



Goodbye to you all !

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Editor, JMS, RIMS, Imphal

Dear members,

My time has come to say goodbye to you all. Thank you so much for your full faith in me to lead our esteemed journal for the past two years. I worked honestly to the best of my abilities. However, I struggled a lot to uplift our journal. Today, we have earned credibility amongst all the reader members in and outside our state.

I knew that authors expect a lot from the editor for the publication of his/her article. However, I tried to solve my homework as early as possible. You must believe that the review and publication process for a particular issue took a long time. There are so many reasons for this. I agree that some may be the fault of the journal editor. Moreover, many of our peer reviewers are not quite comfortable with the process of reviewing, making it unsatisfactory and casual. Therefore, there is always a chance of delay in the publication of the journal.

Today, I am quite happy to acknowledge all our readers that the full text articles of all issues of JMS from January 2008 onwards are available online (Web site: <http://medicalsociety.rims.edu.in/>) free of cost. I convey my sincere thanks and appreciation

to Prof. L. Fimate, Director RIMS, Imphal and Prof. H. Shanti Singh, Anaesthesiology; and also the staff of RIMS networking unit who rendered their valuable time in making JMS in the web site.

Again, I owe a lot for everybody concerned viz. authors, peer reviewers, editorial board members, advertisers and Bir Computer Printing Works (BCPW), Lamphelpat, Imphal who have contributed a lot for the upliftment of the journal. I also thank each and every members who help me, assisted me and encouraged me directly or indirectly for smooth functioning and completion of my term successfully.

Lastly, I am very grateful to Prof. L. Fimate, Director, RIMS, Imphal for his moral support, guidance and financial assistance.

Our new editor has to work more according to his plan. We need the right man, a committed editor who can think and plan very well for the growth of the journal. I am also sure you will elect the right person.

Thanks for allowing me to serve you all.



GUEST EDITOR

Management of common bile duct calculi in laparoscopic era

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Stones in the common bile duct (CBD) is called Choledocholithiasis. It may be either primary or secondary. Primary stones are formed in CBD and secondary stones are migrated from the gallbladder. Untreated CBD stones may give rise to serious complications with significant morbidity and mortality.

Effective CBD stones management started with introduction of intra-operative cholangiography by Mirizzi in 1932 and development of choledoscope. The management of CBD calculi traditionally requires open laparotomy and CBD exploration. With the advent of endoscope and laparoscope technology in the later half of century, Endoscopic Retrograde Cholangiography (ERCP) and Laparoscopic Cholecystectomy(LC) have become the mainstream treatment for CBD stones and gallstones in most medical centres around the world.

Management of CBD stone detected pre-operatively or post-operatively remains controversial in the laparoscopic era due to various management strategies employed by different surgeons. Different treatment strategies include –

- i) Conventional open Cholecystectomy and Choledocholithotomy.
- ii) Pre-operative ERCP with Endoscopic Sphincterotomy (ES) for removal of CBD calculi and Laparoscopic Cholecystectomy.
- iii) Laparoscopic Cholecystectomy followed by ERCP extraction of CBD calculi.

- iv) One stage Laparoscopic Cholecystectomy and Choledocholithotomy.

The classical open Cholecystectomy and Choledocholithotomy though time tested remain in the hands of those surgeons who have not updated themselves in the field of endo-laparoscopic surgery with usual disadvantages of any open operations such as bigger scars, longer hospital stay, delayed return to work and increased morbidity.

The procedure of pre/post operative ERCP and Laparoscopic Cholecystectomy has been practiced by many endo-laparoscopic surgeons with significant success. In fact, it has been considered as one of the most accepted procedures till date. But the ERCP with ES is not without hazards. Even in the best hands and in best centers, this procedures may lead to dreaded complications such as perforation, pancreatitis, bleeding, ascending cholangitis and even septicaemia in few patients, moreover the procedure of ERCP and Laparoscopic Cholecystectomy have to be performed at different times and settings. As the natural orifice of sphincter of Oddi is distorted following endoscopic sphincterotomy, there is frequently reflux of duodenal content to bile duct leading to ascending cholangitis later.

Single-stage laparoscopic treatment of gallstones and common bile duct(CBD) stones is now challenging the traditional two-stage endo-laparoscopic approach. Many surgeons are however reluctant to adopt this

procedure because they believe this operation to be difficult and time consuming. Successful single-stage laparoscopic treatment of gallstones and CBD stones treat two problems during the same operation, avoids the additive complications of a second procedure (endoscopic sphincterotomy) and reduces hospital stay and costs.

In the recent years the surgeons at different centers in the world have started exploring the CBD laparoscopically with excellent results. Lyass S and Phillips ER¹ in their study of laparoscopic trans-cystic common bile duct exploration found the success rate of the procedure as 85 to 95% provided the stones are smaller than 10mm and fewer than 9 stones. They also have shown that the laparoscopic CBD exploration (LCBDE) is more cost effective than pre- or post-operative Endoscopic Retrograde Cholangiography and laparoscopic cholecystectomy.

Lien HH et al² conducted retrospective cohort study to compare LCBDE (n=82) with conventional common bile duct exploration (CCBDE) (n=75) and Endoscopic Sphincterotomy (n=80) in the management of cholelithiasis and choledocholithiasis. All LCBDE were performed through choledochotomy with T-Tube placement. There was no significant difference of operating time between LCBDE and CCBDE while post-operative hospitalization was shorter in both LCBDE (8±5 days) and ES(9±4 days) groups than in the CCBDE group (13±6 days). Morbidity rate was 3.7% (3/82) in LCBDE group including bile leakage in 1 case and bile peritonitis in 2 cases, 6.7% (5/75) in CCBDE group including atelectasis in 2 cases, sepsis in 1, and wound infection in 2 cases. There was 2 cases of post-operative pancreatitis (2.5%) in ES group. The study showed the benefits of LCBDE such as minimal invasiveness, concurrent treatment of gall bladder stones and CBD stones in a single session and shorter hospital stay. However longer learning curve is needed.

Cuschieri A et al³ in 1996 conducted prospective randomized controlled clinical trial and compared two management options. Group A (n=50) received pre-operative ERCP

with ES followed by LC during the same hospital admission, and Group B (n=150) received single stage laparoscopic management. Both groups demonstrated equal success rate and patient morbidity for the two management options but a significantly shorter hospital stay in single stage laparoscopic management group of patients.

Berci G and Morgenstern L⁴ in their study found that, 83% stones were removed through trans-cystic approach and 17% through choledochotomy. In trans-cystic group 5% were converted to open procedure due to technical difficulty as contrast with trans-CBD route where conversion rate was 19%. Retained stones were discovered in 2.6% cases. Authors opined that the LCBDE is feasible approach for CBD stones which permits a definitive procedure in one stage without pre- or post-operative ES.

Following Choledocholithotomy with laparoscopic or open procedure, it is generally accepted these days that T-Tube insertion is no longer mandatory. The T-Tube insertion has become optional. If the surgeon is satisfied that there is no residual stone left behind in the CBD and no ductal anomalies or pathology which requires further investigation, CBD can be closed primarily without any T-Tube. However, a tube drainage must be kept in Morrison's pouch to drain any bile leak should it occur.

Keeping in mind with the fast changing scenario in the management of CBD calculi, we have also started performing single stage Laparoscopic Cholecystectomy and CBD exploration. In our first 20 such procedures, we have removed CBD calculi by trans-cystic approach in 2 patients and rest of the patients by Choledochotomy. We have used Harmonic hook to open the CBD. One of the patient had one adult round worm in CBD which was also removed laparoscopically along with sludge. In all patients, CBD was closed primarily using 3-0 mersilk without any T-Tube. However, one tube drain was routinely kept in Morrison's pouch. In all patients, the tube drained about 50 to 100cc till 3rd post-operative day. On the 4th post-operative day, the tube drain in all patients except one was removed as the

drainage was nil. All those 19 patients were discharged on 5th post-operative day. We had one patient who developed biliary peritonitis on 4th post-operative day which was successfully managed by laparotomy and thorough peritoneal toileting.

To summarize, single stage laparoscopic management of gallstones and CBD calculi is increasingly being performed by expert laparoscopic surgeon these days challenging

the already accepted procedure of pre-operative ERCP management of CBD calculi followed by Laparoscopic Cholecystectomy. Available literatures in the globe and our own experience though limited revealed that single stage laparoscopic treatment of gall bladder and CBD stones solves 2 problems at the same sitting, avoids the additive complications of ERCP and Endoscopic Sphincterotomy related procedures and reduces hospital stay and costs.

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A study of the profiles of cardiovascular manifestations of HIV infection in Manipur

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Abstract

Objective: To study the different cardiovascular manifestations associated with HIV infection and to find out any correlation between CD₄ cell count and such cardiovascular manifestations. **Methods:** Sixty two HIV infected patients with or without antiretroviral therapy and admitted in the Department of Medicine, Regional Institute of Medical Sciences (RIMS), Imphal during the period from September 2006 to August 2008 were studied. Diagnosis of cardiovascular involvement was made from clinical examination, ECG, chest X-ray and echocardiogram. CD₄ cell count was done by FACS counter machine at the Department of Microbiology, RIMS. Logistic Regression was used for statistical analysis. **Results:** Twenty two (35%) out of a total of 62 cases had cardiovascular manifestations of which pericardial effusion constituted the majority (21%) followed by dilated cardiomyopathy (11%). Pulmonary hypertension and or cor pulmonale constituted about 1.6% each. The aetiology of pericardial effusion was unknown in 62% while tuberculosis was detected in the remaining 38%. Pericardial effusion was associated with a mean CD₄ cell count of 64±20.7 cells/cumm (P<0.003) and dilated

cardiomyopathy with 67.7±13.6 cells/cumm respectively which were statistically significant. **Conclusion:** HIV infection was associated with cardiovascular manifestations in about one third of the cases. Pericardial effusion was the commonest condition followed by dilated cardiomyopathy. Both of these were significantly associated with lower CD₄ cell count.

Keywords: HIV infection, pericardial effusion, dilated cardiomyopathy, CD₄ cell count.

Introduction

HIV infection is a global pandemic and at present people living with HIV infection globally is 32.2 million (30.6 – 36.1 million)¹. At present much emphasis has been laid on the diseases associated with respiratory, gastrointestinal, skin and central nervous system. As of now, with the advances in the knowledge of the disease and its management including antiretroviral therapy, patients with HIV infection are living longer. With the increasing lifespan of HIV infected patients, the chance of having HIV related cardiovascular problems especially dilated cardiomyopathy is high.² Patients with cardiovascular problems have increased morbidity as any other chronic disease. So in view of such a situation we decided to study the different cardiovascular manifestations of HIV infection and its correlation with CD₄ counts in Regional Institute of Medical Sciences, Imphal.

Methods

It is a prospective study which was carried

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out in the department of Medicine, RIMS Hospital, Imphal. Sixty two HIV infected cases (documented and newly diagnosed case of HIV infection including patient who were already on antiretroviral therapy) were studied during the period from September 2006 to August 2008. Diagnosed of HIV infection was made by 3 ELISA/RAPID/SIMPLE (E/R/S) test.

A pre-designed proforma was used to record the various parameters including age, sex, high risk behaviours etc. Diagnosis of the cardiovascular involvement was made by clinical assessment followed by cardiogram, chest X-ray and transthoracic 2D echocardiography to confirm the cardiovascular involvement in HIV infected patients.

All the patients were subjected to lipidogram, CD₄ + T cell count apart from routine tests like haemogram, liver function test, kidney function test, random blood sugar, urine routine examination. In a few cases, serum adenosine deaminase and myocodot test were done. Sampling was done by random sampling. Logistic regression was used for statistical analysis and a probability value of ≤ 0.05 was considered significant. An informed consent was taken from the cases taken for the study.

Results

Table 1 shows the age distribution of the study population. The maximum number of patients were in the age group of 30-40 years which constitute about 61% of the total cases in the study.

Table 1. Showing age distribution

Age (years)	No. of patients	%
<30	5	8
30 – 40	38	61
40 – 50	15	24
50 – 60	1	2
60 – 70	3	5
	62	100

Out of the 62 cases, 46 (74%) were males and 16 (26%) were females with a male to female ratio of 3:1 (table 2).

Table 2. Showing sex distribution of the study population.

Sex	No. of patients	%
Male	46	74
Female	16	26

Table 3 shows district wise distribution. Seventy one percent of the patients in the study population were from Imphal and the least number of individuals were from Chandel district (1.6%).

Table 3. Showing district wise distribution of the study population.

Districts	No. of patients	%
Imphal	44	71
Ukhul	5	8
Thoubal	5	8
Lilong	3	4.8
Churachandpur	2	3.2
Chandel	1	1.6
Tamenglong	2	3.2

Table 4 shows religion of the patients. The maximum numbers of cases in the study were from Hindu community (63%).

Fig 4. Showing religion of the study population

Religion	No. of patients	%
Hindu	39	63
Muslim	12	19
Christian	11	18

Table 5 shows the mode of contraction of HIV infection. The mode of transmission of HIV infection was mainly through intravenous drug use which contributed about 59.67% of the cases.

Table 5. Showing mode of contraction of HIV infection

Mode of contraction of HIV	No. of patients	%
Intravenous drug use	37	59.67
Sexual contact	24	38.7
Blood transfusion	1	1.6

Table 6 shows cardiovascular manifestations and CD₄ counts. Out of the total 62 cases, 22 patients (35%) had cardiac manifestation. Pericardial effusion occurred in 13 patients (21%), dilated cardiomyopathy in 7 patients (11%). The mean CD₄ cell count in cases with pericardial effusion was 64.1±20.7 cells/cumm with a maximum of 92 cells/cumm respectively. The mean CD₄ count in HIV infected patients with dilated cardiomyopathy was 67.7±13.6 cells/cumm. Pericardial effusion and Dilated cardiomyopathy show a significant correlation with CD₄ count.

Fig 6. Showing cardiovascular manifestations and its associated CD₄ counts

Types	No. of patients	%	Mean CD ₄ counts	p-value
Normal heart	40	64.5		
Pericardial effusion	13	21	64±20.7(27– 92)	0.003
Causes: Unknown	8			
Tubercular	5			
Dilated cardiomyopathy	7	11	67.7±13.6 (42 – 88)	0.04
Pulmonary hypertension	1	1.6	92	0.298
Cor pulmonale	1	1.6	143	0.280

Discussion

Sixty two cases of HIV infection were studied in the present study. Out of the 62 cases, 46 (74%) were males and 16 (26%) were females with a male to female ratio of 3:1 which is tallying with Manipur AIDS Control Society statistics of 7513 females out of the 29147 HIV positive cases detected since 1986 till March 2008.³

The maximum number of patients were in the age group of 30 – 40 years which constitute about 61% of the total cases included in the study whereas in Manipur AIDS Control Society 2008 report maximum patients were in the age group of 21 – 30 contributing about 43.26% and followed by the age group of 31 – 40 years (35.61%)³. The difference in the findings could be due to the fact that HIV infected patients are living longer with the introduction of antiretroviral therapy and better management of opportunistic infections.

Seventy one percent of the individuals included in the study were from Imphal and

the least number of individuals were from Chandel district (1.6%). This distribution is comparable with Manipur AIDS Control Society reports³ in which 56.33% of individuals similar with HIV infection were from Imphal district and the least from Chandel district (5.07%).

Maximum numbers of cases in the study were from Hindu community (63%). This increased number of HIV infected individuals among Hindus was because of the fact the Manipur is a Hindu dominated state.

The mode of transmission of HIV infection in the present study was mainly through injection drug use which contributed about 59.67% of the cases. Manipur AIDS Control Society³ reported that major route of infection were the injection drug users which contributed 42.38% of the total.

In this study, out of the total 62 cases 22 patients (35%) had cardiac manifestation which is in tune with the findings of Levy WS et al⁴ in the study entitled “Prevalence of cardiac abnormalities in human immunodeficiency virus infection” where Echocardiography abnormalities was identified in 35% (21 out of 60) of patients. Pericardial effusion occurred in 13 patients (21%), dilated cardiomyopathy in 7 patients (11%) which is almost similar with the study by Hakim JG et al⁵ in 157 HIV infected patients who found that 19% (30 out of 157) had pericardial effusion and 9%(14 out of 157) has dilated cardiomyopathy.

In our study, the mean CD₄ cell count in cases with pericardial effusion was 64.1±20.7 cells/cumm with a maximum of 92 cells/cumm respectively which is in agreement with the study by Paul AH et al⁶ in which the average CD₄ count at the diagnosis of pericardial effusion was 59±41 cells/cumm.

Sixty two percent cases with pericardial effusion were of unknown etiology and

tuberculosis contribute to 38% of the total cases with pericardial effusion, which is comparable to the study conducted by Chen Y et al⁷ in which the etiology of pericardial effusion was described to be of Mycobacterium species in 19% of patients, streptococcus pneumonia in 6%, staphylococcus aureus in 6%, Kaposi Sarcoma in 6% and 63% are unknown. The origins of pericardial effusion in patients with HIV and/or AIDS are diverse, but in most cases no etiologic agent has been identified, despite an extensive work-up.⁸ The reason for the unknown aetiology could be a part of a generalised serous effusive process ("capillary leak")⁹. Other organisms causing pericardial effusion were not found in the present study, but among the know aetiology tuberculosis (38%) was the common cause which may be attributed to the high prevalence of tuberculosis in HIV infected patient in this country as stated by National AIDS Control Organisation, India.

In the present study, the correlation of pericardial effusion with CD₄ count is statistically significant (P=0.003). The mean CD₄ count in HIV infected patients with dilated cardiomyopathy in the present study was 67.7±13.6 cells/cumm where all the 7 cases have CD₄ count less than 100 cells/cumm which is consistent with Curie PF et al¹⁰ in which dilated cardiomyopathy was strongly associated with CD₄ cell count of less than 100 cells/cumm (P<0.001). In the present study the correlation of dilated cardiomyopathy with CD₄ count is statistically significant (P=0.049).

In our study, only 1(1.6%) had pulmonary hypertension and its correlation with CD₄ count was insignificant. Fisher DS and Lipshultz RS¹¹ in 2005 stated that primary pulmonary hypertension in estimated to occur in 0.5% of hospitalised AIDS patients. Cor pulmonle occurred in 1(1.6%) patient in the present study and its correlation to CD₄ count was insignificant (p=0.298).

Rangasetty CU et al¹² found that isolated right ventricular hypertrophy and dilation are relatively uncommon in HIV-infected individuals and are generally related to

pulmonary diseases.

In the DAD (Data Collection on Adverse Events of Anti-HIV Drugs) study, a prospective study of 23,000 patients with HIV infection, during the initial study period, 126 patients had myocardial infarction (MI), during the first 4 to 6 years of combination therapy; there was a 26% relative increase in the rate of MI per year of exposure to antiretroviral medication. There was no sufficient power to permit comparisons among patients receiving different types of antiretroviral regimens.¹³ In the present study, no myocardial infarction was seen in any of the cases probably due to the fact that all the cases in the study were taking ART combination of nucleoside analogue reverse transcriptase inhibitors (NNTRIs) as per national AIDS control organisation, India guidelines. In the previous studies, most myocardial infarction were detected in cases taking Protease inhibitors commonly which are proven to cause dyslipidemia and not in patients taking NRTIs AND NNRTIs.

Curie PF et al¹⁴ reported that among HIV-infected patients, infective endocarditis was seen almost exclusively in injection drug users (IDUs), where its prevalence varies from 6.3% to 34% of HIV patients and is rare otherwise. Though most of the cases in the present study were IDUs, none of them had endocarditis which is consistent with the statement above by Curie PF et al¹⁴ which consider it a rare entity.

The introduction of potent antiretroviral therapy led to reduction in the overall incidence of cardiac involvement with Kaposi Sarcoma and non-Hodkin lymphoma. This change may be attributed to the improved immunologic state of the patients and to play an etiologic role in these neoplasms.¹⁵ In the present study none of the cases had any cardiac malignancy (Kaposi Sarcomas and Lymphomas) which is consistent with the above statement because all the patients in the present study were taking antiretroviral therapy.

Reports of vasculitis in HIV-infected patients are increasingly frequent. Many types of

vasculitis have been described in HIV-infected patients, including systemic necrotizing vasculitis, hypersensitivity vasculitis, Henoch-Schoenlein purpura, lymphomatoid granulomatosis and primary agiitis of the central nervous system.¹⁶ In this study, no case of vasculitis or autonomic dysfunction was seen. Cardiac manifestation is an important clinical feature in HIV infected patients. However, a larger study is required to ascertain the outcome of the present study.

Conclusion

HIV infection was associated with cardiovascular manifestations in 35% of the cases. Of these, pericardial effusion was the commonest followed by dilated cardiomyopathy. Aetiology of pericardial effusion was unknown in the majority of the cases while tuberculosis was found in about one third of the subjects. These cardiac manifestations were significantly associated with lower CD₄ cell count.

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Foeto-maternal outcome in HIV infected women and measures to prevent parent-to-child transmission of HIV

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Abstract

Objective: To observe the effect of HIV infection on foeto-maternal outcome and the role of nevirapine in the prevention of parent-to-child transmission of HIV virus in the study.

Methods: Pregnant women attending in the Department of Obstetrics and Gynaecology, RIMS, Imphal, during the period from July 2006 to June 2008 were tested for HIV infection after counselling and obtaining informed written consent. 50 HIV positive women and 100 HIV negative women were taken as study cases and controls respectively in the study. CD₄ cell count was done on all the cases and women with CD₄ cell <250/mm³ was started with antiretroviral therapy (ART). All the cases were given tablet Nevirapine at the onset of labour pain. Birth parameters of the babies were recorded. All the babies were given Nevirapine drops within 72 hours of birth. They were followed up and tested for HIV infection at 18 months. The effects of HIV infection on the maternal and foetal outcome were analysed. **Results:** The incidence of HIV was found to be 0.75%. Maximum numbers of cases were observed among primiparas (46%) in the age group of 26-30 years (38%).

Antepartum complications were significantly higher in the study cases (68%). Anaemia (64%) and preterm labour (28%) were the common complications. Significantly more number of study cases were delivered by elective caesarean section (32% in cases vs. 10% in controls). The mean gestational age (37.33±2.32 weeks in cases vs. 38.13±1.43 weeks in controls) was shorter and mean birth weight (3.08±.494 kg vs. 3.19±.491kg in controls) was lower among study cases. The Apgar score was significantly lower in the study cases. Vertical transmission was observed in 5% study cases. **Conclusion:** There is high prevalence of HIV infection among pregnant women and it is associated with increased pregnancy complications. The vertical transmission is reduced to less than 2% with the use of antiretroviral therapy, Nevirapine prophylaxis, elective caesarean section and replacement feeding.

Key words: HIV, AIDS, Nevirapine, ART, vertical transmission, PET, PROM, VD, LSCS.

Introduction

The prevalence of HIV infection among adult population in India is 0.91%. Although the prevalence is <1%, due to large population of more than one billion, India has larger number of people living with HIV/AIDS, second only to South Africa. Heterosexual mode of transmission is by far the most common mode of transmission in India. The seroprevalence among antenatal women in India is reported between 0.5 to 3.3% in

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various part of the country. The antenatal complications viz. anaemia, preterm labour etc are higher in HIV infected women. The vertical transmission- Mother-to-child transmission (MTCT) occurs antenatally (in utero), intrapartum (during labour and childbirth) and postpartum (breast feeding). It is expected that in India about 75,000 HIV infected neonates are born each year with more than 27 million pregnancies annually. MTCT has been shown to have wide variation among different population groups. The MTCT rate can be reduced by ART or prophylaxis, elective caesarean section and replacement feeding to less than 2%.

Methods

Women attending the Department of Obstetrics and Gynaecology, RIMS, Imphal from July 2006 through June 2008 were counselled for HIV antibody testing. After obtaining written informed consent, they were subjected to Rapid HIV test followed by post test counselling. Positive tests were confirmed by doing another rapid test. If the result of the two tests were different, a third test was done as per revised prevention of parent-to-child transmission of HIV training curriculum trainer manual, December 2004.¹ 50 HIV positive women were taken as study cases and 100 HIV negative women were taken as control. Pregnant women with medical and obstetrical complications were excluded from the study. The study cases were followed up for progress and complications during the pregnancy period. CD₄ cell count was done in HIV positive cases. 24 HIV positive pregnant women were found to have CD₄ cell <250 mm³. These patients were given ART in consultation with ART centre. The regimen followed was Zidovudine, (AZT), Lamivudine (3TC) and Nevirapine (NVP). It was started as soon as the diagnosis was made. The antenatal complications in both the study and control groups were observed. All subjects were given Nevirapine with the onset of labour and the mode of delivery were recorded. Term new born was given weight adjusted dose of Nevirapine drops (2 mg/Kg body of birth weight) as early as possible but not later than

72 hours. Birth parameters of new born viz. period of gestation at birth, birth weight, and Apgar score at birth, one minute and five minutes were observed and recorded. Babies were followed up on OPD basis and tested for HIV seroconversion at eighteen months. All 50 cases were compared with 100 controls.

Statistical analysis was done using Chi square test with Epi. Info version 6 Software. P value less than 0.05 were taken as significant.

Results

Table 1 shows the prevalence of HIV infection among tested gravid women was 0.75% (176/23352).

Table 1. Prevalence of HIV infection

No. of pregnant women tested for HIV during the study period (July,2006-June 2008)	23352
HIV positive pregnant women detected	176
Prevalence of HIV infection among tested women	0.75%

Table 2 shows that maximum numbers of cases were observed in women age group of 26-30 years (38%).

Table 2. Distribution of the cases according to age

Age range(years)	No.	%
<20	1	2
20-25	12	24
26-30	19	38
31-35	14	28
36-40	4	8
Total	50	100

The maximum cases were observed in primiparas(46%), followed by para 1(28%) and minimum cases were observed in para 2(6%). 28% of cases were preterm as against 12% of control, which is statistically significant (P=0.02). Mean period of gestation at delivery among cases were 37.33±2.32 weeks vs. 38.13±1.43 among control (table 3).

Table 4 shows higher incidence of different complications among study cases. Anaemia was observed in 32 (64%) cases against

Table 3. Distribution of the cases according to parity and period of gestation

Parity	Frequency	%
P0+0	23	46
P1+0	14	28
P2+0	03	06
P3+0	04	08
P4 & above	06	12
Total	50	100

Period of gestation	Cases Number(%)	Control Number(%)
<37 (Wk)	14(28)	12(12)
=37 (Wk)	36(72)	88(88)
Mean(Wk)	37.33±2.32	38.13±1.43

21(21%) in controls which is statistically significant ($P=0.0001$). Preterm labour was observed in 14 (28%) of cases against 12(12%) in control. The difference was statistically significant ($P=0.02$). More number of cases were delivered by caesarean section (32%) as compared to control(10%) which is statistically significant ($P=0.001$).

Table 4. Distribution of cases according to antepartum complications & mode of delivery

Complications	Cases		Controls	
	No.	%	No.	%
Anaemia (<11gm %)	32	64	21	21
PET	3	6	8	8
Polyhydramnios	1	2	2	2
PROM	1	2	6	6
Preterm Labour	14	28	12	12
Modes of Delivery				
VD	34	68	82	82
LSCS	16	32	10	10
Instrumental	00	00	06	06
Breech	00	00	02	02

Table 5 shows that preterm births were found to be more in the cases (28%) than in the control(10%). And this difference is statistically significant.

Table 5. Distribution of cases according to foetal outcome

Foetal outcome	Cases		Controls	
	No.	%	No.	%
Term delivery	36	72	88	88
Preterm delivery	14	28	12	10
Live Birth	49	98	99	99
Still Birth	01	02	02	02
Neonatal death	01	02	02	02
Low Birth weight	08	16	10	10
Congenital anomalies	01	02	02	02

Table 6 shows that lower birth weight were found in cases than in control which is not statistically significant ($P= 0.75$). Mean birth weight was 3.08 ± 0.494 kg vs. 3.19 ± 0.491 kg respectively. Apgar score of <7 was seen in 24% of cases compared to 6% in the control group which is found to be statistically significant ($P=0.006$).

Table 6. Distribution of cases according to birth weight and Apgar Score

Apgar score at 5min	Cases		Controls	
	No.	%	No.	%
<7	12	24	6	6
7-10	38	76	94	94
Birth weight				
>2500 gms	8	16	10	10
≥2500 gms	42	84	90	90
Mean birth weight	3.08±.494 Kg		3.19±.491 Kg	

Table 7 shows the distribution of causes of perinatal deaths. Prematurity and respiratory distress in a term birth were the causes of perinatal deaths in 1(one) case each and in 2(two) each among control.

Table 7. Distribution of cases according to causes of perinatal deaths

Causes	Cases		Controls	
	No.	%	No.	%
Preterm	1	2	2	2
Respiratory distress	1	2	2	2
Others	Nil	-	-	-

Numbers of babies who came for follow up at 18 months were 20 (40%). Number of baby tested positive for HIV was 1(5%).

Discussion

The prevalence of HIV infection among tested women in the present study was 0.75%. National AIDS Control Organisation (NACO, 2004)¹ reported the seroprevalance among pregnant women attending the antenatal clinic as 0.5 to 3.3% which is consistent with the present study. However, Gomutbutra V² and Kierere MM et al³ reported high incidences of, 2.2% and 1.9% respectively, whereas Runa B et al⁴ observed lower prevalence of 0.11% in their study.

In the present study, most of the cases were in the age group of 20 - 40 years. The present finding is similar to that of Habib NA et al⁵ who

also reported 94.5% of cases in the age group 20 - 35 years. The maximum number of cases were primigravidas (46%). Similar finding was reported by Gupta A et al⁶ where they observed 50% of cases among primigravidas. The mean gestational age among seropositive pregnant women was 37.3±2.32 weeks compared to 38.12±1.43 weeks among seronegative ones. Habib NA et al⁵, Gupta A et al⁶ and Bodkin C et al⁷ observed mean gestational ages of 39.6 weeks, 38 weeks and 37.92 weeks respectively which are similar to the present findings.

Anaemia was found among 64% of seropositive pregnant women in the present study. Uneke CJ⁸ in his study recorded an incidence of 76.9% anaemic cases and Dario MD et al⁹ also recorded high incidence of anaemia among HIV infected pregnant women. Preterm delivery occurred in 28% of cases which is comparable to the study of Gomutbutra V² who observed 26% of preterm labour in his study.

In the present study, elective caesarean section was found to be 32% which is comparable to the findings of Habib N et al⁵ who observed a caesarean rate of 36.5% in HIV pregnant women who received treatment.

The mean birth weight in the present study among cases was found to be 3080 gm vs. 3180 gm among control whereas Gupta A et al⁶ observed a mean birth weight of 2426 gm in HIV infected pregnant women. Habib N et al⁵ observed mean birth weight of 3090 (498) gm among cases vs. 3127 gm in control and Bodkin C et al⁷ observed mean birth weight of 2969.98 gm in HIV positive cases vs. 3138.43 gm in HIV negative control which are similar to the present findings. Low birth weight was observed in 16%

of cases. Habib N et al⁵ observed low birth weight in 18% of cases which is comparable to the present study finding.

In the present study, only one baby was tested positive at 18 months (5%) whereas Martinelli P et al¹⁰ observed MTCT in 0.6%, Warszawski J et al¹¹ reported in 1.3% of cases, Coetzee D et al¹² found MTCT in 8.8%. Gomutbutra V² reported MTCT in 4% and Zahumensky J et al¹³ recorded it in 4.2% which are similar to the present finding. Apgar score of less than 7 at 5 minutes was observed four times more among cases than control. Habib NA et al⁵ reported low Apgar score of 0-3 three times more common among cases than controls. Habib NA et al⁵ observed perinatal mortality of 66.2 per 1000. In the present study, perinatal mortality rate was 4% among cases and control, and similar observation has been made by Sukwa TY et al¹⁴ in their study.

Conclusion

The prevalence of HIV infection is high among pregnant women in Manipur (0.75%). HIV infected women had higher incidence of pregnancy complications than uninfected control. The course of HIV infection seems to be unaltered by pregnancy as there was no incidence of maternal death or disease progression to AIDS defining disease though CD₄ cell count of less than 250 was found in 48% of cases.

The vertical transmission of HIV in our study is very low (5%). The drop out rate of mother-baby pair for postdelivery review was high (60%). Antiretroviral therapy, Nevirapine prophylaxis, elective caesarean section and replacement feeding were found to be highly effective in reducing the of mother-to-child transmission of HIV infection.

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A comparative study of amelioration of propofol dose in co-induction of anaesthesia by esmolol and midazolam

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Abstract

Objective: To study the amelioration of propofol dose by co-induction with esmolol and midazolam. **Methods:** 105 adult patients of ASA grade I and II undergoing elective surgery under general anaesthesia were divided into three groups viz. control group (Group A) received 10ml of 0.9% saline IV followed by a 0.9% saline infusion, midazolam group (Group B) was given 0.04mg/kg of midazolam diluted to 10ml, followed by an infusion of 0.9% saline and the esmolol group (Group C) received 1mg/kg esmolol diluted to 10ml followed by an infusion of esmolol at 250µg/kg/min. The hemodynamic and respiratory variables along with any adverse events after propofol administration occurring during the study period were recorded. The findings were statistically analysed. **Results:** The present study shows that intravenous esmolol reduced the dose of propofol required for induction of anaesthesia by 7.33% when compared with the effect of midazolam co-induction which also reduced the dose of propofol by 28.66%. **Conclusion:** Esmolol and midazolam were effective up to some extent in amelioration of propofol dose, with midazolam showing slightly better efficacy.

Key words: Propofol, esmolol, midazolam, co induction, amelioration.

Introduction

Induction of anaesthesia usually involves intravenous administration of various induction agents. Co-induction is the administration of a small dose of sedative or anaesthetic agent prior to the induction of anaesthesia, the aim being to reduce the dose of induction agents required and a more stable haemodynamic profile, without substantially compromising recovery.¹ Currently, planned co-induction of anaesthesia is practiced by anaesthetists using drug interactions, particularly synergism, principally between midazolam, fentanyl, sufentanil and alfentanil, and propofol. It can produce an improvement in all phases of anaesthesia, including induction, maintenance and recovery.² Recently, esmolol and midazolam have been commonly used as co-induction agents, and they have been known to act synergistically with propofol, thus reducing the induction dose of propofol. It is also documented that in induction of propofol anaesthesia, administration of esmolol co-induction has been observed to reduce the cardiovascular system (CVS) stress response to laryngoscopy, intubation and electroconvulsive therapy, in addition to reduction in cardiac side effect in healthy subjects through the reduction in stroke volume and cardiac output.³

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Methods

The study was conducted in the Department of Anaesthesiology, Regional Institute of

Medical Sciences Hospital, Imphal. 105 adult patients of ASA grade I and II, who were above 18 years, scheduled to undergo elective surgery under general anaesthesia were included in this study.

Patients with asthma, diabetes, renal and cardiovascular diseases and those taking centrally acting drugs (e.g. benzodiazepines or antidepressants), cardiovascular drugs (including β -blocker) as well as those contraindicated to any of the study drugs in use were excluded from the study. These patients were randomly allocated in equal number to one of three groups, each group of 35 patients (n=35).

Group A: 0.9% saline or placebo (10ml) intravenously followed by a 0.9% saline infusion (Control group)

Group B: midazolam 0.04 mg/kg (diluted to 10 ml), followed by an infusion of 0.9% saline (Midazolam Group)

Group C: esmolol 1mg/kg intravenous bolus (diluted to 10ml) followed by 250 μ g/kg/min

infusion
(Esmolol group)

The anaesthetic regimen was standardized for all the patients. Every patient was pre-oxygenated for 3 minutes prior to induction and continued till the infusion period of the study was over.

Then the control group (Group A) received 10ml of 0.9% saline IV followed by a 0.9% saline infusion. The midazolam group (Group B) was given 0.04mg/kg of midazolam diluted to 10ml, followed by an infusion of 0.9% saline. The esmolol group (Group C) received 1mg/kg esmolol diluted to 10ml followed by an infusion of esmolol at 250 μ g/kg/min. Initial dose of drug was administered over 60 seconds. 3 (Three) minutes after the infusion

of test drug had been started, the heart rate, blood pressure and respiratory rate (tachypnoea if RR>25 breath per minute), SPO₂ were recorded and anaesthesia was induced with intravenous propofol injection at the rate of 1ml (10mg) per 3 seconds till the patient loses response to verbal command. The end point of induction of anaesthesia was taken as the first lack of response to the verbal command of the investigator. At that point, the total dose of propofol administered was noted. Injection of the study drug was stopped and the hemodynamic and respiratory variables along with any adverse events occurring during the study period were recorded. The findings were statistically analysed using ANOVA test. Chi-square test or student t-test was used where necessary.

Results

In the present study, the patients in the three groups had comparable demographic profiles and ASA physical status. Table 1 shows the distribution of baseline heart rate (HR, min⁻¹),

Table 1. Distribution of patients' baseline haemodynamic & respiratory variables with mean \pm SD and range

Patient Profile	Group A	Group B	Group C	ANOVA F-value	P-value
HR min-1	80.37 \pm 12.5	80.17 \pm 10.17	78.89 \pm 10.8	0.28	P>.05 (NS)
SBP mmHg	130.29 \pm 9.85	131.89 \pm 11.80	131.83 \pm 12.03	0.23	P>.05 (NS)
DBP mmHg	82.74 \pm 7.50	84.11 \pm 7.44	84.23 \pm 7.70	0.89	P>.05 (NS)
RR min-1	16.40 \pm 1.19	16.31 \pm 1.78	16.20 \pm 1.41	0.16	P>.05 (NS)
SPO ₂ %	99.37 \pm 1.02	99.34 \pm 0.88	99.43 \pm 0.82	0.08	P>.05 (NS)

HR=Heart rate, SBP=Systolic BP, DBP=Diastolic BP, RR=Respiratory rate

systolic blood pressure (SBP, mm Hg), diastolic blood pressure (DBP, mm Hg), respiratory rate (min-1) and arterial oxygen saturation (SPO₂ %). The pre-anaesthetics variables were not significant statistically (p-value >0.05).

The comparison of the heart rate of the patients in the three groups at different time intervals is shown in table 2. There was significant decrease in heart rate in esmolol

group after administration of the test drug (5.04%) but, there was no change in the heart rate in the control group when compared with the baseline parameter. The midazolam group showed decrease in the heart rate (0.9%) after the test drug. The entire study group showed slight increase in heart rate just after the

induction, with greatest increase in control group (5.87%). However, this was found to be statistically insignificant (P-value >0.05).

The systolic blood pressures at different time interval are shown in table 3. There was reduction of SBP from the baseline in

Table 2. Comparisons of heart rate (mean ± SD) of the three groups at different time intervals i.e. baseline, after test drug & after induction

Group	Baseline (HR1)	After test drug (HR2)	After Induction (HR3)	P-value
Group A	80.37±12.5	80.00±12.56	85.09±13.94	P>.05(NS)
Group B	80.17±10.17	80.94±10.06	83.86±8.44	P>.05(NS)
Group C	78.89±10.8	74.91±12.48	78.89±12.83	P>.05(NS)

HR=Heart rate

Table 3. Comparisons of Systolic blood pressure (mean ± SD) of the three groups at different time intervals i.e. baseline, after test drug & during induction

Group	Baseline (SBP1)	After test drug (SBP2)	After Induction (SBP3)	P-value
Group A	130.29±9.85	126.49±10.25	116.80±12.88	P<.001(HS)
Group B	131.89±11.80	120.94±10.67	113.77±11.16	P<.0001(VHS)
Group C	131.83±12.03	126.17±10.45	110.06±8.74	P<.0001(VHS)

SBP=systolic blood pressure

Table 4. Comparisons of Diastolic blood pressure (mean ± SD) of the three groups at different time intervals i.e. baseline, after test drug & during induction

Group	Baseline (DBP1)	After test drug (DBP2)	After Induction (DBP3)	P-value
Group A	82.74±7.50	76.60±9.75	74.23±12.06	P<.05(S)
Group B	85.11±7.44	79.77±8.12	73.14±10.60	P<.001(HS)
Group C	84.23±7.70	82.80±7.82	72.31±9.61	P<.0001(VHS)

DBP=diastolic blood pressure

Table 5. Distribution of observable abnormal response to the test drugs in the three groups

Sl. No.	Abnormal response	Group A	Group B	Group C	Chi-square value	P-value
1.	Apnoea with induction	12(34.29%)	12(34.29%)	12(34.29%)		
2.	Pain	5(14%)	4(11%)	3(8%)		
3.	Increase in respiratory rate	1(3%)	1(3%)	1(3%)		
4.	Decrease respiratory rate<10 min ⁻¹	01(3%)	0	1.42	P>.05	(NS)
5.	Decrease in heart rate	0	0	1(3%)		
6.	Drowsy with the test drug	0	5(14%)	0		
7.	Limb movement	1(3%)	0	1(3%)		
8.	No response/ observable features	16(46%)	11(32%)	17(49%)		

variables recorded after test drug and after induction of anaesthesia in control group, which was found to be highly significant statistically (P<0.001). In midazolam and esmolol groups, the reduction in SBP were found to be very highly significant statistically (P<0.0001). The systolic blood pressure after test drug and after induction of anesthesia was lowest in midazolam group (8.30% decrease from baseline) and esmolol group (16.50% decrease from baseline) respectively.

The values of diastolic blood pressure at different time intervals are shown in table 4. There was decrease in the diastolic blood pressure 3 min after the test drug and induction of anaesthesia in

all the study groups. These were statistically significant (P <0.05) in control, highly significant (P<0.001) in the midazolam and very highly significant (P<0.0001) in the esmolol group. Thus the decrease in diastolic blood pressures was seen more after giving midazolam (14.06%) and esmolol in our study (14.15%).

The unwanted side effects with the study drug when given as co-induction agent with propofol for co-induction of anaesthesia are shown in table 5. Twelve (34.29%) patients in each group exhibited apnoea with induction dose of propofol and one patient (3%) in each group showed rapid shallow breathing with respiratory rate of 28 min⁻¹. One patient in the esmolol group had transient bradycardia after 2min of test drug administration but resolved spontaneously without pharmacological intervention. Pain of moderate degree was seen with the propofol injection in the entire group. Five (14%) patients in control group, four (11%) patients in midazolam group and three (8%) patients in esmolol group complained of pain on propofol injection.

Table 6. Distribution of Propofol dose requirement (mean \pm SD) at induction in mg per kg body weight

Group	Mean \pm SD	ANOVA or F-value	'P'-value
Group A	1.50 \pm 0.38		
Group B	1.07 \pm 0.30	16.96	P<.001(HS)
Group C	1.39 \pm 0.28		

The mean (SD) doses of propofol required in the 0.9% saline, midazolam and esmolol groups were 1.50 \pm 0.38mg/Kg, 1.07 \pm 0.30 mg/kg and 1.39 \pm 0.28 mg/kg respectively (table 6). There was a significant reduction of induction dose of propofol in esmolol and midazolam co-induction groups (p<0.001). The dose of propofol for induction of anaesthesia with esmolol and midazolam co-induction was reduced by 7.33% and 28.66% respectively (table 7).

Table 7. Difference between mean induction dose (mg/kg) for placebo (A), midazolam (B) and esmolol (C) and dose reduction for midazolam and esmolol as percentage of placebo group.

Group	A vs C	A vs B	C vs B
Difference in mean induction dose (mg/Kg)	0.11	0.43	0.32
Dose reduction as percentage of placebo group	7.33%	28.66%	

Discussion

The mechanism involved in co-induction is poorly understood. It has been suggested that co-induction results from a combination of

both pharmacodynamic synergistic interaction in the receptor level, and the pharmacokinetic effects related to the distribution of the induction agents⁴.

The reduction of the dose of propofol required for induction of anaesthesia observed in the present study was found to be consistent with the study of Wilson ES et al⁵ who observed that esmolol and midazolam co-induction reduced the induction dose of propofol by 25% and 45% respectively compared to 7.33% and 28.66% respectively in the present study. There is always a chance of dose dependent risk of hypotension and bradycardia before laryngoscopy when esmolol is combined with anaesthetic inducing agents. There was also decrease in heart rate in one subject in our study and this is in agreement with the study of Wilson ES et al⁵. They suggested that the decrease in heart rate was due to effective β -blockade. In all the groups, there was a trend for pulse to decrease over the course of induction, which did not affect the study subjects deleteriously. In our study, we found more decrease in heart rate after test drug injection in esmolol group compared to midazolam group and control group. The decrease in blood pressure was more in esmolol group compared with control and the midazolam group which could be predicted to be due to decrease in cardiac output and decrease in renin release⁶. In the study of Menigaux C et al⁷, it was clearly indicated that β -adrenoceptor antagonist not only block the cardiovascular stress response after noxious stimulation, which could mask inadequate anaesthesia, but also could increase the antinociceptive effect of anaesthesia, which was consistent with our study. Three patients (8%) in esmolol group complained of moderate degree of pain when propofol was injected as compared to five patients (14%) in the control group. The mechanism of this effect is unclear. In our study, four patients (11%) in the midazolam group complained of moderate degree of pain with propofol injection compared to five patients (14%) in the control group. This may be due to changes in interactions within the GABA receptor complex, but may also include increased access to other central nervous system

biophases (for example, spinal or subcortical versus cortical) or recruitment of other receptor population with increasing propofol concentration.⁸

One of the patients in midazolam study showed decrease in respiratory rate of 8 breaths per minute with the induction dose of propofol, but the incidence of apnoea (no apparent spontaneous respiratory effort for 60secs) was found to be similar in the entire study group. The overall incidence of apnoea was 34.29% in our study, which was similar to the study finding of Cressy DM et al⁹, who

found 34% apnoea in their study. We also found one case each of nonspecific limb movements with the induction dose of propofol in esmolol and control group of the study but, not in the midazolam group.

Conclusion

The present study shows that intravenous esmolol reduced the dose of propofol required for induction of anaesthesia by 7.33% whereas midazolam co-induction reduced it by 28.66%. In addition, esmolol and midazolam showed antinociceptive effect without causing significant cardiorespiratory adverse effects.

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Umbilical cord prolapse in current practice

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Abstract

Objective: To assess the incidence, risk factors and outcomes of umbilical cord prolapse in current obstetric practice.

Methods: A retrospective study of the obstetric cases delivered over a period from January 2006 to July 2008 at Regional Institute of Medical Sciences (Tertiary Hospital) was undertaken. The mean age, booking status, presentation, gestational age, sex, parity, mode of delivery and the perinatal outcome were analyzed. **Results:** During the study period there were 39 cases of cord prolapse out of 24,856 deliveries giving an incidence of 0.16%. Majority of the cases were unbooked 27/39 (69%) with mean maternal age of 29.3 years. In this series we found an approximately 74% cord prolapse. Apgar score <7 at 5 minutes was found in 23 cases (59%) and out of which there were 12 perinatal deaths (30.77%). Emergency cesarean section was done in 17 cases (43.59%) with 6 breech deliveries (15.38%) and 4 instrumental deliveries (10.26%). **Conclusion:** The higher incidence of cord prolapse was seen among multipara and unbooked cases. Cord prolapse was associated with poor perinatal outcome. The perinatal outcome greatly depends on early diagnosis and timely intervention.

Unbooked cases reaching the hospital late had the worst outcome. The decreased incidence in this study is due to modern obstetric practices leading to early diagnosis and higher incidence of cesarean delivery.

Key words: *Umbilical cord prolapse, perinatal outcome, cesarean section.*

Introduction

Umbilical cord prolapse occurs when the umbilical cord descends in advance of the presenting fetal part during labor. It is a serious obstetric emergency endangering the life of the baby due to compression of the cord.¹ The reported incidence of umbilical cord prolapse varies from 1 in 162 to 1 in 714 births (0.14-0.62%).^{2,3} It is associated with anything that prevents the presenting part from fitting closely into the lower uterine segment and thus shutting off the fore waters from the hind waters. The conditions associated are malpresentation², low birth weight⁴, multiple gestation², multiparity⁵, polyhydramnios⁵ and prematurity⁶. Critchlow CW et al⁷ reported that the excess risk was confined to the second born twin, mostly due to an increased probability of malpresentation. They could find any association with multiparity although the study very large numbers 709 women with cord prolapse. Cord presentation can be detected antenatally by transvaginal sonography usually performed every week, after 36 weeks of pregnancies. Kinugasa M et al⁸ studied incidence of cord prolapse by transvaginal sonography (TVS) in 198 women with breech presentation who delivered after

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36 weeks and found 8 women with cord presentation. On reviewing the literature it is found that there is insufficient data to support universal or selective screening for cord presentation.

The aim of the study was to assess the incidence, risk factors and perinatal outcomes of pregnancies complicated with umbilical cord prolapse in current practice at a tertiary centre.

Methods

The study was conducted retrospectively from January 2006 to July 2008 at the Department of Obstetrics and Gynecology, Regional Institute of Medical Sciences, Imphal. The deliveries complicated with umbilical cord prolapse were analyzed. The parameters studied include maternal age, parity, booking status, gestational age, malpresentation, sex, mode of delivery and perinatal outcome.

Results

There were 39 cases of cord prolapse out of 24,856 deliveries during the study period. Thus, prolapse of the umbilical cord complicated 0.16% of all deliveries in our study. The demographic and clinical characteristics of women in the study are presented in table 1. Women with cord prolapse had a mean age of 29.3 years with mean birth weight of 2.920kg and were of higher parity. Male gender (58.97%) was associated more with cord prolapse. Table 2

Table 1. Demographic and clinical characteristics of women

Characteristics	No. of cases with cord prolapse (n=39)
Maternal age	
≤ 30	23 (58.97%)
> 30	16 (41.03%)
Parity	
Primi	10 (25.64%)
Multi	29 (74.36%)
Gestational age (Days ±SD)	265 ± 19 days
< 37 weeks	12 (30.7%)
≥ 37 weeks	27 (69.3%)
Mean birth weight (kg)	2.920
Fetal gender	
Male	23 (58.97%)
Female	16(41.03%)
Type	
Overt prolapse	29 (74%)
Cord presentation	10 (26%)

Table 2. Risk factors of women

Characteristics	n=39
Malpresentation	20(51%)
Premature rupture of membrane (PROM)	9(23.1%)
Multiple pregnancy	4(12.8%)
Unbooked (lack of prenatal care)	27(69.2%)
Preterm	12(30.7%)

Table 3. Mode of delivery

Parameters	No. of cases
Cesarean section	17 (43.59%)
Types of vaginal deliveries	
Instrumental	4 (10.26%)
Breech	6 (15.38%)
Vaginal delivery	12 (30.77%)

Table 4. Perinatal outcome

Apgar score	Numbers of deliveries	Perinatal deaths
< 7	23 (59%)	12 (30.77%)
≥ 7	16 (41%)	Nil

showed the obstetric risks factors of women with cord prolapse. Out of 39 cases emergency cesarean section was done in 17 cases (43.59%) and all alive births (table 3). Low apgar score <7 was seen in 23 cases and out of which 12 (30.77%) had stillbirths (table 4).

Discussion

The rate of cord prolapse was 0.16% in our population which is comparable to other studies reported¹⁻⁶. Prolapse was more common among multiparous women. Critchlow CW et al⁷ have found a significant relationship between multiparity (above three deliveries) and prolapse of cord. Lack of prenatal care (unbooked cases) was a dominant factor for perinatal mortality with cord prolapse. This is comparable to Twinzer T et al⁹ and Kahana B et al¹⁰. Malpresentation (51%) was also another risk factor associated with prolapse in our study. Fetal malpresentation is indeed a well known risk factor.¹⁰ Male gender was another independent risk factor to cord prolapse and perinatal mortality. There have been many studies reported earlier showing the differences between male and female pregnancies.¹⁰ Perhaps male infants have a longer umbilical cord that could cause cord knots and prolapse.

Conclusion

The perinatal mortality rate of the umbilical cord

prolapse group in our study was 30.77%. Cord prolapse was associated with poor perinatal outcome. The prognosis depends on the condition of fetus at diagnosis and decision to delivery interval. Pregnancies complicated with malpresentation, multiple pregnancy, premature rupture of membrane, should be

carefully evaluated during labour. Early diagnosis, decompression of the cord if the fetus is alive and to deliver at the earliest is the practice of choice. Antenatal detection is difficult and insufficient data to support universal or selective screening for cord presentation on reviewing the literature.¹⁰

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The analgesic effects of tramadol, meperidine and lignocaine in ameliorating propofol injection pain - a comparative study

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Abstract

Objective: Propofol is one of the most commonly used intravenous anaesthetic induction agent. However pain on injection causes a significant drawback to its use. So we compared the analgesic effects of lignocaine, tramadol, meperidine and normal saline (placebo) in ameliorating propofol injection pain. **Methods:** Following the approval of the hospital ethics committee, 200 adult patients of either sex (age 18-60 years, ASA I & II) were divided into four groups (n=50) to receive lignocaine 25 mg, tramadol 50 mg, meperidine 25 mg or normal saline 1 ml in a randomized, double blinded fashion, to compare the pain relieving effects of the drugs during propofol injection before the patients lost consciousness. Verbal analogue scale (VAS) was used to compare the pain score (0=no pain; 10=most excruciating pain). **Results:** Lignocaine (90% patients) and tramadol (80% patients) had complete pain relief. Meperidine caused no significant pain reduction (58% patients complaining of pain) compared with placebo. **Conclusion:** Lignocaine and tramadol can significantly reduce pain during propofol injection.

Key words: Propofol, pain, tramadol, meperidine, lignocaine, Verbal Analogue Scale(VAS).

Introduction

Propofol is widely used to induce and maintain

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anaesthesia as well as for sedation in intensive care patients. However, in anesthetic practice, 30-90% of patients usually complain of pain during propofol injection.¹ This pain on propofol injection has been attributed to irritation of the skin, mucous membrane and venous interna by the phenol group present in the propofol² and contact between aqueous phase propofol and free nerve ending.³ Several drugs can reduce pain of propofol injection and these include lignocaine hydrochloride⁴, meperidine⁵, tramadol hydrochloride,⁶ etc. Hence, the use of pretreatment to reduce the pain of injection of propofol has become standard practice for smooth induction of anaesthesia. The present study was planned to compare the attenuating effects of lignocaine, tramadol, meperidine and placebo (normal saline) during propofol injection.

Methods

After obtaining approval from the hospital ethics committee and informed written consent, 200 adult patients of ASA grade I and II, aged between 18 and 60 years of both sexes scheduled to undergo elective surgery under general anaesthesia were chosen for this study in the Department of Anaesthesiology, Regional Institute of Medical Sciences Hospital, Imphal.

Patients with difficulty in communication and those with a history of adverse response to propofol, tramadol, lignocaine and meperidine; and patients with hepatic, renal, cardiac, haematological, metabolic and thrombophlebotic disorder were excluded from the study.

After premedication with glycopyrrolate 0.2 mg i.m 45 minutes before induction of anaesthesia, intravenous line was accessed.

All the patients were instructed to inform the investigator the severity of pain he/she would experience using a verbal analog scale (VAS) of 0 to 10 - with 0 being no pain and 10 being the most excruciating pain. After exsanguination by elevation of the arm for 15 seconds, a pneumatic tourniquet was placed on the arm with pressure of 70 mmHg to produce venous occlusion.

The patients were divided equally into 4 groups of 50 each in a randomized and double blind fashion to receive the following medications which were handed to the conducting anaesthesiologist in a coded syringe. The patients in group A received tramadol 50

Table 1. Showing the distribution of the patients demographic profile in the four groups (%)

Patients profile	Group A Tramadol	Group B meperidine (n=50)	Group C Lidocaine 2%	Group D placebo (n=50)	Statistical Test (n=50)	"P" Value (n=50)
Age (yrs)	33.50 ±12.11	40.30 ±12.05	36.42 ±10.96	38.36±13.72	ANOVA or "F" value 2.80	p ≥ 0.05 NS
Weigh(Kg) Mean ±SD	53.00 ± 5.88	51.52 ± 5.78	51.32 ± 5.40	51.36±4.75	ANOVA or "F" value 1.08	p ≥ 0.05 NS
Sex(M:F)	11:39	10:40	9:41	12:38	Chi-square, x ² =0.33	p ≥ 0.05 NS
ASA (I : II)	42:8	35:15	40:10	41:9	Chi-square x ² =3.24	p ≥ 0.05 NS

mg; group B received meperidine 25 mg; group C received lignocaine (2%) 25 mg and group D received 1 ml normal saline serving as placebo. VAS was assessed during and immediately after the injection of the studied drugs. At one minute after the injection of the studied drug the tourniquet was released, followed immediately by i.v injection of 10 ml (100 mg) propofol at a rate of 0.5 ml/second for the induction of anesthetic. VAS was reassessed before the patient lost consciousness.

Anaesthesia was maintained with 66% N₂O in O₂ along with traces of volatile anaesthetic and nondepolarizing muscle relaxant. The course of surgery and the postoperative period remained uneventful. Then, the results were analysed with an ANOVA test for demographic data, chi-square test for the incidence of side effects of the pretreatment drugs and propofol injection pain. The results were considered significant (S) statistically, if p-value was less than 0.05, highly significant (HS) if p-value was less than 0.001 and very highly significant (VHS) if p-value was less than 0.0001).

Results

Table 1 shows that there is no statistically significant difference between the four groups in male - female sex distribution with chi-

square value of 0.33 and p- value > 0.05. The mean age in years of the groups were 33.50 ±12.11, 40.30 ± 12.05, 36.42 ± 10.96, and 38.36± 13.72 in group A, group B, group C and group D respectively. The F-value was 2.80, which was not statistically significant (p- value > 0.05). The mean weight in kilograms (kg) of patients in group A was 53.00 ±5.88, group B was 51.52 ±5.78, group C was 51.32 ±5.40

and in group D it was 51.36 ±4.75 respectively. The F- value was 1.08, which was statistically not significant (p>0.05).

Table 2 shows the distribution of the VAS score in the four groups during propofol injection. The number of patients with VAS 0 were 40(80%) in group A, 9(18%) in group B, 45(90%) in group C and 11(22%) in group D. The patients with VAS 10 were 10(20%) in group A, 41(82%) in group B, 5(10%) in group C and 39(78%) in group D. The chi-square value was 68.18 and was found to be highly significant (p< 0.001). Data analysis showed that tramadol and lignocaine significantly reduced the incidence of propofol injection pain more than the placebo. But meperidine was comparable with placebo in reducing propofol injection pain.

Discussion

Lignocaine 0.1mg kg⁻¹ can significantly reduce the incidence of pain⁷ and lignocaine when given after a tourniquet (inflated to 50mmHg) virtually abolishes the propofol injection pain⁸. The possible mechanism could be attributed to the fact that lidocaine block the nerve fibers responsible for pain transmission resulting from direct irritation of propofol on the inner wall of blood vessels. At the same time, it reduces propofol induced

Table 2. Showing the distribution of VAS score in the four groups after injection of the pretreatment drugs (During Propofol Inj.)

Groups	No of pts with VAS score "0"	No of pts with VAS score "10"	Chi-square, χ^2	p-Value
A	40(80%)	10(20%)	68.18	P<0.001, HS
B	9(18%)	41(82%)		
C	45(90%)	5(10%)		
D	11(22%)	39(78%)		

HS-Highly significant

kallikrein-kinin system and the release of bradykinins.

Tramadol hydrochloride is found to be as effective as lignocaine in reducing the incidence and severity of pain on propofol injection in this study. Tramadol hydrochloride is a central acting, weak mu-receptor agonist and inhibits noradrenaline re-uptake as well as promotes serotonin release⁹ and exogenous opioids like tramadol hydrochloride activates opioid receptors increasing potassium currents and decreasing calcium

currents in sensory neuron cell bodies leading to inhibition of signal transmission¹⁰.

In contradiction to present study, Mok SM et al¹¹ found meperidine to have peripheral analgesic effect in reducing propofol injection pain.

However, similar to our findings, Flanagan MT¹² observed that meperidine had no anesthetic ability in inhibiting conduction in human peripheral nerves. The disparity between meperidine's ability to produce spinal anaesthesia and its ability to produce peripheral anaesthesia may be attributed to mechanism other than inhibition of sodium channels.

Conclusion

Pretreatment with lignocaine and tramadol hydrochloride could reduce the propofol injection pain. Meperidine could not be shown to be effective in our study.

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Placentrex gel with electrocauterization in the treatment of cervical erosion

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Abstract

Objective: To compare placentrex gel application and electrocauterization as treatment modalities in the management of cervical erosion. **Methods:** The study participants were randomly allocated into one of the two groups either placentrex gel or electrocautery to assess the response to these treatment and comparison. Electrocauterization was done postmenstrually with needle and ball electrodes using the standard electrosurgical unit. Placentrex gel was applied internally by using an applicator or syringe and about 2ml of placentrex gel was applied for two times daily except during menses. All the subjects were followed up at 2nd week, 4th week, 12th week and 24th week and evaluated for healing, side effects, complications and patients' satisfaction. Healing was graded as good (complete healing), fair (partial healing) and poor (no healing). Statistical analysis was done using Chi-square test, Fisher's exact test. A probability value of less than 0.05 was considered significant. **Results:** Healing took shorter time in electrocautery group than placentrex group but as time elapsed; healing rate improved and ultimately became better in placentrex group. Placentrex gel was technically easier to apply and associated with less complications and side effects.

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Conclusion: Placentrex gel was found to be better than electrocauterization for treatment of cervical erosion in terms of healing rate, side effects, complication, technical ease of application and patients' compliance.

Key words: Cervical erosion, Pap smear, cervical biopsy, healing rate.

Introduction

Cervical erosion is the commonest lesion found in women attending Gynae outpatient department. It is a condition where there is persistence of columnar epithelium of the endocervix into the ectocervix. The normal squamous epithelium of the ectocervix is replaced by inflamed tissue from within the cervical canal. It appears as bright red area surrounding and extending beyond the external os in the ectocervix with clearly demarcated outer edge. It may be congenital or acquired. Leucorrhoea is the most common associated symptom. Various precipitating factors are poor hygiene, child birth trauma, high parity, low literacy, low socio-economic status, early age of marriage and coitarche, multiple sexual partners, genital tract infections and immunosuppression. Many treatment modalities are available like chemical cauterization, diathermy cauterization, cryotherapy, laser ablation, conisation, microwave coagulation, hysterectomy etc.

Placentrex gel is an aqueous extract of human placenta and contains various nucleotide fractions of RNA and DNA, water soluble peptides and trace elements. It has immunomodulatory, anti-inflammatory, anti-oxidant properties and also stimulates growth

factors which are helpful in healing of wound. It has got additional benefit of being non invasive, painless, does not carry complications like sterility, perforation, excessive bleeding and also, it does not interfere with biopsy. Electrocautery involves the use of electric current to heat up a metal conductor and then tissue is cauterized by touching the hot metal object to it. By electrocautery, cystic glands are punctured, ectropion corrected by deep linear burns and any erosion coagulated. The study was undertaken to compare placentrex gel application and electrocauterization in the management of cervical erosion.

Methods

This comparative study was carried out in the Department of Obstetrics and Gynaecology, Regional Institute of Medical Sciences(RIMS), Imphal from September 2006 to August 2008. After obtaining institutional ethics committee approval and informed consent, a total of 124

patients with cervical erosion on per speculum examination attending Gynae. OPD, RIMS were selected. Patients on hormone therapy, having cervical cancer and pregnancy were excluded. After a detailed history and thorough clinical examination, all participants were subjected to Pap smear and cervical biopsy to rule out any malignant lesion. Patients recruited in the study were randomly allocated into two groups - placentrex gel and electrocautery. Both the procedures were done on outpatient basis without analgesia or anaesthesia. Electrocauterization was done postmenstrually with needle and ball electrodes using the standard electrosurgical unit. Placentrex gel was applied internally by using an applicator or syringe and about 2ml of placentrex gel was applied for two times daily except during menses. Electrocauterized women

were advised abstinence for three weeks after the procedure, which was not required in the placentrex group. Each cervix was photographed before treatment as well as serially during follow up visits in order to allow objective documentation of the healing process. All the subjects were followed up at 2nd week, 4th week, 12th week and 24th week and evaluated for healing, side effects, complications and patients' satisfaction. Healing was defined as regression of size of cervical erosion on per speculum examination (i.e. regression in the grades of erosion) and improvement of subjective symptoms. Healing was graded as good (complete healing), fair (partial healing) and poor (no healing). Statistical analysis was done using Chi-square test, Fisher's exact test. A probability value of less than 0.05 was considered significant.

Results

Out of 124 cases studied, 62 cases were treated with placentrex gel application and

Table 1. Background characteristics of the cases in two groups

Background characteristics	Electrocautery Group n(%)	Placentrex Gel Group n(%)	Total n(%)	p-value
Age (yr)				
< 35	12 (36.4)	21 (63.6)	33(26.6)	0.07
= 35	50 (54.9)	41 (45.1)	91(73.4)	
Parity				
< P ₃	17 (50.0)	17 (50.0)	34(27.4)	1.0
= P ₃	45(50.0)	45 (50.0)	90(72.6)	
Socio-economic status				
Low	54 (50)	54 (50)	108(87.1)	1.0
Middle	8 (50)	8 (50)	16 (12.9)	
Residence				
Rural	39 (52)	36 (48)	75(60.5)	0.58
Urban	23 (46.9)	26 (53.1)	49 (39.5)	
Literacy status (standard)				
Illiterate	25 (56.8)	19 (43.2)	44 (35.5)	0.22
< 12	25 (42.4)	34 (57.6)	59 (47.6)	
= 12	12 (57.1)	9 (42.9)	21 (16.9)	
Occupation				
Housewife/unemployed	43(50.0)	43 (50.0)	86 (69.4)	0.79
Employed	20 (52.6)	18 (47.4)	38 (30.6)	
Religion				
Hindu	43 (48.9)	45 (51.1)	88 (71.0)	0.40
Muslim	5 (38.5)	8 (61.5)	13 (10.5)	
Christian	14 (60.9)	9 (39.1)	23 (18.5)	
Presenting complaints				
White discharge	21 (48.8)	22 (51.2)	43 (34.7)	df=3, 0.67*
Mucopurulent discharge	23(57.5)	17 (42.5)	40 (32.3)	
Pain abdomen	11 (44)	14 (56)	25 (20.2)	
Bleeding p/v or contact bleeding	5 (45.5)	6 (54.5)	1 (8.8)	
Others (itching, backache)	2 (40.0)	3 (60.0)	5 (4.0)	

*Last two rows were combined

another 62 with electrocauterization. The mean age of the patients was 40.6 years. Twenty seven cases were lost on follow up (electrocautery 18 and placentrex 9) and 1 case underwent total hysterectomy. These cases were excluded from the final outcome analysis.

Table 1 shows background characteristics of the study subjects in both the groups. There were no significant differences between the two groups in these variables. The mean age for marriage was 21.13 ± 4.4 years in electrocautery group and it was 20.05 ± 4.2 years in placentrex group. No significant difference was seen between these two groups ($t=1.39$; $p=0.166$).

The initial healing rate was less in placentrex group (4.8%), but it was better than the electrocautery group at 24th week (100.0% vs 95.3%) (table 2).

During the procedures, placentrex gel application was painless and associated with minimal complications. In electrocauterized women, 48.9% had leucorrhoea during treatment whereas only 7.6% in placentrex. Mild or moderate vaginal bleeding in 70.2%, mild or moderate pain in 97.9% of electrocautery group whereas in placentrex gel group it was 1.9% for bleeding and none for pain (table 3). In the electrocautery group, there were 20 cases complaining of pain, 2

Table 2. Healing rate on follow up in both the groups

Follow up at	Electrocautery			Placentrex			Inflammatory on Pap smear (87.1%) and chronic cervicitis on cervical biopsy (94.4%) which were similar with other studies. ^{1,5} The initial healing rate in electrocautery was
	poor N (%)	fair & good N (%)	total N (%)	poor N (%)	fair & good N (%)	total N (%)	
2 weeks	11 (17.7)	51 (82.3)	62	59 (95.2)	3 (4.8)	62	(43.5% and 30.7%),
4 weeks	2 (4.3)	45 (95.7)	47	11 (19.3)	46 (80.7)	57	inflammatory on Pap smear
12 weeks	2 (4.7)	42 (95.30)	44	1 (1.9)	52 (98.1)	53	(87.1%) and chronic cervicitis
24 weeks	2 (4.7)	42 (95.3)	44	0 (0)	52 (100.0)	52	on cervical biopsy (94.4%)

Table 3. Distribution of cases by vaginal bleeding, pain and leucorrhoea during treatment

	Electrocautery N(%)	Placentrex N(%)	Total
Vaginal bleeding			
No	14 (29.8)	52 (98.1)	66
Mild & Moderate	33(70.2)	1 (1.9)	34
Pain			
No	1 (2.1)	53 (100)	54
Mild & Moderate	46 (97.9)	0 (0)	46
Leucorrhoea			
No	24 (51.1)	49 (92.4)	73
Mild & Moderate	23 (48.9)	4 (7.6)	27

$P < 0.001$ (Fisher's exact test)

cases having dyspareunia, 1 case each of PID and secondary bleeding during follow up. None of the patients in the placentrex gel group complained of these complications.

Discussion

This prospective study was undertaken to compare the effect of placentrex gel on cervical erosion with electrocauterization. In the present study, cervical erosion was most common in the multiparae (72.6%) which was comparable to that reported by Kulkarni RN and Durge PM (75.6%)¹. The increase incidence of cervical erosion with parity was also reported by other workers.²⁻⁴ Again, maximum cases were encountered in illiterate or low literacy status (83.1%), low socioeconomic strata (87.1%), housewives or unemployed (69.4%) and majority married between 18 to 30 years (69.4%) with first deliveries before 30 years of age (73.4%). These were comparable to the reports made by other authors.^{1,4,5} The main underlying reason for cervical erosion may be correlated with low socio-economic status, low literacy and poor hygienic standards. Moreover, women with low socioeconomic status tend to marry young and have frequent pregnancies and child birth and hence high parity. Goldacre MJ et al³ reported that most patients presented with white or mucopurulent discharge (38.5%) which was lower than 67.0% in our study.

Majority had grade 2 or 3 erosion on first visit (43.5% and 30.7%), inflammatory on Pap smear (87.1%) and chronic cervicitis on cervical biopsy (94.4%) which were similar with other studies.^{1,5} The initial healing rate in electrocautery was 82.3% with a failure rate of 17.7%, which were comparable to that reported by Richart RM and Sciarra JJ⁶(89%) and Schuurmans SN et al⁷(85.9%). Chanen W and Hollyock VE⁸, Hollyock VE and Chanen W⁹ also reported a success rate of 90% while Chanen W and Rome RM¹⁰ as 97.3% and 93.9% by Giles JA et al¹¹. However, Ostergard DR et al¹² reported only 33% as success rate for electrocauterization. Majority of patients in electrocautery group (97.9%) had mild or moderate pain during treatment but none of

the placentrex group experienced any pain. Only 7.6% of the placentrex group complained of leucorrhoea whereas 48.9% of electrocauterised women had leucorrhoea and 70.2% of electrocautery group had mild or moderate vaginal bleeding during treatment. Richart RM and Sciarra JJ⁶ reported complications in 7.6% while Chanen W and Hollyock VE⁸, Hollyock VE and Chanen W⁹ in 3% with cervical stenosis in 0.8%. Warwick DJ¹² found a significant vaginal discharge in 70% of the patients with diathermy cauterization. However, placentrex gel application being noninvasive procedure was totally pain free with minimal complications. Hence, the complications were observed in electrocautery group only which was statistically significant ($P < 0.001$). On the other hand, fair and good healing rate was less in placentrex group at 2 weeks (4.8%) but on follow up visits, healing rate improved and caught up with electrocautery group and finally became better. Also, the patients compliance was better in placentrex gel group. The number

of patients lost in the follow up was double in the electrocautery group. Shukla M and Wati C¹³ also reported cervical erosion to be completely healed in 30% cases in placentrex group and 40% in cryocauterization after 3 months of treatment and healing rate increased to about 60% and 70% respectively after 6 months. In their studies, both cryocauterization and placentrex gel had almost equal effect and 10% cases failed to heal after 6 months in both modalities.

Conclusion

Healing took shorter time in electrocautery but overall healing rate was better in placentrex inspite of longer duration of healing time. Placentrex gel application for treatment of cervical erosion was a non-invasive, painless procedure with overall good healing rate and better compliance compared to those treated with electrocautery. Hence this treatment modality was cost effective for cervical erosion with high efficacy, minimal side effects, complications and was technically easier treatment.

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A comparative study of accelerated fractionation radiotherapy with concomitant boost regimen vs conventional fractionation radiotherapy in locally advanced head and neck squamous cell carcinoma - a preliminary report

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Abstract

Objective: To evaluate the efficacy and tolerability of accelerated fractionation radiotherapy with concomitant boost and to compare it with that of conventional fractionation radiotherapy in locally advanced head and neck squamous cell carcinoma.

Methods: A prospective non-randomised study of 25 patients in the study arm and 26 patients in the control arm during November 2006 to February 2008 was conducted at Radiotherapy department of Regional Institute of Medical Sciences Imphal, Manipur. Patients in the control arm were treated with external beam radiation for a tumoricidal dose (T.D.) of 6660 cGy to 7200 cGy over 7 to 8 weeks by using conventional fractionation schedule of 1.8 Gy per day 5 days a week with the help of Theratron 780-C telecobalt unit. The same treatment equipment was used for the study arm and T.D. of 6600 - 7200 cGy was delivered. However, fractionation schedule was changed by giving 1.8 Gy per fraction per day during the main phase of treatment and then adding a second fraction of 1.5 Gy as concomitant boost during the last 12 treatment days keeping a gap of 4-6 hrs between the two fractions. The overall treatment period was shortened and completed over 5 to 6 weeks. All patients were monitored weekly during the treatment period and assessed at

the end of one month and 3 months of completion of treatment for response and toxicities. **Results:** One patient in control arm was out of protocol due to incomplete dose and one in study arm dropped out of treatment on his own. Complete response (CR) to treatment was obtained in 13 of 25 patients (52%) in the control arm and 19 of 24 patients (79%) in the study arm at primary sites. The CR for nodal sites were 13 of 24 (54%) for the control and 18 out of 22 (81%) for the study arm which was significant statistically ($P < 0.05$). When analysed for survival advantage, no significant difference was observed between the two arms either in disease-free survival rate (60% Vs 66%; $P > 0.05$) or overall survival rate (76% Vs 75%; $P > 0.05$) at 13 months and 14 months of median follow-up respectively. This could be due to short period of follow up since the median follow up was not mature at the time of reporting. There were significant increase in early treatment related side effects like mucositis, laryngitis and pharyngitis and late treatment related sub cutaneous fibrosis and xerostomia in the study arm compared to the control arm. However, the increase toxicities were tolerable. **Conclusion:** Accelerated fractionation radiotherapy with concomitant boost regimen significantly increases the complete response rates in both primary and nodal sites with manageable increase in toxicities compared to conventional fractionation radiotherapy schedule. Whether this increase in response rate will translate into longer overall survival can only be known after adequate long term follow up.

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Key Words: *Head and neck cancer, Accelerated fractionation radiotherapy, Concomitant boost radiotherapy.*

Introduction

The term "Head and neck squamous cell carcinomas" usually refers to the most common epithelial malignancies arising from below the skull base to the region of the thoracic inlet excluding thyroid cancers. Histologically, more than 90% of cancers arising in this area are of squamous cell carcinomas.¹

Head and neck cancer accounts for 15 to 30% of all cancers in South East Asian countries and Imphal West District of Manipur had 28.56% according to the ICMR 2006 Cancer registry.²

The male to female ratio for head and neck cancers is 2.1:1.0 in Manipur and major sites were nasopharynx (40.9%), hypopharynx (12.7%) and larynx (11.9%).

Unlike tumors at other sites, head and neck cancer tends to present with advanced loco-regional disease, and only 18%-20% developed distant metastases. Less than 15 % can be treated with definitive surgery with accompanying morbidities and mortality. Thus control of the primary site and nodal metastasis is paramount in the management of this disease.³

Chemoradiation in various sequences has proven to be superior to the conventionally fractionated radiotherapy alone but treatment-related toxicities are higher. Hence, radiotherapy alone would be a more appropriate treatment choice when proper selection of cases suitable for radical radiation dose delivery with correct technique and fractionation schedule can be done.⁴

Results of large randomized trials addressing the optimization of radiation fractionation collectively show that a number of biologically sound altered fractionation schedules improved the loco-regional control rate to the order of 10 to 15%, but they have only a modest impact on overall survival.⁵

Generally when accelerated fractionation radiotherapy with concomitant boost is planned for head and neck tumours, a shrinking field technique is employed during the course of treatment. In the first phase, the tumour and regional nodal areas are encompassed and irradiated; following this a smaller volume is irradiated to include the areas of known-tumour with a safe margin. In this way, the smallest possible volume is given the highest dose, minimizing problems that may occur when radiation is delivered to large portals. Following pilot studies in which the boost was given during various phases of the main treatment, it was found that the best results were achieved by boosting during the last 2 weeks of treatment course.³

In the background of these evidences and in an effort to find the best optimal fractionation schedule of radiotherapy to be followed in head and neck cancer, this study was undertaken with aims to evaluate the efficacy of accelerated fractionation radiotherapy with concomitant boost in locally advanced head and neck squamous cell carcinoma and also to analyze the associated side effects thereof.

Methods

Histologically confirmed cases of head and neck squamous cell carcinoma (Stage III and IV) attending the Department of Radiotherapy, Regional Institute of Medical Sciences, Imphal, Manipur, form the materials of this study. 25 consecutive OPD patients were recruited in study arm for accelerated fractionation with concomitant boost and 26 patients in control arm were enrolled for conventional fractionation schedule. Only patients who are previously untreated were taken up. The required qualifying criteria for performance status (Karnofsky score) was 60% or above, adequate haematological function (11b-9gm% or above, TLC-4,000/mm³ or above and platelet count - 1,00,000/mm³ or above), normal kidney function test (KFT) and liver function test (LFT) and no major co- morbid medical problems.

The study was a prospective non-randomized clinical study to compare the efficacy and the side effects of accelerated fractionation

radiotherapy with concomitant boost in locally advanced head and neck squamous cell carcinomas to that of the conventional fractionation standard radiation. After the proper work-up and the confirmation of the disease, the patients were grouped into either of the following 2 arms:

Control arm (n=26)

All the patients were treated by Cobalt-60 (Theratron-780 C) external beam radiation treatment (EBRT) unit available in our Department to a T.D. of 6660 cGy-7200 cGy at a dose rate of 180 cGy. per day 5 days a week. Spinal cord was spared after 4320 cGy/ 24 exposures and uninvolved areas excluded at 5040 cGy over 28 exposures. All the patients planned by using Simulix HQ simulator and tissue compensators, bolus, wedge filters and immobilization system were used as necessary.

Study arm (n=25)

The same treatment equipments and techniques used for the control arm were used in this arm as well and same dose delivered i,e T.D. of 6600-7200 cGy. but with the altered hyperfractionation schedule leading to shortened treatment period. The initial treatment volume covered the primary disease area along with regional areas with safe margins at a dose rate of 180 cGy. one fraction a day and 5 days a week. But for the last 12 exposures, a concomitant boost only to the grossly involved primary and secondary sites were incorporated at a dose rate of 150 cGy per exposure. The treatment gap in between the two fractions was maintained at 4 to 6 hrs. Spinal cord was shielded at 4230 cGy after day 21 exposures.

During the whole period of treatment in both the arms, patients were checked up twice a week for side effects and untoward events. At one month and three months of completion of treatment, patients were assessed for treatment response. Early treatment response was assessed in accordance with WHO Miller's criteria. Calculation on long-term survival was done using standard chi-square test. Treatment related early and late side effects were analyzed in accordance with RTOG criteria.

Results

In this non-randomized prospective study, 25 patients were accrued in the study arm and 26 patients in the control arm in the period spanning November, 2006 through February, 2008.

Table 1 shows that majority of patients belonged in the age group of 50 - 59 years in control arm (38.5%) and in study arm (36.0%). The accrual of patients by stagewise was also found to be matching in both arms.

Table 1. Patient characteristics

Characteristics	Study Arm (n = 25)	Control Arm (n=26)	p-value
Sex :	No. (%)	No. (%)	
Male	17(68%)	19(73%)	
Female	8 (32%)	7 (28%)	
Age (Y) :			
range	28 - 78	25 - 80	x ² - test = 0.76
median	56	53	
20 - 29	2 (8.0%)	2 (7.7%)	p-value > 0.50
30 - 39	3 (12.0%)	4 (15.4%)	
40 - 49	4 (16.6%)	5 (19.2%)	
50 - 59	9 (36.0%)	10 (38.5%)	
60 - 69	4 (16.0%)	3 (11.6%)	
70 - 79	2 (8.0%)	1 (3.8%)	
80 - 89	1 (4.0%)	1 (3.8%)	
TNM Staging (AJCC, 2002)			
III	9 (36.0%)	10 (38.5%)	x ² - test = 0.01
IV	16 (64.0%)	16 (61.5%)	p - value > 0.50
Karnofsky Score			
90 - 100%	3 (12.0%)	4 (15.4%)	x ² - test = 0.23
80 - 90%	13 (52.0%)	12 (46.1%)	
70 - 80%	7 (28.0%)	8 (30.7%)	p - value > 0.50
60 - 70%	2 (8.0%)	2 (7.6%)	

Table 2 shows the distribution of the primary sites. The most common primary tumor site was the pyriform fossa in both the arms: 7 cases (27.0%) in control arm and 8 cases (32.0%) in study arm.

Table 2. Distribution of the primary site

Primary Tumor Site	Study - Arm (n = 25)	Control Arm (n = 26)	p-value
	No. (%)	No. (%)	
Ca. Pyriform fossa	8(32.0%)	7 (27.0%)	
Ca. Larynx	7(28.0%)	6 (23.0%)	x ² - test = 1.12
Ca. Alveolus	2(8.0%)	2 (7.7%)	
Ca. Post Pharyngeal Wall	2(8.0%)	2 (7.7%)	p - value > 0.05
Ca. Tongue	1(4.0%)	2 (7.7%)	
Ca. Nasopharynx	3(12.0%)	3 (11.5%)	
Ca. Tonsillar Region	1(4.0%)	2 (7.7%)	
Ca. Maxilla	1(4.0%)	2 (7.7%)	

The maximum number of patients (42.3%) have T3 stage in the control arm and 36.0% in the study arm. The majority of patients in control arm have stage IV disease contributing 61.5% and in study arm also 64% was stage IV. The nodal and primary sites status in both

Table 3. Early Treatment Response (primary sites)

Type of Response	Study Arm (n=24)	Control Arm (n=25)	p-value
CR	19 (79.1%)	13 (52.0%)	<0.05
PR	5 (20.9%)	7 (28.0%)	>0.05
NR	0	2 (8.0%)	-
PD	0	3 (12.0%)	-

CR - Complete Response, PR - Partial Response, NR - No Response, PD - Progression of Disease

Table 4. Early Treatment Response (neck nodes)

Type of Response	Study Arm (n=22)	Control Arm (n=24)	p-value
CR	18 (81.8%)	13 (54.1%)	<0.05
PR	3 (13.6%)	5 (20.8%)	>0.05
NR	1 (4.5%)	2 (8.3%)	-
PD	0	4 (16.7%)	-

Table 5a. Early side effects

Toxic effects Grade	Study arm (n=24)			Control arm (n=25)			P-value
	I	II	III	I	II	III	
Skin	13 (54.1%)	9 (37.5%)	2 (8.3%)	15 (60.0%)	8 (32.0%)	2 (8.0%)	>0.05
Mucosa	2 (8.3%)	5 (20.8%)	17 (70.8%)	6 (24.0%)	10 (40.0%)	9 (36.0%)	<0.05
Salivary Gland	16 (66.6%)	8 (33.0%)	0	18 (72.0%)	7 (28.0%)	0	>0.05
Larynx	9 (37.5%)	3 (12.5%)	12 (50.0%)	16 (64.0%)	6 (24.0%)	3 (12.0%)	<0.05
Pharynx	3 (12.5%)	11 (45.8%)	10 (41.6%)	11 (44.0%)	13 (52.0%)	1 (4.0%)	<0.05

Table 5b. Late side effects

Toxic effects Grade	Study arm (n=24)				Control arm (n=25)				P-value
	0	I	II	III	0	I	II	III	
Skin	2 (8.3%)	15 (62.5%)	4 (16.7%)	3 (12.5%)	3 (12.0%)	14 (56.0%)	6 (24.0%)	2 (8.0%)	>0.05
Mucosa	1 (4.2%)	3 (12.5%)	4 (16.6%)	16 (66.6%)	3 (12.0%)	8 (32.0%)	10 (40.0%)	4 (16.0%)	<0.05
Salivary Gland	1 (4.2%)	5 (20.8%)	14 (58.3%)	4 (16.7%)	2 (8.0%)	8 (32.0%)	10 (40.0%)	5 (20.0%)	>0.05
Subcutaneous	5 (20.8%)	13 (54.2%)	6 (25.0%)	0	6 (24.0%)	15 (60.0%)	4 (16.0%)	0	>0.05
Trismus	14 (58.3%)	8 (33.3%)	2 (8.3%)	0	16 (64.0%)	7 (28.0%)	2 (8.0%)	0	>0.05

arms were comparable and statistically insignificant. 1 patient in control arm did not complete treatment with major protocol deviation and 1 patient in study arm dropped out of treatment. Thus, only 25 and 24 cases were evaluable for result analysis for control and study arm respectively. The patients in the study arm had a median follow-up of 14 months (7 -22 months). Likewise, in the control arm, median follow-up was 13 months (6 - 22 months).

Table 3 shows response in primary sites where 19 patients (79.1%) had complete response (CR) in the study arm as compared to 13 (52.0%) patients in the control arm (P < 0.05). Partial response (PR) was noted in 5 patients (20.9%) in the study arm, 7 patients (28.0%) in the control (P > 0.05). 2 patients (8.0%) in the control arm did not show any response whereas 3 (12.0%) patients developed progressive disease in the control arm. The CR in the study arm was significantly higher compared to that of the control arm for this site.

In table 4 response in the nodal sites follow similar pattern with 18 (81.8%) patients in study arm as compared to 13 patients (54.1%) in control arm had complete response which is statistically significant (P < 0.05) but the difference in partial response in both arms was insignificant in nodal sites.

Mucositis (Grade 3) resulted in 17 out of 24 patients in the study arm as compared to 9 out of 25 patients in control arm. Similarly, more early side effects occurred at

pharynx and larynx in study arm as compared to control arm. The difference of early side effects in both arms at mucosa, pharynx and larynx are significant statistically.

Late treatment related mucositis was significantly higher in the study arm as compared to the control arm ($P < 0.05$). The other late side effects were comparable (table 5a & b).

The late treatment response in both arms in terms of disease free survival, survival with disease and overall survival were comparable statistically (table 6).

Table 6. Late treatment response in study arm (13 months) and control arm (14 months)

Type of response	Study arm (n=24)	Control arm (n=25)	p-value
DFS	16(66.6)	15(60.0%)	>0.05
SWD	2(8.3%)	4(16.06%)	>0.05
OS	18(75.0%)	19(76.0%)	>0.05

Discussion

Accelerated radiotherapy with concomitant boost technique has been studied on the basis of the radiobiological aspects reported by many authors.⁶⁻⁸ We took up the concept of accelerating radiotherapy using concomitant boost from week 3, after 4 - 6 hrs interval keeping in mind the radiobiological advantages reported by Chris HJ et al⁹, and Bentzen SM et al¹⁰. Ang KK et al¹¹ reported that if the boost be given during the last 2 - 2½ weeks of basic treatment, a slightly better primary control rates than of the boost delivered during the first 2 - 2½ weeks or twice a week throughout the basic treatment. The present study though small in size and non randomised was a pilot study designed to evaluate the efficacy and tolerance of concomitant boost over conventional RT in locally advanced head and neck carcinomas. The fractionation schedule followed is a quasi accelerated type of altered fractionation since the acceleration is done during the end phase of treatment only.

Analysis of the primary sites showed that 19 (79.1%) patients in study arm achieved complete response (CR) as compared to 13 (52%) patients in the control arm ($P < 0.05$). 7 (28%) and 5 (20.9%) cases in the control and

study arms respectively achieved partial response (PR) and in the control arm, no response (NR) rates was noted in 2 (8%) patients, 3 (12%) patients had progressive disease (PD) during treatment. None of the patients in the study arm had NR and PD. The results are comparable to a similar pilot study by Mackenzie R et al¹² who obtained the CR in 77% of patients assigned to concomitant boost techniques.

For nodal sites, the CR in the study arm, 18 (81.8%) compared to 13 (54.1%) patients in the control arm ($P < 0.05$) were similar to findings reported by Valentine K and Simonida C¹³ where the complete nodal response rate was 16 of 27 patients (59.2%) treated with conventional fractionation and in 18 of 25 patients (72.0%) treated with concomitant boost technique. These studies further reinforce our belief that the radiobiological advantage of delivering smaller size fractions as accelerated concomitant boost and contracting the overall treatment period will translate into better tumour control while keeping the radiation reactions within acceptable limits.

In the present study, there were no significant difference in disease-free survival rate (DFS), survival with disease and overall survival rates (OS). Similar survival findings were reported by Valentina and Simonida C¹³ and Fu KK et al¹⁴. However our study period is too short to comment for a meaningful survival benefit. Longer follow up is continuing and median survival is yet to be reached. In a study by Morris MM et al¹⁵, the DFS of 64% at a longer follow up of 2 years is comparable to 66.6% of our study arm but the overall survival rate of 59% in that study is inferior to OS rate of 75% in our study.

In comparison to the control arm, our study arm had more acute reactions of mucositis, pharyngitis and laryngitis which are significant statistically. No patient experienced grade 4 acute reactions. The reactions were manageable and treatment interruptions were within acceptable limits of protocol. None of the patients in the treatment arm got interrupted beyond the 1 week limit of

admissible rest for acute reactions. On the contrary, study of Schmidt-Ullrich RK et al¹⁶ found no difference in acute reactions between conventional fractionations and concomitant but few studies of Fu KK et al¹⁴ and Horiot JC et al¹⁷ supported our results. In our study arm, 70.8% of patients experienced acute mucositis (Grade 3) which is higher than the findings of Mackenzie R et al¹² and Johnson CR et al¹⁸ (50% and 52% respectively). Acute pharyngitis (Grade 3) 41.6% was also higher than 27% reported by Mackenzie R et al¹².

Late reactions were also higher in our study in patients treated with concomitant boost radiotherapy (16/24) compared with conventional fractionation radiotherapy (4/25) which is significant statistically ($P < 0.05$). Our finding is similar with those findings of Valentine K and Simonida C¹³ where grade 3 late mucosal reactions were modestly enhanced in the study arm. In contrast to our study Fu KK et al¹⁴ found there were no significant increase of late effects. The discordance in acute and late radiation side effects could be due to different radiation equipments, energies,

delivery system, nutritional and oral hygienic care and use of radio protectors by the different investigators.

With the gain achieved in therapeutic ratio by using concomitant boost regimen we can incorporate chemotherapy schedules to further enhance the response rate and future studies can be directed in this avenues of clinical research.

Conclusion

The preliminary results from this pilot study reaffirms that accelerated fractionation radiotherapy with concomitant boost regimen significantly increases the complete response rates in both primary and nodal sites with manageable increase toxicities compared to conventional fractionation radiotherapy schedule in loco regionally advanced head and neck cancers. However, whether this increase in response rate will translate into longer overall survival can only be known after adequate long term follow up. Future studies can incorporate chemotherapy to further enhance the treatment response.

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Impact of HCV co-infection with HIV infected individuals on CD₄ cell count

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Abstract

Objective: To find the impact of HCV co-infection on CD₄ cell count (immunocompetence) in HIV infected individuals of Manipur.

Methods: Known HIV infected blood samples were tested for HCV antibody and immunophenotyping (CD₄ cell count) was carried out on the stained blood samples using FACS Calibur flow cytometer (Becton Dickinson) in the department of Microbiology, JN Hospital, Porompat, Imphal. Statistical analysis for significance was performed by calculating p values using student's t test. **Results:** The mean CD₄ count of HIV infected individuals without laboratory evidence of HCV infection (HIV+, HCV-) was found to be 366/μl and that of the dual infection (HIV+HCV+) was found to be 277/μl of blood. The mean CD₄ count of dual infected subjects (HIV+, HCV+) was found lower as compared to HIV without HCV infection (HIV+, HCV-) but statistically not significant (p value = 0.086). The mean CD₄ count among sexually transmitted HIV infected subjects was found to be 385/μl and that of the intravenous drug users (IDU) were found to be 228/μl of blood irrespective of HCV serostatus. The mean CD₄ cell count of intravenous drug users (IDU) was significantly lower than sexually transmitted HIV infected individuals (p value < 0.001). **Conclusion:**

Though this study could not determine that HCV co-infection hasten deterioration of immuno-competence among HIV infected subjects, we concluded that progression of immune-suppression is reasonably faster in HIV positive subjects transmitted through intravenous route (IDU).

Key words: Co-infection, phenotyping, CD₄ cell.

Introduction

Human immunodeficiency-virus (HIV) and hepatitis C virus (HCV) infection are pandemic, affecting people everywhere. Both share many characters. Because both are transmitted through the sharing of contaminated needles, many injecting drug users (IDUs) acquire both viruses. In person with HIV infection, its prevalence is estimated to be approximately 50%.¹ Backus LI et al² reported prevalence rate of 37% among high risk group in USA. In many studies, more than 90-95% of IV drug users are co-infected.³ On the other hand, only 4-8% of heterosexual (gay men) who are HIV positive also HCV positive³ since HCV are not as easily transmitted by sexual contact. Of HCV positive persons, approximately 10% are also HIV positive, and of HIV positive persons, approximately 25% are also HCV positive.⁴ In one study, the prevalence of HCV infection among the IDUs of Manipur were found to be exceptionally high (90.4%).⁵ Main source for HIV and HCV transmission includes IV drug use, transfusion of blood products prior to screening, and to a less extent sexual intercourse.⁴

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Many studies indicate that HIV can worsen HCV. HIV/HCV co-infection has been associated with a faster rate of Hepatitis C disease progression, higher HCV viral loads and a greater risk of developing severe liver damage, and HCV can affect HIV treatment by increasing the frequency of liver toxicity to HIV drugs. Since it takes about 20 to 40 years for HCV to cause clinically significant liver damage, most clinicians initially presumed that individuals with both HIV and HCV would die of AIDS before liver disease become a concern.

About 70 to 80% of acute HCV infection becomes chronic. Factors that promote progression of HCV include alcohol intake, age over 45 at the time of infection, HIV co-infection, male gender, and co-infection with Hepatitis B or other viruses. HIV infection and alcohol consumption are independently associated with accelerated progression of fibrosis.⁶ The diagnosis of HCV is made by a serological test which is sensitive and specific. In immune-suppressed person, however, there may be a false negative test in presence of hepatitis C viremia. Therefore, in a high risk HIV infected patient who has a negative antibody test, a quantitative PCR is also recommended.⁷

Many physicians have also opined that HCV co-infection may act as cofactor for HIV disease progression. Though there have been several studies on impact of HIV on HCV infection, there are sparse studies on impact of HCV on HIV infection and also there are hardly any conclusive studies on CD₄ cell count level among co-infected individuals. Therefore, the aim of this study is to find the impact of HCV co-infection with HIV infected individuals on CD₄ cell count (immunocompetence). This study would be highly relevant in a state like Manipur where prevalence of HIV/HCV co-infection is exceptionally high among the injecting drug users (IDU).

Methods

This study was conducted in the department of Microbiology, JN Hospital, Porompat, Imphal from March 2007 to December 2008. A total of 159 HIV infected adults were included in this study.

The mean age of the study population was 34 years. The median age group was 35 years, the range being 21 to 50 years. The male and female ratio of the population included in this study was more or less 1:1 (80 males and 79 females). Risk factors included both sexual as well as IDUs. Confidentiality was strictly maintained throughout the study. This study population was divided into two matched groups.

Group (1) consisted of clinically healthy HIV infected individuals without laboratory and clinical evidence of HCV infection (HIV+, HCV-). Group (2) included of apparently healthy individuals with laboratory confirmation of HIV and HCV infection (HIV+, HCV+).

Samples collection and processing

After thorough clinical examination, 5 (five) ml of fresh whole blood sample was collected from known HIV infected (HIV+) individuals in vacutainers (Becton Dickinson) containing EDTA. Sample collection was done strictly between 9 to 11 am to minimize diurnal variation and no samples were accepted if collected elsewhere. Analysis was always performed on the same day. HCV antibody test was carried out using SD bioline test kits. Blood sample for flow cytometric analysis was kept at room temperature until analyzed, after which the rest of the samples were stored in deep freezer after separation of plasma for further reference and analysis. Guidelines for internal quality control and biosafety measures were strictly followed.

Flow cytometry

20µl fluorescent dye conjugated antibodies containing CD₃, CD₄ and CD_{4,5}, and 50µl of fresh whole blood were added respectively in Trucount tube supplied by Becton Dickinson and mixed thoroughly using vortex. It was then incubated at room temperature for 15-20 minutes in the dark after which RBCs were lysed using 450 µl of lysing solution and vortex for 5 seconds. Further, incubation was done for another 15-20 minutes in the dark. Analysis was always carried out on the same day.

Analysis

Multi color phenotypic analysis was carried out on the stained blood on a FACS Calibur flow

cytometer (Becton Dickinson). Manufacturer's instructions were strictly followed.

Statistical analysis

The data was analyzed for significance by calculating p values using student's t test.

Results

A total of 159 individuals, 35 co-infected with both HIV and HCV (HIV+, HCV+), and 124 HIV infected individuals without HCV infection (HIV+, HCV -) completed the study.

Cell surface markers

Table 1. CD₄ count in different study groups

Study groups	No . of cases	Mean CD ₄ count	Std Deviation
HIV +, HCV -	124	366/ μ l	294/ μ l
HIV + HCV+ (co-infection)	35	277/ μ l	157/ μ l

The mean CD₄ count of HIV infected individuals without laboratory evidence of HCV infection (HIV+, HCV-) was found to be 366/ μ l and that of the dual infection (HIV+, HCV+) was found to be 277/ μ l of blood (table 1). The mean CD₄ count of dual infected subjects (HIV+, HCV+) was found lower as compared to HIV without HCV infection (HIV+, HCV-) but statistically not significant (p value = 0.086).

Table 2. CD₄ count in different risk groups irrespective of HCV co-infection

Risk groups	No . of cases	Mean CD ₄ count	Std Deviation
Sexual route	75	385/ μ l	268/ μ l
IDUs	84	228/ μ l	167/ μ l

The mean CD₄ count among sexually transmitted HIV infected subjects was found to be 385/ μ l and that of the intravenous drug users (IDU) was found to be 228/ μ l of blood irrespective of HCV serostatus (table 2). The mean CD₄ cell count of intravenous drug users (IDU) was significantly lower than sexually transmitted HIV infected individuals (p value < 001).

Discussion

Hepatitis C virus (HCV) co-infection is reported to be common among HIV infected subjects due to shared routes of transmission.¹ There are many reports that HIV hastens progression of liver disease in HCV co-infected subjects

leading to early death in HIV infected patients.⁴ But, whether HCV infection directly instigates deterioration of the immune competence (CD₄) of HIV infection or hastens the HIV disease progression has not been widely publicized. Though our preliminary study indicates that the immunocompetence (CD₄) cell count is lower in dual infection, we need to evaluate in a larger study group. This slight lowering of CD₄ cell count in dual infection may not be only due to the direct affect of HCV infection, but other factors like nutrition or other opportunistic infections other than HCV may also play a role. We also need to investigate further with the inclusion of other HIV disease progression markers like HIV-RNA viral load, serum neopterin and β -2 microglobulin.⁷ This would of highly relevant in a state like Manipur where a good number of IDUs are co-infected both with HIV and HCV.

Unexpectedly, our study could verify that intravenous drug users (IDU) have significantly lower CD₄ count as compared to sexually acquired HIV infection. Our traditional belief that the inhabitants of North Eastern part of the country have comparatively lower CD₄ cell count because the virus in the region is a more virulent strain as they come from Thai region. However, now it is more or less obvious that the same strain of virus can influence the rate of disease progression differently depending on the route of transmission. This could be also due to unhygienic practices among the IDUs while injecting themselves or other co-infection introduced during such practices.

Conclusion

Though this study could not determine that HCV co-infection hasten deterioration of immuno-competence among HIV infected subjects, we concluded that progression of immune-suppression is reasonably faster in HIV positive (HIV+) subjects transmitted through intravenous route (IDU) than those cases transmitted through several route.

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Caroli's disease- a case report

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A 57 years old female came to surgery OPD of Regional Institute of Medical Sciences (RIMS), Imphal, with the complaints of pain abdomen off and on for about three months. The pain was associated with fever, which was with chills and rigor. She was then referred to Radiodiagnosis Department, RIMS for radiological investigations. On examination, the general physical condition of the patient was normal. Per abdominal examination revealed tenderness over the right upper quadrant. Other systemic examinations were normal. Routine blood examination showed Hb-11.3 gm%, total WBC count -8190 cells/cu mm (P:63, L: 28, M: 7, E: 2 and B: 0); ESR- 90mm/ 1st hr; Platelet count- adequate. Liver function test showed Alkaline phosphatase - 345 IU/L; total serum protein - 6.8 g% ; A :G ratio 7.0; rest of the LFT parameters were within normal limits.

Chest X-Ray was normal. USG examination of the whole abdomen revealed multiple rounded cystic lesions of varying sizes that communicate with the biliary tree, in both the lobes of liver, more pronounced towards the centre. On Doppler interference, no colour filling or flow within the lesion was elicited (fig 1).

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Fig 1. USG picture of liver showing cystic dilatation of IHBR

MRI of upper abdomen was performed in the Institution with 1 Tesla (Siemens Magnetom) machine with the following protocols viz. T1fs, T2 haste gated, T2 haste thin slices, T2 haste thick slabs in coronal. Multiple cystic lesions were noted on both the lobes of liver giving low signal intensity in T1w and high signal intensity in T2w images (fig 2). On MIP

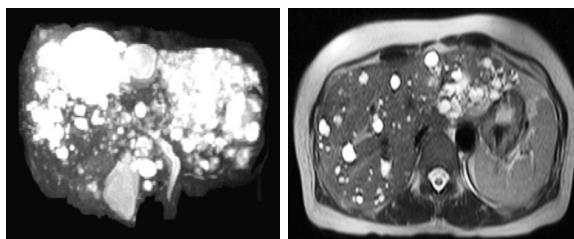


Fig 2. T2W MRI liver showing multiple cystic lesions on both lobes

Fig 3. MRCP showing multiple intrahepatic biliary dilatation

images these lesions were seen communicating with the intra-hepatic biliary tree. MRCP demonstrates irregular cystic dilatation of intrahepatic bile ducts with normal ducts in between. The cystic lesions were in continuity with the biliary tree (fig 3). Considering the above imaging findings, the patient was diagnosed as a case of pure form

of Caroli's disease. Liver biopsy for exclusion of associated congenital hepatic fibrosis was not done since imaging studies did not show any evidence of portal hypertension. The differential diagnosis of Caroli's disease are polycystic liver disease (cysts are rounder, smoother, do not communicate with bile ducts); obstructive bile duct dilatation (dilatation is most marked centrally, tapers towards periphery in an organized pattern which lacks focal areas of cystic dilatation); choledochal cyst and sclerosing cholangitis.

Discussion

Caroli's disease which is also known as communicating ectasia of the intrahepatic bile ducts was first described by a French gastroenterologist, Jacques Caroli in 1958. It is a very rare congenital condition which is characterised by non-obstructive saccular or fusiform multifocal segmental dilatation of the intrahepatic bile ducts. Jacques Caroli observed cavernous ectasia in the biliary tree causing a chronic, often life threatening hepatobiliary disease.¹ The disease affects about 1 in 10, 00000 people.² Caroli's disease is typically found in Asia and diagnosed in children and under the age of 22 years.³ Females are prone to Caroli's disease than males.⁴ Mode of inheritance is still unclear but in majority of cases it is transmitted in autosomal recessive fashion. One recent observation in a family from Japan (1995) suggested an autosomal dominant mode of inheritance. This abnormality may remain asymptomatic and undetected throughout life but often presents in adolescence or later with episodes of recurrent cholangitis, complicated by multiple biliary calculi. Caroli's disease is distinct from other diseases that cause ductal dilatation caused by obstruction, in that it is not one of the many choledochal cyst derivatives.³

Caroli's disease is a developmental anomaly and there are many theories explaining its pathogenesis. It is postulated to be due to a combination of disproportionate overgrowth of biliary epithelium and of its supporting connective tissue. Alternatively, it may be due to ductal plate malformation in which there is arrest in foetal organogenesis of the biliary tree

at the level of the larger intra-hepatic bile ducts. Another interesting hypothesis is that the cystic dilatation is a result of ischaemic infarction secondary to peripheral hepatic artery occlusion. Development of communicating biliary cyst in women with polyarteritis nodosa and hepatic artery occlusion, and in 13 monkeys subjected to hepatic artery embolisation, supports this theory. On a genetic level, unbalanced translocation between chromosome 3 and 8 or the structural rearrangement of genes located therein seems to be responsible. This explains the familial clustering and its association with polycystic kidney disease.⁵ Out of these four theories, the second one is the most widely accepted theory.⁶

Caroli described two entities of this disease: Caroli's Disease and Caroli's syndrome. Caroli's disease (pure form, less common) is characterised by ectasias of intra-hepatic bile ducts without fibrosis. Patient presents with symptoms of cholangitis or hepatic abscess, including recurrent attacks of right upper quadrant pain and fever, but do not develop cirrhosis. It may be associated with autosomal recessive polycystic kidney disease⁷ or rarely autosomal dominant polycystic kidney disease⁸. Caroli's syndrome (complex form) relatively has less bile duct dilatation, but is associated with hepatic fibrosis that results in portal hypertension and terminal liver failure. Patient presents with portal hypertension including haematemesis and lower GI bleed. Caroli's disease can be associated with choledochal cyst, in such cases there is no associated hepatic fibrosis or renal anomalies, and the ductal dilatation is usually confined to one lobe.⁹

Modern imaging techniques allow the diagnosis to be made more easily and without Invasive imaging of the biliary tree.¹⁰ USG is the initial investigation of choice. Dilated segmental intra-hepatic biliary radicles are easily detected. No obstruction is seen. The cystlike tubular anechoic spaces converge towards the porta hepatis. They are largest in the superior part of the liver. The "intraluminal portal vein sign" which consists of portal vein radicles surrounded by the dilated bile ducts

is considered to be pathognomonic of Caroli's disease. Color flow Doppler ultrasonography is helpful in showing blood flow in these branches but no flow is present in the bile-containing spaces. Portal branches bridge the cyst wall. Ultrasonography can also help in the diagnosis of complications (peripheral ductal dilatation is indicative of development of cholangiocarcinoma) and in the follow up of patients with Caroli's disease. Caroli's disease can be diagnosed antenatally on USG, by late second or third trimester. The earliest reported cysts are at 25 weeks of gestation and there is an instance of regression of antenatally diagnosed localised Caroli's disease. Hence a period of observation appears warranted.¹¹

CT scan is an excellent means to demonstrate the extent of the disease by noting the many fluid-filled, tubular structures to the liver.⁹ "Central dot sign" corresponding to intraluminal portal vein sign on USG can be seen on CT. A high contrast CT must be used to distinguish the difference between stones and widened ducts.

MRI appearance of Caroli's disease are of three patterns according to Guy F et al¹². (a) Fusiform and cystic dilatation of the intrahepatic bile ducts, and central dot sign on gadolinium enhanced scans. (b) Isolated fusiform intrahepatic ductal dilatation. (c) Dilatation of left intrahepatic ducts in addition to hepatic cysts. The dilated and cystic biliary system appears hypointense on T1WI and markedly hyperintense on T2WI. The intraluminal portal vein radicles enhance strongly after IV gadolinium administration. It usually demonstrates bridges across dilated IHD resembling internal septa which is consistent with the wall of an insufficiently resorbed, malformed ductal plate that surrounds the portal vein radicles. In the absence of central dot sign, MR cholangiography can be extremely valuable, by demonstrating the pathognomonic features of saccular dilated and non-obstructed IHBDs that communicate with the biliary tree.

Hepatobiliary scintigraphy with technetium

99m iminodiacetic acid agents reveals large, irregular, multifocal collections of the radiotracer in the liver. A beaded appearance in the dilated ducts, if present, is somewhat pathognomonic². Single photon emission computed tomography(SPECT)may better outline the ductal pattern but it is most helpful in the evaluation of focal disease.

PTC can allow direct visualization of the dilated biliary tree and ERCP also can aid in the diagnosis. However these two techniques are invasive and has limitations; are now rarely indicated with the availability of non-invasive diagnostic methods.

Complications of Caroli's disease are stone formation (95%), recurrent cholangitis, liver abscess, and cholangiocarcinoma (occurring in 7% of patients¹³).

There is no cure of the disease, so the treatment is symptomatic. Antibiotics are used for cholangitis, litholytic therapy with Ursodeoxycholic acid or endoscopic sphincterotomy for hepatolithiasis, internal biliary bypass procedure and liver transplantation for selected cases.

The reported case is a pure form of Caroli's disease with no evidence of periportal fibrosis and renal cystic disease. The case is reported because of the rarity of this disease (incidence: 1 in 10,00000) and also the late onset of clinical symptoms. Plain abdominal radiographs are not helpful unless hepatic calculi are found. Archaic I.V. or oral cholangiography is not beneficial. However, ERCP is helpful. USG is an excellent tool for the diagnosis of the disease as well as for the detection of complications and also in the follow up of patients. CT and MRI can aid in the diagnosis. Also MRCP shows the ductal anatomy well. Mortality in Caroli's disease is indirect and caused by complications . After cholangitis occurs, a large number of patients die within 5-10 years. Although Caroli's disease is a rare congenital anomaly, it should be included in the differential diagnosis in children presenting with abdominal pain and hepatomegaly.

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Anaesthetic management of temporomandibular joint ankylosis release - a case report

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A 17 years old boy was posted for release of bilateral temporomandibular joint (TMJ) ankylosis at Regional Institute of Medical sciences, Imphal. History dated back to childhood, he had a severe episode of illness at the age of 8 years which was followed by restriction of mouth opening along with deformity of left leg and complete inability to open his mouth since 4 years.

On examination, mouth opening was 0mm and two teeth were absent in the upper jaw which were served as the channel for ingestion of liquid and semisolid foods (fig 1). His neck was extensively elongated and chin was very small but there was no restriction of neck movements (fig 2).



Fig1. Showing full mouth opening (0-mm)



Fig 2. Preoperative photograph showing the long neck

His vital signs were stable and systemic examination revealed no abnormality. All the

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hematological and biochemical tests were within normal limits.

He was scheduled for release of TMJ ankylosis under general anaesthesia with controlled ventilation. We decided to perform an elective tracheostomy when the patient was fully conscious because of anatomical variations in this specific patient and lack of facilities availability.

When the tracheostomy tube was in situ (fig 3), the patient was anaesthetized with propofol (1%) 2mg/kg body weight IV. Anaesthesia was maintained with



Fig 3. Showing the tracheostomy tube in situ

N_2O , O_2 , isoflurane, muscle relaxant and systemic analgesics. Intraoperative monitoring included pulse oximetry, continuous ECG, non-invasive blood pressure measurement and capnometry.

Release of right and left temporomandibular joint ankylosis with gape arthroplasty was done. Total mouth opening of (3-4)cm was achieved with no significant blood loss.

At the end of surgery, residual neuromuscular block was reversed with IV neostigmine and glycopyrrolate. The postoperative course was unevenful. He maintained oxygen saturation between (98-100)% and was haemodynamically stable.

Discussion

TMJ ankylosis, especially with mandibular hypoplasia presents a serious problem for airway management.¹ In a patient with nil or limited mouth opening, various alternatives for securing the airway are blind nasal intubation, retrograde intubation technique via cricothyroid membrane, fibre-optic guided intubation and tracheostomy.

All these have their own advantages and disadvantages and hence, any particular technique has to be selected keeping in mind the patients age, clinical condition, availability of equipments and patient safety during the procedure.

Blind nasal intubation was traditionally recommended for TMJ ankylosis release but in the presence of associated airway anomaly failure of the technique is still high.^{2,3}

In our patient we could not attempt blind nasal intubation because the neck of the patient was excessively long and repeated unsuccessful attempts could cause soft tissue trauma, and bleeding.

Although different modifications of retrograde intubation in temporomandibular joint ankylosis has been studied,^{4,5} in our case we have not advised this technique because of the position of trachea which was situated so much lower down due to an extremely long neck.

Again, facilities for fibre-optic intubation may not be available in most centres like ours due to its cost factor.⁶

It is concluded that for release of TMJ ankylosis associated with anatomical variations, elective tracheostomy is a safe, simple and effective method of airway management for the safety of the patient.

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Primary lymphoepithelial carcinoma of the buccal minor salivary gland -a case report

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A 42 years old tribal female presented to the Plastic surgery O.P.D., Regional Institute of Medical Sciences (RIMS), Imphal with complaints of a painless slow growing swelling near right angle of mouth for the last 3 years. She had no significant past history. On examination, the patient was of average Indian build, no pallor, oedema, cervical lymphadenopathy or organomegaly. On local examination, the swelling was slightly mobile, nontender, irregular, firm around 1.5cms in diameter. Routine haematological investigation showed haemoglobin 9.8 gms/dl, total leucocyte count 6500/cumm, differential count-polymorph 68%, lymphocytes 30%, monocytes 1% and eosinophil 1%. Platelet count was 1.2 lacs/cumm. Liver function test showed total bilirubin 0.7mg%, S.G.O.T. 31U, S.G.P.T. 28U, serum alkaline phosphatase 167KAU, total protein 6.6gm%, serum albumin 4.2gms%, serum globulin 2.4gms%, . Serum urea and serum creatinine were 32mg% and 0.9mg% respectively. FNAC of the swelling showed moderately cellular smear with a heterogenous population of lymphoid cells admixed with malignant tumour cells. The tumour cells were arranged in cohesive clusters. Individual cell have a variable amount of cytoplasm and mildly pleomorphic vesicular nuclei with prominent nucleoli (fig 1).

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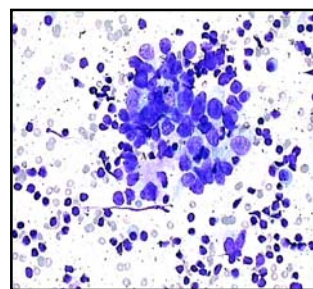


Fig 1. Aspiration smear showing pleomorphic tumour cells with indistinct cell border and lymphoid stroma (Geimsa stain, x 400 magnification)

A diagnosis of metastatic undifferentiated carcinoma was rendered. Subsequently, a search for the primary tumour was made with CT scan of the nasopharynx, ultrasonography of the whole abdomen and various serum

markers including serum alpha fetoprotein, serum HCG etc. Despite of all efforts, no evidence of a primary tumour was detected.

Surgical excision of the swelling was planned. Under local anaesthesia and aseptic precautions, the swelling along with some portion of the normal surrounding tissue were excised and the material were sent to the Pathology Department for histopathological examination. On gross examination, the excised mass was found to be partly brownish, partly grayish tissue measuring (1.5x1.2x 0.8)cms. No mucosal part was identified. Microscopic examination showed several sheets, anastomosing islands and nests of large pleomorphic cells with vesicular nuclei and prominent nucleoli. The cytoplasm was eosinophilic with indistinct cell borders. The tumour was densely infiltrated by lymphoid cells. Occasional lymphoid follicles with germinal centres were also noted. There were prominent desmoplastic stroma separating the lymphoid nodules. A few lobules of normal

minor salivary gland along with skeletal muscle fibres were also noted (fig 2 and 3). Considering all the clinical and other findings,

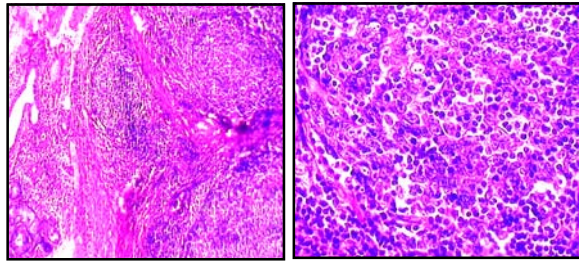


Fig 2. Section showing nests and sheets of tumour cells, dense lymphoid stroma, desmoplasia and occasional lymphoid follicle & a few remnant of salivary acini (H&E stain x100 magnification)

Fig 3. Showing pleomorphic tumour cells with prominent nucleoli & the tumour densely infiltrated by lymphoid cells (H & E stain x 400 magnification)

a diagnosis of primary lymphoepithelial carcinoma of right buccal submucosal salivary gland was made. The patient was referred to the Radiotherapy Department for further management.

Discussion

Primary lymphoepithelial carcinoma of salivary gland is a rare tumour, most frequently arising in the parotid.¹ Cases of lymphoepithelial carcinoma affecting submandibular gland have been reported.² Even rarer is the primary lymphoepithelial carcinoma of minor salivary gland with only a few case reports.^{3,4} It usually affects age group of the fourth to seventh decade of life with slight female preponderance. Among all

salivary gland tumours, it is the only carcinoma that is associated with EBV infection. In situ hybridization studies showed strong EBV positivity in Chinese and Eskimos but only rarely positive in other ethnic groups. Large sized tumour cells nests and dense lymphoid stroma, as in our case, occurred more frequently in minor salivary gland while small sized nests with fibrous and lymphocyte-depleted stromata occurred more frequently in the parotid.¹ Diffuse growth pattern, absence of granuloma and/or germinal centres and metastases to lymph nodes are regarded as bad prognostic features.⁵ Lymphoepithelial carcinoma of salivary gland is morphologically identical to undifferentiated carcinoma of nasopharynx. As the undifferentiated carcinoma of nasopharynx is more common than lymphoepithelial carcinoma, carcinoma of nasopharynx should be ruled out before rendering a diagnosis of primary lymphoepithelial carcinoma of salivary gland. In the past, lymphoepithelial carcinoma was thought to arise from lymphoepithelial sialadenitis through malignant transformation. This contention is now rejected by many investigators.⁵⁻⁷ Among all undifferentiated carcinomas, lymphoepithelial carcinoma has the best prognosis.⁸ Lymphoepithelial carcinoma should be included in the differential diagnosis of the minor salivary gland tumours. Prognosis of lymphoepithelial carcinoma is better when compared with undifferentiated carcinomas.

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Percutaneous nephrolithotomy under combined spinal epidural anaesthesia - an alternative

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A 79 years old female was scheduled for elective percutaneous nephrolithotomy (PCNL) at Shija Hospital and Research Institute, Langol, Manipur. Her ultrasonography reveals moderate right renal hydronephrosis with a calculi measuring 7mm and pelvic ureteric junction calculi measuring 1.3cm. A detailed preanaesthetic evaluation was done. She gave history of exertional dyspnoea and chronic cough with expectoration, suggestive of COPD. She was also a chronic smoker. On examination she weighed only 35kgs, her pulse rate was 80/min, blood pressure was 130/80mmHg and temperature was 98.6 0F. Respiratory system examination revealed bilateral basal crepitations and air entry was decreased on both sides with chest expansion of less than 1cm. SpO₂ ranged from 91- 92% on room air. A complete investigation which includes a full blood count, blood coagulation profile, renal function test and urine analysis were within normal. Plain KUB radiograph and an intravenous urogram (fig 1) were performed to determine the exact anatomy of the pelvicaliceal system. There was no abnormality detected in the ECG but the X-ray chest (fig 2) showed bilateral increased



Fig 1. IVP of the patient

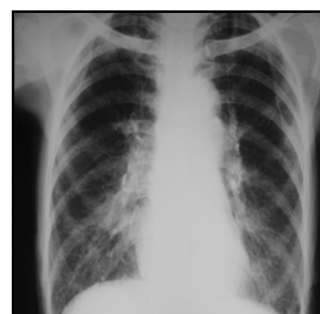


Fig 2. X-ray chest showing increased bronchopulmonary markings and opacities in the middle and lower zones of right lung.

bronchopulmonary markings and opacities in the middle and lower zones of right lung.

Considering the prevailing respiratory problems we decided to choose combined spinal epidural (CSE) anaesthesia instead of general anaesthesia for PCNL of the patient. The patient was counseled about the procedure and an informed consent was taken. Before the procedure, intravenous infusion of Ringer lactate was started. Ondansetron 4mg IV and an IV antibiotic were administered prior to the procedure. In the operating theatre, pulse, blood pressure, ECG and SpO₂ were monitored. A two-level approach of CSE anaesthesia was undertaken with patient in lateral position. A lumbar epidural puncture at the level of L₁-L₂ intervertebral space was performed using a 16- gauge Touhy epidural needle and loss of resistance technique and a catheter was inserted into the epidural space. The correct position of the catheter in the epidural space was assured with negative aspiration test and a test dose of 3ml of 2% lignocaine with epinephrine(1/200,000), then the catheter was fixed. A standard spinal

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anaesthesia using 2.2ml of 0.5 % bupivacaine (heavy) was given with a 25 gauge spinal needle at L₂-L₃ intervertebral space. The patient was then placed in supine position and both sensory and motor blocks were assessed. Sensory block reached T₅-T₆ thoracic dermatomes and a motor block of grade IV Bromage score.

Ureteric catheterization and Foley catheter insertion were done in supine position, then the patient was turned to prone position and the surgery was performed in this position (fig 3)



Fig 3. Patient under CSE anaesthesia undergoing PCNL

which took around two hours. Oxygen supplementation by nasal cannula at two litres per minute was administered throughout the procedure. SpO₂ remained around 96-97 % during the entire surgery. Blood pressure was monitored every five minutes during the surgery and remained stable during the entire procedure, except for a short period of hypotension (80/60), ten minutes after the spinal block which required 5mg of mephentermine injection. A second IV line with hydroxyl ethyl starch 6%(Haes-steril) was started. One hour after the spinal block, a bolus dose of 7 ml bupivacaine (plain) with 0.1 ml of 7.5% (w/v) sodium bicarbonate was given through the epidural catheter. At the end of the surgery, another 5 ml bupivacaine (plain) was given through the epidural catheter for postoperative analgesia. The whole procedure was well tolerated except for some minor discomfort due to the position. The postoperative vitals were pulse rate of 86 per minute, blood pressure 110/60 mmHg and SpO₂ of 93 % on room air. There were no significant intraoperative problems related to surgery or anaesthesia. The patient did not require any further analgesic during the postoperative period. The epidural catheter was removed on the second postoperative day and the patient was shifted to the ward.

Discussion

Percutaneous nephrolithotomy, first described by Fernstrom I and Johansson B¹ in 1976, has become an established procedure for the treatment of renal calculi. PCNL has almost entirely replaced open surgery in the management of renal stone. As a minimally invasive procedure, PCNL significantly reduces morbidity. Usually, PCNL is performed under general anaesthesia with some form of postoperative analgesia, but, sometimes, to avoid general anaesthesia related morbidity, alternative anaesthesia² techniques have been described by some authors.

In our patient, considering the existing comorbid conditions (elderly with COPD), we preferred to avoid general anaesthesia in order to avert postoperative respiratory complications. We choose CSE anaesthesia³ since it combines the benefits of both spinal and epidural anaesthesia. The spinal component gives a rapid onset of a predictable block and the indwelling epidural catheter gives the ability to provide postoperative analgesia and to titrate the dose given to the desired effect.

The main concern for performing PCNL under regional block is patients discomfort as the procedure is performed in prone position. In our case, CSE anaesthesia was used effectively and safely. The patient was able to control her own ventilation during the operation and there was no postoperative respiratory complications. Opioid requirement in the postoperative period was also reduced. Regional anaesthesia avoids many of the respiratory problems associated with general anaesthesia and has an added advantage of providing postoperative analgesia. Effective analgesia is vital in order to optimize respiratory functions. Lack of effective pain relief may result in diminished chest expansion and ineffective cough, leading to basal atelectasis, hypoxemia and nosocomial infections. Combined spinal epidural anaesthesia and analgesia is beneficial as it may prevent the above complications. In case of general anaesthesia, to provide adequate pain relief, more opioids may be required which

in turn depresses the respiration which was not desirable in our patient. It is not uncommon for patients with absolute indications for PCNL not to be operated on because of high risk of general anaesthesia. These are the patients which can be given CSE anaesthesia.

Singh I et al⁴ in their study reported that PCNL under regional anaesthesia speeds up recovery shortens the length of hospitalisation and analgesic requirement. Aravantinos E et al⁵ demonstrated the feasibility of PCNL under local anaesthesia in a selected group of patients. They suggested that patients who are at higher risk of anaesthesia related morbidity could undergo PCNL under assisted local anaesthesia. PCNL under multimodal analgesia regime had been described by

Aravantinos E et al⁶. Regional anaesthetic technique like CSEA can be an option in patients undergoing surgical procedure who are contraindicated for general anaesthesia. Our method of CSE anaesthesia also offers some advantages - 1. It is suitable for patients who are at risk under general anaesthesia, 2. It provides a safe, effective and cheap anaesthesia, 3. It provides postoperative analgesia and lastly, 4. It does not affect the technical aspects of PCNL. However, regional block has its own disadvantages which include patient's discomfort due to prone position and long duration of the procedure. In such cases, sedation and assurance may be of help. In conclusion, combined spinal epidural anaesthesia is a feasible safe and well tolerated alternative anaesthesia technique for the management of patients undergoing PCNL.

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Giant vesical calculus - a case report

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A 68 year old male illiterate patient from a remote hill village of Manipur came to urology OPD, RIMS, Imphal on 8th April 2009 with complaints of suprapubic pain for the last seven years, hematuria off and on for last 10 months, dysuria for last 10 months and intermittent fever for 5 months.

Seven years back he had no symptoms except for a slight suprapubic pain, burning sensation while passing urine and occasional hematuria.

Systemic examination showed no abnormality. Locally, mild swelling was observed in the hypogastrium. On palpation, there was a non-tender and immobile hard mass in suprapubic area. On digital rectal examination, a hard lump could be felt bimanually probably in urinary bladder.

X-ray KUB showed a huge radio-opaque shadow in urinary bladder. All routine laboratory investigation were done. Blood routine examination showed haemoglobin 8g%, total leucocyte count 11000/Cumm, differential count-polymorph 72%, lymphocyte 24%, monocytes 3% and eosinophil 1%. LFT was found to be within normal limit, whereas in KFT S.Urea(58mg/dl) and S.Creatinine(2.7mg/dl)

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were mildly raised. Serum electrolyte were normal. Findings of routine examination of urine showed pus cells 15-20/hpf, RBC 8-10/HPF, epithelial cells 2-3/hpf, appearance turbid and reaction alkaline. Routine blood sugar was 108mg%.

USG showed a huge vesical calculus with mild hydroureteronephrotic changes in both the kidney.

Patient underwent suprapubic cystolithotomy 13th April 2009. On cystotomy, a large stone was removed using obstetric forceps, as the stone was too big to have a grip on with the cystolithotomy forceps.

This stone measured around 7x10x12cm, and weighed 750g, it was pearly white with blood stained patchy areas and very hard in consistence (fig 1 and 2). After delivery of stone, cystostomy wound was closed in single layer with a Vicryl 2-0 suture. Skin closed with a retropubic drain and urinary bladder drained by Foley's catheter for a week. Postoperative period was uneventful, patient was discharged on postoperative day 8.



Fig 1. Showing huge vesical calculus delivered by obstetric forceps

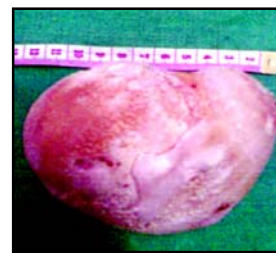


Fig 2. Showing vesical calculus measuring 7x10x12 cm and weighing 750gm

Discussion

Urinary bladder calculi are a rare clinical entity in developed countries.¹ Giant vesical calculus weighing more than 100g is even rarer, especially in modern setting of urologic practice.² However, vesical calculus is not uncommon in this part of India.

The largest vesical calculus reported so far in literature was of 6294g(6.3kg).³ In our case, stone weighing 750g was found to be rare in this part of the country. Giant bladder stone may be found synchronously with smaller stones in urinary bladder or in prostate.⁴

Becher RM et al⁵ have reported a giant uric acid vesical calculus of 235g with a minor

component of calcium oxalate.

Presentation of patient with giant vesical calculus is commonly with recurrent UTI, hematuria, inability to pass urine and azotemia.⁶

There are various modalities for treatment of vesical calculus which include open Suprapubic cystolithotomy, cystoscopic fragmentation and evacuation, extracorporeal fragmentation, and endoscopic crushing followed by extraction of pieces. Open surgery is the best modality for a giant vesical calculus.⁶ However, obstetric forceps delivery of giant vesical calculus is a rarest modality of treatment of vesical calculus.⁷

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Retrograde tracheal intubation with a gum elastic bougie in a penetrating neck injury - a case report

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A 42 years old male was brought to emergency room, Regional Institute of Medical Sciences, Imphal following an alleged gun shot injury around the neck. Entry wound was at the angle of mandible on right side which existed through the nape of neck. There was profuse bleeding in the oral cavity with spurting of blood from the injured areas. The areas around the face, neck and oral cavity were edematous and diffusely swollen. In the neck region, the anatomical landmark were so much distorted because of swelling and haematoma. The patient was in state of agony and the profuse bleeding demanded immediate operation as the risk to life increased every moment.

When the patient reached the operation theatre, his BP was 110/70mmHg, pulse rate was 126/min and SpO₂ was between 80-85%. Despite giving 100% O₂ with mask ventilation, his SpO₂ was not improved as the edematous and lacerated tissues partially obstruct the airway. Laryngoscopy and intubation were attempted after proper suctioning of blood and debris, and instillation of 4% lignocaine spray(2ml). Visualization of laryngeal inlet was extremely difficult as there was extensive tissue damage and bleeding in the oral cavity, thereby distorting the whole anatomy. In

addition to that, tongue was enormously swollen.

As laryngoscopy was unsuccessful, retrograde intubation was planned. But the nature of injury and haematoma around the neck made it difficult to find the landmark for cricothyrotomy puncture. With much effort, the trachea was palpated and a small nick was made at the cricothyroid membrane under local anaesthesia. Retrograde intubation with a flexible guide wire was attempted through that nick, but because of the nature of the injury, the flexible wire could not be passed effectively. So little choice was left and a bit rigid but non-traumatic gum elastic bougie was introduced through that nick in a cephalad direction. With slight manipulation in and around the oral cavity, it was guided out through the mouth(fig 1).



Fig 1. Showing retrograde intubation using non-traumatic gum elastic bougie.



Fig 2. Showing successful intubation with a 8mm ID ETT rail loading over the bougie from mouth.

Then the patient was successfully intubated with a 8 mm ID endotracheal tube(ETT) rail loading over the bougie from the oral cavity (fig 2). When the ETT reached the tracheal rent, the bougie was removed from oral cavity and airway secured. End tidal CO₂ was

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detected, bilateral breath sounds and chest rise were auscultated while SpO₂ gradually rose to 98%.

After that, patient was anaesthetised and surgeons were allowed to operate to secure the bleeding areas and repaired of the lacerated tissues. During the long 3 hours operation, anaesthesia was maintained with O₂, N₂O, isoflurane and atracurium. After the operation patient was reversed, ETT was kept in-situ and shifted to ICU for further management and treatment. Patient recovered gradually in the ICU.

Discussion

Emergency difficult airway if not acted promptly or rather timely may cause most disastrous outcomes. Therefore, awareness of the potential difficult airway and accessing the probable outcome and employing the appropriate technique to maximize visualization can minimize the risk to a great extent. There are various techniques which could be employed in emergency difficult airway management. Some of the techniques include LMA, intubating LMA, McCoy laryngoscope, bougie, cricothyrotomy, fiberoptic laryngoscope etc.

Fiberoptic intubation¹ could be one of the option but its use in emergency case with bleeding and airway edema like ours seems difficult. Moreover, it is not currently available at our institute.

Tracheal tube placement over gum elastic bougie² can also one of the option in difficult airway management but in our case, introduction of gum elastic bougie orally was

not successful because of the extensive tissue damage of upper airways and oral cavity with profuse bleeding.

LMA³⁻⁶ used was also contraindicated as there was extensive damaged of upper airways with distorted anatomy with marked bleeding though it was postulated to have been used to facilitate difficult airway management in adults. Similarly I-gel^{7,8} used was also contraindicated.

Blind nasal intubation was not attempted as there was massive bleeding and tissue damage of upper airways and oral cavity.

Classically retrograde intubation^{9,10} is performed in presence of unstable cervical spine fracture or temporomandibular joint ankylosis or tissue damage around face with difficult mask ventilation. But in our case as the flexible guide wire could not be introduced effectively, other technique like retrograde introduction of bougie in cephalad direction which passed out orally was adopted. ETT was then rail-loaded caudally over the bougie from mouth.

Marciniak D and Smith CE¹¹ described retrograde intubation with the use of a gum elastic bougie to secure the airway in a trauma patient. We also used gum elastic bougie for retrograde intubation in our patient. Retrograde intubation with bougie¹¹ will never be a good option for securing an airway as it has the chances of producing retropharyngeal haematoma, vocal cord injury, false passage with bougie and injury to other vital structures. But if there are limited means available for securing the airway, this can also be one of the option to save the patient life and indeed this option saves our patient life.

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Erdheim - Chester Disease

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A 27 year old male from Arunachal Pradesh presented with pain in the right side of the mid back for the past 5 years. The pain was of dull aching type. There was no history of dry cough, fever, dyspnea, weight loss, breathlessness, loss of appetite, abdominal swelling and excessive micturition. There was no evidence of exophthalmos, bilateral involvement, hepatomegaly or clubbing, skin lesions and neurological signs. Local examination revealed tenderness over the right sixth rib, medial and superior to the inferior angle of the scapula. There was no axillary lymph node involvement. Routine investigations-blood, urine, renal function and liver function tests were within normal limits. Alkaline and acid phosphatase levels were normal and the cholesterol level was 110mg/100ml, with normal triglycerides. The erythrocyte sedimentation rate was 51mm/hr. Chest X-ray and computed tomography with three dimensional reconstruction of chest showed a lytic lesion with sclerosed margin in the shaft of right 6th rib near its angle (fig 1).

Open bone biopsy was done. A cystic lesion about the size of 2cms by 2cms, circular in shape was found in the 6th rib near its angle medial to the right scapula. It was soft, friable and the cavity was filled with soft yellowish

tissue. Histologic examination revealed infiltration of lipid laden foamy histiocytes, lymphocytes and scattered multinucleated Touton typed giant cells with extensive coagulative necrosis which are the diagnostic features of Erdheim - Chester disease (fig 2).



Fig 1. CR-scan showing a lytic lesion with sclerosed margin.

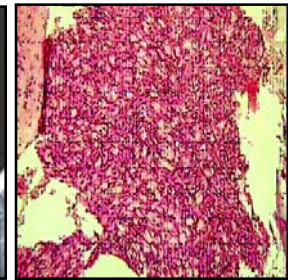


Fig 2. Histological picture showing foamy histiocytes in diffuse sheets.

Discussion

It was first described by Chester W, an American Pathologist who had been working with J. Erdheim in Vienna in 1930.¹ Symmetric osteoblastic lesions usually are found restricted to the diaphysis and metaphysis of long bones. Flat membranous bones are less frequently involved but includes the mandible, ribs, pelvis and skull.² In our case, the lesion was found in the shaft of right 6th rib near its angle. 37% of the patient also had some lytic components in addition to the classic sclerotic changes. In affected bones, coarse woven trabeculation and some loss of corticomedullary differentiation have been observed, with production of both endosteal and periosteal appositional bone.² In our patient the lesion was of mixed osteolytic and osteosclerotic lesion. Extraskelatal

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involvement also has been described and includes the skin, conjunctiva, pituitary gland, brain, meninges, choroid plexus, orbits, gingival, false vocal cord, thyroid gland, heart, lungs, mediastinum, pleura, liver, pancreas, spleen, small bowel, kidneys, adrenal glands, retroperitoneum, pelvis and testis.^{3,4} There was no extraosseous involvement in our case. Erdheim - Chester disease is a disease of adults 26-70 years old, with a male

predominance clinically, the disease can range from a focal asymptomatic process to a multisystemic fatal condition. Bone pain is the usual symptom.³ Our patient was a 27-year-old man who presented with bone pain. Histologically, the disease is characterized by an infiltrate of lymphocytes, foamy histiocytes, Touton-like giant cells with coagulative necrosis.⁵ Histologic findings in our case were consistent with these histologic changes.

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Penicillium marneffeii infection of the eyelids - a case report

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A 31 years old female patient with HIV infection presented with progressive swelling of left eyelids causing difficulty in opening of the left eye at J.N. Hospital, Porompat, Imphal on 19/06/2009 (fig1). The patient also had low grade fever, general weakness and weight loss. The patient was diagnosed as having HIV infection five years back but not on ART.



Fig 1. Photograph of the patient with swelling of left eyelids.

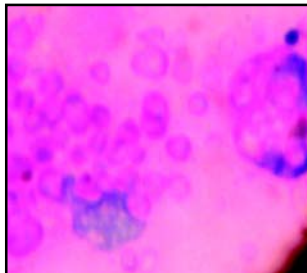


Fig 2. Intracellular and extracellular yeast forms of *P.marneffeii*, PAS, X1000

On clinical examination the patient was found to be febrile. The pulse rate was 100/minute and blood pressure was 130/80 mm of Hg. The physical examination revealed mild pallor, oral candidiasis and mild hepato-splenomegaly. Local examination of the left eye showed massive swelling of the eyelids with two subcutaneous nodules one on each eyelid measuring 3 x 2.5 cm were detected. There were no other relevant clinical findings on the left eye.

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Laboratory data included Hb 6.4gm/dl., TLC4800/cumm, DLC-P77, L20, M2, E1, ESR 70 mm with adequate platelet count. Patient tested negative for HBsAg and HCV Ab. T-helper lymphocyte (CD₄+) absolute count was 26/microL. Liver function tests showed elevated levels of alkaline phosphatase (578.7IU/L), SGPT (55IU/L) and SGOT (59IU/L). Serum bilirubin, total proteins, albumin, globulin, urea and creatinine were within normal limits. Chest x-ray revealed minimal pleural effusion on right side. Ultrasonography of the abdomen showed hepato-splenomegaly, minimal ascites with mesenteric lymphadenopathy.

Fine needle aspiration cytology of the subcutaneous nodules of the eyelids detected yeast like tissue forms of *Penicillium marneffeii*; many of them showing prominent central septum (bars) indicating multiplication of the organism by fission and this finding aids in the differentiation from *H. capsulatum* and most other fungi that divide by budding. Leishman, PAS (fig 2) and GMS (fig 3) stains were used in the study.

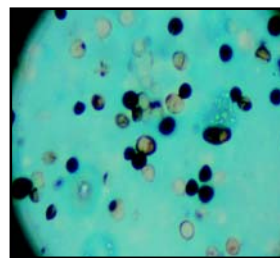


Fig 3. Yeast form of *P. marneffeii*, GMS, X1000



Fig 4. Mycelial growth of *P. marneffeii* showing the characteristic red pigment

A portion of the aspirate was transferred to

Sabouroud dextrose agar and was incubated at 25 C for a period of seven days. The characteristic red pigment diffused into the medium was seen as early as third day after inoculation (fig 4). The mycelial phase of P. marneffeii having the characteristic conidiphores,metulae,phialides and conidia were observed under LCB (Lacto Phenol Cotton Blue) mount. The patient was treated with tablet itraconazole 200mg. bid for 14 days followed by a maintenance dose of 200mg once daily and the swelling in the eye lids decreased gradually which disappeared subsequently.

Discussion

Penicillium marneffeii, the only dimorphic (a mould at 25°C and a yeast at 37°C) species of the genus *Penicillium* is an emerging opportunistic fungal infection observed among HIV infected individuals in South East Asia including North-East India^{1,2} and stands today as an important clinical entity. With the start of HIV pandemic systemic infection with *P. marneffeii* has developed from a rare diagnosis to the third most common opportunistic infection after extra-pulmonary TB and Cryptococcal meningitis in HIV co-infected patients in South-East Asia.³ It is also considered as an AIDS defining illness.⁴ Even though a proper study has not been conducted yet, *P. marneffeii* infection appears to be more common than Cryptococcal infection in HIV

positive patients attending JN Hospital, Imphal.

Seventy to eighty per cent of the patients with *P. marneffeii* infection developed skin lesions; the umbilicated papules resembling molluscum contagiosum being the commonest presentation which are usually located in the face, upper trunk, extremities and genitalia. Folliculitis subcutaneous nodules abscesses and rarely oral lesions may be seen.⁵ Subcutaneous nodules with excessive swelling of the eye lids due to inflammatory oedema may mimic some other serious eye disease creating diagnostic difficulty as in this case. *P. marneffeii* infection appears usually late in the course of HIV infection and usually occurs when CD₄ count is less than 50/microL. *P. marneffeii* infection in immunocompromised patients is a dangerous clinical situation with significant mortality if not diagnosed early and promptly treated with appropriate antifungal drugs.⁶ Diagnosis of *P. marneffeii* infection by FNAC is a rapid procedure compared to tissue biopsy and culture thereby allowing early institution of therapy which is of particular importance in immunocompromised patients. Though early diagnosis by serology and molecular based methods have been developed, it is not available in most of the centers for routine use.⁷ The successful treatment of *P. marneffeii* is dependant on early and accurate diagnosis for prompt treatment.

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