Journal of BSA, Vol. 20, No. 2, July 2007

Original Article

SEDATION FOR ERCP - COMPARISON BETWEEN KETAMINE DIAZEPAM COMBINATION WITH PROPOFOL FNTANYL COMBINATION

Iqbal Hossain Chowdhury[1], Abdullah Al Maruf[2], Kazi Ashkar Lateef[3], Sayeed Mahmud Ali Reza[4], M. Abdul Hye[5]

SUMMARY

For Endoscopic Retrograde Cholangio-pancreatography, an anaesthesiologist usually administers sedation to patient and search for more suitable regimen continues. This prospective randomized study was carried out to compare the efficacy, safety, tolerability and cost effectiveness of ketamine, diazepam combination to propofol, fentanyl combination for sedation during ERCP. One hundred and fifty patients of both sex, age between 18 to 70 years, ASA physical status I and II scheduled to undergo ERCP were included in this study. Patients were randomly allocated into two groups. Group A (n=75) sedated with ketamine 1.5mg/Kg body weight and diazepam 5-10 mg intravenously. Group B (n=75) sedated with propofol 1mg/Kg body weight and fentanyl 1µg/Kg body weight intravenously and intravenous infusion of propofol maintained at 50µg/Kg body weight/min throughout procedure. Both groups showed satisfactory sedating condition for ERCP. Incidences of hypertension and tachycardia were more in group A than group B and differences between two groups were statistically significant (P< 0.01). Agitation and nightmares were found in 10 (13.33%) patients in group A. Mean recovery time was more in group A than group B and difference between two groups was statistically highly significant (P<0.001). Sedation regimen of group B found 7 times more costly than group A. Both regimens found safe, effective, and tolerable for ERCP. However, recovery time is more with ketamine, diazepam but it found more cost effective than propofol fentanyl that is a concern in developing country like Bangladesh.

Key Words: Endoscopic Retrograde Cholangio-pancreatography (ERCP), Sedation, Ketamine, Diazepam, Propofol, Fentanyl, Intravenous.

INTRODUCTION

ERCP is used primarily to diagnose and treat biliary and pancreatic diseases. These include removal of common bile duct stones, stenting of biliary stricture and resolution of pancreatic duct disruption[1]. Despite an increase number of patients with hepato-biliary-tract disease, surgical treatment is limited along with risky outcome such as bleeding, infection or improper postoperative pain control. ERCP is another treatment of choice, which has some advantages over surgery-.[2] There are two basic choices of anaesthesia available for completion of the procedure, sedation and general anaesthesia. Sedation is commonly administered in order to carry out the procedure successful.[3] General anaesthesia is usually provided for ERCP in children and when prior attempts using sedation have failed. For sedation, there has been debate over appropriate drugs and their dosage and those who sedate have their favorite sedation regimens. It is important that person administering the drug is familiar with them and cocktails of more than two drugs are to be avoided because of unpredictability of drug interactions, and the increased incidence of side effects. So search for suitable sedation regimen continues.

The phencyclidine derivative ketamine has been described as a safe and effective sedative agent. Ketamine produces a dissociative state, combination of analgesia, amnesia and sedation at subanaesthetic dose, with minimal effects on the airway and vital reflexes[4]. It is best if combined with an anticholinergic for control of secretion and with a benzodiazepine to prevent agitation and nightmares. Combination of short acting drugs like propofol and fentanyl is another useful procedural

1. Associate Professor (Intensive Care Unit), Department of Anaesthesia, Analgesia, & Intensive Care Medicine. BSMMU, Dhaka-
2. Graded Specialist in Anaesthesiology, Department of Anaesthesia & Intensive Care, CMH, Dhaka
3. Graded Specialist in Anaesthesiology, Department of Anaesthesia & Intensive Care, CMH, Dhaka.
4. Assistant Professor Department of Anaesthesia, Analgesia, & Intensive Care Medicine, BSMMU, Dhaka.
5. Associate Professor, Department of Anaesthesia, Analgesia, & Intensive Care Medicine, BSMMU. Dhaka

sedation regimen. Propofol produces sedation and amnesia and fentanyl produces analgesia and sedation[4] and this combination is useful for upper gastrointestinal endoscopic procedures[5].

This prospective randomized study was designed to compare the efficacy, safety; tolerability and cost effectiveness of ketamine, diazepam combination to propofol, fentanyl combination for sedation during ERCP.

MATERIALS AND METHODS

We performed a prospective randomized study on 150 patients of both sex, age between 18 to 70 years, ASA physical status I and II scheduled to undergo ERCP at Gastro Liver Hospital & Research institute Ltd, Dhaka in two calendar years from July 2005 to June 2007. Patients with anatomic airway abnormalities, severe cardiovascular and respiratory disease and severe psychological problem were excluded from the study. During preprocedural assessment, every patient underwent thorough physical examination with ASA classifications. Total sedation procedure was explained to every patient and informed consent was taken for sedation. A baseline pulse, blood pressure, respiratory rate, ECG and SpO_2 were recorded.

Patients were randomly allocated into two groups. Group A contained 75 patients received atropine 0.4mg intravenously to prevent excess secretion. Then a loading dose of Ketamine 1.5 mg/Kg body weight was given intravenously over 60 seconds and diazepam 5-10mg given intravenously. Group B contained 75 patients, received Propofol lmg/Kg body weight intravenously over 60 seconds, then fentanyl 1 μg/Kg body weight intravenously. Intravenous infusion of propofol was maintained at rate 50 μg/Kg body weight/min throughout ERCP. After 05 minutes patient was taken to examination room. ERCP was done in prone position. Anaesthesiologist was constantly available to observe and record patient's heart rate, blood pressure, respiratory rate, SpO_2 and continuous ECG in lead II. If initial sedation was inadequate or if repeated dose was necessary to accomplish the procedure, additional incremental dose of Ketamine 0.5 mg/Kg body weight was given intravenously to patient in group A and intravenous infusion of propofol was increased up to 100 μg/Kg body weight/min to patient in group B. Additional oxygen was given with nasal canula if SpO_2 found 93% or less.

After completion of ERCP, the patient was brought to recovery area and nursed in prone position. Patients level of consciousness, heart rate, blood pressure, respiratory rate, SpO_2 and ECG were monitored until recovery of the patient from sedation. The recovery time was defined as the time from the procedure completion until the patient attained presedation level of verbalization, awareness and purposeful neuromuscular activity. A full set of resuscitation equipments including suction apparatus, oxygen, a bag valve mask, age appropriate airway, resuscitation drugs and defibrillator were available throughout sedation and recovery to combat any adverse event. Side effects during sedation and recovery like desaturation (SpO_2 less than 93%), hypertension (systolic BP more than 30% of baseline record), hypotension (systolic BP less than 90 mm of Hg), arrhythmia, vomiting, agitation and nightmares were observed, recorded, managed in both groups. The cost of sedation regiments in both groups also calculated and recorded. All results were expressed in percentage or mean±SEM as applicable. Statistical analyses were carried out using Statistical Package for Social Science (SPSS). Results were considered statistically significant if P value less than 0.05.

RESULTS

Patients characteristics were almost similar in both groups and differences were statistically not significant (Table-I). Indications for ERCP in patients were also similar in both groups (Table-II). ERCP was done successfully in every patient of both groups. There were no serious adverse events reported in any patients of both groups. Anaesthetic complications during procedure and recovery were observed and recorded (Table –III). Twelve (16%) patients in group A and 10(13.33%) patients in group B required additional dose of sedative drugs during procedure. Desaturation was noted in 7(9%) patients in group A and 9(12%) patients in group B and difference between two groups was statistically not significant. Hypertension was observed in 12(16%) patients in group A and 3(4%) patients in group B and difference between two groups was statistically significant ($P<0.01$). Hypotension was recorded in 5(6.66%) patients in group B and no occurrence of hypotension in group A. Tachycardia observed in 12(15%) patients in group A and 3(4%) patients in group B and difference between two groups was statistically significant ($P<0.01$). Bradycardia

observed in 5(6.66%) patients in group B and no occurrence of bradycardia in group A. Vomiting was observed in 7(9.33%) patients in group A and G(8%) patients in group B and difference between two group was statistically not significant. Agitation and nightmares were reported in 10(13.33%) patients in group A and no occurrence of agitation and nightmares were reported in group B. Mean procedure time and mean recovery times were calculated in both groups (Table-IV). Mean procedure time was 23.21±5.58 minutes in group A and 25.23±6.15 minutes in group B and difference between two groups was statistically not significant. Mean recovery time was 91.13f8.7G minutes in group A and 56.25+5.69 minutes in group B and the difference between two groups was statistically highly significant (P < 0.001). Cost status of sedation regimen in both groups was calculated. It was 50 taka in group A and 350 taka in group B. Statistics showed that it was 7 times more costly in group B than group A.

Table-I
Characteristics of patients

Parameters	Group A n=75	Group B n=75	Result
Age (years)	57.2 ± 15.9	58.3 ± 14.8	NS(Student 't' test, unpaired)
Sex (M/F)	39/36	38/37	NS(Chi- square test)
Body Weight (kg)	52.26 ± 4.59	53.7 ± 5.28	NS(Student 't' test , unpaired)
Height(cm)	158.76 ± 6.23	159.16 ± 5.14	NS(Student 't' test, unpaired)
ASA Grading (I/ II)	51 ± 24	48 ± 27	NS(Chi- square test)

Results are mean ± SEM NS-No significant difference.

Table-II
Indications for ERCP

Indication	Group A (n=75)	Group B (n=75)	Total (n=150)
Biliary tract stone removal	36(48%)	34(45.33%)	70(46.66%)
Stent insertion/removal	27(36%)	25(34.66%)	53(35.33%)
Diagnosis	10(13.33%)	12(16%)	22(14.66%)
Others	2(2.66%)	3(4%)	5(3.33%)

Table-III
Anaesthetic complications during procedure and recovery

Anaesthetic complications	Group A (n=75)	Group B (n=75)	Result Chi-square test
Inadequate sedation	12(16%)	10(13.33%)	NS
Desaturation	7(9.33%)	9(12%)	NS
Hypertension	12(16%)	3(4%)	P< 0.01
Hypotension	0	6(8%)	-
Tachycardia	12(16%)	3(4%)	P<0.01
Bradycardia	0	5(6.66%)	
Vomiting	7(9.33%)	6(8%)	NS
Agitation and nightmare	10(13.33%)	0	

P<0.01 -Significant.
NS -No significant difference.

Table-IV

Comparison of mean procedure time and mean recovery time between two groups.

Groups	Mean procedure time (minutes)	Mean recovery time(minutes)
Group A (n=75)	23.21 ± 5.58	91.13 ± 8.76
Group B (n=75)	25.23 ± 6.15	56.25 ± 5.69
Result Student's 't' test (Unpaired)	NS	P < 0.001

Results are mean ± SEM

NS - No significant difference.

P < 0.001- Highly Significant.

DISCUSSION

ERCP is an effective treatment with fewer complications than surgery especially for biliary tract abnormalities. The two basic choice of anaesthetic technique; sedation and general anaesthesia which have advantages and disadvantages. Sedation is usually preferred for ERCP unless otherwise, general anaesthesia is indicated for complex painful procedures, paediatric patients and refusal of sedation. [6, 7] A spectrum of sedation may exist and lies on a continuum between complete wakefulness and general anaesthesia. Every patient responds to sedative agents differently. Sliding into general anaesthesia with loss of protective airway reflexes is an important complication of sedation. Sedative dose should be adjusted based on route of drug administration, drug interaction and patient's age and physical fitness[8]. In this prospective randomized study, we tried to compare the effectiveness of sedation in patient during ERCP between Ketamine, diazepam combination with propofol, fentanyl combination. ERCP was done successfully in patients of both groups. There were few incidences of inadequate sedation in both groups, which required additional dose of sedation drugs. Desaturation was noted in 7(9%) patients in group A and 9(12%) patients in group B and the difference between two group was statistically not significant. Transient hypoxia can occur occasionally, but are usually recognized and managed appropriately without clinical consequence and incidence is less common with prone position[9]. Hypertension was observed in 12(16%) patients in group A and 3(4%) patients in group B and difference between two groups was statistically significant (P< 0.01). Tachycardia observed in 12(15%) patients in group A and 3(4%) patients in group B and difference between two groups was statistically significant (P<0.01). This hypertension and tachycardia may be related to sympathomimetic property of the drug ketamine and observed in ketamine administered other endoscopies.[10] Hy-potension and bradycardia observed in few patients with propofol, fentanyl in group B and no occurrence of hypotension and bardycardia observed in group A with ketamine, diazepam. These few incidences of hypotension and bradycardia were transient and minor inconveniences. Adverse cardiopulmonary events can occur during any endoscopic procedure and myocardial ischaemia has been studied during ERCP[11,12]. In this study no signs of cardiac ischaemia recorded in ECG tracing in both groups during *ERCP. Risk* factors for cardiopulmonary complications include known or unsuspected premorbid conditions and can be avoided with careful patient selection, preparation and adequate monitoring[13,14]. Vomiting was observed in few patients of both groups and this vomiting may be due to with ketamine and fentanyl as well as for the endoscopic procedure. [15] Though diazepam was given but agitation and nightmares reported in 10(13.33%) with ketamine. Overall, this agitation and nightmares were transient and managed with additional doses of diszepam. Mean recovery time was more with Ketamine diazepam than with propofol fentanyl and difference between two groups was highly significant (P<0.001). Ketamine is a safe, useful procedural sedation agent but it delays recovery when used with long acting benzodiazepine like diazepam[14,10]. Ketamine does not fit easily into standard drug classification. At low doses full general anaesthesia is not achieved rather a dissociative state in which airway and respiratory tone are maintained. The specific dangers of airway compromise and cardio respiratory instability are suggested to be less with ketamine[16]. Propofol provides safe and effective sedation during ERCP as well as improved recovery[17] and in this study with shorter acting opioid fentanyl also results rapid recovery. Upper gastrointestinal endoscopy is widely used procedure that is generally considered safe, although deaths after endoscopy may be unavoidable[18]. ERCP in low ASA grading (III-V)

patients should be provided with oxygen therapy and cardiovascular monitoring[19]. The involvement of an anaesthesiologist in administration of intravenous sedation and airway management should be actively considered.

In developing country like Bangladesh, cost of drug is a matter of consideration during sedation procedure. Both the sedation regimen proved effective for *ERCP* but cost is very much higher (7 times more) in group B, with propofol, fentanyl than in group A with Ketamine, diazepam.

CONCLUSION

ERCP is a procedure for diagnosis and treatment of hepatobiliary tract abnormalities. However, this procedure still needs not only endoscopic but also anaesthesiologist to observe and take care of the patient. Procedure usually done by different sedation regimen, unless general anaesthesia is indicated. Result from this study we can conclude ERCP can be successfully done administering both sedation regimens. Complications like hypertension, tachycardia, agitation and nightmares were more with ketamine, diazepam but easily correctable and manageable. Recovery time was also more with Ketamine. However, regarding the cost of sedation regimen ketamine, diazepam found more cost effective than propofol, fentanyl, which is a considerable matter in developing country like Bangladesh.

REFERENCES

1. Nicholas A Boon, Nick), R colledge, Brian R, John A A Hunter . Davidson's Principles and Practice of Medicine. 20th edn. UK. Churchill Livingstone 2006; 859-860.
2. Fleischer DE, Van de Mierop F, Eisen GM, AL Kawas , FH, Benjamin SB, Lewis JH, Nguyen CC, Avigan M, Tio TL, Kidwell JA. A new system for defining endoscopic complications emphasizing the measure of importance. Gastrointest Endosc 1997; 45(2):128-33.
3. Steven M Yentis, Nicholas P Hirsch, Gary B Smith. Anaesthesia and Intensive care A-Z. 3rd edn. UK. Butterworth Heinemann 2004; 464-465.
4. Edward Morgan Jr, Maged S. Mikail, Michael J. Murry. Clinical Anaesthesiology. 4th edn. USA. Lange Medical Books McGraw-Hill 2006; 197-202.
5. Graber RG. Propofol in the endoscopy suit: An anesthesiologist's perspective [editorial; comment]. Gastrointest Endosc 1999; 49:803.
6. Raymendos K, Panning B, Bachem I, Manns MP, Piepenbrock S, Meiev PN, Evaluation of Endoscopic Retrograde Cholangiography under Conscious Sedation and General Anaesthesia Endoscopy 2002; 24: 721-726.
7. Etzhom KP, Diab F, Brown RD et al. Endoscopic retrograde cholangiopancreatography under general anaesthesia: indications and results. Gastrointest Endose 1998; 47: 363-367.
8. Faigel DO, Baren TH, Goldstein JL et al. Guidelines for the use of deep sedation and anaesthesia for GI endoscopy. Gastrointest Endosc 2002; SG:G13.
9. Ferreira L. Comparison of safety and efficacy of ERCP performed with patient in supine and prone position. Gastrointest Endosc 2003; 39: 279-282.
10. Varadarajulu S, Elobeidi MA, Tamhane A, Wilcox CM. Prospective randomized trial evaluating Ketamine for advanced endoscopic procedures in difficult to sedate patients. Alimentary Pharmacology & Therapeutics 2007; 25(8): 987-997.
11. American Society of Anesthesiologist Task Force on Post anesthesia Care: Practice Guidelines for Post anesthesia Care. Anesthesiology 2002; 96; 742.
12. Lee 3F, Leung JWC Cotton PB. Acute cardiovascular complications of endoscopy : prevalence and clinical characteristics. Dig Dis 1995; 13(2): 130-135.
13. Lieberman DA, Wuerker CK, Katon RM. Cardiopulmonary risk of endoscopic diameter and systematic sedation. Gastroenterology 1985; 88: 468-472.
14. Johnston SD, Mckenna A, Than TC. Silent myocardial ischaemia during endoscopic retrograde cholangiopancreatography. Endoscopy 2003; 35(12): 1039-42.
15. Amomyotin S, Na pomphet S, Wongwathanyoo T, Chalayonnavin V. Anaesthesia for

Endoscopic Retrograde Cholangio-Pancreatography-(ERCP) from 1999-2003 in Sirraj Hospital: A prospective study. J Med Assoc Thai 2004: 87(12):1491-95.

16. Drummond GB. Comparison of sedation with midazolam and ketamine: effects on airway muscle activity. Br. J Anaesth 1996; 776: 663-7.
17. Ong WC, Santosh D, Lakhtakia S, Nageshwar Reddy D. A Randomized controlled trial on use of propofol along versus propofol with midazolam, ketamine and Petazocine "sedate-analgesic cocktail" for sedation during ERCP. Endoscopy 2007; 39: 807-812.
18. Thompson AM, Wright DJ, Murray W, Ritchi GL, Burton HD, Stonebridge PA. Analysis of 153 deaths after upper gastrointestinal endoscopy: room for improvement. Surgical Endoscopy 2004; 18:22-25.
19. Rosenberg J, Jorgensen LN, Rasmussen V et al. H3,poxaemia and myocardial ischaemia during and after endoscopic cholangio-pancreatograpy: Call for further studies. Scand J Gastroenterol 1992; 27:717-720.