ORIGINAL ARTICLE

Comparison of Injection Dexmedetomidine with Injection Ketamine in Alleviation of Propofol Injection Pain

Mushtaq Ahmed Wani, Suhail Wani, Sandeepika Dogra, Mukta Jitendra

Abstract

Propofol is the drug of choice for intravenous induction because of quick onset of action and fast recovery .Most popular complication of propofol is pain during injection also called PIP(Propofol Injection Pain). In our study we compared injection Dexmedetomidine (0.5µg/kg) with injection Ketamine (0.25mg/kg) to alleviate PIP. In our present study, 100 ASA 1 and 2 patients aged between 18 to 60 yrs, undergoing elective surgeries under general anesthesia were randomaly allocated into two groups. Group I received injection Dexmedetomidine (0.5µg/kg and GROUP II received injection Ketamine(0.25mg/kg) loaded in identical 20 ml syringes labeled as study drug ,over 10 mins using syringe pumps. Propofol 2mg/kg I/V was administered slowly over 25 secs. Pain score was advocated by McCrirrick and Hunter scale,every 5 secs after the onset of propofol injection until the patient became unresponsive. Statistical Analysis was conducted with SPSS, Student's t test, Chi-square test and Fisher's exact test as appropriate. The significance level was set as $p<0.05$. No pain was reported by 20% and 58 % patients in group I and group II respectively. Mild pain was reported by 64% and 40% patients respectively in group I and group II. While severe pain was reported by 6% patients only in group I. Our study concluded that I/V injection of ketamine 0.25 mg/kg is more effective in alleviating mild PIP than injection dexmedetomidine 0.5µg/kg. Also, ketamine was slightly more effective in alleviating moderate to severe PIP than dexmedetomidine, however he difference was statistically insignificant. The study observed significantly more incidence of tachycardia and HTN in group II.

Key Words

Anaesthesia, Dexmedetomidine, Ketamine, Pain, Propofol, I/V (Intravenous)

Introduction

Propofol is a popular intravenous anaesthetic agent for induction as it results in quicker onset, faster recovery and earlier return of psychomotor function . However, disadvantage of propofol is pain on injection, which is sometimes very unpleasant to the patients. The pain on injection of propofol has been widely investigated and is reported to occur in 70 percent of the patients without any pretreatment (1). In children, the incidence of propofol pain has been reported to be around 8%(2). Pain on propofol injection is immediate as well as delayed after 10 to 20 seconds (3). Immediate pain is due to irritation of vein endothelium where as delayed pain is due to the release of mediators of pain such as kininogens from kinin cascade.(4). Slower injection of propofol causes more pain than rapid injection since slow injection increases the concentration and duration of exposure of propofol to the venous wall and rapid injection may clear the drug quickly to replace it with the blood.

A number of drugs with different anti nociceptive actions have been employed with varying efficacy to reduce the PIP (5). Dexmedetomidine is a highly selective alpha 2 agonist with diverse clinical profile consisting of systemic analgesia, sedation, anxiolysisand sympatholysis without the risk of respiratory depression (6). Its

From the Department of Anaesthesiology and Intensive Care, Government Medical College, Jammu

Correspondence to : Dr Mushtaq Ahmed Wani, Lecturer, Department of Anaesthesiology and Intensive Care, Government Medical College, Jammu

antinociceptive action is due to the analgesic modulation at the level of dorsal hornby activation of alpha-2B adrenoreceptors and inhibition of substance P release (7). Rapid intra venous bolus may lead to biphasic response with initial hypertension followed by prolonged hypotension, bradycardia and even sinus arrest(8). Ketamine has analgesic and local anesthetic properties(9). Local anesthetic properties are caused by antagonism of NMDA receptors. Ketamine given as premedicant acts as pre emptive analgesic preventing sensitization of local nerve endings by noxious inputs. However, ketaminehas some undesired effects, including sympathetic stimulation and increased secretions(10). The reported effective dose of ketamine varies from 0.1mg/kg to 1 mg/kg. It is postulated that the low dose ketamine may be effective due to local anesthetics effects where as with high dose central analgesic sedative effect may be playing a role(11).

Material and Methods

The present prospective, randomized, double blinded study was conducted in GMC Jammu, in Post Graduate Department of Anaesthesiology and Intensive Care after attaining approval from the hospital ethical committee and informed consent from the patients, 100 patients of either sex, age group between18 to 60 years ASA I and II scheduled for routine elective surgical procedures undergoing general anaesthesia were included in the study. Patients with difficulty in communication, history of allergy to the study drugs, requiring rapid sequence induction, having difficulty in venous access, presence of renal or hepatic impairment, patients with the history of drug abuse, pregnant and lactating women,morbidly obese, patients who received any kind of analgesic or sedatives in 24 hours prior to surgery were excluded from the study. The patients were explained about the procedure in detail and thorough pre anaesthetic check up was done a day before surgery. Relevant demographic characteristics and baseline hemodynamic parameters were recorded. Routine investigations included hemoglobin, BT/CT, urine routine,ECG, RFT's, blood glucose fasting and chest radiograph. No premedication other than study drug was administered to the patients. The patients were fasted for 8 hours pre operatively.

In the operating room , monitors including NIBP, ECG and SpO2 were applied. A 20 gauge IV cannula was secured in the vein on the dorsum of the non dominant hand. Depending upon the drug used for premedication patients were randomly allocated into two groups(Group I for dexmedetomidine 0.5µg/kg or Group II for ketamine 0.25 mg/kg) using computer generated table with random numbers.The study drugs were loaded in identical 20 ml syringes labeled as ' study drug' by an (2) independent anaesthesiologist not involved in the study and infused over 10 minutes using a syringe pump. Immediately after infusion of the study drug, injection propofol 2 mg/kg I/V was administered slowly over 25 seconds. Starting from the time of injection patients were assessed for pain by asking and open ended question ' does it hurt'? every 5 seconds until the patient became unresponsive, and the degree of pain was scored as advocated byMcCrirrick and Hunter rating scale(verbal rating scale). Both the patients as well as the anaesthesiologist monitoring the response were unaware of the group allocation. The above pain assessment methodology was selected because PIP starts immediately after injection and McCrirrick and Hunter scale has been validated previously for evaluation of PIP (12).

After the assessment of pain , induction of anaesthesia was completed with the remaining dose of propofol, and tracheal intubation was facilitated with the injection of succinylcholine. Anaesthesia was maintained with injection of vecuronium, O2, N2O, and isoflureand on IPPV. Intraoperatively, heart rate, blood pressure, SpO2, and ETCO2 were monitored. Any episode of bradycardia, hypotension hypertension or tachycardia were recorded and managed accordingly.

Statistical testing was concluded with the SPSS for windows. Demographic data was presented as mean plus minus SD and compared utilizing Student's t test. Categorical variables were compared using Chi-square test or Fisher's exact as appropriate. For all tests, p value < 0.05 was considered as significant.

Results

A total of 100 patients were included in the study and divided randomly into two groups each comprising of 50 patients (n=50). The demographic data and baseline vitals were comparable in both the groups (*Table2*). According to McCrirrick and Hunter scale, no pain was reported by 20% and 58% patients respectively in Group I and GroupII. The difference was statistically significant (p= 0-0002). Mild pain was reported by 64% and 40% in Group I and Group II respectively (p=0-02), which is again statistically significant.

Moderate and severe pain was reported by more patients in GroupI1 as compared to Group II, but the difference between both the groups is statistically not significant. No patient in Group 2 (ketamine group) reported severe pain on propofol injection.

In GroupII, thereis significantly higher incidence of tachycardia and hypertension as compared to Group 1. In Group I only one patient experienced hypotension.

Table.1 Severity of Pain

Degree of Pain	Response
None (0)	No response to questioning
Mild (1)	Pain reported in response to questioning alone without any behavioral sign
Moderate (2)	Pain reported in response to questioning and accompanied by behavioral sign or pain reported without any questioning
Severe (3)	Strong Vocal Response or Response accompanied by facial grimacing arm withdrawal or tears

Table.2 Demographic Data and Base Line Vitals

Variable	Group I Injection Dexmedetomidine (N=50)	Group II Injection Ketamine (N=50)	P Value
Age	37.82±11.42	39.16 ±10.20	0.53
Sex (M:F)	27:23	19:31	0.15
Wt (Kg)	65.04±10.04	65.26±6.77	0.94
Height (Cm)	167.06±8.34	166.33±4.68	0.76
ASA I:II	43:7	38:12	0.30
Heart Rate (BPM)	77.84±7.65	77.20±7.75	0.41
SBP	120.08±9.84	122.96±7.67	0.10
DBP	74.62±5.22	76.78±7.60	0.10
Spo2	92.26±	98.60	0.33

Table . 3 Distribution of the Patients according to the Incidence of Propofol Injection Pain (PIP)

Degree of pain.	Group I	Group II	P Value
None (0)	10 (20.00)	29(58.00)	0.0002
Mild (1)	32 (64.00)	20(40.00)	0.02
Moderate (2)	5 (10.00)	1 (2.00)	0.020
Severe (3)	3 (6.00)	0 (0.00)	0.24

Table: 4 Distribution of the patients according to the incidence of side effects

Side Effects	Group I	Group II	P Value
None	47 (94.00)	38 (76.00)	0.02
Bradycardia	2 (4.00)	0	0.49
Hypotension	1 (2.00)	0	1.00
Tachycardia	0	6(12.00)	0.02
Hypertension	0	6(12.00)	0.02

Discussion

Propofol is a popular drug in anaesthesiology and is widely used for induction and maintainance of anaesthesiadue to its good CNS absorption and short half life and also minor side effects which include propofol injection pain (PIP). A study has revealed that around 60% of the patients experience pain on injection propofol and this includes 20% of the patients experiencing severe PIP (5).The PIP is said to be influenced by temperature of the solution, size of the vein and speed of the injection. The gets abolished by pre treatment with a kallikrein inhibitor before propofol injection (13). Dexmedetomidine isa potent alpha 2 agonist with the added advantage of systemic analgesia by inhibition of Substance P(7).Ketamine when mixed with propofol decreases the pH of the solution and reduces PIP (8), also it is less cardio depressant as compared to the other anaesthetic drugs. However, there are a few reports (3) comparing the efficacy of these two drugs in I/V boluses to alleviate PIP. We, therefore studied and compared the efficacy of these two drugs. A total of 100 patients of comparable demographic data and baseline vitals were randomally divided into two equal groups. Group I patients were given injection dexmedetomidine 0.5µg/kg while Group II patients were given injection ketamine 0.25mg/kg. The degree of pain score was advocated by McCrirrick and Hunter scale.

The present study showed that ketamine whencompared with dexmedetomidine pre treatment was more effective in reducing incidence and severity of PIP. The incidence of moderate to severe pain during propofol injection was 16% and 2% in Group 1 and Group 2 respectively suggesting both are effective in reducing moderate to severe pain. Our results are in accordance with Sarkilar *et al* (14). A number of studies have combined drug pre treatment, including ketamine and dexmedetomidine with venous occlusion, however, it has failed to become a standard technique (1). A number of drugs with varying antinociceptive efficacy to reduce PIP

have been employed. Ketamine produces analgesia both by local anaesthetic action and also by analgesic modulation by NMDA and mu opiate receptors at the neuraxial level (15).

In the present study, dexmedetomidineand ketamine were administered as 10 minutes infusion to avoid acute haemodynamic changes associated with the rapid bolus doses(7).We did not observe any initial hypertensive response in dexmedetomidine which occurs as a first part of biphasic response during rapid injection, but bradycardia was observed in two patients subsequent to dexmedetomidine infusion. One patient observed hypotension, but it was statistically insignificant. Present study observed statistically significant incidence of intraoperative hypertension and tachycardia in six patients in the ketamine group.

Conclusion

The study concluded that intravenous infusion of ketamine 0.25 mg/kg before propofol injection is more effective in alleviating the incidence of pain when compared to infusion dexmedetomide 0.5µg/kg, as more than half of the patients in ketamine group experienced absolutely no pain. Also, the incidence of mild pain was significantly higher in dexmedetomidine group as comp ketamine group. However, the study observed that there was significantly more incidence of tachycardia and hypertension in ketamine group patients.

References

1. Picard P, Tramer MR. Prevention of pain on injection with . . . . . *Anesth Analges* 2000; 90(4): 963-69.
2. Borazan H, Sahin O, Kececioglu A, Uluer MS, Et T, Otelcioglu S. Prevention of propofol injection pain in children: A comparison of pre treatment with tramadol and propofol-lidocaine mixture. *Int J Med Sci* 2012; 9(6): 492-97.
3. Scott RP, Saunders DA, Norman J. Propofol: Clinical strategies for preventing the pain of injection. *Anaesthesia* 1988; 43: 492-4.
4. Tan CH, Onsiong MK, Kua SW. The effect of ketamine pretreatment on propofol injection pain in 100 women. *Anaesthesia* 1998; 53(3): 302-05.
5. Jalota L, Kalira V, George E, *et al*. Prevention of pain on propofol injection: Systemic review and meta-analysis. *BMJ* 2011; 342:d1110.
6. Uzun S, Karazog H, Kose A,Canabay O, Ozgen S. Dexmedetomidine fo prevention of propofol injection pain. *J Anaesth Clin Pharmacol* 2008; 24:406-8
7. Jooste EH, Muhly WT, Ibison JW, *et al*. Acute hemodymnamic changes after rapid intravenous bolus dosing of dexmedetomidine in pediatric heart transplant patients undergoing routine cardiac catheterization. *Anaesth Analg* 2010; 111: 1490-6.
8. Ingersoll-Weng E, Manecke GR, Jr, Thistlehwaite PA. Dexmedetomidine and cardiac arrest . *Anaesthesiology* 2004; 100: 738-9.
9. Tobias JD, Leder M. Procedural sedation: A review of sedative agents, monitoring and management of complications. *Saudi J Anaesth* 2011; 5(4): 395.
10. Hui TW, Short TG, Hong W, Suen T, Gin T, Plummer J.Additive interactions between propofol and ketamine when used for anaesthesia induction in female patients. *Anaesthrsilogy* 1995; 82: 641-8.
11. Desousa KA. Pain on propofol injection: Causes and remedies. *Ind J Pharmacol* 2016; 48: 617-23.
12. Rahimzadeh P, Faiz SH, Nikoobakht N, Ghodrati MR.Which one is more efficient on propofol 2% injection ;pain? Magnesium sulphate or ondansetron: A randomized clinical trial. *Adv Biomed Res* 2015; 4: 56.
13. Iwama H, Nakane M, Ohmori S, Kenako N. A kallikrein inhibitor, prevents pain on injection with propofol. *Br J Anaesth* 1998; 81:963-4.
14. Sarkilar G, Kara I, Duman A, Okesli S. Effect of dexmedetomidine on pain caused by injection of propofol. *Nobel Med* 2012; 8: 83-8.
15. Visser E, Schug SA. The role of ketamine in pain management. *Biomed Pharmacother* 2006; 60: 341-8.
16. WHO. Model List of essential medicines, 19th list. World Health Organisation, April 2015.
17. Tan CH, Onsiong MK. Pain on injection of propofol. *Anaesthesia* 1998; 53(3): 302-05.
18. Persson J. Ketamine in pain management. *CNS Neurosci Therap* 2013; 19(6): 396-402.
19. Cormack JR, Orme RM, Costello TG. The role of alpha 2 agonists in neurosurgery. *J Clin Neurosci* 2005; 12(4) : 375-78.
20. Dundee JW, Wyant GM. Ketamine. In: Intravenous Anaesthesia New York: Churchill Livingstone; 1988 .pp. 135-59.