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Comparison of Ketamine Intravenous Infusion with Dexmedetomidine Intravenous Infusion to Alleviate Propofol Injection Pain.

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Abstract
Background and Aims: For induction of anaesthesia propofol is the most widely used intravenous anaesthetic agent. The induction of anaesthesia is rapid with propofol and also is recovery .But propofol injection pain (PIP) still remains a problem. The incidence of pain on its injection is 28-90%. The high prevalence of pain makes it necessary to find an ideal drug or drug combination to alleviate the pain on propofol injection. The aim of this study was to compare ketamine 0.5 mg/kg intravenous (IV) infusion with dexmedetomidine 0.5mcg/kg IV infusion to alleviate PIP. Methods: In this prospective observational study 70 patients undergoing elective surgeries under general anaesthesia were randomly enrolled to two groups. 35 patients (group K) received ketamine 0.5 mg/kg IV and 35 patients (group D) received dexmedetomidine 0.5mcg/kg in 20ml normal saline over 10 minutes. Soon after the infusion, 1% propofol 2mg/kg IV was injected over 25 seconds. The pain was assessed by asking 'does it hurt' every 5 seconds, until the patient lost consciousness. McCririck and Hunter scale was used for pain scoring. Statistical analysis done-using-SPSS 22 version. Results: 97.1% of patients in group K had no PIP where as 2.9% of group D had no PIP. In the dexmedetomidine group, 17.06% had severe pain, 37.12% had moderate pain. The incidence of PIP was significantly higher in group D compared to group K (P<0.05) Conclusion: IV ketamine infusion is more effective than IV dexmedetomidine infusion to alleviate PIP.

Keywords: *Ketamine, dexmedetomidine, propofol, anaesthesia, pain.*

Introduction

Propofol is the most commonly used intravenous induction agent due to its smooth induction and rapid recovery. Propofol induced pain is considered to be one of the most important problem in current anaesthesia practice. It is rated as the 7th most disturbing experience to the patient in anaesthesia practice.[1] The use of adjuvant medication before propofol has become a common practice. The use of lignocaine with propofol is almost since many years and hence maximum number of clinical trials were with lignocaine either alone or in combination with other drugs.[3] Another effective drug is IV Ketamine as pretreatment. The reported effective dose varies from 0.1-0.4 mg/kg IV. It is postulated that low dose of ketamine may be effective due to its

peripheral local anaesthesia and also by analgesic modulation via NMDA and μ opioid receptors at the neuraxial level where aswith high dose central and sedative effect may be playing a role[5]. It is also found that injection dexmedetomidine before propofol be more effective than injection normal saline in alleviating pain of propofol injection.[8] α_1 and α_2 stimulation by dexmedetomidine might be a possible mechanism in decreasing propofol injection pain and resultant release of prostaglandins which causes vasodilatation, that antagonise vasoconstrictor response.[10]Dexmedetomidine is a highly selective specific α_2 agonist, potent analgesic and sedative along with sympatholytic effect without respiratory depression. Dexmedetomidine has been shown to promote peripheral antinociption.[11]

Methods

After obtaining due ethical clearance from the institutional review board and written informed consent from the patients, 70 patients aged 18 to 70 years of either sex belonging to American society of Anaesthesiologists (ASA) Physical Status I and II undergoing elective surgeries under general anaesthesia were enrolled for this prospective observational study. Patients with history of drug abuse, psychiatric disease, seizures, uncontrolled hypertension, renal or hepatic impairment, allergy to the study drugs and pregnant females were excluded from the study. All patients were evaluated and assessed in the preoperative period. All patients were kept fasting for 8 hours preoperatively. No premedication was administered to the patients.

In the operation theatre, IV line was secured on the dorsum of hand and fluid started. Monitors, electrocardiography, pulse oximetry and noninvasive arterial pressures were applied. Patients getting ketamine are group K and those receiving dexmedetomidine are group D. The study drugs ketamine or dexmedetomidine are loaded in 20ml syringes and labelled and infused over 10 minutes using a syringe pump. Immediately after infusion of the study drugs, injection propofol of 2mg/kg IV was administered slowly over 25 seconds. Starting from the time of injection, the patients were assessed for pain by asking an open ended question "does it hurt" every 5 seconds until the patient became unresponsive and the degree of pain was scored according to McCririck and Hunter Scale (Table 1). This pain assessment method was selected because pain of propofol injection starts immediately after injection and MCcririck and Hunter scale has been used previously for evaluation of pain of propofol injection.[8]

The sample size was calculated based on previous studies and stastistical analysis was done using SPSS version22.

Age, weight, height and body mass index are presented as mean ± standard deviation Chi-Square frequency and independent sample t test used to find out the level of significance at 0.05 with the help of SPSS software 22version.

For all statistical tests, $p < 0.05$ was taken to indicate significant difference.

Table 1: McCririck and Hunter Pain Scale.

Numerical score	Response	Interpretation	Interpretation for Statistical analysis.
0	Negative response(no) to question	No pain	No pain
1	Pain reported yes only in response to the question without any behavioral change.	Mild pain	Mild pain
2	Voluntary complaint of pain or behavioral change	Moderate pain	Moderate pain
3	Strong vocal response or facial grimacing or arm withdrawal or tears on injection	Severe pain	Severe pain.

Results

A total of 70 patients were included in the study and randomly distributed into two groups. All of them completed the study. Both groups were comparable

with regard to demographic data and base line vitals (Table 2). The incidence of PIP was significantly lower in group K compared to Group D. Only one patient in Group K had mild pain. All the remaining patients in the Group K did not have any pain on propofol injection. No patient in two groups exhibited arm withdrawal on injection of propofol. The incidence of pain on propofol injection was significantly higher the Group D compared (Figure-1 and Table -3) to Group K. The incidence of severe PIP is lowered even in group D Table.3.

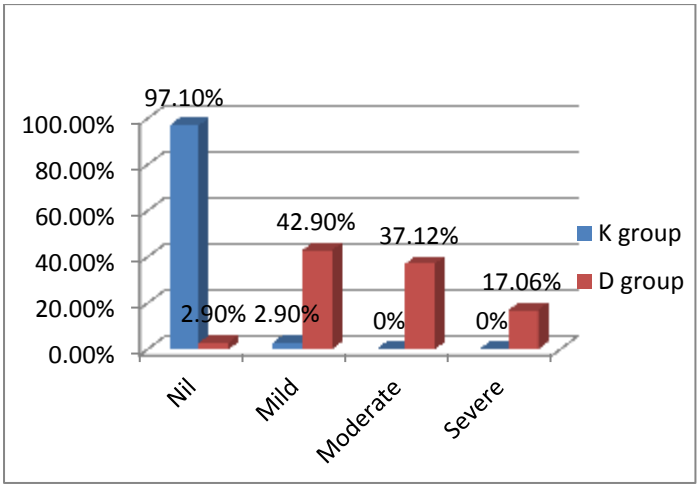
Table 2: Demographic Data and Baseline Vitals

Variables	K group N=35	D group N=35	P value
Age	44.60±12.51	49.94±14.54	.104
Male/Female	29/6	29/6	.213
Weight	56.31±8.30	58.66±6.72	.199
Height	155.27±27.09	160.57 ±2.59	.254
BMI	22.088±2.80	22.69±2.15	.310
ASA (I/II)	31/4	31/4	1.00
HR	80.80±10.02	83.20 ±13.03	.391
BP	80.82±6.22	83.65±8.62	.121

BP -Blood Pressure; BMI-Body Mass Index
ASA -American Society of Anaesthesiologists
HR -Heart Rate.

Table 3: Pain Scores

Pain score	Kgroup N=35	Dgroup N=35	P value
Nil	34 (97.1%)	1 (2.9%)	.000
Mild	1(2.9%)	15(42.9%)	.000
Moderate	0	13(37.12%)	.000
Severe	0	6(17.06%)	.016



Pain severity

Statistics used

Present study investigator used Chi-square, Frequency and independent sample t test used for find out the level of significance at 0.05. with help of SPSS software 22version

Discussion

Propofol is a popular intravenous anaesthetic agent that causes pain on injection. Three and one of every five patients report pain on propofol injection and severe PIP respectively[13]. The present study showed that ketamine pretreatment was more effective then dexmedetomidine pretreatment in reducing the incidence and severity of PIP. Nature of vascular pain is experienced by the patient as aching, burning and crushing. Propofol has a phenol group which is irritating to the skin, mucous membrane and venous intima. Mechanism of pain is due to activation of kallikrein-Kinin system bypropofol there by generating kinin probably bradykinin. The incidence of PIP injection in a study by Deepa Raveendra Shryan et al was reduced from 93.3% in control Group to 20% in ketamine group[6]. The incidence of PIP is 2.9% in the present study that too is mild. 97.1% of patients the Group K had no pain. The incidence of moderate and severe pain on propofol injection in dexmedetomidine group is 37.12% and 17.06% respectively. Moderate to severe pain is less with dexmedetomidine also. These results are in accordance with study by Sarkilaret el who found an incidence of 17.6% of severe pain with dexmedetomidine 0.5% mcg/kg pretreatment [18]. In this study, there is a higher overall incidence of pain on propofol injection with dexmedetomidine. In group D, majority of patients had mild pain 42.9% 2.9% had no pain, where as 37.12% had moderate and 17.06% had severe pain. The moderate to severe pain in also associated with physical and psychological distress with chance to be remembered by the patients postoperatively. (13,14).

Many drugs with different mechanisms acting peripherally, alleviate or producing analgesic modulation at spinal and supraspinal level have been used to alleviate the PIP [13] Ketamine acts through NMDA and μ opiate receptors at the

neuraxial level [5]. Saadwy et al used 0.4 mg/kg Ketamine as pretreatment for PIP and found to be effective in reducing the pain on propofol injection but they combined this with venous occlusion.[4]

The dose of 0.5 mg/kg ketamine was selected in this study on the basis of a study conducted by SeemaThukral et al who found this dose to be effective in reducing PIP. [17] The anti nociceptive action of dexemedetomidine is mediated by the analgesic modulation at the level of dorsal horn by α & β receptor activation and inhibition of substance p release.[11] 0.5 and 1 mcg/kg dexmedetomidine was equally found effective by Sarkilar et al.[18] Dexmedetomidine and ketamine were administered as intravenous infusion to avoid acute hemo dynamic changes associated with their bolus administration. Rapid IV injection of dexmedetomidine is associated with hypotension and bradycardia. In this study no patient had any of the advance effects.

Conclusion

Ketamine 0.5mg/kg slow IV infusion immediately before propofol injection is found to be more effective in reducing the incidence of pain on propofol injection than dexmedetomedine 0.5 mcg/kg IV infusion pretreatment.

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