ORIGINAL ARTICLE

To Study the Effect of Injection Dexmedetomidine for Prevention of Pain Due to Propofol Injection and to Compare It with Injection Tramadol and Injection Lignocaine

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Abstract

Propofol induced pain (PIP) is considered to be one of the most important problems of current clinical practice. The pain may cause hand withdrawal and dislodging of the venous cannula.We conducted a prospective,randomized study to evaluate the effect of intravenous dexmedetomidine and compared it to injection lignocaine and injection tramadol for reducing the incidence and severity of propofol injection pain. WE found that both injection dexmedetomidine and injection tramadol are equally effective in reducing propofol injection pain and can be used as an alternative to injection lignocaine without any significant side effects.

Keywords

Propofol, Dexmedetomidine, Tramadol, Lignocaine, PIP.

Introduction

Propofol is the drug of choice for induction of anaesthesia in millions of patients every year because of it's rapid onset, short duration of action, easy titration, and favorable profile for side effects (1).Although propofol has these positive characteristics, it has some unwanted effects like injection pain which impairs patient comfort (2).Propofol induced pain is rated as the 7th most disturbing experience to the patient in anaesthesia practice by a group of experts (3). The pain may cause hand withdrawal and dislodging of the venous cannula (4). In the absence of treatment regimens, 28 to 90% of patients experience moderate to severe pain when propofol is injected into peripheral vein (5).

Nature of the vascular pain is expressed by the patients of as aching, burning and crushing. It is due to phenol group present in propofol. Phenol group is irritating to skin, mucous membrane and venous intima. The mechanism of pain is attributed to the activation of kinin-kallikrein system that releases bradykinin, causing vasodilatation and hyperpermeability, thereby increasing contact between the aqueous phase propofol and the free nerve endings (6). Numerous studies have been done to investigate the most effective method and drug to reduce propofol-induced pain with variable results.

A systemic review and meta-analysis showed that propofol infusion via the antecubital vein and pretreatment with lidocaine in conjuction with venous occlusion were the two most efficient interventions to reduce pain on injection of propofol (7). However, some unexpected adverse side effects have been associated with the two methods.Tramadol is a centrally-acting drug which is effective in the treatment of moderate to severe pain. In addition to its systemic effect, the local anesthetic effect of tramadol has been shown in both clinically and laboratory studies (8). According to this action, pretreating the vein with intravenous tramadol has proved to be effective in preventing propofol injection pain in adults. The incidence of tramadol treated pain was 23% vs 69% in the control group (9). Dexmedetomidine, a newer alpha adrenergic agonist, has been used to alleviate propofol injection pain (10). It has a potent analgesic and sedative effect along with sympatholytic effect.Dexmedetomidine has been shown to promote peripheral antinociception. Therefore, dexmedetomidine can also be used for relief of propofol pain. In the present study, we investigated the effect of injection dexmedetomidine for prevention of propofol injection pain and compared it with injection lignocaine and injection tramadol.

Materials and Methods

After obtaining approval from hospital ethics committee, the present prospective, randomized study was conducted in the Government Medical College and Associated Hospitals, Jammu in the Postgraduate Department of Anaesthesiology and Intensive Care. A total of 105 patients were taken up in the study in the age group of 18 to 60 years of either sex scheduled for

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routine elective surgical procedure under general anesthesia with endotracheal intubation.

Inclusion criteria:

ASA grade I, II

Exclusion criteria:

Difficult in communication
History of adverse effects to propofol and other study drugs
Patients who require rapid sequence induction
Having difficulty in venous access
Presence of hepatic or renal dysfunction
Patients with cardiac failure, rhythm abnormalities
Patients with seizure disorder
History of drug abuse
Uncontrolled hypertension
Morbidly obese patients
Pregnant and lactating women
Patients who received any kind of analgesic or sedative in the 24 hours prior to surgery

Informed written consent was taken from each patient fulfilling inclusive criteria. Pre-anaesthetic check-up was done a day before surgery.

Routine investigations were done. No premedication other than the study drug was administered to the patients. The patients were fasted for 8 hours preoperatively.

In the operating room, monitors including non-invasive arterial pressure, electrocardiography, and pulse oximetery were applied. A 20 gauge IV cannual was secured in the vein on the dorsum of the non-dominant hand. Depending upon the drug used for premedication, patients were randomly allocated to three groups (Group I, Group II or Group III) using computer generated table with random numbers. The study drugs kept at room temperature was divided into equal volumes of 5 ml with addition of normal saline. The patients enrolled were divided randomly into three groups of 35 patients each. Group I received 0.2 g/kg of dexmedetomidine diluted in 5 ml normal saline. Group II received 0.2 mg/kg of lignocaine diluted in 5 ml normal saline. Group III received 1 mg/kg tramadol diluted in 5 ml normal saline.The patients were asked to report their pain according to the verbal rating scale (11).

With the aim of keeping the drug within the vein, the forearm was squeezed with a pneumatic tourniquet up to 70 mmHg to occlude the vein for 1 minute. The study drug was injected through the cannula over 5 seconds. After 1 minute, the occlusion was released and 25% of the induction dose of propofol (2mg/kg) was administered over 10 seconds by a mechanical syringe. During propofol injection, the patients were asked standard questions regarding the comfort of the injection and were continuously observed for vocal response, facial grimacing, arm withdrawal, or tears suggesting severe pain. The above pain assessment methodology was selected because the propofol injection pain (PIP) starts immediately after injection and McCririck and Hunter scale (11) has been validated previously for evaluation of PIP.After the assessment of pain, induction of anesthesia was completed with the remaining dose of propofol, and tracheal intubation was facilitated with the injection of succinylcholine. Anesthesia was maintained with injection of vecuronium, oxygen, nitrous oxide (66% and isoflurane on intermittent positive pressure ventilation.

Statistical analysis

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

Sttistical testing was conducted with the statistical package for the social science (SPSS) for Windows. Demographic data was presented as mean standard deviation and compared utilizing Student's t'test. Categorical variable were expressed as frequencies and percentages and compared using Chi-square test or Fisher's exact test as appropriate. For all statistical tests, $p < 0.05$ was taken to indicate a significant difference.

Result

All patients (n = 120) completed the study. There was no statistical difference in patients' demographics or the ASA grading as shown in *Table 1.* Mean baseline vital characteristics like heart rate, peripheral oxygen saturation and noninvasive blood pressure of the patients in all the three groups are comparable. (*Table 2*)

As per McCririck and Hunter scale15, no pain is reported by 57.14%, 62.86% and 45.71% patients in injection dexmedetomidine (Group I), injection lignocaine (Group II) and injection tramadol (Group III) drug groups ,respectively. Mild pain is reported by 42.86%, 37.41% and 54.29% patients in injection dexmedetomidine, injection lignocaine and injection tramadol drug groups

respectively(*Table 3*).No patient reported moderate or severe propofol injection pain.

In the present study, in comparing results of incidence of propofol injection pain (PIP), no significant difference (p>0.05) is seen when injection dexmedetomidine drug group is compared with injection lignocaine drug group. Similarly, no significant different (p>0.05) is seen when injection dexmedetomidine drug group is compared with injection tramadol drug group.(*Table 4*)

Discussion

The present prospective, randomized study was carried out in order to evaluate the effect of intravenous dexmedetomidine in comparison with intravenous lignocaine and tramadol for reducing the incidence and severity of propofol injection pain. The possible mechanism involved in decreasing propofol injection pain by dexmedetomidine is not fully understood. It might be due to alpha 1 and 2 stimulation causing release of vasodilator prostaglandins that antagonize the vasoconstrictor response. This modulation of the sympathetic response of the venous smooth muscle might be important in endothelial dysfunction caused by propofol (12). So far, there have been only a few studies investigating the inhibiting effect of dexmedetomidine on the pain of propofol injection. Ayoglu *et al.* (13) demonstrated that pretreatment with 0.25 g/kg dexmedetomidine was not effective in reducing propofol injection pain. Yet the research done by Turan *et al.* (14) contradicted this, showing that pretreatment with 0.25 g/kg dexmedetomidine decreased propofol injection pain as effectively as pretreatment with lidocaine 0.50 mg/kg. In our study, there was no case of moderate or severe pain in any of the three groups. On comparing results of incidence of propofol injection pain , no significant differentce (p>0.05) was seen when injection dexmedetomidine drug group was compared with injection ligocaine drug group. Similarly, no significant difference (p>0.05) was seen when injection dexmedetomidine drug group was compared with injection tramadol drug group.

Ebert *et al.* (15) showed that increasing concentrations of dexmedetomidine in humans resulted in a progressive increase in analgesic effect. Dexmedetomidine was most effective when 1 g/kg was injected 5 minutes before propofol injection in their study.

Table 1.Demographic Profile in Three Groups

	Group I (Injection dexmedetomidine n=35)	Group II (Injection lignocaine n=35)	Group III (Injection tramadol n=35)	p value
Age (years)	39.51±11.18	42.6±9.57	42.42±10.17	>0.05
Sex(M:F)	17:18	15:20	16:19	>0.05
Height (cm)	168.20±6.81	169.66±4.32	168.10±4.27	>0.05
Weight (kg)	78.33±6.81	82.13±6.20	80.70±6.03	>0.05
ASA Grade I:II	04:07	23:12	24:11:00	>0.05

Table 2. Mean baseline heart rate, peripheral oxygen saturation and noninvasive blood pressure of the patients in the three groups

Variable	Group I (Injection Dexmedetomidine) Mean ± Standard deviation	Group II (Injection lignocaine) Mean ± Standard deviation	Group III (Injection Tramadol) Mean ± Standard Deviation
Mean heart rate (beats/minute)	75.65 ± 7.53	75.45 ± 7.22	74.82 ± 7.17
Mean SpO_2 (%)	98.45 ± 0.81	98.17 ± 0.82	98.28 ± 0.85
Mean SBP (mmHg)	120.82 ± 10.32	123.97 ± 10.64	123.42 ± 11.19
Mean DBP (mmHg)	74.22 ± 5.73	74.91 ± 7.73	73.82 ± 6.79

Table 3. Distribution of the patients according tot he incidence of propofol injection pain (PIP)

Degree of pain	Group I (Injection Dexmedetomidine) No. (%)	Group II (Injection lignocaine) No. (%)	Group III (Injection Tramadol) N0. (%)
None (0)	20 (57.14)	22 (62.86)	16 (45.71)
Mild (1)	15 (42.86)	13 (37.14)	19 (54.29)
Moderate (2)	0	0	0
Severe (3)	0	0	0
Total	35 (100.00)	35 (100.00)	35 (100.00)

Table 4. Comparison of injection dexmedetomidine (Group I) with injection lignocaine (Group II) and injectiont ramadol (Group III) as per incidence of propofol injection pain (PIP)

Comparison	No pain No.	Mild Pain No.	Statistical inference
Group I versus Group II	20 versus 22	15 versus 13	Chi-square = 0.06; p=0.80*
Group I versus Group II	20 versus 16	15 versus 19	Chi-square = 0.51; p=0.47*

* Not significant

We observed that 42.86% of the patients in the dexmedetomidine group experienced mild pain as compared to 37.14% in 15ligocaine group. Our findings were also comparable to the ones in studies by Uzun *et al.* (16) and Sarkilar *et al.* (17) who demonstrated pain in 43% (0.25 g/kg) and 45.5-66.3% (0.5-1 g/kg) of the patients, respectively, in the dexmedetomidine group.

Thukral *et al.* (18) reported higher incidence of propofol injection pain and moderate-severe propofol injection pain when 0.5 g/kg of dexmedetomidine was given (79.6%; 16.7%), which is not in accordance with our study. They chose to administer dexmedetomidine as 10 minute infusions to avoid acute haemodynamic changes associated with it's rapid bolus injection.

Overbaugh *et al.* (19) showed that lidocaine, (2 ml of 2% i.e. 40 mg) when mixed with propofol was more effective in reducing the pain on propofol injection than when given as a pretreatment. Lee and Russel (20) reported a decreased incidence of propofol injection pain in the propofol mixed group (2 ml of 2% lidocaine) compared to the lidocaine (4 ml 1%) pretreatment group. We used 2% lignocaine concentration at a dose of 0.2 mg/kg, which was effective in reducing the pain of propofol injection.

In our study, 62.86% of the cases had no pain and 37.12% had mild pain in the lignocaine group that is comparable to the study conducted by Singh *et al.* (6), who reported 80% of the cases had not pain and 17.14% had mild pain.

Tramadol, is a centrally acting weak -receptor agonist, inhibits noradrenaline re-uptake as well as promotes seratonin release and can be used to treat moderate and severe pain (21). In addition to its systemic effect, the local anesthetic effect of tramadol on peripheral nerves has been shown in both clinically and laboratory studies (22).Desmolues *et al.* (23) have confirmed in humans that the analgesic effect of tramadol is apportioned between the opioid and monoaminergic componenets. Jou *et al.* (8) suggested that tramadol affects sensory

and motor nerve conduction by a similar mechanism to that of lidocaine which acts on the voltage dependent sodium channel leading to axonal blockage.

In our study, 47.71% of the patients had no pain and 54.29% had mild pain in tramadol group. Borazan *et al* (24) showed that pretreatment with intravenous tramadol to be equally effective in relieving propofol injection pain compared to lidocaine mixed with propofol and it is also useful for intraoperative and post operative analgesia when minor operations are under taken.

Conclusion

In conclusion, injection dexmedetomidine is equally effective and can be used as an alternative to time tested injection lignocaine for relief of pain due to propofol injection without any significant effects. Also, injection tramadol can be used alternatively to injection lidocaine as seen in the present study. Further studies are needed to justify use of dexmedetomidine as an alternative to lignocaine and tramadol for prevention of propofol injection pain.

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