Original Article

Comparison of intravenous dexmedetomidine and intravenous lignocaine for the prevention of conventional propofol injection pain: A prospective randomised double-blind study

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Abstract

Background: Pain on injection with propofol is a well recognized problem sometimes very distressing to patient. Current study compared the effectiveness of intravenous dexmedetomidine and lignocaine pretreatment for the prevention of propofol pain during induction of general anaesthesia.

Methods: Ninety, American Society of Anesthesiologists (ASA) grade I and II patients were randomised into three groups of 30 each, Group D, Group L and Group N. Group D, patients received dexmedetomidine 0.2 μg/kg diluted to 5 ml of normal saline, group L, patients received 0.5 mg/kg preservative free lignocaine diluted to 5 ml of normal saline and group N, patients received 5 ml of normal saline. Intravenous access was secured with 20 G cannula and venous occlusion was applied to forearm using a pneumatic tourniquet inflated to 90 mm of Hg for 1 minute. The study drugs were injected over 5 seconds and after 1 minute venous occlusion was released and 25% of total calculated dose of propofol (2 mg/kg) was given intravenously over a period of 60 seconds. Severity of pain was evaluated using McCrirrick and Hunter scale at 0 seconds, 30 seconds and 60 seconds respectively and then remaining propofol and neuromuscular blocking agent was given.

Results: The groups were comparable demographically. There was significant difference in pain scores assessed at 0 seconds, 30 seconds and at 60 seconds between the three groups.

Conclusions: Dexmedetomidine in a dose of 0.2 μg/kg before applying venous occlusion by tourniquet for one minute in the same vein before inducing the patient with propofol was effective in decreasing the propofol injection pain when compared to lignocaine in a dosage of 0.5 mg/kg and placebo.

Keywords: Dexmedetomidine, lignocaine, McCrirrick and Hunter scale, propofol

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INTRODUCTION

Propofol is an intravenous (IV) sedative and hypnotic agent commonly used for induction of anaesthesia. Its rapidity and reliability in causing loss of consciousness, pleasant sleep, quick smooth recovery and little postoperative nausea

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are favourable features. However, pain on injection when given intravenously is a common problem with propofol. This pain may be distressing to the patients and can reduce the acceptability of an otherwise useful agent. In the absence of treatment regimens, 28%–90% of patients experience moderate to severe pain when propofol is injected into the peripheral vein.[1]

Propofol by an indirect action on the endothelium[2] activates the plasma kallikrein–kinin system thereby generating kinins probably bradykinin. Bradykinin produces local vasodilation and hyperpermeability which increases the contact between the aqueous phase of propofol and free nerve endings, resulting in pain on injection.[3] The pain on injection of propofol could be due to other factors such as the osmolality of the solvent used for the preparation, the pH of the solution[4,5] and concentration of the propofol in the aqueous phase of the emulsion.[6]

The main aim of the study was to know the reduction of the pain to conventional propofol when given by IV route. The reduction of pain to propofol was compared with test drugs IV dexmedetomidine (0.2 μg/kg), IV lignocaine (preservative free) (0.5 mg/kg) and control, normal saline.

MATERIAL AND METHODS

After obtaining approval from Institutional Thesis Approval Committee and Institutional Ethics Committee, 90 patients posted for elective surgery were randomly allocated into three groups by using computer-generated random numbers and opaque-sealed envelope technique: (i) Group D: (n = 30) All these patients received IV dexmedetomidine (0.2 μg/kg) diluted to 5 mL of normal saline; (ii) Group L: (n = 30) All these patients received IV lignocaine (0.5 mg/kg) diluted to 5 mL of normal saline; and (iii) Group N: (n = 30) All these patients received 5 mL of IV normal saline.

Preanaesthetic check-up was done the day before surgery and reassurance was given to all the patients participating in the study. Written informed consent was obtained from all the patients. No premedication was given as we erroneously thought that sedating the patients might have a bearing on the patient's response to pain on injection with propofol. Patients were informed about the McCrirrick and Hunter scale [Table 1][7] for assessing the intensity of pain during propofol injection. On arrival of the patient to the operating theatre, standard ISA monitors were connected. A 20-gauge IV cannula was inserted at the dorsum of the nondominant hand. We intentionally took a smaller vein for IV cannulation and subsequent study drug and propofol administration as we observed nonsignificant pain intensity scores postpropofol injection even in the saline group when we cannulated larger forearm veins as part of the pilot cases. A pneumatic tourniquet was applied on the same upper arm with a pressure inflated up to 90 mmHg to produce venous occlusion. The study drugs were preservative free and kept at room temperature. Each of the study drugs was prepared by an independent anaesthesiologist blinded to the study. The study drugs were injected over 5 s, and after 1 min, venous occlusion was released and 25% of calculated dose of propofol was given intravenously over a period of 60 s. Patients were assessed for pain intensity at 0 s, 30 s and 60 s after injection of propofol using McCrirrick and Hunter scale.[7] Post 60 s assessment of pain, remaining propofol was given and endotracheal intubation was facilitated with injection vecuronium 0.1 mg/kg.

Statistical analysis

The quantitative data such as age, weight, height and body mass index (BMI) were expressed as mean with standard deviation and compared between normal saline group, lignocaine group and dexmedetomidine group using ANOVA test. The qualitative data (categorical data) such as sex (male/female), pain scores during propofol induction at 0 s, 30 s and 60 s were expressed in frequencies with percentages, and comparison was done with Chi-square test. $P < 0.05$ is considered statistically significant. In ANOVA test if $P < 0.05$, then *post hoc* Bonferroni test was done to identify between which of the two groups got the significant difference. Statistical analysis was done using software Micrsoft Excel 2010 and SPSS version 22.

RESULTS

The patients were compared with respect to their mean age, sex, weight, height and body mass index [Table 1]. There was no statistically significant difference between the mean age, weight and mean BMI in the three study groups. The number of females outnumbered the males in the dexmedetomidine group, and the male to female ratio is more altered in the said group [Table 2].

Table 1: McCrirrick and Hunter scale

Pain intensity	Degree of pain response
None (0)	No response to questioning,
Mild (1)	Pain reporting in response to questioning only
Moderate (2)	Pain reporting in response to questioning and or pain reported spontaneously without questioning
Severe (3)	Strong vocal response accompanied by facial grimace, arm withdrawals or tears

At 0 s, i.e., at initiation of induction with propofol, the patients in the 3 groups had varying intensity of pain as assessed by McCrirrick and Hunter scale.[7] Patients in dexmedetomidine group had a comparatively milder intensity of pain when compared with lidocaine and saline groups [Table 3].

At 30 s of initiation of induction with propofol, most of the patients in dexmedetomidine and lidocaine groups had a lessened pain severity score than the saline group. Of the 3 study groups, dexmedetomidine group patients had a highly significant reduction in pain severity score ($P < 0.0001$) [Table 4].

One minute into the injection of propofol, none of patients in dexmedetomidine group and 70% of patients who received lidocaine had any pain. Twenty-three patients complained of moderate pain in the placebo group. There was a very statistically significant attenuation in pain score at 1 min of injection of propofol in the dexmedetomidine group ($P < 0.0001$) [Table 5].

DISCUSSION

Ninety, American Society of Anesthesiologists (ASA) physical Status I and II patients were randomised into 3 groups of 30 each receiving dexmedetomidine 0.2 mg/kg IV made up to 5 ml, 0.5 mg/kg lidocaine IV made up to 5 ml and normal saline 5 ml as per the group allocation. The study drugs were injected, and venous occlusion of cannula arm will be done for 1 min. After the release of venous occlusion, 25% of calculated induction dose of propofol was injected over 1 min and severity of pain to propofol injection was measured by McCrirrick and Hunter scale.[7] At all time points of assessment of pain severity (0 s, 30 s and 60 s.) following IV administration of propofol, patients in both dexmedetomidine and lidocaine groups experienced lesser pain scores than the placebo saline group patients. Of all the 3 agents, dexmedetomidine, by far, attenuates the response to pain of patients to injection of propofol [Tables 3-5].

Ever since introduction of propofol into clinical practice, it has attained unmatched popularity as an agent for IV induction. It is used for short duration surgery, day care surgery, sedation and ambulatory surgery. Very often, it has the disadvantage of causing pain or discomfort on injection. This pain may be distressing to the patients and can reduce the acceptability of an otherwise useful agent. Nature of the vascular pain is expressed by the patients as aching, burning and crushing. Mechanism of immediate pain is due to irritation of

Table 2: Comparison of demographic data between the three study groups

Variable	Group D	Group L	Group N	*P*
Age (years)	41.00±9.87	44.73±11.25	38.73±11.46	0.104
Weight (kg)	55.13±7.96	57.83±9.16	57.30±7.12	0.399
Height (cm)	157.40±7.75	161.67±7.74	164.93±9.16	0.003
BMI (kg/m^2)	22.337±3.22	22.114±3.17	21.184±3.57	0.367
Male/female	4/26	10/20	16/14	0.005

Data expressed as mean±SD.
SD=Standard deviation; BMI=Body mass index

Table 3: Severity of pain during propofol induction at 0 s

Group	None (0)	Mild (1)	Moderate (2)	Severe (3)	Total
Dexmedetomidine (%)	0	21 (70)	9 (30)	0	30
Lignocaine (%)	1 (3.33)	6 (20)	20 (66.66)	3 (10)	30
Normal saline (%)	0	0	1 (3.33)	29 (96.66)	30
Total	1	27	30	32	90
P - value			<0.0001		

Table 4: Severity of pain during propofol induction at 30 s

Group	None (0)	Mild (1)	Moderate (2)	Severe (3)	Total
Dexmedetomidine (%)	21 (70)	9 (30)	0	0	30
Lignocaine (%)	1 (3.33)	24 (80)	4 (13.33)	1 (3.33)	30
Normal saline (%)	0	1 (3.33)	6 (20)	23 (76.66)	30
Total	22	34	10	24	90
P - value			<0.0001		

Table 5: Severity of pain during propofol induction at 60 s

Group	None (0)	Mild (1)	Moderate (2)	Severe (3)	Total
Dexmedetomidine (%)	30 (100)	0	0	0	30
Lignocaine (%)	21 (70)	7 (23.33)	1 (3.33)	1 (3.33)	30
Normal saline (%)	1 (3.33)	0	23 (76.66)	6 (20)	30
Total	22	34	10	24	90
P - value			<0.0001		

afferent nerve endings within the vein. Mechanism of the delayed pain is due to activation of kallikrein–kinin system by propofol, thereby generating kinin, probably bradykinin. It produces local vasodilation and hyperpermeability which increases contact between propofol and free nerve endings resulting in pain on injection.[4]

The use of adjuvant medication before propofol to reduce the pain of injection has become a common practice. To attenuate this pain, several adjuvants have been used, such as addition of lignocaine,[8,9] pretreatment with ondansetron,[2] metoclopramide,[10] opioids[11] and thiopentone.[12] Lignocaine pretreatment is most commonly used to decrease the injection-related pain.[8,9] Unfortunately, even with the use of adjuvants, the failure rate is between 13% and 32%.[8]

Lignocaine pretreatment is most commonly used to decrease the injection-related pain. It not only works as

a local anaesthetic on the venous nociceptors but also decreases the pH value which decreases the percentage of free propofol in the aqueous phase of the emulsion and thus reduces pain on injection. Alpha$_1$ and alpha$_2$ stimulation is the mechanism involved in decreasing propofol pain by dexmedetomidine resulting in release of vasodilator prostaglandins that antagonise the venoconstrictor response. This modulates the sympathetic response of venous smooth muscle and plays an important role in endothelial dysfunction caused by propofol. Another possible mechanism is by hyperpolarisation-activated conductance in peripherally mediated antinociception, and local release of enkephalin-like substance is also possible mechanism.

Picard and Tramèr[9] conducted a systematic review of literature data from 6264 patients of 56 reports to find the best intervention to prevent pain on injection of propofol. They concluded that 0.5 mg/kg lignocaine should be given with a rubber tourniquet on the forearm, 30–120 s before the injection of propofol and found that this method will prevent pain in approximately 60% of patients.

Mangar and Holak[13] have evaluated efficacy of IV lignocaine, with and without of tourniquet, to decrease the intensity of pain during IV injection of propofol and concluded that IV lignocaine before propofol injection attenuated the painful response; whereas lignocaine administered after a tourniquet inflated to 50 mmHg for 1 min virtually abolished the pain associated with IV propofol.

Johnson *et al*.[14] studied the efficacy of lignocaine on the pain produced by IV injection of propofol using lignocaine pretreatment (20 mg and 40 mg) and lignocaine (20 mg and 40 mg) mixed with propofol. They found lignocaine 20 mg or 40 mg in either dose reduced the discomfort in comparison with propofol alone.

Turan *et al*.[15] conducted a study to determine the efficacy of dexmedetomidine and compared it with lidocaine in decreasing pain due to injection of propofol. They concluded that when compared with lidocaine, dexmedetomidine in a dosage of 0.25 μg/kg was equally effective in reducing the pain associated with the IV injection of propofol.

Feray Akgul *et al*.[16] conducted a prospective randomised double-blind study of 100 patients and compared the efficacy of single-dose premedication of dexmedetomidine for pain on injection of propofol and its effect on the incidence and the severity of the pain after propofol injection. They concluded that IV administration of a single dose of dexmedetomidine (0.6 μg/kg) as a premedication reduced the incidence and severity of pain on propofol injection without significant adverse haemodynamic effect.

Mizrak *et al*.[17] studied the effects of dexmedetomidine and fentanyl on the injection pain due to propofol, and they concluded that pretreatment with subclinical doses of dexmedetomidine (0.15 μg/kg) or fentanyl (1 μg/kg) 60 s before the administration of propofol was effective to reduce the injection pain of propofol without any significant haemodynamic side effects.

He *et al*.[18] conducted a prospective, randomised, double-blind and placebo-controlled study to evaluate the effect of dexmedetomidine for reducing the incidence and severity of propofol injection pain. Pretreatment with IV dexmedetomidine 1 μg/kg, 5 min before injection of propofol is effective and safe in reducing the incidence and severity of pain due to propofol injection.

Sapate *et al*.[19] conducted a randomised prospective study to evaluate the effect of dexmedetomidine for prevention of pain due to propofol injection in comparison with injection lignocaine and found that dexmedetomidine (0.2 μg/kg) was equally effective and can be used as an alternative to time-tested drug lignocaine (0.2 mg/kg) for relief of pain due to propofol injection without any significant side effects.

The 0.2 μg/kg dexmedetomidine dose was chosen according to the studies of Turan *et al*.[15] Sapate *et al*.[19] and Uzun *et al*.[20] found that 0.2 μg/kg dexmedetomidine decreased propofol injection pain without any adverse haemodynamic effects.

In our study, venous occlusion was applied to forearm using a pneumatic tourniquet for 1 min. The study drugs were preservative free and kept at room temperature. Each of the study drugs was prepared by an independent anaesthesiologist blinded to the study. The study drugs were injected over 5 s, and after 1 min, venous occlusion was released and 25% of calculated dose of propofol was given intravenously. Severity of pain was evaluated using McCrirrick and Hunter scale[7] at 0 s, 30 s and 60 s of propofol injection.

At 0 s, 30 s and at 60 s of induction of propofol, there was statistically significant difference in pain scores in between the three groups with $P < 0.0001$. Dexmedetomidine group was found to have lesser pain severity when compared to lignocaine group and placebo.

The main finding of the present study was the use of dexmedetomidine when given as IV pretreatment in a dosage of 0.2 μg/kg by applying venous occlusion by tourniquet for 1 min in the same vein before inducing the patient with propofol was effective in decreasing the propofol injection pain when compared to preservative-free lignocaine in a dosage of 0.5 mg/kg and placebo.

The study would have more credence if we had used a larger forearm vein for IV cannulation. The results of the study would have been more appropriate if we had included more number of patients. We were unable to access the gender difference in pain perception to propofol injection as there was no equitable distribution of sexes among the 3 groups.

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Conflicts of interest
There are no conflicts of interest.

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