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Research Article

Comparison of Effect of Lidocaine and Dexmedetomidine for Prevention of Propofol Induced Pain: A Prospective, Randomized, Double Blind Controlled Study

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Abstract: Propofol, an intravenous anesthetic widely used for general anaesthesia cause severe pain in most of people. The aim of this study was to compare effect of lidocaine and dexmedetomidine for prevention of propofol induced pain. The patients received normal saline (5 ml) in Group I, 0.5µg/kg of dexmedetomidine diluted in 5 ml normal saline in Group II, and 0.5 mg/kg of lidocaine diluted in 5 ml normal saline in Group III through intravenous route. The study drug was injected through the cannula over 5s and 25% of the induction dose of propofol (2 mg/kg) was administered over 10s by a mechanical syringe and Pain was graded using the four point scale. In control group 10%, 12%,32%, and 46% patients said no, mild, moderate, severe pain respectively while in dexmedetomine group 52%,44%, and 4% patients said no, mild and moderate pain respectively. In the lidocaine group 64%,34% and 2% patients said no, mild and moderate pain respectively. In both groups none of the patient complained severe pain. These drugs were effective in reducing the propofol injection pain compared to control group, but lidocaine was better than dexmedetomidine.
Keywords: Propofol, pain, Lidocaine and Dexmedetomidine

INTRODUCTION

Propofol is the drug of choice for induction of anaesthesia in millions of patients every year because of its rapid onset and short duration of action, easy titration, and favourable profile for side effects [1]. Despite these positive attributes, about three out of five patients experience pain on injection of propofol, with one of these patients reporting severe or excruciating pain. Some patients recall the induction of anaesthesia as the most painful part of the perioperative period. As a result several interventions have been investigated to alleviate the pain associated with propofol injection [2]. The quality of pain was described as extremely sharp, aching, or burning. It has been arranged as the seventh most important problem in current practice of clinical anesthesia by American anesthesiologists [3].

Many methods have been proposed to reduce the incidence of pain on propofol injection, including varying injection speed and carrier fluid, adjusting dilution temperature, and adding other concomitant drugs.

Peripheral veins are innervated with polymodal nociceptors that mediate the responses to an injection that cause pain [4]. Pain on injection of propofol can be immediate or delayed. Immediate pain may result from a direct irritant effect, where as delayed pain may be caused by an indirect effect via kinin cascade [5,6]. A high concentrationof free propofol in the aqueous phase of an emulsion activates the kallikreinkinin system in plasma, liberating bradykinin. Bradykinin acts on the local vein to dilate it and make it permeable. In this bradykinin-modified vein, the aqueous phaseof propofol may contact more free nerve endings outside the endothelial layer of the vessel, causing pain [7].

Among the interventions, intravenous (IV) lidocaine, atime-tested local anesthetic of the amide group, is the most commonly used drug but it has a sucess rate of 68-84% [8] in redcing propofol pain. Picard *et al.* [9] in a systematic review suggested pretreatment using lidocaine (lignocaine) in conjunction with venous occlusion as the most effective intervention.One well-accepted technique is the use of a premixture of lidocaine in propofol. Mixing lidocaine with propofol has been reported to reduce injection pain [10-12]. Lidocaine may act by local anesthetic effect on the vein and by stabilizing the kinin cascade.

On the other hand, dexmedetomidine, a highly selective, specific, and potent α2 adrenoceptor agonist, has sedative, analgesic, and sympatholytic actions, along with supraspinal, spinal, and peripheral actions, anxiolytic property and without producing significant respiratory depression It has been shown to promote

anti nociception and can be used to provide relief to propofol injection pain [13]. Its sympatholytic effect had shown to decrease MAP and HR by reducing norepinephrine release. They had also shown to decrease BIS value in the intra operative period when used as an adjuvant with other drugs given as continuous i.v. infusion [14].

The alpha-2 adrenoceptor agonist clonidine was found to alleviate the pain of injected propofol effectively [15]. Dexmedetomidine is also an alpha-2 adrenoceptor agonist, but is more selective than clonidine and has analgesic and sedative properties [16]. Dexmedetomidine has been evaluated for reducing the incidence and intensity of propofol-induced pain, but reported results are inconsistent [17].

The purpose of this study is to compare the effects of prior administration of dexmedetomidine, lidocaine and normal saline in reducing propofol injection pain.

MATERIALS AND METHODS

After the approval of the Hospital Ethics Committee of Mamatha General Hospital of Khammam,Telangana state 150 patients, aged 18 to 52 years, ASA (American Society of Anesthesiologists) physical classification I to II, and scheduled for minor elective surgery, were included in the study. All patients signed a written informed consent form. Patients were excluded if they had a history of drug abuse, chronic use of any medication, presence of neurological or psychiatric diseases, uncontrolled hypertension, or renal or hepatic insufficiency. Patients were also excluded if they had a known history of hypersensitivity to the study drugs.

Before surgery (24 h) the patients did not receive analgesics or sedatives. Upon arrival to the operating room, a 20-gauge cannula was inserted into the dorsum of the patient's hand and connected to a T-connector for drug administration. Standard ASA monitors were attached, including non-invasive arterial pressure, electrocardiography, and pulse oximetry.

All the patients were premedicated with injections of 50 mg of IV ranitidine and 0.005 mg/kg of intramuscular (IM) glycopyrrolate at least 1h before the surgery. The study drug kept at room temperature was prepared by an independent anesthesiologist not involved in the study and was divided into equal volumes of 5 ml with the addition of normal saline. The patients received normal saline (5 ml) in Group I, 0.5µg/kg of dexmedetomidine diluted in 5 ml normal saline in Group II, and 0.5 mg/kg of lidocaine diluted in 5 ml normal saline in Group III through intravenous route. The study drug was injected through the cannula over 5s and 25% of the induction dose of propofol (2 mg/kg) was administered over 10s 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, ortears suggesting severe pain. Pain was graded using the four point scale of McCrirrick *et al.* [18].

Assessment of propofol injection pain according to the McCrirrick and Hunter scale.

Degree of pain Response

None (0) No response to questioning

Mild (1) Pain reported in response to questioning alone without any behavioral signs

Moderate (2) Pain reported in response to questioning and accompanied by behavioral signs, or pain reported without any questioning

Severe (3) Strong vocal response or response accompanied by facial grimacing, arm withdrawal, or tears

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 injection of fentanyl with controlled ventilation. Patients were monitored hourly for 24 hours post surgery by a blinded investigator for adverse effects at the injection site (eg, pain, edema, wheal, flare response).

The data collected were tabulated and analyzed by usingthe statistical package for social sciences, Windows-based version 16.0 (SPSS Inc., Chicago, IL, USA). The patients' characteristics were analyzed by using one-way analysis of variance (one-way ANOVA) and chi-square test was used for comparison of the categorical data.

RESULTS AND DISCUSSION

All patients sucessfully completed the study. There were no statistically significant differences among the three groups with regard to age, weight, gender, or ASA class ($p > 0.05$).

The main objective of this study was to know the reduction of propofol pain by using Dexmedetomidine and Lidocainein different groups. In the control group about 90% people felt pain while using Dexmedetomidine 48% felt pain and lidocaine 36%people felt pain. The incidence of pain was given in table.1

Table-1: Incidence of pain on propofol injection in different groups

S.N0	Parameter	Group I Control	Group II Dexmedetomidine	Group III Lidocaine
1	Age (Mean± SD)	32.7±12.6	33.8±11.7	30.5±13.4
2	Weight (Mean± SD)	44.5±8.9	48.6±12.2	45.3±11.4
3	Sex M/F (N0)	16/34	19/31	17/33
4	Pain gradation (%)			
a	No	10%	52%	64%
b	Mild	12%	44%	34%
c	Moderate	32%	4%	2%
d	Severe	46%	0%	0%

Propofol, an excellent IV anesthetic belonging tothe phenol group, can irritate the skin, the mucousmembrane, and the venous intima. The mechanism of pain is attributed to the activation of the kinin-kallikrein system that releases bradykinin, causing vasodilatation and hyper permeability, thereby increasing contact between the aqueous phase propofol and the free nerveendings [6].

Considering the extensive use of propofol in clinical practice, the pain frequently reported on induction of anesthesia cannot be neglected. Although it is not a serious complication, efforts are assumed to reduce the severity of the pain or discomfort. Propofol belongs to the group of phenols that can irritate the skin, mucous membranes, and venous intima[18]. Injection pain associated with propofol characteristically occurs immediately or later after the drug injection with a delayed response of 10-20s [5]. The explanation for the pain includes endothelial irritation, osmolality differences, unphysiological pH, and the activation of pain mediators [19].

The number of patients who had experienced pain in contrlol was 90. % that was similar to the studies of Turan *et al.* [16] Uzun *et al.* [20] and Sarkilar *et al.* [21] who reported pain in 86.7%, 80%, and 71.1% of the patients, respectively, in their control groups.

Many methods have been used to reduce the incidence of pain on propofol injection with variable results. Lignocaine added to or given before injection of propofol is widely employed [22]. Gajraj and Nathanson[23] studied the optimal dose of lidocaine for propofol pain and concluded that 30 mg lidocaine is the optimal dose for attenuation of propofol pain. Cooling the propofol to 4°C reduces its injection pain possibly by delaying the activation of enzyme cascade of pain mediators [18]. Injecting into a large forearm vein also reduces the pain, probably by reducing contact between drug and endothelium [22].

A recent systematic review and meta-analysis showed that propofol infusion via the antecubital vein and pretreatment with lidocaine in conjunction with venous occlusion were the two most efficient interventions to reduce pain on injection of propofol [22]. However, some unexpected adverse side effects have been associated with the two methods. For some patients undergoing short-time surgery with general anesthesia, propofol infusion via a hand vein is more convenient than via an antecubital vein. Tourniquets are the most common compressive devices for venous occlusion, but can cause tourniquet-induced hypertension or even ischemia-reperfusion injury [24,25]. Therefore, venous occlusion before propofol injection may be contraindicated in patients with moderate to severe hypertension. The same condition was taken for consideration in our study.

In this study 2% lidocaine at a dose of 0.5mg/kg was used was effective in reducing the propofol pain. 64% patients had no pain, 34% people had mild pain,2% had moderate pain and no one reported severe pain. These results were in accordance with the previous studies.

King *et al* [11] observed that 20 mg of lidocaine premixed in 200 mg propofol significantly reduced the incidence of injection pain from 73% to 32%. Scott *et al*. [10] reported incidence of pain has been between 25.7% and 48.9% by addition of lidocaine. Tan and Hwang [12] reported that the incidence of propofol injection pain was reduced to 25.7% in their study population using a mixture of lidocaine 1% and propofol 1% at a 1:10 ratio. In a study Jinseok[27] by using 2 mg/kg of premixed lidocaine 1% in propofol 1% in a 1:10 ratio the incidence of pain was significantly lower in patients (36.7%) than in group C (83.3%). Lee and Russel [28] reported a decreased incidence of propofol injection pain in the propofol mixed group (2 ml of 2% lidocaine).

So far, there have been only a few studies investigating the inhibiting effect of on the pain of propofol injection using dexmedetomidine, and the question of its efficacy remains controversial.

Although the mechanisms of the analgesic effect of Dexmedetomidine have not been fully elucidated, many studies have shown that Dexmedetomidine acted by inhibiting the release of substance P from the dorsal horn of the spinal cord[28]. A recent study reported that dexmedetomidine effected strong analgesia through inhibition of the spinal ERK1/2 signaling pathway [29]. These studies suggest that dexmedetomidine has an important role in nociceptive transmission at the spinal level.

Park *et al* .[30] demonstrated that dexmedetomidine DEX had a dose-dependent analgesic effect in rat models, and Ebert and colleagues showed that increasing concentrations of in humans resulted in a progressive increase in analgesic effect. Dexmedetomidine was most effective when 1 µg/kg was injected 5 min before propofol injection. It is possible that, given this time interval, dexmedetomidine concentrations at the spinal level increased enough to result in an analgesic effect [31].

The possible mechanism reducing propofol pain might be due to alpha1 and alpha2 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 [32]. It may be due to hyperpolarization activated conductance in the peripherally mediated antinociception, but the peripheral analgesic effects of dexmedetomidine have not yet been fully elucidated. But as dexmedetomidine is more potent α2 adrenergic agonist compared to clonidine, the peripheral antinociception produced by clonidine-like drugs mediating the local release of enkephalin-like substances is also possible [33].

In this study 0.5µg/kg of dexmedetomidine was given and 52% had told no pain,44% told mild pain and 4% felt moderate pain and no one reported severe pain. Uzun et al[33] and Sarkilar et al[21] who demonstrated pain in 43% (0.25 µg/kg) and 45.5-66.3% (0.5-1 µg/kg) of the patients, respectively in the dexmedetomidine group. In a study, singh et al [34] observed that 37.14% of the patients in the dexmedetomidine(0.2µg/kg) group experienced pain as compared to 20% in the lidocaine(0.5 mg/kg) group. Turan *et al.* [16] who had reported pain in 33.34% of the patients in the dexmedetomidine (0.25 µg/kg) group as compared to 23.34% in the lidocaine (0.50 mg/kg) group. Ayoğlu et al [17] demonstrated that pretreatment with 0.25 µg/kg dexmedetomidine was reducing propofol injection pain to 60% was not effective and 0.5 mg/kg lidocaine to 36.7% is more effective. Liang He *et al.* [35] reported 0.25-0.5 µg/kg of dexmedetomidine was not effective but when the pretreatment dose of was increased to 1.0 µg/kg, the incidence rate of pain scores >2 decreased from 17/30 to 1/30.

Pretreatment with dexmedetomidine has been reported to cause significant hemodynamic adverse side effects However, Liang He et al [35] a showed that at doses of 0.5 -1 µg/kg can be safely used pre operatively, with stable hemodynamics. In this study also no one reported the bradycardia.

CONCLUSION

This study concludes that pretreatment with 0.5 µg/kg dexmedetomidine and 0.5mg/kg of lidocaine were effective in reducing the propofol injection pain compared to control group, but lidocaine was better than dexmedetomidine.

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