

Original research article

A Study of comparison of efficacy of ketamine and dexmedetomidine for prevention of pain due to propofol injection

¹Dr. Smita Vivek Harkare, ²Dr. Anita N Rao, ³Dr. Vaijayanti Sheetal Gandhi

^{1,2}Associate Professor, Department of Anesthesia, Srinivas Medical College and Research Institute, Mukka, Surathkal, Mangaluru, Karnataka, India

³Department of Anesthesia, Srinivas Medical College and Research Institute, Mukka, Surathkal, Mangaluru, Karnataka, India

Corresponding Author:

Dr. Vaijayanti Sheetal Gandhi

Abstract

Pain upon injection with propofol is a typical problem that can be quite painful to the patient. However, propofol is a popular intravenous anaesthetic induction drug that offers a smooth, quick induction with rapid clearance and recovery. Inducing agents like ketamine, which is a derivative of the drug phencyclidine, and dexmedetomidine hydrochloride, which is an imidazole molecule, are both examples of the drug class known as alpha 2 agonists. In the current study, a comparison was made between the efficacy of ketamine (0.5 mg/kg) and dexmedetomidine (0.5 mcg/kg) in lowering the severity of pain caused by propofol injection and preventing its occurrence. Ketamine was given at a dose of 0.5 mg/kg, while dexmedetomidine was given at 0.5 mcg/kg.

Keywords: Ketamine, dexmedetomidine, Comparison, efficacy, propofol injection

Introduction

Propofol is the intravenous (IV) anaesthetic medication that is used the most frequently for induction and maintenance of anaesthesia as well as for sedation inside and outside of operating theatres ^[1]. Propofol is a well-liked intravenous anaesthetic induction drug, particularly for shorter procedures, day surgeries, and situations in which a laryngeal mask airway is going to be utilised. Propofol is another drug that can be utilised in the total intravenous anaesthesia (TIVA) procedure for the purpose of keeping the patient sedated and under anaesthesia. Propofol has been shown to provide an induction that is both smooth and quick, as well as rapid clearance and recovery ^[2]. In addition to these applications, it has been utilised in the treatment of pruritis, the avoidance of emesis, and tracheal intubation without the need of neuromuscular blocking medications. Following the administration of propofol, there have been case reports of epileptiform movements, facial paraesthesia and bradycardia; nonetheless, the discomfort associated with its injection continues to be a serious problem ^[3]. Propofol is a type of alkylphenol that is also known as 2,6-diisopropyl phenol; it is a solid at room temperature and is insoluble in water, but it has a high solubility in lipids. The most recent formulation of propofol contains 1% (weight/volume) of the drug, which is then combined with 10% soybean oil, 2.25% glycerol and 1.2% purified egg phosphatide. Additionally, a bacterial growth retardant in the form of disodium edetate (0.005%) is added. Because the oil droplets that contain the majority of the propofol in this formulation are large enough to considerably reflect and refract white light, the product gives the appearance of being milky ^[4]. It's not uncommon for patients to experience pain when getting an injection of propofol, which can be very upsetting for them. It is possible for people to experience pain during the induction of anaesthesia, and the severity of this pain can range anywhere from 28% to 90% ^[5]. The prevalence of pain in children ranges anywhere from 28% to 85% of the population. Pain from a propofol injection is more common and severe in younger children ^[5]. This is especially true for very young children. The incidence of this pain is significantly higher in females ^[6]. When compared to other intravenous anaesthetic medications, propofol is known to cause a greater amount of pain during the injection process. It's possible that the discomfort won't always be a major problem, but it has the potential to clinically cause tachycardia in patients. Tachycardia is something that patients with ischemic heart disease, critical stenotic lesions, coronary artery diseases and a wide variety of other cardiac pathologies need to avoid at all costs. Patients who have pheochromocytoma and receive an injection of propofol for severe pain run the risk of experiencing an abrupt myocardial infarction ^[7]. Pain caused by propofol may provoke movements of the limbs, which may result in the unexpected removal of an intravenous line in paediatric patients. This may cause previously cooperative youngsters to become uncooperative. Chronic smokers are more likely to

get severe bronchospasm when they take propofol for pain^[8]. The vast majority of patients recall it as one of their most unpleasant experiences with their anaesthetists^[1]. All phenols are known to irritate the skin and mucous membranes. Since propofol is an alkylphenol, it is reasonable to anticipate that taking it, even if it is nearly isotonic, may result in some degree of discomfort. Some people have also referred to POPI as angialgia, which indicates that the pain is caused by involvement of the vascular system. Both an immediate and a delayed response to POPI after 10-20s are possible. The acute pain is brought on by the irritation of the venous endothelium, but the delayed pain is brought on by the release of mediators from the kinin cascade, such as kininogen^[1].

In the past, it was hypothesised that propofol might interact with sensory nerve fibres that are situated in the venous adventitia either indirectly or directly. According to a study that was published not too long ago, the nonselective ligand-gated cation channels that include transient receptor potential (TRP) ankyrin 1 (TRPA1) and TRP vanilloid 1 (TRPV1) are the primary molecular entities that are responsible for the activation of peripheral nerve endings by general anaesthetics. The ion channel known as TRPA1 can be found on the plasma membrane of many different types of cells. It is well recognised for its function as a sensor for irritants, pain, cold, and strain. It has been demonstrated that 97% of sensory neurons that are positive for TRPA1 also express TRPV1, and that 30% of neurons that are positive for TRPV1 also co-express TRPA1^[9, 10].

Aims and Objectives

Comparison of efficacy of ketamine and dexmedetomidine for prevention of pain due to propofol injection:

Materials and Methods

The current investigation was a prospective, randomised controlled trial that was conducted on 150 patients with ASA I and ASA II who were scheduled to undergo elective surgical operations under general anaesthesia. The patients were seen before to the operation, and a comprehensive pre-anesthetic checkup was performed after first receiving clearance from the relevant institutional ethical council. All of the patients who participated in this research were required to give their informed consent in writing. Participants in this study had to be between the ages of 18 and 60, have an ASA I or II classification, and be having elective surgery done while under general anaesthesia. Patients with an ASA score of III or higher, pregnant women, patients with any kind of hepatic or renal impairment, and patients with a known history of hypersensitivity to the study medicines were not allowed to participate in this research. A computer was used to assign each of the 150 patients to one of the three groups in a random fashion (there were 50 patients in each group). An anesthesiologist who was unaware of the medicine's components gave the patient the drug solution while he or she was under general anaesthesia. A pretexted proforma was used throughout the data collection process to ensure that it adhered to the aims of the study. The patients' histories, investigations, pre-anesthesia checkups, consents to surgery and anaesthesia, and neuromuscular blockade (NBM) statuses were recorded and verified. It was successful in obtaining written informed permission for the study. Patients were given the instruction to recline in the supine position with their arms resting by their sides. Baseline measurements of heart rate, blood pressure and SpO₂ were collected after the non-invasive blood pressure monitor, electrocardiogram, and pulse oximeter were installed. It was decided to begin providing supplemental oxygen at a rate of 6 litres per minute. On the dorsum of the forehead, an intravenous line was inserted using a 20-gauge gangiocath and secured in a big, clearly visible peripheral vein. An anesthesiologist who was not involved in the trial prepared all of the drugs for the study in a syringe that had a capacity of 10 millilitres and was wrapped in black tape.

Study that did not participate in the study. Premedication in the form of injections of ondansetron (0.08 mg/kg), glycopyrrolate (0.004 mg/kg), fentanyl (2 mcg/kg), and midazolam (0.02 mg/kg) was carried out as per standard procedure. Following the administration of the premedication, HR, BP, SPO₂, and Pain Scores were recorded. After this, an infusion pump was used to slowly give the test subjects their medication over a period of ten minutes, as seen in the chart further up. At 3,5 and 10 minutes, several measures of heart rate, blood pressure, oxygen saturation, and pain scores were recorded. After initiating the propofol injection at a rate of 0.2 ml/sec, several readings of the patient's heart rate, blood pressure, oxygen saturation, and pain scores were taken at the start of the propofol injection, after injecting half of the propofol dose, after injecting the whole dose of propofol, and at 1, 3, and 5 minutes after injecting the full dose of propofol.

We kept a close eye on the patient's vocal communication, as well as the frequency and severity of any discomfort they experienced, as well as any involuntary movements. A four-point scale that is going to be discussed below was used to rate how painful the injection was. After the administration of propofol injections, the level of pain was evaluated by a third anesthesiologist who was not aware of the grouping that had been assigned. After the patient had lost their corneal reflex and was able to be ventilated using a bag and mask, the patient was given an injection of vecuronium at a dose of 0.1 mg/kg. After five minutes of oxygenation, patients were intubated using direct laryngoscopy equipped with the proper

laryngoscope blade and an ET tube of the appropriate size. The ETCO₂ level was examined, and the bilateral air entry was validated. Patients were maintained within a confined space and given controlled breathing. A combination of oxygen, nitrous oxide, and sevoflurane was used to keep the patient under anaesthesia during the procedure. Additional doses of vecuronium were administered at sporadic intervals. Antagonising the remaining neuromuscular blockade was accomplished at the conclusion of the procedure by administering 0.05 mg/kg of neostigmine and 0.008 mg/kg of glycopyrrolate. When the patients were completely conscious and responding to commands, the endotracheal tubes were removed. Patients were moved to the recovery room, where an experienced staff nurse was instructed to keep a close eye on them for the next half an hour. Patients were moved to the subsequent area shortly after that. The degree of pain, their vital parameters were noted.

Note:

- Group C = Group Control.
- Group K = Group Ketamine.
- Group D = Group Dexmedetomidine.

Results

Table 1: Age Distribution

	Group C (n=50)	Group K (n=50)	Group D (n=50)
Age (year)	41.2 ± 9.37	39.6 ± 8.56	37.79 ± 7.48

Table 2: Sex Distribution

	Group C (n=50)	Group K (n=50)	Group D (n=50)
Gender (M/F)	24/26	25/25	24/26

Table 3: Pain scores

Time	Group C Mean ± S.D.	Group K Mean ± S.D.	Group D Mean ± S.D.	C vs K P value	C vs D P Value	K vs D P Value
				One way ANOVA followed by post hoc		
Base	0.059 ±0.3	00	0.082 ±0.28	>0.05	>0.05	>0.05
After Premedication	00	00	00	>0.05	>0.05	>0.05
During Injecting Study Drug	00	00	00	>0.05	>0.05	>0.05
3 minutes After	00	00	00	>0.05	>0.05	>0.05
5 minutes After	00	00	00	>0.05	>0.05	>0.05
10 minutes After	00	00	00	>0.05	>0.05	>0.05
During Injecting Propofol	2.1 ±0.85	0.07±0.24	0.31 ±0.57	.000**	.000**	>0.05
After Injecting half Propofol	1.74 ±0.77	00	0.16 ±0.37	.000**	.000**	>0.05
After Injecting Complete Propofol	1.32 ±0.62	00	0.08 ±0.27	.000**	.000**	>0.05
1 minute After Propofol	0.08 ±0.34	00	00	>0.05	>0.05	>0.05
3 minutes After Propofol	00	0.02 ±0.141	00	>0.05	>0.05	>0.05
5 minutes After Propofol	00	00	00	>0.05	>0.05	>0.05

Discussion

In the current investigation, it was found that all of the hemodynamic parameters (HR, SBP, DBP, MAP and SPO₂) and pain scores were comparable between the study groups with P values that were not statistically significant. This was the case both at the beginning of the trial and after premedication. After the drug infusion for the trial, it was discovered that the control group did not experience any significant changes in their hemodynamic parameters (HR, SBP, DBP, MAP and SPO₂) or their pain levels. In contrast, HR, SBP, DBP, and MAP were all marginally elevated compared to the baseline.

Values in group K and values that are only marginally lower than the baseline in group D. It is possible to draw the following conclusions from this research:

1. An infusion of dexmedetomidine induces a dose-dependent suppression of the central sympathetic outflow.
2. This explains the observations of bouts of bradycardia and hypotension in Group D.
3. These conclusions are supported by the data presented.

All of these shifts in parameters fell well within the range of what is considered acceptable. These shifts in group K and group D were determined to be statistically significant (P value less than 0.001) when contrasted with one another using the test. None of the aforementioned groups experienced any noteworthy shifts in their Pain Scores or SPO₂ readings during the study. Because three patients in group C experienced tachycardia (heart rate more than 120), an additional dose of one milligramme of midazolam was administered. In the group D patients who experienced episodes of bradycardia, an injection of atropine 0.6 mg bolus was administered. While injecting their respective study medicines, 2

patients in group C and 1 patient in group K had blood pressure readings that were higher than 160 millimetres of mercury (Hg), which led to the administration of a bolus of injection esmolol 30 mg.

Conclusion

According to the results of our research, it is possible to draw the conclusion that ketamine at a dose of 0.5 mg/kg and dexmedetomidine at a dose of 0.5 mcg/kg are both beneficial in lowering the frequency of Propofol injection-related pain as well as its intensity.

References

1. Desousa KA. Pain on propofol injection: Causes and remedies. *Indian journal of pharmacology*. 2016;48(6):617.
2. Aboian M, Johnson JM, Ginat DT. Propofol. In *Neuroimaging Pharmacopoeia*; c2015. p. 347-349.
3. Springer Cham, Wijesundera DN, Kavanagh BP. Prevention of pain from propofol injection.
4. Egan TD. Exploring the frontiers of propofol formulation strategy: is there life beyond the Milky Way?
5. Picard P, Tramèr MR. Prevention of pain on injection with propofol: a quantitative systematic review. *Anesthesia & Analgesia*. 2000;90(4):963-9.
6. Kang HJ, Kwon MY, Choi BM, Koo MS, Jang YJ, Lee MA. Clinical factors affecting the pain on injection of propofol. *Korean journal of anesthesiology*. 2010;58(3):239.
7. Morishima T, Sobue K, Arima H, Tanaka S, So M, Ando H, *et al*. Profound pain due to propofol injection triggered myocardial ischemia in a patient with a suspected pheochromocytoma. *Anesthesia & Analgesia*. 2003;96(2):631.
8. Zeidan A. Profound pain due to propofol injection triggered severe bronchospasm in a smoker-A case report. *Middle East journal of anaesthesiology*. 2006;18(5):939.
9. Fischer MJ, Leffler A, Niedermirtl F, Kistner K, Eberhardt M, Reeh PW, *et al*. The general anesthetic propofol excites nociceptors by activating TRPV1 and TRPA1 rather than GABAA receptors. *Journal of Biological Chemistry*. 2010;285(45):34781-92.
10. Scott RP, Saunders DA, Norman J. Propofol: clinical strategies for preventing the pain of injection. *Anesthesia*. 1988;43(6):492-4.