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Original research article

Ketamine and dexmedetomidine for prevention of pain due to Propofol injection

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Abstract

Patients frequently report experiencing excruciating discomfort upon receiving an injection of propofol, which is understandable given the nature of the situation. Propofol, on the other hand, is a well-liked intravenous anaesthetic induction agent. It allows for a smooth and speedy induction, as well as a speedy clearance and recovery. Inducing substances like ketamine, which is a derivative of the drug phencyclidine, and dexmedetomidine hydrochloride, which is an imidazole molecule, are both examples of the class of drugs known as alpha 2 agonists. Ketamine is a derivative of phencyclidine, while dexmedetomidine hydrochloride is an imidazole molecule. In the present study, a comparison was done between the efficacy of ketamine (0.5 mg/kg) and dexmedetomidine (0.5 mcg/kg) in reducing the intensity of the pain generated by propofol injection and preventing its occurrence. Both medications were given. The dose of ketamine that was administered was 0.5 mg/kg and the dose of dexmedetomidine that was administered was 0.5 mcg/kg.
Keywords: Ketamine, dexmedetomidine, Comparison, efficacy, propofol injection

Introduction

Propofol is the intravenous (IV) anaesthetic medication that is used for induction and maintenance of anaesthesia as well as for sedation inside and outside of operating theatres [1]. It is also the intravenous medicine that is used the most commonly for sedation. Propofol is a well-liked intravenous anaesthetic induction agent, particularly for shorter procedures, day surgeries, and circumstances in which a laryngeal mask airway is going to be used. It is also utilised in scenarios where a halothane gas is going to be used. Propofol is another medication that may be administered to the patient during the total intravenous anaesthesia (TIVA) process in order to maintain the patient's state of anaesthesia and sedation throughout the duration of the treatment. It has been demonstrated that propofol enables an induction that is both smooth and rapid, in addition to rapid clearance and recovery [2]. In addition to these applications, it has been used in the treatment of pruritis, the prevention of emesis, and the intubation of the trachea without the use of drugs that impede neuromuscular activity. There have been case reports of epileptiform movements, facial paraesthesia, and bradycardia following the administration of propofol; despite this, the discomfort associated with its injection continues to be a significant issue [3]. Propofol is a form 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. Propofol is used to treat a variety of medical conditions, including sedation and respiratory depression. The most recent formulation of propofol includes the medication at a concentration of 1% (weight/volume), which is then mixed with 10% soybean oil, 2.25% glycerol, and 1.2% purified egg phosphatide. This results in the formulation. In addition to that, 0.005% of disodium edetate is included as a growth inhibitor for bacteria in the form of a bactericide. The product gives the appearance of being milky because the oil droplets that contain the majority of the propofol in this formulation are large enough to significantly reflect and refract white light [4]. This gives the product its characteristic milky appearance. When receiving an injection of propofol, it is not unusual for patients to experience pain, which can be quite distressing for them. It is conceivable for individuals to feel pain during the process of inducing anaesthesia and the degree of discomfort that these individuals report can range anywhere from 28% to 90% [5]. The percentage of children who experience pain might range anywhere from 28-85 percent of the total population. Younger children are more likely to experience and be more distressed by the pain caused by a propofol injection [5]. This is something that should be emphasised to children who are very young. There is a statistically significant gender difference in the prevalence of this discomfort [6]. Propofol is

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known to induce a larger level of discomfort during the injection process as compared to other drugs that are administered intravenously for the purpose of providing anaesthesia. Although it's likely that the pain won't always be a severe issue, it still has the potential to create tachycardia in patients when it comes to practical applications. Patients who suffer from ischemic heart disease, critical stenotic lesions, coronary artery illnesses, and a broad variety of other cardiac pathologies should do everything in their power to steer clear of tachycardia. Patients diagnosed with pheochromocytoma who receive an injection of propofol for the treatment of severe pain run the risk of suffering an unexpected myocardial infarction [7]. Pain brought on by propofol may prompt movement of the limbs, which in paediatric patients may result in the unexpected removal of an intravenous line. It's possible that kids who were previously agreeable will become uncooperative as a result of this. When chronic smokers take propofol for pain, there is an increased risk that they will get severe bronchospasm [8, 1]. It was one of the most terrible encounters that the vast majority of patients had with their anaesthetists, according to their recollections. It is common knowledge that skin and mucous membranes become irritated when exposed to any phenol. Because propofol is an alkylphenol, it is realistic to predict that ingesting it, even though it is almost isotonic, may result in some level of discomfort. This is the case even though it is nearly isotonic. Some people have also referred to POPI as angialgia, which suggests that the pain is caused by involvement of the vascular system. This is a term that has been used by some people. It is possible to have an immediate response to POPI as well as a delayed response after 10-20 seconds. Pain can be divided into two categories: acute pain and delayed pain. Acute pain is caused by the irritation of the venous endothelium, while delayed pain is caused by the release of mediators from the kinin cascade, such as kininogen [1].

In the past, it was hypothesised that propofol could interact with sensory nerve fibres that are located in the venous adventitia in either a direct or indirect fashion. This was one of the hypotheses that was tested. According to a study that was published not too long ago, the primary molecular entities that are responsible for the activation of peripheral nerve endings by general anaesthetics are nonselective ligand-gated cation channels. These channels include transient receptor potential (TRP) ankyrin 1 (TRPA1) and TRP vanilloid 1 (TRPV1). There is a wide variety of cell types, each of which contains a plasma membrane that contains an ion channel called TRPA1. Its role as a sensor for irritants, discomfort, cold, and strain is well-known and well-respected in the medical community. It has been proven 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]. Additionally, it has been shown that TRPA1 is co-expressed by 97% of neurons that are positive for TRPV1.

Aims and Objectives

Evaluation of the analgesic effects of ketamine and dexmedetomidine in comparison to the painkilling effects of propofol injection.

Materials and Methods

- This study was a prospective, randomised controlled experiment that was carried out on 150 patients with ASA I and ASA II who were scheduled to undergo elective surgical operations under general anaesthesia. The patients were all planned to receive general anaesthesia during the procedures. After obtaining approval from the appropriate institutional ethical committee, the patients were evaluated prior to the operation, and a thorough pre-anesthetic checkup was carried out on each one of them. It was needed that each and every patient who took part in this study submit a written statement indicating that they had read and understood the information provided to them. In order to take part in this study, individuals needed to be between the ages of 18 and 60, classified as ASA I or II, and in the process of undergoing elective surgery while under the influence of general anaesthesia. Patients with an ASA score of III or higher, pregnant women, patients with any form of hepatic or renal impairment, and patients with a known history of hypersensitivity to the study drugs were not permitted to take part in this research. Patients with an ASA score of IV or higher were also excluded.
- A computer was used to randomly place each of the 150 patients into one of the three groups (there were 50 patients in each group). There were three groups totaling 150 patients. While the patient was under general anaesthesia, the drug solution was administered by an anesthesiologist who was unaware of the components of the medication. Throughout the entirety of the process of data collection, a pretextted proforma was utilised to guarantee that the data collected was in line with the objectives of the study. We documented and checked the patients' histories, investigations, pre-anesthesia examinations, consents to surgery and anaesthesia, and neuromuscular blockade (NBM) statuses. The written informed permission needed for the investigation was successfully obtained. Patients were given the order to lie down in the supine position with their arms at their sides while they were being examined. After the non-invasive blood pressure monitor, ECG and pulse oximeter were implanted, baseline measures of heart rate, blood pressure, and SpO2 were acquired. It was agreed that supplemental oxygen should be administered at a rate of 6 litres per minute. An intravenous line was placed on the dorsum of the forehand with the assistance of a 20-gauge

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gangiocath and then secured in a large peripheral vein that was easily discernible. A syringe with a volume of 10 millilitres that was wrapped in black tape was used by an anesthesiologist who was not participating in the trial to prepare all of the medicines that were going to be used in the study.

- Study participants who opted out of taking part in the study. Premedication was administered in the form of injections of fentanyl (2 mcg/kg), ondansetron (0.08 mg/kg), glycopyrrolate (0.004 mg/kg), and midazolam (0.02 mg/kg). This was done in accordance with the standard operating procedure. After the premedication was given, readings were taken of the patient's heart rate, blood pressure, oxygen saturation, and pain score. Following this, an infusion pump was used to provide the test subjects' medication over a period of ten minutes in a gradual and steady manner, as can be seen in the chart further up. At 3.5 and 10 minutes, a number of measurements including pain scores, heart rate, blood pressure, and oxygen saturation were recorded. At the beginning 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, several readings of the patient's heart rate, blood pressure, oxygen saturation, and pain scores were taken. The propofol injection was started at a rate of 0.2 ml/sec.
- We maintained a close check on the patient's vocal communication, as well as the frequency and degree of any discomfort they encountered, in addition to any involuntary movements they could have made. To determine how painful the injection was, we employed a four-point scale, which will be covered in more detail in the following paragraphs. After the patient had been given injections of propofol, the intensity of pain was assessed by a third anesthesiologist who was unaware of the grouping that had been allocated to the patient. After the patient had lost their corneal reflex and was able to be ventilated using a bag and mask, the patient was then given an injection of vecuronium at a dose of 0.1 mg/kg. This was done in order to prevent the patient from experiencing any further complications. After five minutes of oxygenation, patients were intubated using direct laryngoscopy utilising equipment that included the appropriate laryngoscope blade as well as an ET tube of the appropriate size. Both the $ETCO_2$ level and the bilateral air entry were investigated and tested for accuracy. Patients were kept in a confined environment and their breathing was monitored and controlled at all times. During the procedure, the patient was maintained in a state of anaesthesia with a mixture of oxygen, nitrous oxide, and sevoflurane. Vecuronium was given in random doses as a supplement throughout the course of the procedure. At the end of the procedure, 0.05 mg/kg of neostigmine and 0.008 mg/kg of glycopyrrolate were given to the patient in order to reverse the neuromuscular blockade that had been produced. After the patients had regained full consciousness and were able to respond to the doctors' instructions, the endotracheal tubes were removed. The patients were transferred to the recovery room, where an experienced member of the nursing staff was given the directive to keep a watchful eye on them for the subsequent thirty minutes. Almost immediately after that, patients were transferred to the subsequent area. The patients' vital data, as well as the level of pain, were recorded.

Note:
Group A= Group Control.
Group B= Group Ketamine.
Group C= Group Dexmedetomidine.

Results

Table 1: Age Distribution

	Group A (n=50)	Group B (n=50)	Group C (n=50)
Age (year)	39.2 ± 7.37	38.6 ± 7.56	41.2 ± 6.87

Table 2: Sex Distribution

	Group A (n=50)	Group B (n=50)	Group C (n=50)
Gender (M/F)	26/24	24/26	24/26

Table 2: Pain scores

Time	Group A Mean ± S.D.	Group B Mean ± S.D.	Group C Mean ± S.D.	A vs BP value One way ANOVA followed by post hoc	A vs CP Value One way ANOVA followed by post hoc	B vs C 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

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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 this examination, it was discovered 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 for all of the hemodynamic measures and pain scores. This was the situation both before and after the premedication was administered throughout the trial. Following the medication infusion that was part of the experiment, it was found out that the control group did not experience any significant changes in either their hemodynamic parameters (HR, SBP, DBP, MAP, and SPO2) or their levels of discomfort. In contrast, heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were all slightly higher than their baseline values in group K, whereas values in group D were only slightly lower than their baselines.

The following are some of the conclusions that can be drawn 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 that have been presented.

Every one of these alterations to the criteria fell squarely within the realm of what might be categorised as permissible. When compared to one another using the test, these changes in group K and group D were found to be statistically significant (with a P value that was lower than 0.001). During the course of the research, the participants in none of the aforementioned groups reported any appreciable changes in either their Pain Scores or their SPO_2 values. As a result of the occurrence of tachycardia (defined as a heart rate of more than 120 beats per minute) in three of the patients in group C, an additional dose of one milligramme of midazolam was given. An injection of atropine 0.6 mg bolus was given to the patients in group D who had bouts of bradycardia. These patients had previously been evaluated. During the process of injecting their individual study medications, two patients in group C and one patient in group K had blood pressure readings that were higher than 160 millimetres of mercury (Hg). As a result, a bolus of injectable esmolol 30 mg was given to each patient as an additional precautionary measure.

Conclusion

According to the findings of our study, it is feasible to draw the conclusion that a dose of ketamine at 0.5 mg/kg and a dose of dexmedetomidine at 0.5 mcg/kg are both useful in minimising the frequency of Propofol injection-related pain as well as its intensity. This is the conclusion that can be drawn from the findings of our study.

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