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ORIGINAL RESEARCH

Determination of low dose Intravenous Ketamine for Pain Relief associated with Intravenous Propofol Injection

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Abstract

Background: Propofol is a common intravenous drug for anaesthetic use which is responsible for distressing pain at the site of injection. Pre medication with Ketamine is one of the methods recommended to alleviate the pain at the site of Propofol injection because of its local anaesthetic characteristic. The purpose of this study was to determine the efficacy of a low dosage (100 mcg/kg body weight) intravenous Ketamine in reducing intravenous Propofol injection pain using the McCrirrick and Hunter scale. **Materials and Methods:** Total 88 adult patients of American Society of Anesthesiologists (ASA) Physical status I and II of both genders undergoing elective surgical procedure under general anaesthesia were randomly assigned into two groups. Group-A has 44 patients who were Pre-treated with Ketamine 100 mg/kg body weight or 1ml where as Group- B with same number of patients (44 patients) were pre-treated with 0.9% of Normal Saline or 1ml. Both, group A and group B were evaluated using McCrirrick and Hunter method at 5,10 and 15 seconds of interval. **Results:** The comparison of groups A and B using the McCrirrick and Hunter Evaluation Scale at 5, 10, and 15 second intervals was statistically significant (p value 0.005). In comparison to group B, none of the individuals in group A suffered moderate or severe pain at all three periods. Mc Crirrick and Hunter assessment score's mean values were statistically significant across all time periods. The two group's hemodynamic parameters, EtCO2 and SpO2 were equivalent. There was no evidence of any negative consequences in either group. **Conclusion:** Intravenous Ketamine injection at a dosage of 100mcg/kg body weight with a tourniquet as a pretreatment before Propofol was effective in considerably lowering the occurrence and severity of pain while having no adverse haemodynamic impact.

Key words: Anesthetic drug, Pain, Ketamine, Propofol

Introduction

Since its introduction into clinical practise in the early 1980s, propofol has become the most popular intravenous (IV) anaesthetic for sedation, maintenance, and induction of anaesthesia. It is linked to restful sleep, quick healing, and little postoperative nausea and vomiting. Its

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main disadvantage is that it hurts where the injection is made [1]. Propofol injections intravenously result in injection site discomfort, which is commonly characterised as extreme or intolerable. Sixty percent of patients who got propofol report feeling discomfort, where as twenty percent reporting severe pain. The incidence of discomfort following a propofol injection varies from 28% to 90%. For numerous patients, the most agonising part of the perioperative phase was the propofol induction of anaesthesia [2,3]. Clinical dosages of 1-2 mg/kg body weight of ketamine, an anaesthetic drug, produce dissociative anaesthesia. It is well renowned for having strong analgesic and topical anaesthetic effects [4,5]. When used at subanesthetic dosages, it can help lessen the pain associated with propofol injections because of its local anaesthetic characteristic[6,7]. The release of kininogens upon propofol's interaction with the vascular endothelium may be one of the chemical mechanisms responsible for the discomfort associated with propofol injections. The afferent free nerve terminals that connect the media and the intima make up the sensory pathway [8]. Ketamine's local anaesthetic effects are attributed to voltage-sensitive sodium channel interactions or opioid mu-receptor antagonism at the N-methyl D-aspartate (NMDA) receptors, which have been identified [9] in the vascular endothelium. Thus, ketamine administered prior to therapy may function as a preventive analgesic, preventing unpleasant inputs from sensitising the nearby nerve endings. In this study, we investigated the potential of low-dose ketamine to alleviate the pain associated with propofol injections in the dorsal hand vein, as well as the hemodynamic effects of this combination of medications and any potential side effects, such as emergence phenomena, that may arise from the administration of low-dose ketamine.

Material and method

This study was carried out at the Rama Medical College Hospital and Research Centre, Kanpur in the Department of Anaesthesia. It took the shape of a double-blind, prospective, randomised, placebo-controlled study. Patients with ASA grades 1 or 2, who were between the ages of 18 and 65 and weighted between 35 and 75 kg, were listed for minor surgery. Individuals with a documented history of allergies or convulsions, those taking sedatives, analgesics, or antipsychotics, expectant mothers and nurses, patients in need of quick sequence induction, and those in whom problematic airway was predicted were excluded from the study.Following Ethics Committee approval, 88 patients were signed up with their informed, valid, and written consent. Group B received normal saline as a control, while Group A received ketamine as a pretreatment. The investigation was carried out for duration of one year. The night before surgery, every patient received a visit and an explanation of the entire process. Before surgery, they were given instructions to rate any pain every ten seconds while propofol was being administered. Prior to surgery, they were kept off food for six hours. According to institutional procedure, they were given a tablet of Diazepam 0.2 mg/kg body weight, a tablet of Pantoprazole 40 mg the night before surgery, and an intramuscular injection of morphine 0.1 mg/kg, promethazine 12.5 mg, and glycopyrrolate 0.2 mg 45 minutes before operation. A functional suction was tested, the anaesthesia machine and circuit were examined, different sized laryngoscope blades were examined and maintained, and facemasks of various sizes, oropharyngeal and nasopharyngeal airways, and stylets were maintained. Every emergency medication was kept on hand. In the initial attempt, a 20 gauge venous cannula was put into a vein on the dorsum of the patient's non-dominant hand, and a bivalve was attached to enable injections. It was linked to a 5 ml/kg/hr saline 0.9% infusion. The pretreatment medication was injected after the three-way tap was shut off to saline. The patients were administered 10 mg of ketamine in a volume of 1 ml or 1 ml of 0.9% normal saline by a blinded operator who did not know the contents of the injection solution.The three-way tap was opened to the saline infusion and a 3 ml bolus of 1% propofol was administered over the course of three seconds following a 30-second pretreatment with either saline or the study medication. Prior to the procedure, the pain scale was explained to each

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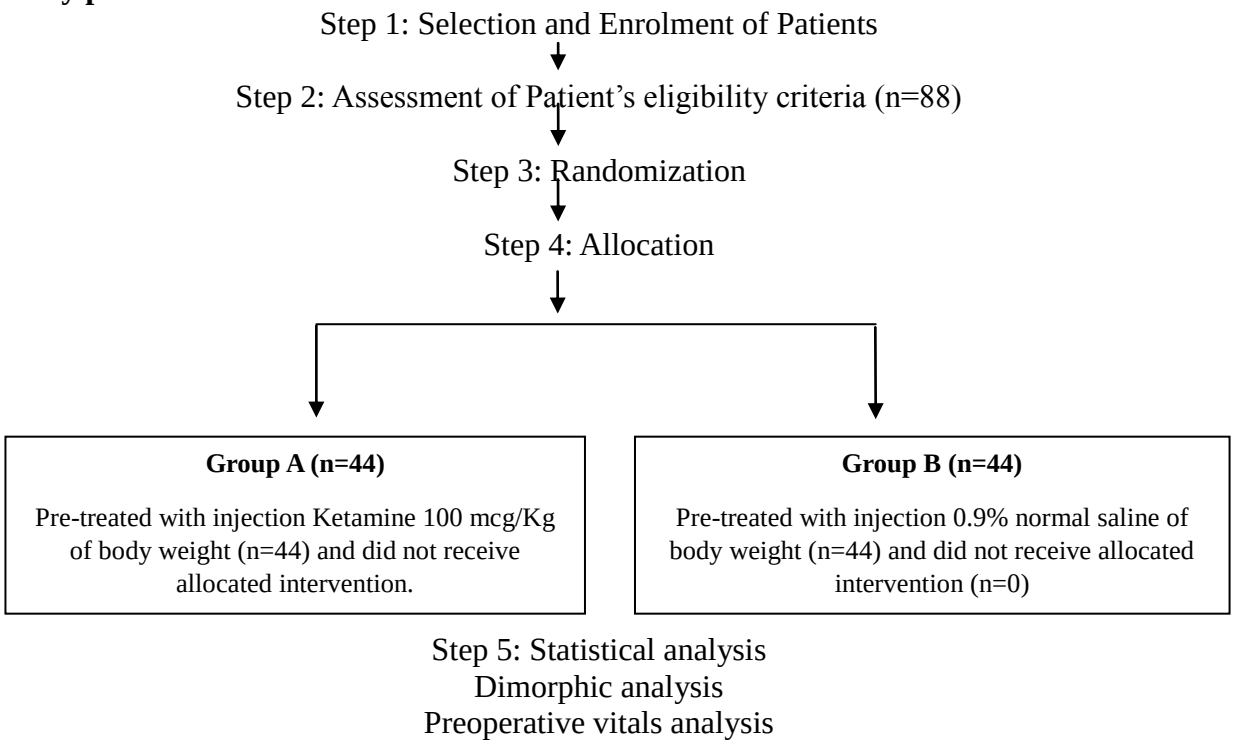
patient. Before administering a propofol injection, a question about any discomfort in the hand or arm was asked of each patient. Based on the verbal pain score, it was scored.
0 – No pain.
1 – Mild pain (discomfort in the hand or arm which is acceptable to the patient)
2 – Moderate pain (discomfort in hand or arm which is unacceptable)
3 – Severe pain (grimace or limb withdrawal)

Verbal rating scale by McCrirrick		
Scale	**Response**	**Interpretation**
0	No response to the questions	No pain
1	Pain recorded 'yes' but only in response to the question without any behavioral change.	Mild pain.
2	Voluntary complaint of pain or behavioural Changes.	Moderate pain
3	Strong verbal response or facial grimacing or arm withdrawal or tears on injection	Severe pain

Prior to the test medication being administered and shortly before intubation, the initial vital signs were recorded. Additionally, the peripheral oxygen saturation was noted. Peripheral nerve stimulators were used to monitor the patients during the procedure, and vecuronium top-up doses were supplemented based on train of four responses. Following surgery, intravenous neostigmine (0.05 mg/kg body weight) and glycopyrrolate (0.01 mg/kg body weight) were used to reverse the neuromuscular blockade. Following the completion of the reversal, patients were extubated on a table.
All patients were kept under observation in the post-operative ward following surgery. Patients were monitored for any irregularities in their behaviour, such as delirium, illusions, or hallucinations, which were promptly reported.

Study plan



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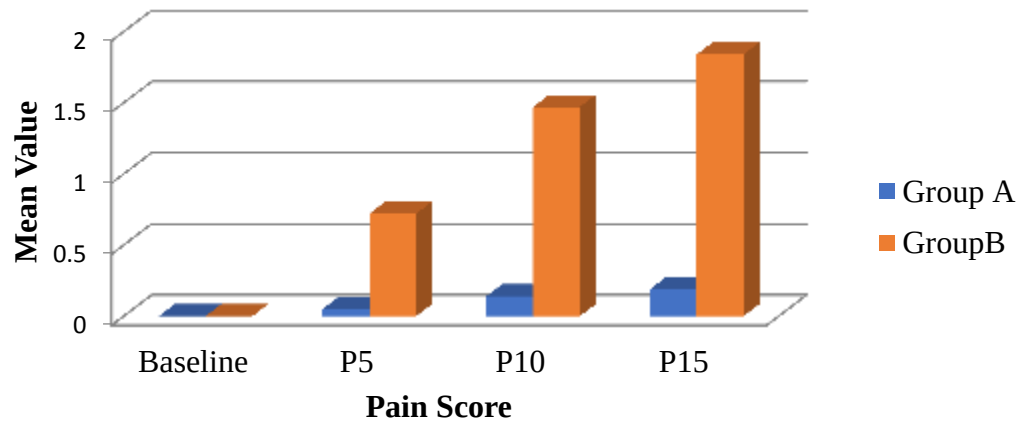
Result

Total 88 patients were selectedduring the study period and randomly divided into two groups of 44objects in each group. Both groups were compared in terms of patient demographics and preoperative vitals as mention in material and methods. Equal number of males and females were set in both groups. The mean age of groups was as group-A patients 32.8 (± 4.1SD) years and group B 34.3 (± 6.4SD) years. Mean body weight of group-A 60.2 (± 5.3) and group-B 63.8 (± 7.3SD) years. The demographic profile of both groups is mentioned in table no.1.

Table No. 1: Demographic profile of the patients

Parameters		Group A	Group B
Mean Age ± SD (in year)		32.8 ± 4.1	34.3 ± 6.4
Gender	Male	22 (50%)	22 (50%)
	Female	22 (50%)	22 (50%)
Body weight		60.2 ± 5.3	63.8± 7.3

Chart No. 1: Comparision of McCrirrick and Hunter Evaluation for mean of pain score Group-A and Group-B



Pain score by McCrirrick and Hunter evaluation method has been observed. The score mean values were statistically significant at all three time intervals between both the groups A and B (Chart No 1).

The difference in pain scores according to the McCrirrick and Hunter assessment scale between groups A and B at P5, P10, and P15 intervals was statistically significant (*p* value 0.005). None of the patients in group A has experienced moderate or severe pain at all three time intervals as compared to group B (saline group) patients, (Table 3).

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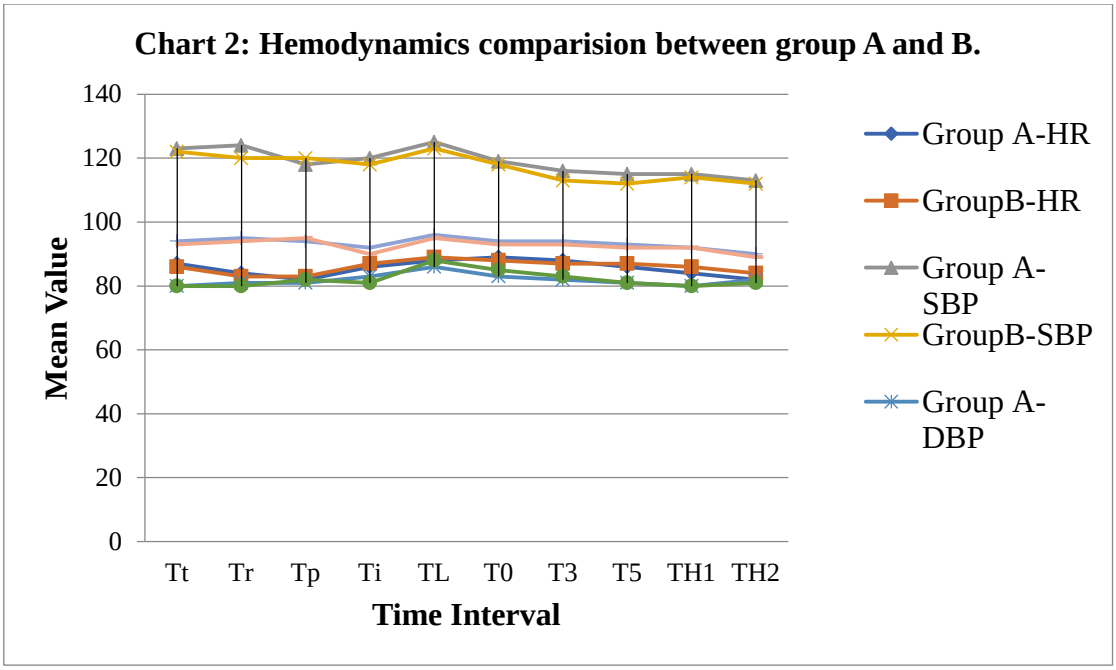

Both groups A and B were equivalent, with no significant differences in the patients' hemodynamic profiles, as shown in Chart no. 2. Furthermore, the mean EtCO2 and SpO2 levels remained within normal limits and were similar. There was no evidence of any detrimental effects in either group of patients.

Table No. 2: Preoperative profile of the patients

Parameter	Group A	Group B
Heart Rate (per minute)	87.4±10.8	85.3 ± 11.6
Systolic Blood Pressure (mmHg)	121.3 ± 12.4	123.8 ± 9.7
Diastolic Blood Pressure (mmHg)	78.8 ± 8.6	79.3 ± 12.3
Respiratory Rate (per minute)	18.6 ± 2.6	19.4 ± 3.1
SpO2 (%)	99.1 ± 0.6	99.3 ± 0.7

The table presents a comparison of vital signs between Group A and Group B. The key points include heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate, and SpO2 levels. Both groups show similar values, with slight variations in their respective averages and standard deviations.

Table 3: Comparison of patient's pain score according to McCrirrick and Hunter scale evaluation between two groups.

		Number of Patients					
		At P5 interval		At P10 interval		At P15 interval	
Score	**Interpretation**	**Group A**	**Group B**	**Group A**	**Group B**	**Group A**	**Group B**
0	**None**	44	18*	29	28	38	12*
1	**Mild**	0	12*	7*	12	5	17*
2	**Moderate**	0	13	3	3	1	8*
3	**Severe**	0	11*	5*	1	0	7*
Total no. of patients with pain		0	36*	15	16	6	32*
***P* value < 0.005 Statistically Significant**							

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A concise summary of the data shows that there is a statistically significant difference (*P* value < 0.005) between Group A and Group B in terms of pain experienced by patients at various intervals (P5, P10, P15). The total number of patients with pain was higher in Group B at all intervals, which suggests potential variations in pain management and outcomes between the two groups.

Discussion

Propofol is first medication for day care surgery preferred by many anaesthesiologists s a result of its quick induction along with clear-headed recovery. It is reported to induce hypnosis in one arm brain circulation time with minimum excitement. Propofol, a Phenol group medication, has the drawback of irritating mucous membranes and skin. The mechanism of pain induced by Propofol has been related to the release of kininogen from the vein wall, which results in the activation of the local kinin cascade. Now a day patients assess the quality of anesthesia in anaesthesia practice by recalling any pain or discomfort they experienced during operation. When solely Propofol is used for induction, it has been observed that two third of patients would suffer discomfort after the first dose. As a result, preventing pain during Propofol injection is particularly desirable because pain appears to be a limiting factor in an otherwise beneficial medicine.We employed a tourniquet at 70 mmHg for 60 seconds to isolate the arm vein from the rest of the circulatory system in order to evaluate the drug's peripheral activity in the absence of its central action.It also permits analgesics to operate on endothelium nociceptors, which are the primary location of local anti-nociceptive activity. Ketamine pretreatment is a well-established pharmacological method for reducing the nociceptive response to Propofol injection. Ketamine (a Phenylcyclidine derivative) is a powerful analgesic and local anesthetic. [5]As an NMDA receptor antagonist, Ketamine may activate these receptors in the vascular endothelium or the central nervous system. At low doses, Ketamine has a powerful analgesic effect. Ketamine, like cocaine, has structural similarities and hence generates analgesia via a local mechanism.Ketamine is linked with less cardiorespiratory depression than other local analgesic medications.It has been noted that discomfort after a Propofol injection might be immediate or delayed. Mattila MA et al colleagues hypothesized that acute pain is caused by a direct irritating action, but delayed pain is caused by an indirect impact via the kinin cascade. [6]It has been realized that discomfort from Protocol injections can be instantaneous or delayed. C.H. Tan and coworkers hypothesized that acute pain is caused by a direct irritating action, but delayed pain is caused by an indirect impact via the kinin cascade. The latency of delayed pain is 15 to 20 seconds. [9]Therefore, we decided to perform a time graded response assessment to determine the effect of Ketamine on both immediate and delayed pain generated by Propofol injection.The pain score was measured every 5 seconds until 15 seconds after receiving one-fourth of the total estimated dosage of Propofol.At 5 seconds interval, 12 patients (27.3%) experienced mild pain and 13 patients (29.5%) experienced moderate pain and 11 (25.0%) patient experienced severe pain in group B (Saline group) as compared to none in group A (Ketamine group). Thus, total patients who experienced pain in group B was 36 (81.8%) patients as compared to none in group A which was statistically significant (p value <0.005). At 10 seconds interval, 7 (15.9%) patients experienced mild pain, 3 (6.8%) patients experienced moderate pain and 5 (11.4%) patients experienced severe pain in group A as compared to 12 (27.3%) patients in group B mild pain, 3 (6.8%) patients moderate pain and only 1 (2.3%) patients severe pain was reported in group B. Thus, total number of patients experiencing pain were 16 (36.4%) patients in group B as compared to 15 (34.1%) patients in group A (p value<0.005). Whereas at 15 seconds interval, mild pain was experienced in 5 (11.4%) patients in group A as against 17 (38.6%) patients in Group B. Moderate pain was reported by 8 patients (18.2%) of Group B as compared to 1

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(2.3%) in Group A. In group A 9 (20.5%) patient experienced severe pain as compared to 7 (15.9%) patients in Group B. Thus, total patients 32 (72.7%) experienced pain in group B as compared to 15 (34.1%) patients in group A, which was significant statistically, (*p* value <0.005). These results are similar to the studies conducted by Johnson RA et al, [7], Roehm KD et al [8], Sangwar MA et al [10] and Kad N et al [11].

Conclsion

Pain due to propofol injection is still a general problem in practice of anesthesia despite introduction of new formulations. The approach to reduce or eliminate pain due to propofol, pretreatment with Ketamine before Propofol gave an excellent result. It significantly reducing the incidence and severity of pain related to Propofol administration as an induction agent.

Conflict Of Interest

None

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