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Original Research Article

A CLINICAL STUDY COMPARING PROPOFOL-KETAMINE AND PROPOFOL-BUTORPHANOL COMBINATIONS FOR TOTAL INTRAVENOUS ANESTHESIA FOR SHORT SURGICAL PROCEDURES

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ABSTRACT

Background: Aim: To compare the effects of total intravenous anaesthesia using the propofol-ketamine and propofol-butorphanol combinations.
Materials and Methods: Sixty patients of Siddhartha Medical College & Hospital, scheduled to undergo short surgical procedures, with physical status ASAI and ASAII, in the age group 18 - 60 years, of both sexes were randomly selected. They were divided into 2 groups at random and given propofol-ketamine in group PK and propofol-butorphanol in group PB. Propofol 1. 5 mg/kg IV was used to induce in both groups, and propofol 9 mg/kg IV was used for maintainance.
Results: In the TIVA approach, maintaining hemodynamic stability, minimising pain from propofol injections, and preventing PONV are controversial issues that cannot be fully resolved. Both systolic and diastolic blood pressure decreased after induction in both groups. Group PB experienced a significant difference in systolic and diastolic blood pressure upon arrival, during induction, and at various points throughout the course of surgery. Group PK did not experience such a significant difference. Instead of ketamine, butorphanol pretreatment reduced pain after a propofol injection. Group PB (propofol-butorphanol) experienced more postoperative sedation than group PK. (propofol –ketamine). PONV: No statistically significant difference existed between the two groups.
Conclusion: In conclusion, we discovered that the combination of propofol and ketamine (GroupPK) had the benefit of providing greater hemodynamic stability and postoperative recovery in terms of sedation.
Keywords: Ketamine, Propofol, Hemodynamic, Postoperative sedation.

INTRODUCTION

Present-day total intravenous anaesthesia (TIVA) employs a number of different medication types, each of which serves a particular purpose. According to conventional thinking, all of them should have a quick rate of clearance and a short latency between changes in infusion rates, plasma levels, and pharmacological effects. This enables quick induction, a stable plane of anaesthesia during surgery, smooth emergence afterward, and quick recovery.[1]

Due to the increased accessibility of syringe/infusion pumps with the requisite capabilities, interest in TIVA for the induction and maintenance of anaesthesia is developing.

A more recent intravenous anaesthetic with a favourable pharmacokinetic profile is propofol. It has already become widely used for the induction and maintenance of anaesthesia during brief surgical procedures.[5] Almost all patients find propofol to be pleasant. It is eminently suitable for infusion because of its high clearance rate and quick drop in blood concentration. When the propofol infusion is

stopped, the patient quickly comes out of the anaesthetic state.[2,3]

The phencyclidine medication class includes the water-soluble intravenous anaesthetic ketamine. In addition to being less expensive than fentanyl and butorphanol, it is the only intravenous anaesthetic with hypnotic, analgesic, and amnesic effects.[3]

Ketamine and propofol are not suitable as the only anaesthetic agents. The most typical adjuvant, an opioid analgesic, is adequate to deliver full anaesthesia. While ketamine elevates both the cardiac index and mean arterial pressure, propofol decreases both.[4]

Therefore, in this study, we contrasted two medication regimens for the TIVA technique in patients having brief surgical operations, namely propofol-ketamine and propofol-butorphanol.

Propofol is combined with the synthetic opioid butorphanol to generate analgesia. Although butorphanol offers effective analgesia, it is also known to have side effects such drowsiness, dizziness, and cardiodepressant activity.[5]

Aims and Objectives

To compare the effects of total intravenous anaesthesia using the propofol-ketamine and propofol-butorphanol combinations in terms of:

1. Stable hemodynamics
2. To investigate how propofol injections affect the effects of eliminating pain
3. Postoperative nausea and vomiting as well as postoperative sedation

MATERIAL AND METHODS

Data Source

Sixty patients of Siddhartha Medical College & Hospital scheduled to undergo short surgical procedures, with physical status ASAI and ASAII, in the age group 18 - 60 years, of both sexes were randomly selected.

Following the patient's informed consent, the study was conducted with the ethics and research committee of the hospital's clearance. Patients who needed muscle relaxation, those who anticipated having a difficult time breathing through their mask, those with psychological illnesses, those using thyroid medication, those who were hypertensive, and those who had heart disease were not included in the study.

Design

60 participants were enrolled in the trial and were divided into two groups at random.

30 individuals in Group PK received a propofol-ketamine combo.

Group PB: Thirty patients received a combination of propofol and butorphanol.

For the purpose of excluding cardiorespiratory disease and determining any drug and method contraindications, a thorough history and physical examination were performed before to the administration of anaesthesia.

For each patient, routine investigations such as haemoglobin %, bleeding and clotting times, and others were performed. No additional research was conducted specifically for this study.

Thirty minutes prior to surgery, diazepam IV injection (0. 1 mg/kg) was administered to all of the patients. A line of 18 gauge cannulas was begun for an infusion as soon as the patient entered the operating room. Each patient had a connection to an ECG monitor, NIBP, and pulse oximeter.

Methods for data collection

Propofol-ketamine was used to produce anaesthesia in Group PK, and propofol-butorphanol was used in group PB, both at the proper dosage based on body weight. At regular intervals, readings from the pulse oximeter, NIBP, and ECG were taken.

While administering propofol, patients were continuously monitored for verbal response, grimacing, arm withdrawal, or tears that would indicate pain. Ramsay Hunt's sedation scoring system was utilised to assess sedation in the post-operative period. PONV incidence was observed.

Statistical Analysis

Data were entered in MS-Excel and analyzed in SPSS V25. Descriptive statistics were represented with percentages for qualitative data, Mean with SD for quantitative data. Shapiro wilk test was applied to find normality. Chi- square test, Fisher Exact test were applied for comparison of proportions. Independent t-test was applied for comparison between mean. P& lt;0.05 was considered as statistically significant.

RESULTS

The current study involved 60 patients who were undergoing elective brief surgical procedures under TIVA and who met the physical standards for Grade I and Grade II anaesthesia by the American Society of Anesthesiology. Patients of both sex between the ages of 18 and 60 were included in this study.

In the ketamine group, the age distribution was 41.07□9.42 years, while it was 39.77□10.5 5 years in the butorphanol group. [Table 1]

Comparing the two groups revealed that it was statistically insignificant.

Out of 30 patients in the ketamine group, 15 (50%) were male and 15 (50%) were female. Out of 30 patients in the butorphanol group, 12(40%) were male patients, and 18 (60%) were male patients. Between the two groups, there was no statistically significant difference. [Table 2]

The baseline SBP was 134. 57±13. 64mm of Hg in the ketamine group and

135. 53 ±13. 20 mm of Hg in the butorphanol group. Statistics-wise, both groups were comparable.

SBP was 135. 10±14. 50mm mm of Hg in the ketamine group and 140. 50±11. 02 mm of Hg in the butorphanol group at arrival. Both groups were statistically comparable.

SBP was measured at induction in the ketamine group at 137. 07□12. 74mm mm of Hg and in the group butorphanol at 120. 10±13. 89 mm of Hg. With a p value of <0.001.

The difference in SBP between the two groups was statistically highly significant.

SBP measured at10 minutes inketamine group was 135. 60±12. 59 mm of Hg and in butorphanol group it was 119. 13±13.36mm of Hg. The difference inSBPin2groupswas Statisticallyhighly significant with ap value <0.001 which is highly significant.

SBP at 20 minutes in the ketamine group was 135.90±12. 46 mm of Hg, while it was 119.13±13.36mmhg in the butorphanol group. SBP in the two groups differed statistically significantly from one another. Thep value is, 0.001 which is highly significant.

SBP at 30 minutes was 133.33±11.51mmhg in the ketamine group and 123.63±13.36mmhg in the butorphanol group. Statistically, the difference in SBP between the two groups was highly significant (p 0. 004).

SBP at 40 minutes was 134.22±10.54mmhg in the ketamine group and 126.40±14. 22 mm of Hg in the butorphanol group. SBP between the two groups differed in a statistically significant way with a p value 0.045. [Table 3]

The baseline DBP was 84.40 7±.07mmhg for the ketamine group and 81.17±6.38 mmhg for the butorphanol group. Both groups had comparable statistical characteristics

DBP was 84.40±7. 07mm of Hg in the ketamine group and 82.50 ±6.64 mm of Hg in the butorphanol group upon arrival. Both groups were statistically comparable

On induction, DBP in the butorphanol group was 81.97 ±7. 47mm of Hg and 69.07 ±7.48 mm of Hg in the ketamine group. Statistics showed that there was a significant difference with a p value,0.001.

DBP was 79.57 4±.19 mm Hg in the ketamine group and 68.40±5.68 mm Hg in the butorphanol group at 10 minutes. Statistically, the difference in DBP was highly significant. P value (<0.001).

DBP was 80.90±7.0 mm of Hg in the ketamine group and 70.87±6.00 mm of Hg in the butorphanol group at 20 minutes. The difference between the two groups was statistically significant. P value (<0.001)

DBP at 30 minutes was 78.00± 6.54 mm of Hg in the ketamine group and 71.93±4.47 mm of Hg in the butorphanol group. The difference was statistically significant with a p value <0.001

DBP was statistically significant at a 40-min interval and was 79.09±6.54 for the ketamine group and 72.80± 6.30 for the butorphano l group.the difference. [Table 4]

Baseline heart rates for the ketamine group were 76. 80±5.52 and 73.47± 4.92 in the ketamine group, respectively. Both groups can becompared statistically. But clinically not significant.

The mean heart rate upon arrival in the ketamine group was 77.93±5.38 while in the butorphanol group it was 78.50±7.74 Statistics-wise, both groups were comparable.

The difference in the mean heart rates at induction in the ketamine andbutorphanol groups 78.57±5.33 and 73.00±8.22, respectively was statistically significant. Pvalue=0.003

At 10 minutes, the mean heart rates were 78.07±35.53 in the ketamine group and 71.07±. 6.57 in the butorphanol group. There was statistically significant difference between the two groups. P value <0.001

There was a substantial difference between the mean heart rates at 20 minutes between the group ketamine and group butorphanol, which was 79. 47±7.10 and 71.07±6.57 respectively. two groupswere statistically significant. p value 0.002

At 30 minutes, the mean heart rate in the ketamine group was 78.30±6.23 and in thebutorphanol group was 69.37±4.86Statistics showed that the difference was significant with p value 0.0023. [Table 5]

At 40 minutes, the mean heart rates in the ketamine and butorphanol groups were 80. 70±8.35and 70.10±5.58±respectively. This difference was extremely significant. P value<0.001

In group PK, 18 of the 30 participants reported experiencing discomfort after receiving a propofol injection (60%). Only 6 patients (20%) in groupP B complained of pain after receiving a propofol injection. etween the two groups, there was a statistically significant difference. P value 0.003. [Table 6]

Out of the 30 patients investigated in groupPK, 10 (33.3%) had postoperative sedation, compared to 18 (60%) in group PB. Although there was no statistically significant difference between the two groups when compared, it is obvious that group PB had a high prevalence of sedation. [Table 7]

6 of the 30 participants in group PK who were studied—or 20%—complained of PONV after surgery. In group PB, 6 participants (20%) reported having PONV. When the incidence of PONV in the two groups (40%) was examined, it was not statistically significant. P value=1. [Table 8]

Table 1: Distribution of age in study groups

Age	Group-PK		Group-PB	
	Count	%	Count	%
20-30	7	23.3%	7	23.3%
30-40	5	16.7%	7	23.3%
40-50	13	43.3%	11	36.7%
50-60	5	16.7%	5	16.7%
Total	30	100.0%	30	100.0%
P=0.92				

Table 2: Sex distribution in study groups

Sex	Group-PK		Group-PB	
	Count	%	Count	%
Male	15	50.0%	12	40.0%
Female	15	50.0%	18	60.0%
Total	30	100.0%	30	100.0%
P=0.6				

Table 3: Comparison of SBP in both study groups

SBP	Group-PK		Group-PB		P-value
	Mean	SD	Mean	SD	
At Base Line	134.57	13.64	135.53	13.20	0.781
At Arrival	135.10	14.50	140.50	11.92	0.121
At Induction	137.07	12.74	120.10	13.89	**<0.001**
At 10 min	135.60	12.59	119.13	13.36	**<0.001**
At 20 min	135.90	12.46	123.73	12.10	**<0.001**
At 30 min	133.33	11.51	123.63	13.36	**0.004**
At 40 min	134.22	10.54	126.40	14.22	**0.045**

Table 4: Comparison of DBP in both study groups

DBP	Group-PK		Group-PB		P-value
	Mean	SD	Mean	SD	
At Base Line	84.40	7.07	81.17	6.38	0.068
At Arrival	82.93	7.32	82.50	6.64	0.811
At Induction	81.97	7.47	69.07	7.48	<0.001
At 10 min	79.57	4.19	68.40	5.68	<0.001
At 20 min	80.90	6.70	70.87	6.00	<0.001
At 30 min	78.00	6.14	71.93	4.47	<0.001
At 40 min	79.09	6.54	72.80	6.30	0.003

Table 5: Comparision of heartrate changes in both groups

HR	Group-PK		Group-PB		P-value
	Mean	SD	Mean	SD	
At Base Line	76.80	5.52	73.47	4.92	**0.016**
At Arrival	77.93	5.38	78.50	7.74	0.743
At Induction	78.57	5.33	73.00	8.22	**0.003**
At 10 min	78.07	5.53	71.07	6.57	**<0.001**
At 20 min	79.47	7.10	71.33	4.18	**<0.001**
At 30 min	78.30	6.23	69.37	4.86	**<0.001**
At 40 min	80.70	8.35	70.10	5.58	**<0.001**

Table 6: Comparision of POI in both study groups

POI	Group-PK		Group-PB	
	Count	%	Count	%
Positive	18	60%	6	20%
Negative	12	40%	24	80%
Total	30	100%	30	100%
P=0.003				

Table 7: Comparison of POS in both groups

POS	Group-PK		Group-PB	
	Count	%	Count	%
Positive	10	33.3%	18	60.0%
Negative	20	66.7%	12	40.0%
Total	30	100.0%	30	100.0%
P=0.04				

Table 8: Comparison of PONV in both study groups

PONV	Group-PK		Group-PB	
	Count	%	Count	%
Positive	6	20%	6	20%
Negative	24	80%	24	80%
Total	30	100%	30	100%
P=1				

DISCUSSION

Total intravenous anaesthesia, the most current version of GA, has experienced significant modification since it was first used in surgery. Total intravenous anaesthesia (TIVA) is a procedure where volatile medications are replaced with intravenous

drug administration. In addition to providing a quick and painful recovery and a lower incidence of PONV. TIVA has other advantages over inhalation anaesthetic that make it suitable for daycare procedures. The risk of malignant hyperthermia and environmental dangers are reduced by its relative lack of noxiousness. TIVA provides many advantages over inhalational anaesthesia, including less cardiac depression, a negligible neuro-humoral reaction, and lower oxygen use.[1]

All anesthesiologists have been interested in total intravenous anaesthesia since it is the most effective way to prevent operating room contamination. TIVA was initially explored with a single medication (such as thiopentone or propofol), however this was linked with adverse effects, andit was discovered that no agent could provide total anaesthesia.

The availability of quick-acting analgesics, muscle relaxants, and sedative hypnotics has brought total intravenous anaesthesia back into focus. The introduction of the continuous infusion device has increased the popularity and practicality of TIVA administration.

But as of right now, there isn't a single intravenous medication that can fulfil all of anesthesia's needs (i. e. unconsciousness, analgesia and muscle relaxation).

Therefore, it is necessary to administer a variety of agents in order to get the desired outcomes. Drug interactions become crucial and significant as a result.

Exaggerated reactions could happen when utilising higher total ketamine dosages, giving it more quickly than usual, combining ketamine with sedatives, barbiturates, or opiates, and lengthier recovery durations should be anticipated,[6], Propofol-ketamine (group PK) and propofol-butorphanol (group PB) medication regimens were tested for the TIVA approach.

When comparing group PK to group PB in our study, there was no statistically significant difference in heart rate, systolic blood pressure, or diastolic blood pressure throughout the post-induction and maintenance of anaesthesia throughout the procedure in group PK.

A different study from 2016 assessed the efficacy of two medication combinations, Propofol with ketamine (PK) and Propofol with fentanyl, (PF)on 100 elective surgery candidates. This study demonstrates that, as compared to ketofol, PF composition causes a noticeably lower pulse rate, SBP, and DBP during the anaesthesia induction stage. The effects of PK are more stable during the maintenance period. In the recovery phase, the PF group scored higher for movement and awaking than the ketofol group did for ventilation. Overall, it has been found that both medication groups provide anaesthesia quickly, safely, and with little side effects and hemodynamic consequences.

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Dunnihoo and colleagues used propofol-ketamine to evaluate the effects on cardiovascular response and wakefulness. The y value indicated that this combination maintained greater haemodynamic stability, and heart rate and arterial blood pressure did not significantly fluctuate during the surgery.[7]

The primary results of this study are typical peak increases of 34% in pulse rate (PR), SBP is 22%, 24% in DBP, and 23% in mean arterial pressure (MAP). These results are close to Virtue et al. 16's research, which noted a 34% rise in PR and a 23% elevation in the MAP following the anaesthesia induction with 2.2 mg/kg in adults.

Heart rate, systolic and diastolic blood pressure, as well as post-induction and intraoperative haemodynamic variables, were tracked in the current investigation in group B. We discovered that the heart rate significantly decreased statistically following induction and throughout the maintenance phase of anaesthesia. When propofol-butorphanol was used to induce and maintain anaesthesia, a considerable reduction in both systolic and diastolic blood pressure was also seen.

Mayer and colleagues,[4] carried out a study in which they contrasted the hemodynamic and analgesic effects of propofol-ketamine.

A randomised, double-blind trial was carried out by Saha and colleagues8 they had taken 60 patients undergoing minor surgery, to determine the effectiveness of the combination of propofol, ketamine, and fentanyl. Following the administration and maintenance of anaesthesia with propofol and

fentanyl,[1] they demonstrated a substantial reduction in heart rate. Additionally, a considerable drop in systolic blood pressure was seen.

We came to the conclusion that a single dose of ketamine administered during the induction of anaesthesia was sufficient to counteract propofol's cardiodepressant effects. Ketamine group had greater hemodynamic stability during anaesthesia maintenance than butorphanol group. Patients in this group were more sedated because butorphanol accelerated the reduction in arterial blood pressure that occurred following propofol induction.

Sedation incidence varied between the two groups, it was discovered. In the butorphanol group, the incidence was 60%, compared to 33.[3]

In a different investigation, Croizer and colleagues 9 contrasted the impact of TIVA with that of ketamine-propofol on the haemodynamic, endocrine, and metabolic stress response to alfentanyl-propofol. 2mg/kg Ketamine or 0.05 mg/kg alfentanil, followed by 1 mg/kg propofol, were used to produce anaesthesia. Propofol was infused to maintain anaesthesia at a starting rate of 15 mg/kg/hr, which was later decreased to 5 mg/kg/hr after 30 minutes. In contrast to propofol alfentanil, they discovered that the combination of propofol and ketamine maintained hemodynamic stability throughout the procedure.

Sheppard's 10 study compared the effects of ketamine and propofol on breathing, postoperative mood, perception, and cognition. They came to the conclusion that a propofol and ketamine combination induced a positive mood state during the recovery period without causing any negative side effects.

The combination also appeared to prompt early recovery of cognitive function. This may be due to the fact that propofol inhibits NMDA receptors in hippocampus neurons, which may have contributed to the positive effect on mood. Sedative effects of propofol are partially antagonized by arousal effect of ketamine.[10]

In a double-blinded trial with ambulatory surgical patients, butorphanol IV preinduction dosages of 20 micrograms/kg, 40 micrograms/kg, or a 2 micrograms/kg dose of fentanyl were compared for the frequency of postanesthesia adverse effects and durations to reach "benchmarks" in the recovery process. In all study areas, the authors predicted that all medications would perform equally well. 60 ASA physical status I and II females undergoing laparoscopic tubal ligation were divided into one of three groups at random: As a preinduction agent, butorphanol was given to Group I (n = 20), Group II (n = 20), and Group III (n = 20) at a rate of 20, 40, and 2 micrograms per kilogramme, respectively. Anesthesia management for all groups was the same. Statistically significant variance was found in time to discharge-ready status and duration of nausea (p value less than 0.05) between 40 micrograms/kg butorphanol and 2 micrograms/kg fentanyl, but no significant difference was found between 20 micrograms/kg butorphanol and 2 micrograms/kg fentanyl in these areas. Statistically significant variance was found in duration of dizziness and time to obtain a 10 on the Aldrete Post Anesthesia Recovery Score (APARS) between 40 micrograms/kg butorphanol and 20 micrograms/kg butorphanol and 40 micrograms/kg butorphanol and 2 micrograms/kg fentanyl. From the study, 20 micrograms/kg butorphanol appears to be as suitable as 2 micrograms/kg fentanyl for use as a preinduction narcotic analgesic, whereas 40 micrograms/kg butorphanol appears to be unsuitable due to increased duration of nausea, dizziness, and time to score 10 on APARS and reach discharge-ready status.As a result of the study, it appears that 20 micrograms/kg butorphanol is equally suitable to be used as a preinduction narcotic anti - inflammatory agent as 2 micrograms/kg fentanyl, whilst 40 µg butorphanol does seem to be unsuitable due to the prolonged duration of nausea and dizziness as well as the longer time it takes to score 10 on the APARS and become discharge-ready status.

Propofol injection pain can be reduced using a variety of techniques, including injecting the drug into a big vein or carrier fluid and using antiemetics, analgesics, and anaesthetic medications.

Of the 2 groups under study, the butorphanol group was able to eliminate the pain from a propofol injection. In group PB, the prevalence of pain was 20%, whereas in the ketamine group, it was 60%. This is congruent with research by Agarwal and colleagues, who discovered that straightforward and Butorphanol pretreatment before to taking propofol is an efficient way to reduce the pain it causes.

PONV, which is the rate limiting factor in patient discharge from the postoperative ward, is one significant drawback of TIVA. In our study, group PK had a 20.0% incidence of PONV while group P B had a 20.05% incidence. Between the two groups, there was statistically negligible difference.

These findings are comparable to those of a study by W. Etchler and group 10 which discovered no difference between butorphanol and fentanyl in the incidence of PONV when used as a pre-induction agent.

Fospropofol is the brand name for the sodium salt of 2,6-diisopropylphenoxymethyl phosphate, which itself is water-soluble and less painful to inject.[11] To produce sedative effects, propofol, a prodrug, must initially be transformed from fospropofol. The liver and endothelium both contain alkaline phosphatases, which are in charge of the enzymatic conversion. So, 4–8 minutes after injection, the effect starts to take effect. In contrast to propofol's quick commencement of action, when a dosage of,[10] mg/kg is utilised, the onset of effect takes place almost 7 minutes later.[12]

All phenols irritate mucosal membranes and skin. Propofol is an alkylphenol, therefore even though it is practically isotonic, it is expected to produce pain. Some people have also referred to POPI as angialgia,[13] implying that the pain is caused by

vascular involvement. POPI is both immediate and delayed after 10–20 seconds.[14] While delayed pain is caused by the generation of mediators like kininogen from the kinin cascade, immediate pain is caused by irritation of the venous endothelium.

The type of operation, the level of intraoperative stimulation, the use of local anaesthetic blocks, and the patient's ventilatory condition all affect the recommended target levels for propofol and remifentanil. Target-controlled infusion anaesthesia and paediatric complete intravenous anaesthesia benefit from the use of processed eeg monitoring, especially when neuromuscular blockade is present.

CONCLUSION

In conclusion, we discovered that the combination of propofol and ketamine (GroupPK) had the benefit of providing greater hemodynamic stability and postoperative recovery in terms of sedation. The sole additional benefit of the propofol-butorphanol (Group PB) combination was a reduction in the pain experienced after injection. With either medication, PONV occurred at the same rate.

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