

# Assessment of Efficacy of Two Drug Combinations in Patients Undergoing Total Intravenous Anesthesia: A Comparative Study

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## ABSTRACT

**Background:** Propofol/ketamine combination, used in total intravenous anesthesia (TIVA), is assayed in patients with abdominal diseases presenting surgical and anesthesiological risk of a varying degree. Combining local anesthesia and sedation which provides a painless condition without reflexes is definitely accompanied by maximum cooperation of the patients and a more practical situation to perform the surgeries. Hence; present study was done to assess and compare the efficacy of two drug combinations in patients undergoing total intravenous anesthesia.

**Materials & Methods:** The present study included assessment and comparison of efficacy of two drug combinations in patients undergoing total intravenous anesthesia. A total of 50 patients were included in the present study and were broadly divided into two study groups as follows: Group 1: patients who were given intravenous Propofol–ketamine combination, and Group 2: patients who were given intravenous Propofol–fentanyl combination. Recording of the baseline parameters was done. Induction of anesthesia was done in all the subjects according to their respective study groups. Stopping of all the anesthetic drugs was done five to seven minutes before the anticipated end of the surgery. Re-recording of all the parameters was done half an hour after the surgery. All the results were recorded in Microsoft excel sheet and were analyzed by SPSS software.

**Results:** Significant results were obtained while comparing the mean pulse rate in between both the study groups at induction, intubation and intraoperative time. However; postoperatively no-significantly results were obtained while comparing the mean pulse rate in between subjects of the two study groups. Non-significant results were obtained while comparing occurrence of side-effects in between subjects of both the study group.

**Conclusion:** Both the drug combinations used in the present study with equal efficacy.

**Key words:** Anesthesia, Intravenous, Propofol.

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## Article History:

Received: 24-01-2017, Revised: 20-02-2017, Accepted: 15-03-2017

### Access this article online

Website: <a href="http://www.ijmrp.com">www.ijmrp.com</a>	Quick Response code 
DOI: 10.21276/ijmrp.2017.3.2.091	

## INTRODUCTION

Propofol/ketamine combination, used in total intravenous anesthesia (TIVA), is assayed in patients with abdominal diseases presenting surgical and anesthesiological risk of a varying degree. Ketamine has already played a safe and effective role as a sole anaesthetic agent with a few limitations like delayed recovery, emergence phenomenon and nausea and vomiting.<sup>1,2</sup> Subsequently, there is an increase in the use of propofol due to its favourable pharmacokinetics. However, propofol is associated with dose-dependent respiratory depression, hypotension and no intrinsic analgesic property. Addition of fentanyl to propofol compliments the analgesic property.<sup>3,4</sup>

Combining local anesthesia and sedation which provides a painless condition without reflexes is definitely accompanied by maximum cooperation of the patients and a more practical

situation to perform the surgeries. There are several methods of sedation; however, propofol results in rapid recovery and no atmosphere pollution with anesthetic pollutants, the features which were considered from the beginning of its use in anesthesia. It has always been tried to reduce the adverse effects of propofol regimen by adding other drugs such as sedatives and narcotics as much as possible.<sup>5,6</sup>

In the quest for complete anesthesia, various combinations of these new drugs have been tried which include midazolam–ketamine, propofol–ketamine, propofol–fentanyl and many more each with varying results.<sup>7-9</sup>

Hence; present study was done to assess and compare the efficacy of two drug combinations in patients undergoing total intravenous anesthesia.

**MATERIALS & METHODS**

The present study was carried out in the Department of Anaesthesia, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, Uttar Pradesh (India) and it included assessment and comparison of efficacy of two drug combinations in patients undergoing total intravenous anesthesia. Ethical approval was obtained from the ethical committee of the institution and written consent was obtained from all the patients after explaining in detail the entire research protocol. A total of 50 patients were included in the present study and were broadly divided into two study groups as follows:

**Group 1:** Patients who were given intravenous Propofol–ketamine combination, and

**Group 2:** Patients who were given intravenous Propofol–fentanyl combination

Complete demographic data and clinical details of all the patients were obtained. Exclusion criteria for the present study included:

- Patients with presence of any other co-morbid condition,
- Patients with history of any known drug allergy
- Patients with presence of any metabolic disorder

Ranitidine tablets were given as premedication 2 hours prior to induction of anesthesia. In all the subjects of both the study groups, standard anesthetic technique was used. Recording of the baseline parameters was done. Induction of anesthesia was done in all the subjects according to their respective study groups. Stopping of all the anesthetic drugs was done five to seven minutes before the anticipated end of the surgery. Re-recording of all the parameters was done half an hour after the surgery. All the

results were recorded in Microsoft excel sheet and were analyzed by SPSS software. Chi-square test was used for assessment of level of significance. P-value of less than 0.05 was taken as significant.

**RESULTS**

A total of 50 patients were analyzed in the present study and were broadly divided into two study groups. Mean age of the subjects of the group 1 and group 2 was 45.2 and 44.2 years respectively. Mean weight of the subjects of the present study was 69.8 Kg and 73.1 Kg respectively. There were 15 males and 10 females in group 1 and 14 males and 11 females in the group 2 as shown in Table 1. Mean pre-induction pulse rate among subjects of group 1 and group 2 was 83.50 and 84.12 respectively. Mean pulse rate at the time of induction of anesthesia among subjects of group 1 and group 2 was 83.25 and 75.24 respectively. Mean pulse rate at the time of intubation among subjects of group 1 and group 2 was 89.64 and 78.76 respectively. Significant results were obtained while comparing the mean pulse rate in between both the study groups at induction, intubation and intraoperative time as shown in Table 2. However; postoperatively no-significantly results were obtained while comparing the mean pulse rate in between subjects of the two study groups. Most common side effects seen in subjects of both the study groups were nausea, vomiting, secretions and laryngospasm. Non-significant results were obtained while comparing occurrence of side-effects in between subjects of both the study group.

**Table 1: Demographic data**

Demographic parameter		Group 1	Group 2
Mean age (years)		45.2	44.2
Gender	Males	15	14
	Females	10	11
Mean weight (Kg)		69.8	73.1

**Table 2: Comparison of pulse rate**

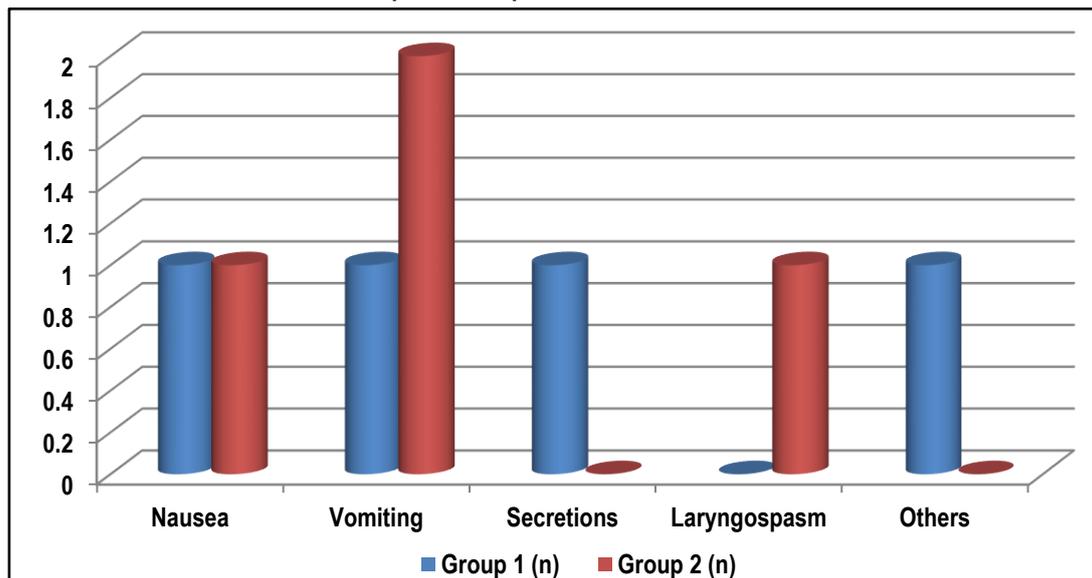
Mean Pulse rate	Group 1	Group 2	P- value
Pre-induction	83.50	84.12	0.22
Induction	83.25	75.24	0.02*
Intubation	89.64	78.76	0.03*
Intraoperative	85.78	88.94	0.01*
Postoperative	86.87	84.25	0.85

\*: Significant

**Table 3: Occurrence of postoperative adverse effects**

Side effect	Group 1 (n)	Group 2 (n)	P- value
Nausea	1	1	0.52
Vomiting	1	2	
Secretions	1	0	
Laryngospasm	0	1	
Others	1	0	

Graph 1: Postoperative adverse effects



## DISCUSSION

Propofol is the most suitable agent for total intravenous anaesthesia (TIVA), as it has a short context-sensitive half-time. Fentanyl, a  $\mu$  (MOP) opioid agonist, is used in many species to provide analgesia during propofol anaesthesia. In goats, it has a short half-life following intravenous (IV) injection, and is therefore suitable for CRI. Midazolam, a water-soluble benzodiazepine, is used as a sedative, muscle relaxant and an anticonvulsant in human patients.<sup>10,11</sup> In the present study, a total of 50 patients were analyzed in the present study and were broadly divided into two study groups. Mean age of the subjects of the group 1 and group 2 was 45.2 and 44.2 years respectively. Mean weight of the subjects of the present study was 69.8 Kg and 73.1 Kg respectively. Singh Bajwa SJ et al compared two drug combinations of TIVA using propofol-ketamine and propofol-fentanyl and to study the induction, maintenance and recovery characteristics following anesthesia with these techniques. A hundred patients between the ages of 20 and 50 years of either gender were divided into two groups of 50 each, and they underwent elective surgery of approximately 1 h duration. Group I received propofol-ketamine while group II received propofol-fentanyl for induction and maintenance of anesthesia. Propofol-fentanyl combination produced a significantly greater fall in pulse rate (PR; 9.28% versus 0.23%) and in both systolic (7.94% versus 0.12%) and diastolic blood pressures (BP; 8.10% versus 0.35%) as compared to propofol-ketamine during induction of anesthesia. Propofol-ketamine combination produced stable hemodynamics during maintenance phase while on the other hand propofol-fentanyl was associated with a slight increase in both PR and BP. During recovery, ventilation score was better in group I while movement and wakefulness score was better in group II. Mean time to protrusion of tongue and lifting of head was shorter in group I. Both propofol-ketamine and propofol-fentanyl combinations produce rapid, pleasant and safe anesthesia with only a few untoward side effects and only minor hemodynamic effects.<sup>10</sup>

In the present study, mean pre-induction pulse rate among subjects of group 1 and group 2 was 83.50 and 84.12 respectively. Mean pulse rate at the time of induction of

anesthesia among subjects of group 1 and group 2 was 83.25 and 75.24 respectively. Mean pulse rate at the time of intubation among subjects of group 1 and group 2 was 89.64 and 78.76 respectively. Significant results were obtained while comparing the mean pulse rate in between both the study groups at induction, intubation and intraoperative time. However; postoperatively no-significant results were obtained while comparing the mean pulse rate in between subjects of the two study groups. Hernández C et al compared the characteristics of induction, maintenance and awakening for three techniques of combined total intravenous anesthesia (TIVA): propofol-ketamine, midazolam-ketamine and propofol-fentanyl. Sixty patients were randomly assigned to three TIVA groups. Group 1 (n = 20) received midazolam, ketamine and vecuronium. Group 2 (n = 20) received propofol, ketamine and vecuronium. Group 3 (n = 20) received propofol, fentanyl and vecuronium. Perfusion of midazolam-ketamine was accompanied by a significantly higher number of hypertensive peaks. Time to awakening was significantly shorter in Group I (11.8 +/- 5 min) than in group 2 (20.2 +/- 12.5 min); in group 2 time to awakening was 16.6 +/- 5.6 min. Eight patients in group 1, 5 in group 2 and 1 in group 3 reported having bad dreams, the difference between groups 1 and 3 reaching statistical significance. TIVA with ketamine and propofol is comparable to the most commonly used combination of propofol and fentanyl and may be an appropriate choice when hemodynamic stability is of great importance; withdrawal 15 min before ending surgery prevents prolonged awakening.<sup>11</sup>

In the present study, most common side effects seen in subjects of both the study groups were nausea, vomiting, secretions and laryngospasm. Non-significant results were obtained while comparing occurrence of side-effects in between subjects of both the study group. Mayer M et al investigated whether the combination of propofol and ketamine can give better hemodynamic stability during the induction and maintenance of general anesthesia than propofol used with fentanyl, whose cardiodepressant actions may cumulate. For induction of general anesthesia 10 patients (ASA I and II) each received 3-5 boluses of propofol (0.5 mg.kg<sup>-1</sup> during 35 s until predetermined level of anesthesia was reached (stage D2/E0 according to [20]) followed

by a continuous propofol infusion (0.120 mg.kg-1.min). Fentanyl 0.1 mg was administered to each patient in group A for induction of anesthesia and again if evident pain was present. In group B ketamine was given following a pharmacokinetic model based on computer-simulated calculation. In both groups a moderate drop of mean arterial pressure (MAP) was observed after the induction of general anesthesia. Two patients in each group showed a distinct decrease in MAP (-32%). The heart rate dropped slightly (-9%) in group A, but did not change in group B. Following intubation the MAP rose by less in group A (+8%) than in group B (+21%). The dose of ketamine administered during the induction of general anesthesia may have been not high enough to neutralize the cardiodepressant effect of propofol.<sup>12</sup>

## CONCLUSION

Under the light of above obtained data, the authors conclude that both the drug combinations used in the present study with equal efficacy. However; further studies are recommended.

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**Source of Support:** Nil. **Conflict of Interest:** None Declared.

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**Cite this article as:** Rangit Priyakar Pandey. Assessment of Efficacy of Two Drug Combinations in Patients Undergoing Total Intravenous Anesthesia: A Comparative Study. *Int J Med Res Prof.* 2017; 3(2):434-37. DOI:10.21276/ijmrp.2017.3.2.091