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Original Research Article

Comparative Evaluation of Propofol-Ketamine and Propofol-Fentanyl Combination For minor Surgical Procedures

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Conflict of interest: Nil

Abstract

Combining a sedative agent with an analgesic agent for short surgical procedures done under intravenous sedation can offer a lot of advantages especially when short acting agents are chosen. In our study we combined propofol with either ketamine or fentanyl and formed two groups of patients undergoing short surgical procedures with 40 members in each group. Group I received Inj ketamine 0.5 mg/kg over 2 minutes followed by Inj propofol at rate of 1 ml over 3 seconds tillthe end point of induction. Group II received injection fentanyl 1.5 µg/kg followed by 1 ml propofol till the end point of induction. Parameters assessed include hemodynamics, recovery profile and complications. Data were collected and analysed using appropriate statistical tests.

Results: Demographic profile was comparable between the two groups. Pulse rate, systolic bloodpressure, respiratory rate were statistically better in Group I(Ketamine) and diastolic blood pressure and saturation were comparable. But clinically the changes were insignificant. Recoveryprofile was better with Group II. Complications like pain at the site of injection, PONV were morein Group II.

Conclusion: Both combinations are clinically effective and comparable with some advantages favouring Ketamine group (Group I).

Keywords: Propofol, Ketamine, Fentanyl, Hemodynamics, Recovery.

Introduction

The concept of ambulatory anaesthesia has emerged as an important element in day care surgical procedures. The ambulatory anesthesia for day care surgeries should be simple, economically safe, cost effective and easy to practice.

Total intravenous anesthesia (TIVA) currently practiced uses several types of drugs, each performing a specific role. There is a perceived wisdom that they should have rapid clearance rate and little delay between change in infusion rates, plasma levels and pharmacological actions and less side effects. This allows for rapid induction, good plane of anesthesia and at the end of surgery, smooth emergence, early recovery and return to preoperative functional status with minimal side effects.

There is a growing interest in TIVA for the induction and maintenance of anesthesia, because of increasing availability of syringe or infusion pumps with the necessary features. Total intravenous anesthesia overcomes some of the disadvantages of inhalation anesthesia in thefollowing ways:

1. The components of TIVA can be regulated independently as the need for each component changes during surgery. Both somatic and autonomic responses to varying degrees of surgical stimulation
   can be controlled.
2. Use of precision vaporizers can be avoided.
3. Operation theatres remain minimally polluted by trace concentrations of nitrous oxide and volatile agents.

Propofol is a newer intravenous anesthetic agent, having favorable pharmacokinetic profile. It has already achieved considerable popularity for induction and maintenance of anesthesia for short duration surgeries. Propofol is pleasant for most

patients. It has a high clearance rate and rapid decline in blood concentration, making it eminently suitable for infusion. When propofol infusion is discontinued there is rapid recovery from anesthetic state. Various studies suggested that propofol can be used satisfactorily for day care surgery when analgesic agents are used as an adjuvant along with it.

Ketamine which is water soluble intravenous anesthetic belongs to phencyclidine group of drugs. It is the only intravenous anesthetic which has hypnotic, analgesic and amnesic properties, and cheaper than fentanyl and Butorphanol. Ketamine in sub-anesthetic doses along with propofol has picked up consideration in total intravenous anesthesia because of its potent analgesic action a in small dose without causing myocardial and respiratory depression. Neither propofol nor ketamine are suitable as sole anesthetic agents. The most common adjuvant is an opioid analgesic, and this is sufficient to provide complete anesthesia. Propofol produces a reduction in both cardiac index and mean arterial pressure, in contrast, ketamine increases the same.

Fentanyl, a synthetic opioid is the most commonly used opioid in clinical anesthesia today. It is used in short surgical procedures and as a part of balanced anesthetic technique. Its persistent respiratory depression vagally mediated bradycardia are worrisome side effects. Hence, in this study we compared two drug regimens, namely propofol-ketamine and propofol fentanyl for TIVA technique in patients undergoing short surgical procedures to assess the intraoperative stability of the hemodynamics, respiratory parameters as well as recovery profile.

Aim and Objectives of the Study

To compare the combination of propofol-ketamine with propofol-fentanyl for total intravenous anesthesia in terms of

- Hemodynamic stability
- Recovery profile
- Side effects

Materials and Methods

This study was approved by our institutional ethical committee, and it was conducted in institute of anesthesiology and critical care, Thanjavur medical college and hospital, Thanjavur.

After obtaining informed written consent from patient, the study was conducted on 80 patients of ASA I& II of both sexes undergoing short surgical procedures.

Inclusion Criteria

Age: 20 – 50 years, ASA: 1& 2, short surgical procedures: incision and drainage of abscesses, dilatation and curettage, closed reduction of fracture upper limb, fibroadenoma, patients who have given written informed consent.

Exclusion Criteria

Patients who received any analgesic or narcotic in the preceding 48 hours,

Patients of ASA grade III and above, allergic to medications, anticipated difficult mask ventilation, patients with cardiovascular, respiratory, neurological and liver disease,

patients with psychiatric disorders

Materials

Drugs: Injection ranitidine, inj glycopyrrolate, inj midazolam, inj propofol, inj fentanyl and inj ketamine

- Monitors – NIBP, ECG and SPO2

Method

The study included 80 patients randomly allocated into two groups.

- Group I :40 patients received propofol-ketamine combination.
- Group II :40 patients received propofol-fentanyl combination.

Preoperative

Age, weight, height, comorbid conditions, any history of previous surgery, vitals like heart rate, blood pressure, respiratory rate, spo2, baseline investigations like hemoglobin, blood sugar, blood urea, serum creatinine, ECG and chest X ray were checked. Thorough systemic examination and airway examination were done and patients were allocated into two groups. All patients were kept fasting for at least 6 hours prior to anesthesia.

Intraoperative

Patients were shifted on the morning of surgery to operating room as scheduled. Monitors were connected and baseline parameters like heart rate, blood pressure, spo2, respiratory rate were recorded.

A peripheral intravenous line was established. All patients were premedicated with inj ranitidine 50 mg + inj glycopyrrolate 0.2 mg + midazolam 1 mg 5 min prior to induction.

- **Group I** received i.v. injection ketamine 0.5 mg/kg over 2 minutes followed by propofol at rate of 1 ml over 3 seconds till the end point of induction (till loss of consciousness and loss of eye lash reflex).
- **Group II** received i.v. injection fentanyl 1.5 µg/kg followed by 1 ml propofol till the end point of induction.

Intraoperatively, heart rate, blood pressure, respira-

tory rate and oxygen saturation were recorded at different time intervals of 1, 3,5,10,15 and 20 minutes following induction of anesthesia in both the groups.

Top up dose of propofol (25 mg) was given when the plane of anesthesia became lighter during anesthesia as indicated by rise in heart rate, blood pressure, lacrimation or any movement to surgical stimulus. Recovery from anesthesia at the end of surgery was assessed by observing spontaneous eye opening and the response to verbal commands i.e. orientation of time,place and person. Postoperatively, all vital parameters were recorded every 10 minutes. Any complication like nausea, vomiting, delirium, giddiness, sedation, pain, headache, diplopia were noted for 1 hour in the recovery room.

Observation and Statistical Analysis of Results

Table 1: Comparison of mean age with study Group (N=80)

Parameter	Study Group		P VALUE
	Group I	Group II	
Age	33.00 ± 1.95	33.65 ± 2.18	0.164

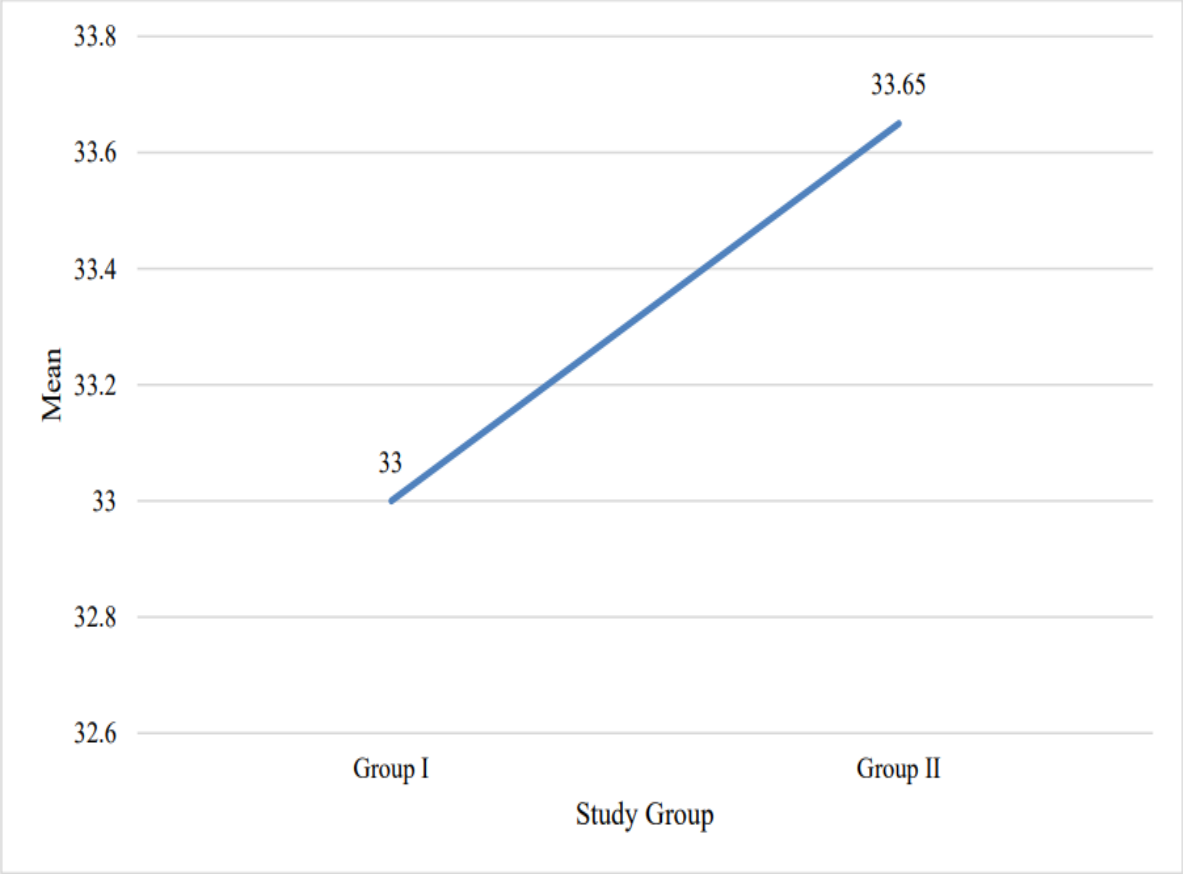

Figure 1: Line chart for Comparison of mean age with study Group (N=80)

Table 2: Comparison of mean Heart Rate at different follow ups with Study group (N=80)

Heart Rate	Study Group (Mean ± SD)		P Value
	Group I (N=40)	Group II (N=40)	
HR @Baseline	86.83 ± 1.28	87.05 ± 1.84	0.527
HR @1 min	94.53 ± 4.74	83.03 ± 4.76	<0.001
HR @3 min	95.97 ± 3.87	86.00 ± 4.34	<0.001
HR @5 min	98.08 ± 3.28	83.95 ± 4.27	<0.001
HR @10 min	92.40 ± 3.67	84.85 ± 4.23	<0.001
HR @15 min	90.33 ± 3.65	85.33 ± 4.03	<0.001
HR @20 min	90.33 ± 3.72	83.53 ± 4.25	<0.001

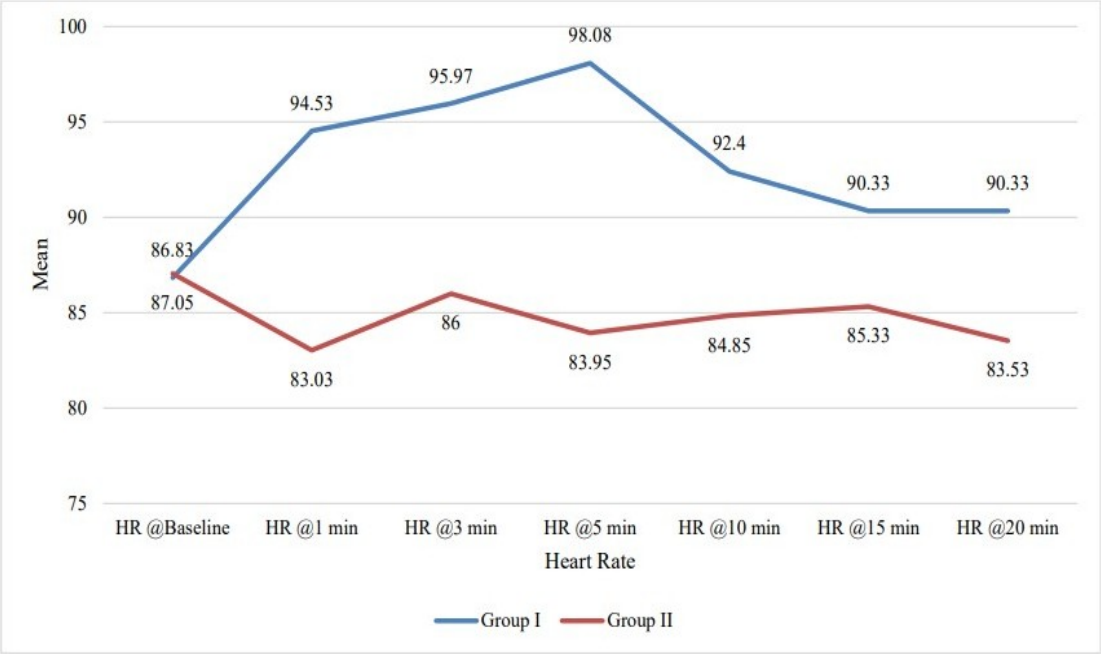

Figure 2: Line chart for Comparison of mean Heart Rate at different follow ups with Study (N=80)

Table 3: Comparison of systolic blood pressure at different follow ups with Study group(N=80)

Systolic Blood Pressure	Study Group (Mean ± SD)		P Value
	Group I(N=40)	Group II(N=40)	
SBP @Baseline	115.63 ± 4.11	114.40 ± 1.34	0.077
SBP @1 min	113.28 ± 4.36	107.35 ± 3.63	<0.001
SBP @3 min	115.33 ± 4.24	106.35 ± 3.26	<0.001
SBP @5 min	116.30 ± 3.93	108.30 ± 2.42	<0.001
SBP @10 min	117.55 ± 3.61	109.50 ± 2.89	<0.001
SBP @15 min	116.70 ± 2.70	110.55 ± 3.04	<0.001
SBP @20 min	116.95 ± 3.10	111.60 ± 2.65	<0.001

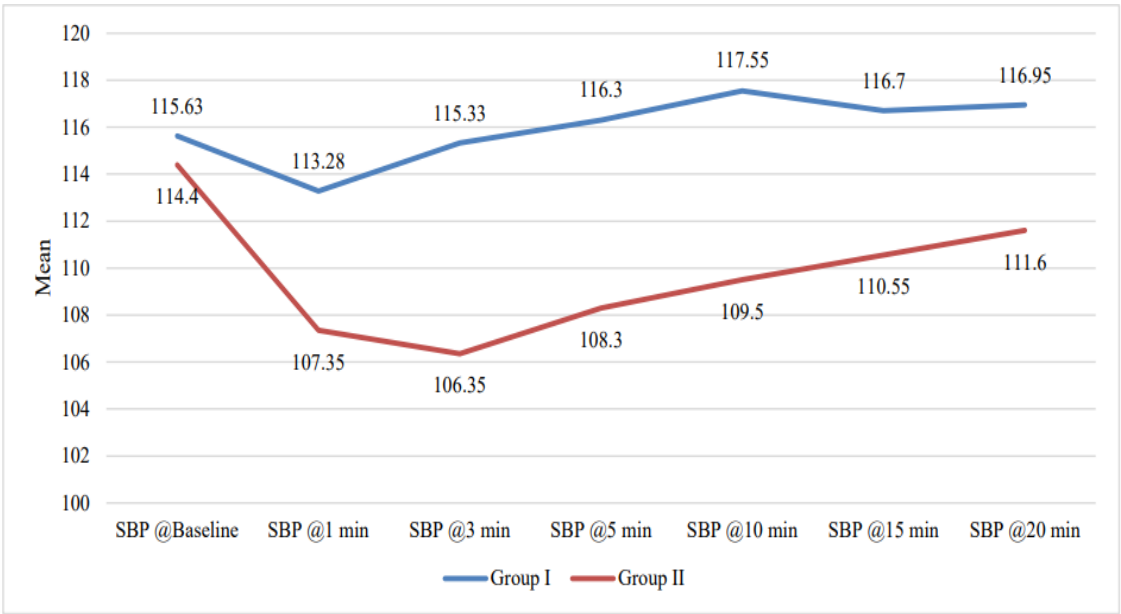

Figure 3: Line chart for Comparison of mean Systolic Blood Pressure at different follow ups with Study group (N=80)

Table 4: Comparison of mean Respiratory Rate at different follow ups with Study group(N=80)

Respiratory Rate	Study Group (Mean ± SD)		P Value
	Group I(N=40)	Group II(N=40)	
RR @Baseline	17.02 ± 1.56	16.98 ± 1.39	0.8800
RR @1 min	15.82 ± 1.85	13.40 ± 1.40	<0.001
RR @3 min	17.43 ± 2.04	13.95 ± 1.20	<0.001
RR @5 min	18.38 ± 1.93	14.50 ± 1.11	<0.001
RR @10 min	19.52 ± 1.78	15.55 ± 1.13	<0.001
RR @15 min	18.05 ± 1.69	16.23 ± 1.21	<0.001
RR @20 min	16.75 ± 1.84	13.93 ± 1.31	<0.001

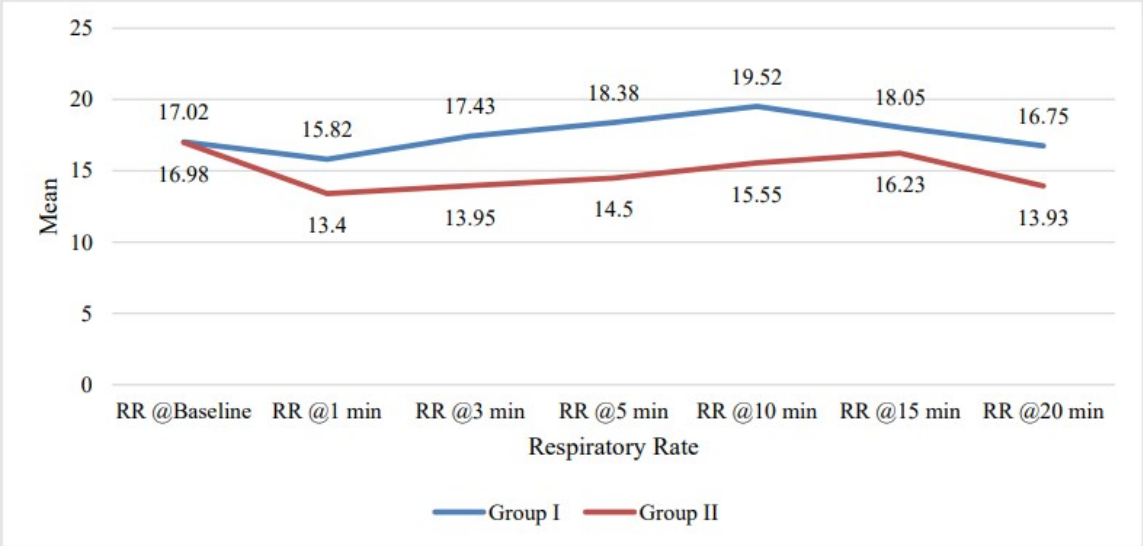

Figure 4: Line chat for Comparison of mean Respiratory Rate at different follow ups with Study group (N=80)

Table 5: Comparison of mean Response to verbal commands with study group (N=80)

Parameter	Study Group (Mean ± SD)		P Value
	Group I(N=40)	Group II(N=40)	
Response to verbal commands (in mins)	20.48 ± 2.31	18.63 ± 1.53	<0.001

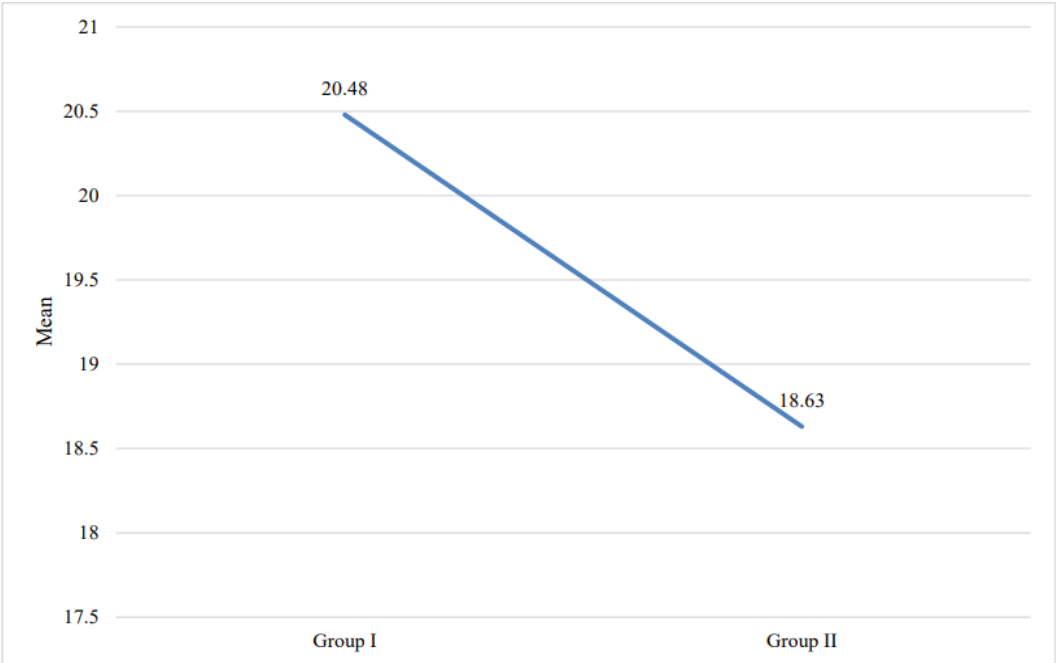

Figure 5: Line chart for Comparison of mean Response to verbal commands with studygroup (N=80)

For normally distributed quantitative parameters the mean values were compared between study groups using independent sample t-test (2 groups) P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

The present study was conducted on 80 patients undergoing short surgical procedure under TIVA belonging to American society of anesthesiology grade I and II physical status.

The two groups were compared with respect to age, sex, weight, height and ASA physical status. The parameters were comparable between the study groups with a P value > 0.05.

While comparing the type of surgical procedure undergone by patients in both the groups, P valueof 0.72 shows there is no significant difference between two groups.

The mean baseline HR was 86.83 ± 1.28 in group I & it was 87.05 ± 1.84 in group II. The difference in baseline HR between the study groups was not statistically significant. (P value 0.527). Intraoperatively, the pulse rate was slightly increased in group I with a maximum rise at 5minutes which was statistically significant (P<0.001) compared to preinduction value (86.83±1.28to 98.08±3.28/min). Group II patients showed minimal decrease in pulse rate post induction and maintenance from basal 87.05±1.84 to 83.95±4.27/min (P<0.001).

The difference in pulse rate in both the groups was statistically significant (P<0.001) The mean baseline SBP was 115.63 ± 4.11 in group I & it was 114.40 ± 1.34 in group II. The difference in baseline SBP between study group was not statistically significant (P value 0.077). In group I we found no statistically significant change in intraoperative mean systolic blood pressure, when baseline mean value of 115.63±4.11 mmHg was compared to 3 minutes (115.33±4.24 mmHg) and at 5 minutes (116.30±3.93 mmHg). Mean value of systolic blood pressure at 10,15and 20 minutes minimal change was observed showed hemodynamic stability. In group II, we found statistically significant fall in mean systolic blood pressure throughout intraoperative period from baseline mean value of systolic blood pressure. The difference in mean systolic blood pressure at different time intervals between two groups was statistically significant. The difference in mean diastolic blood pressure at different time intervals between two groups was statistically insignificant with a P value >0.05 at all time points.

Respiratory rate at baseline was comparable between the study groups. In group I there was minimal change in respiratory rate during post induction and maintenance at different time intervaleven up to 20 minutes. In group II the respiratory rate decreased from the preinduction value and the decrease was statistically significant till 20 minutes post induction The difference in mean respiratory rate at different time intervals between two groups was statistically significant with P value < 0.05 at all time points.

The mean arterial oxygen saturation in the perioperative period in group I was found to be in the range of 98.15±0.66% to 98.68±0.47% whereas in group II mean arterial oxygen saturation was 97.93±0.57 to 98.53±0.51%. The changes in mean arterial oxygen saturation at different time interval was statistically insignificant (P>0.05)

The mean value of spontaneous eye opening (in minutes) was 12.80 ± 1.52 in group I and it was ± 1.35 in group II. The difference in mean value between two groups was statistically significant (P<0.001)

The mean value of response to verbal comments (in minutes) was 20.48±2.31 in group I and it was 18.63±1.53 in group II. The difference in mean value between two groups was statistically significant (P value<0.001)

Discussion

Total intravenous anesthesia has been a subject of interest for all anesthesiologists, as this is the best route to avoid operation theatre pollution. TIVA was initially attempted with a single drug (like thiopentone, propofol) but was associated with side effects and no drug was found to give complete anesthesia. The availability of rapid and short acting sedative hypnotics, analgesics and muscle relaxants has refocused the attention on complete anesthesia by intravenous route. The advent of continuous infusion system has made administering TIVA more popular and convenient.But even today, we are still without any one intravenous drug that can alone provide all the requirements of anesthesia (i.e. unconsciousness, analgesia and muscle relaxation). Hence there is need to administer several different agents to produce the desired results. This in turn leads to important and significant drug interactions.

We studied two drug regimen: propofol - ketamine (group I) and propofol - fentanyl, (group II) for TIVA technique. Variables like Age, sex, weight, ASA grading, type of surgery were comparable between the two study groups. Baseline hemodynamic parameters also were comparable. In the present study, group I (P-K) received ketamine 0.5 mg/kg as well as group II (P-F) received fentanyl 1.5µg/kg two minutes before induction. After giving ketamine and fentanyl, propofol was given in concentration of 1% at the rate of 1 ml/3 sec till loss of eye lash reflex. We found statistically significant changes in pulse rate in both the group's up to 10 minutes but no episodes of brady cardia or tachy-

cardia. Although the increase in pulse rate in group I may be due to the sympathetic stimulation by ketamine and the decrease in pulse rate in group II can be attributed toaction of fentanyl on CVS.

When comparing intraoperative systolic blood pressure in both the groups, it was noted that majority of the patients had stable hemodynamic throughout the procedures. The minimal rise in post induction systolic blood pressure was observed after 5 minutes in group I receive ketamine. In group II, a significant decrease in mean systolic blood pressure from baseline mean value was observed.

There were minimal changes in mean respiratory rate in post induction and maintenance at different time intervals up to 10 min in group I and even at 15 and 20 min while in group II decrease in mean respiratory rate was found up to 20 minutes. The decrease in respiratory rate in group II may be due to respiratory depressant action of fentanyl and propofol.

Intraoperatively, there was no significant difference observed in SpO2 in both groups, when compared with respective base line values.

We found prolong recovery time in ketamine group as compared to fentanyl group, prolongation could be because of maximum peak effect of ketamine (5 to 10 min).

Although the mean time required for orientation of time, place and person from time of onset of induction was longer in group I than group II. The P value <0.001 showed significant difference in both the group. Less than 4% of ketamine was excreted unchanged in urine and 16% of ketamine appears as hydroxylated derivative, so large fraction of ketamine remained in unchanged form resulting in cumulative effect leading to delayed recovery. Therefore, patient in propofol-ketaminegroup might have delayed recovery.During procedure, patients were observed for any complication e.g. pain on injection, episode of hypoventilation (RR<8/min), laryngeal spasm, apnoea, involuntary movement, episode of desaturation (SpO2<90%). In group II, 12.5% patients had pain at injection site compared to nonein group I. This could be attributed to local anaesthetic action shown by ketamine on intravenous injection. Episodes of PONV were higher in group II because of fentanyl's central emetic action. To sum up, patients in both the groups shows minor hemodynamic changes and did not differ significantly, recovery time was longer in group I as compared to group II, incidence of postoperative nausea and vomiting was higher in group II as compared to group I, pain on injection was observed in group II alone.

Conclusion

Both propofol-ketamine and propofol-fentanyl combinations were comparable to each other hemodynamically, till end of surgery. The recovery was delayed in group I. There were no complications of serious type except nausea and vomiting which was higher in group II. Thus it can be concluded that both combinations were useful for short surgical procedures, but still ketamine has an upper edge.

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