Ketamine- Propofol or Fentanyl- Propofol intravenous infusion a better combination for short surgical procedures in paediatric patients, a comparative study

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Abstract

Introduction: Paediatric patients usually present with various painful conditions that require immediate surgical interventions. Many studies have been done on ketamine propofol combination to prove its efficacy.

Aim: The aim was to compare the effect of propofol-ketamine and propofol-fentanyl infusion in terms of haemodynamic stability, postoperative sedation, postoperative nausea and vomiting and adverse effects if any.

Materials and Methods: This was a prospective, randomized, double blind controlled trial conducted in 60 patients of ASA Grade I & II of age group 3 to 14 years. Patients were randomly allocated into two groups to receive either ketamine 1mg/kg before induction (group PK, n=30) or fentanyl 1.5 ug/ kg before induction (group PF, n=30) and patients in both groups were induced with propofol 2 mg kg and maintained on propofol infusion at rate of 50 ug/ kg /min. Heart rate and blood pressure were monitored throughout the procedure. Sedation was monitored by Ramsay sedation score and side effects were noted.

Results: In PF group there was a fall in heart rate as compared to PK group. There was a statistically significant fall in systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) in PF group (P 0.05). In PK group there is no significant fall in SBP, DBP and MAP. The patients in group PF were more sedated postoperatively and there was increased incidence of postoperative nausea and vomiting in group PF as compared to group PK.

Conclusion: Propofol-ketamine combination is better as compared to propofol-fentanyl in terms of haemodynamic stability and better recovery with less side effects.

Keywords: Propofol, Ketamine, Fentanyl, Paediatric procedures.

Introduction

Anaesthesia in the mid and late nineteenth centuries was based entirely on the use of inhalational agents. With the invention of new safe drugs and more appropriate means of delivering these drugs e.g. syringe pumps enthusiasm for total intravenous anaesthesia (TIVA) has markedly increased.[1]

Total intravenous anaesthesia is a technique in which induction and maintenance of anaesthesia is achieved with intravenous drugs alone thus avoiding both volatile agents and nitrous oxide. It can be safely used for a number of procedures lasting for a short duration. A variety of pediatric surgical procedures that need prompt innervation can be managed with total intravenous anesthesia.

Propofol (2, 6, di-isopropyl phenol) is the most recent intravenous anaesthetic to be introduced into clinical practice and is being widely used due to its hemodynamic property.[2] Propofol is a non-opioid, non-barbiturate, sedative hypnotic agent.[3,4] It possesses anti emetic effect & reliably produces sedation.[5] Because of its clear headed recovery nature it is preferred in ambulatory surgeries. Side effects include dose related cardiovascular & respiratory depression, bradycardia and hypotension. It also lacks analgesic property.

Ketamine is phencyclidine derivative & known to produce analgesia & amnesia.[5] It causes minimal respiratory depression and does not cause myocardial depression.[6,7] However ketamine when used as a sole agent for procedural sedation & analgesia results in occurrence of emergence reactions, which are associated with dreaming, delirium and illusions.[5,8,9] In few cases laryngospasm and airway obstruction has also been noted.

Fentanyl is potent opioid with no intrinsic anxiolytic or amnestic properties. It produces respiratory depression. There is fall in blood pressure which is primarily due to a reduction in systemic vascular resistance through centrally mediated reduction in systemic tone and often associated with bradycardia. Fentanyl when combined with propofol endorses the analgesic property. Opioids interact synergistically and markedly reduce the dose of propofol to produce loss of consciousness. However it attenuates the respiratory depression.

Propofol causes hypotension and bradycardia whereas ketamine because of its sympathetic stimulation leads to hypertension and tachycardia. In view of this opposing effects propofol ketamine combination is favoured.[5]

A number of studies have been done in the past to prove propofol ketamine combination is superior in terms of hemodynamic stability when compared with other drugs such as midazolam, fentanyl or dexmedetomidine. This combination has proved to be safe and effective in both adults and children undergoing different procedures in and outside the operation theatre. Ketamine and propofol combination

has been used successfully in paediatric patients for cardiac catheterization,[4] dental procedures,[10] endoscopies[11] as well as for debridement and dressing of burn patients.[12]

This study was designed to compare the haemodynamics & safety of intravenous infusion of ketamine–propofol with fentanyl-propofol for short surgical procedure in paediatric patients. Postoperative sedation and adverse effects were also noted.

Materials and Methods

This study was a prospective, randomized, double-blind, single center study. The study was conducted in a tertiary care level institute and a clinical research organization after ethical committee approval. 60 cases between 3-14 years of age of both sex with ASA grade 1 and 2 were included in the study. Procedures lasting for half an hour were included. Patients with comorbidities and anticipated difficult airway were excluded from the study.

Patients were randomly allocated to one of two groups using computer-generated random number table. Each group was consisting of 30 patients. The preparation of drugs was done by anaesthesiologist who was not the part of data collection and analysis. Administration of drug and data collection was done by anesthetist who was blinded to study drugs.

Patients under the study underwent thorough preoperative assessment including detailed case history, clinical examination & all necessary investigations. Written informed consent was obtained from parents or guardian of patients. After taking patients inside operation theatre intravenous access was obtained and Ringers Lactate solution was started. All patients received premedication 15-20 min prior to induction with Inj Ranitidine (1mg/kg) and Inj Metoclopromide (0.15mg/kg) i.v. Monitoring included heart rate, electrocardiography, non-invasive blood pressure and pulse oximetry (SpO2).

In group (PF) patient received 1.5 ug/kg Inj Fentanyl prior to induction and then induced with Inj propofol 2mg/kg as an initial bolus and then infusion was started at the rate of 50 ug/kg/min.

In other group (PK) patient received Inj ketamine 1mg/kg followed by Inj. propofol 2 mg/kg as a bolus dose and then infusion was started at the rate 50 ug/kg/min.

The rate was increased based on requirements namely spontaneous movement, appearance of tears, increase in respiratory rate, tachycardia, high blood pressure.

As soon as patient is anaesthetized the patient was maintained on O_2 by mask on spontaneous respiration.

Heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP) were measured before induction (baseline), 0, 5, 10, 15, 20, 25 and 30 minutes of procedure. Baseline reading was taken before induction. 0^{th} minute reading indicates values after induction. We defined hypotension when mean arterial pressure reduced by >20% of baseline value. Bradycardia was defined as heart rate <60 beats per minute. For correction of hypotension vasopressors were kept ready. Bradycardia was treated with atropine 20 ug/kg iv. SpO2 was monitored continuously throughout the procedure.

Postoperative sedation was evaluated using Ramsay sedation scale and side effects such as postoperative nausea and vomiting and emergence reaction were noted.

Statistical Analysis

Preliminary sample size estimation showed that approximately 30 patients should be included in each group in order to ensure power as 80% considering the level of significance as 0.05 (95% confidence interval).

Patient characteristics were compared using two independent sample *t*-test and Chi-square test. HR, SBP, DBP and MAP were compared using two independent sample *t*-test. Sedation score was compared using Fishers exact test. $P < 0.05$ was considered significant, $P > 0.05$ not significant and $P < 0.001$ highly significant.

Results

Demographic data did not show any significant difference in age, weight, height and sex ratio among two groups and thus the two groups were comparable [Table 1].

In our study there was no episode of hypotension or bradycardia in any patient. However it can be seen that there is increase in heart rate in PK group and a drop in the PF group which is statistically significant as p-value<0.001 [Fig. 1]. The peak effect of rise in heart rate in the PK group was seen in the 0^{th} minute whereas peak fall in heart rate in the PF group was seen in the 15^{th} minute. The heart rate returned to baseline at 15^{th} minute in the PK group and never dropped more than 5.47% of baseline in PF group.

From Fig. 2, 3 and 4 respectively it can be seen that the difference in the blood pressure in both the groups is statistically significant. The peak fall in SBP, DBP and MAP in PF group is at 15^{th} minute by 10.05%, 10.01% and 9.90% respectively. In PK group there is no significant fall in SBP, DBP and MAP.

There is difference in postoperative sedation in group PK and group PF. In PK group 19 patients had Ramsay Sedation Score (RSS) of 1 and 11 had RSS of 2 and none patients has RSS of 3. In PF group 9 patients had RSS of 1, 12 had RSS of 2 and 9 had RSS of 3.Thus it can be seen that, the patients in group PF were more sedated postoperatively as compared to patients in group PK [Table 2].

Side effects such as postoperative nausea and vomiting (PONV) were noted. 7 patients in group PK while 11 patients in group PF had PONV. Thus the

incidence of PONV was more in group PF as compared to group PK [Fig. 5].

Table 1: Demographic parameters

	Group PK (n=30)	Group PF (n = 30)	P
Age in years (means±SD)	9.37±1.97	9.43±1.96	0.846
Weight in Kg (means±SD)	28.43±5.65	28.33±5.95	0.947
Sex (male/female)	6/14	16/14	0.999s

SD = Standard Deviation

Table 2: Comparison of sedation score in group PK and group PF

Ramsay Sedation score	Group		Total	P-value
	Group PK	Group PF		
1	19	9	28	0.001
2	11	12	23	
3	0	9	9	
4	0	0	0	
5	0	0	0	
6	0	0	0	
Total	30	30	60	

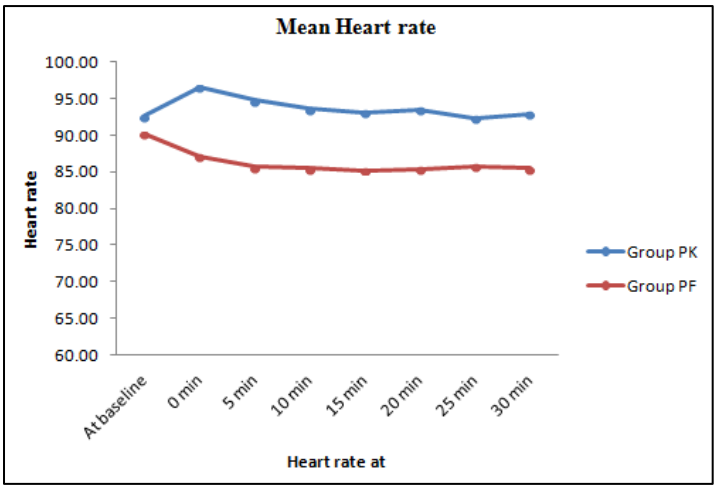

Fig. 1: Comparison of mean heart rate in group PK and group PF

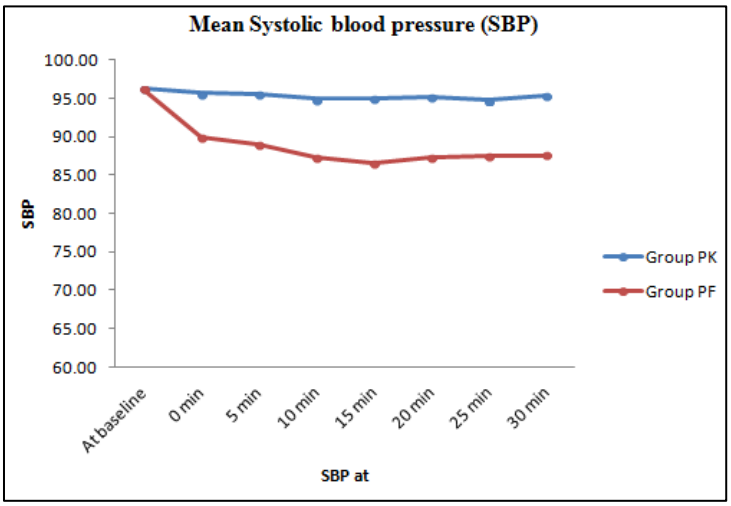

Fig. 2: Comparison of mean systolic blood pressure (SBP) in group PK and group PF

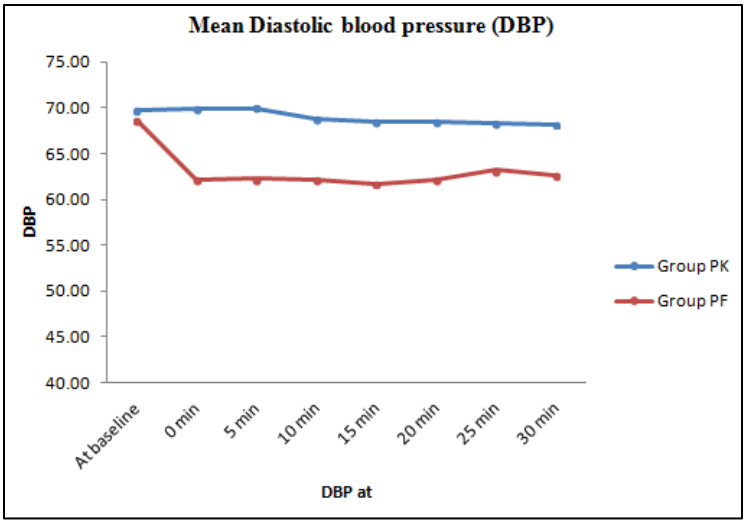

Fig. 3: Comparison of mean diastolic blood pressure (DBP) in group PK and group PF

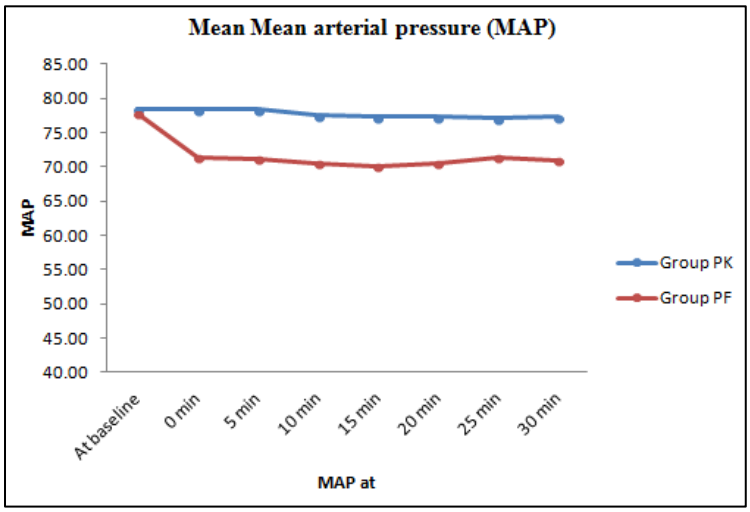

Fig. 4: Comparison of mean arterial pressure (MAP) in group PK and group PF

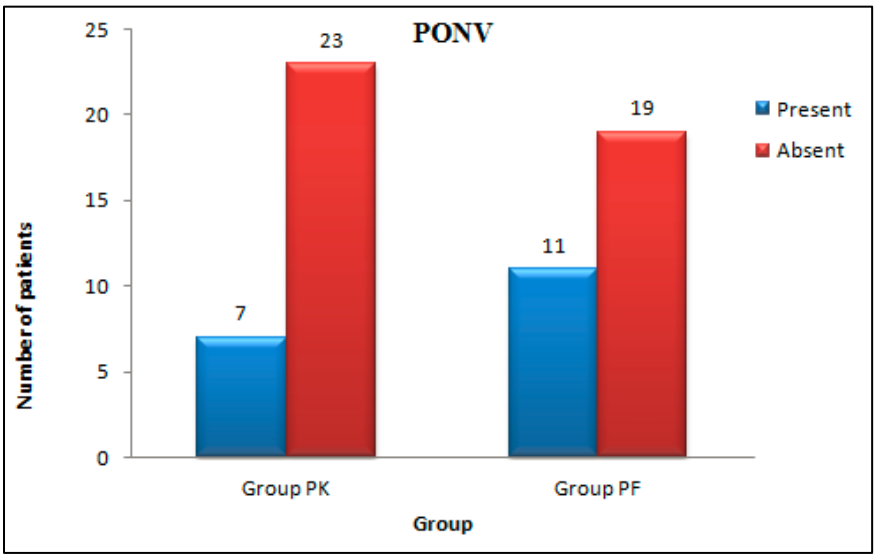

Fig. 5: Distribution of patients with respect to occurrence PONV in PK group and PF

Discussion

Total intravenous anaesthesia (TIVA) has gained popularity in recent decades, as this is the best route to avoid operation theatre pollution. TIVA was initially attempted with a single drug (egthiopentone, propofol) but was associated with side effects and no drug was found to give complete anaesthesia. Also with single drug large amounts are required which may lead to significant adverse effects.

The availability of rapid and short acting sedative hypnotics, analgesics and muscle relaxants has reinforced the attention on complete anaesthesia by intravenous route. With the invention of continuous infusion system TIVA gained popularity. But even today, we are still without any one intravenous drug that can alone provide all the requirement of anaesthesia (i.e. unconsciousness, analgesia and muscle relaxation). Hence there is need to administer several different agent to produce the desired results. This inturn leads to important and significant drug interactions.[13]

In the present study comparison of haemodynamic parameters was main objective. We measured heart rate before induction, after induction and then after every 5 minutes. It was seen that after induction there was increase in heart rate in Group PK. This can be attributed to central stimulation of sympathetic nervous system. The fall in heart rate after induction in Group PF was due to effect of fentanyl on cardiovascular system. The heart rate returned to baseline after 15 minutes in Group PK while in Group PF it never returned to baseline. These results were similar to those of Sukhminder Jit Singh Bajwa, Sukhwinder Kaur Bajwa1, Jasbir Kaur[14] on the comparison of two drug combinations in total intravenous anesthesia that is propofol–ketamine and propofol–fentanyl.

Nalini KB, Anusha Cherian et al[15] conducted a study comparing propofol-ketamine versus propofol-fentanyl for puerperal sterilization. They compared 60 patients belonging to ASA class 1.In their study in Group PK there was no significant change in heart rate but in Group PF showed reduction in heart rate. They measured SBP and DBP at 5 minute interval. In Group PK, SBP and DBP did not show significant variations from baseline readings at any time during anaesthesia. But in Group PF reduction which occurred in SBP and DBP from 5^{th} and 10^{th} minutes respectively were significant. In our study also in Group PF reduction which occurred in SBP and DBP from 5^{th} and 10^{th} minutes respectively were significant. These results were nearly similar with our study.

Mayer and co-worker[16] conducted a similar study. They compared the haemodynamic and analgesic effect of propofol- ketamine with propofol-fentanyl. They compared 10 patients of class ASA 1 and 2. In this study, the heart rate dropped in Group PF (9%) but did not change in Group PK. These results were similar to our study which showed the heart rate had dropped by (5.47%). In both groups a moderate drop of mean arterial pressure (MAP) was observed after the induction of anaesthesia. But during the maintenance of anaesthesia, there was better haemodynamic stability in Group PK as compared to Group PF. In our study also haemodynamic stability was better in PK group during maintenance of anaesthesia.

In another study done by Sukhminder Jit Singh Bajwa, Sukhwinder Kaur Bajwa1, Jasbir Kaur[14] on the comparison of two drug combinations in total intravenous anesthesia that is propofol–ketamine and propofol–fentanyl. They found an increased incidence of nausea and vomiting in propofol–fentanyl group. In our study also the occurrence of nausea and vomiting was more in Group PF as compared to Group PK.

A similar study was done by Dunnihoo and co-workers[17] using Propofol-Ketamine on cardiovascular response and wake up time. They showed that this combination maintained better haemodynamic stability and there was no significant change in heart rate and arterial blood pressure throughout the procedure.

A prospective randomised double blinded study was conducted by Tosun Z et al to compare clinical efficacy and safety of propofol ketamine with propofol fentanyl in pediatric patients undergoing diagnostic upper gastrointestinal endoscopy.[11] The results of this study were similar with our study with respect to haemodynamic stability.

A randomized double blind study was conducted by Tosun Z et al to compare propofol ketamine and propofol fentanyl combinations for deep sedation and analgesia in pediatric burn wound dressing changes.[12] The results of this study were similar to the results in our study.

Propofol a modern intravenous hypnotic produces a reduction in both cardiac index and mean arterial pressure (MAP). Ketamine a potent analgesic in contrast causes an increase in mean arterial blood pressure and cardiac index. Thus propofol when combined with ketamine counteract the effects of each other leading to maintenance of stable hemodynamics.

Ketamine has certain side effects like emergence reactions, vomiting and increased secretions. However in our study there was reduced incidence of PONV and emergence in group PK compared to group PF. This is contributed by the sedative and anti-emetic properties of propofol which leads to reduced adverse effects.

Antisialogogue was avoided in our study as it can cause tachycardia causing misleading results. There were no adverse effects like laryngospasm, bronchospasm or oxygen desaturation.

Conclusion

Our study concluded that Propofol-ketamine (Group PK) combination provides better hemodynamic stability as compared to propofol fentanyl (Group PF). Propofol–ketamine combination reduces the incidence of post-operative sedation and post-operative nausea

and vomiting (PONV) is less in propofol-ketamine (Group PK) group as compared to propofol fentanyl (Group PF).

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