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COMPARISON OF KETAMINE-PROPOFOL COMBINATION WITH OR WITHOUT FENTANYL FOR SEDATION IN CHILDREN UNDERGOING INFRAUMBILICAL SURGERIES UNDER SPINAL ANESTHESIA

Anaesthesiology

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ABSTRACT

Background: General anaesthesia has always been the preferred mode of anaesthesia for children. However, paediatric regional anaesthesia has been gaining popularity over the last few decades. It offers advantages such as rapid onset and recovery, reduced opioid consumption, increased haemodynamic stability, postoperative pain relief, preservation of airway patency to name a few. Spinal anaesthesia in paediatric patients invariably requires procedural sedation as children fail to offer cooperation during the procedure. Propofol and ketamine have been used alone and in combination for procedural sedation. This study was aimed at assessing the safety and efficacy of combination of fentanyl-propofol-ketamine combination in comparison with combination of propofol ketamine only for procedural sedation in children. **Objectives:** To assess intraoperative pediatric sedation state scale, haemodynamic, respiratory parameters and postoperative Modified aldrete score using ketamine and propofol combination with or without fentanyl for sedation in these children. **Material and Methods:** A Prospective and Interventional Randomized Comparative study was conducted at the Department of Anaesthesia And Critical Care, VMMC And Safdarjung hospital, tertiarty care hospital, India after taking ethical clearance and CTRI registration. A total of 50 children between 3-8 years, ASA I and II, scheduled for short duration infraumbilical surgeries were included in the study. Patients with any contraindications for neuraxial blockade- spinal deformities, local site infection, known case of coagulopathy, raised ICP etc,Known allergy to local anaesthetic agents, propofol, Patients with systemic disease, neurological impairment, airway abnormality, Intercurrent URTI were excluded. All patients received premedication with oral midazolam 0.5mg/kg in 10% dextrose. EMLA cream was applied on site of IV cannulation and skin puncture site of spinal block 45 mins prior to surgery. The heart rate and oxygen saturation were monitored. Patient was shifted to operation theatre, all standard monitors connected and IV line secured. Group KPF received bolus of Fentanyl at 2 mcg/kg followed 5 mins later by a bolus of ketamine at 0.2 mg/kg and propofol at 0.8 mg/kg IV which was followed by infusion of ketamine and propofol at 150 ug/kg/hr and 600 ug/kg/hr. Group KPS received a saline bolus followed 5 mins later by combination of ketamine and propofol at 0.2 mg/kg and 0.8 mg/kg IV respectively followed by an infusion at 150 ug/kg/hr and 600 ug/kg/hr respectively. The infusion was titrated to keep the paediatric sedation state score of 2. Haemodynamics and pediatric sedation state score were monitored at an interval of 5 mins intraoperatively. IV Inj paracetamol 15mg/kg was given at the end of surgery for post op analgesia. Recovery in the postoperative period was assessed using Modified Aldrete score, patient was followed upto 24 hours for any complications. Statistical analysis was done using SPSS version 21.0. **Results:** Group KPF faired significantly better in comparison to Group KPS in terms of the requirement of boluses to perform lumbar puncture ($p<0.001$). 92% patients required only a single bolus dose of ketamine-propofol combination as compared to KPS group where84% patients did require a second bolus dose of ketamine-propofol combination to perform lumbar puncture. Need of intraoperative boluses was also significantly higher in KPS group as compared to KPF group ($p = 0.006$). The total dose of Propofol required was 1265.52 ±250.22 mcg/kg body weight in KPF group and 1772.16 ±261.51mcg/kg body weight in KPS group ($p<0.001$). The total dose of Ketamine was 304.38± 67.16 mcg/kg body weight and 411.04± 97.18mcg/kg body weight in KPF and KPS group respectively ($p<0.0001$). **Conclusion:** Addition of fentanyl to low dose PK combination during spinal anaesthesia in paediatric patients provides better quality of sedation and quick recovery without any haemodynamic or respiratory compromise.

KEYWORDS

Propofol- ketamine combination, fentanyl, pediatric spinal anaesthesia, pediatric infraumbilical surgeries, procedural sedation.

INTRODUCTION

General anaesthesia has always been the preferred mode of anaesthesia for children. However, paediatric regional anaesthesia has been gaining popularity over the last few decades. It offers advantages such as rapid onset and recovery, reduced opioid consumption, increased haemodynamic stability, postoperative pain relief, preservation of airway patency to name a few.[1,2,3] Spinal anaesthesia in paediatric patients invariably requires procedural sedation as children fail to offer cooperation during the procedure.

Both propofol and ketamine have been used individually and in combination for procedural sedation.[4,5,6,7,8] The combination of the two should theoretically offer better haemodynamic control and safety profile considering their contrasting action on haemodynamics and ventilation. However propofol and ketamine in combination has been associated with airway complications like hypoxia, desaturation, airway obstruction, excessive salivation, postoperative psycho-mimetic effects.[9,10] The addition of an opioid such as fentanyl may help reduce the doses of propofol and ketamine combination and further mitigate their side effect profile and complications. It may also provide better sedation, haemodynamic stability and quicker recovery. To our knowledge, there is no study comparing the effect of fentanyl-propofol-ketamine combination with propofol ketamine only combination for procedural sedation in children undergoing spinal anaesthesia for infraumbilical surgeries.

This study was aimed at assessing the safety and efficacy of combination of fentanyl-propofol-ketamine combination in comparison with combination of propofol ketamine only for procedural sedation in children posted for spinal anaesthesia in infraumbilical surgeries like herniotomy, orchidopexy, strayers procedure.

MATERIALS AND METHODOLOGY

A Prospective and Interventional Randomized Comparative study was conducted at the Department of Anaesthesia And Critical Care of a tertiary care hospital, New Delhi, India from 01st May 2018 to 28th February 2019 after taking ethical clearance Institute Ethics Committee, VMMC & Safdarjung hospital, New Delhi, India. CTRI registration number-REF/2018/03/018073. A total of 50 children between 3-8 years, ASA I and II, scheduled for short duration infraumbilical surgeries were included in the study. Those having any contraindications for neuraxial blockade, known allergy to local anaesthetic agents, propofol, any systemic disease, neurological impairment, airway abnormality, intercurrent upper respiratory infection were excluded from the study.Participants were randomly allotted into two groups using block randomization with sealed envelope system. All patients received premedication with oral midazolam 0.5mg/kg in 10% dextrose. EMLA cream was applied on site of IV cannulation and skin puncture site of spinal block 45 mins prior to surgery. The heart rate and oxygen saturation were monitored. Patient was shifted to operation theatre, all standard monitors connected and IV line secured. Group KPF received bolus of Fentanyl at 2 mcg/kg followed 5 mins later by a bolus of ketamine at 0.2 mg/kg and propofol at 0.8 mg/kg IV which was followed by infusion of ketamine and propofol at 150 ug/kg/hr and 600 ug/kg/hr. Group KPS received a saline bolus followed 5 mins later by combination of ketamine and propofol at 0.2 mg/kg and 0.8 mg/kg IV respectively followed by an infusion at 150 ug/kg/hr and 600 ug/kg/hr respectively. The infusion was titrated to keep the paediatric sedation state score of 2. Although we used ketamine and propofol separately, their combination in a single syringe has been used by various anaesthesiologists and is called as ketofol.[11] Haemodynamics and pediatric sedation state score were monitored at an interval of 5 mins intraoperatively. Episodes of spontaneous body movements, requirement of supplemental sedation, complications were noted and interventions were made accordingly. Inj paracetamol 15mg/kg IV was given at the end of surgery for post op analgesia. Recovery in the postoperative period was assessed using Modified Aldrete score, patient was followed upto 24 hours for any complications.

Statistical Analysis

Statistical analysis was done using SPSS version 21.0. A p value of<0.05 was considered statistically significant. Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. Quantitative variables were compared using Independent t test/Mann-Whitney Test. Qualitative variables were correlated using Chi-Square test/Fisher's Exact test. Spearman rank correlation coefficient was used to assess the association of time of achieving 9 in Modified Aldrete score with total dose in each group.

RESULTS

Figure 1 illustrates that group KPF faired significantly better in comparison to Group KPS in terms of the requirement of boluses to perform lumbar puncture (p<0.001). 92% patients required only a single bolus dose of ketamine-propofol combination as compared to KPS group where84% patients did require a second bolus dose of ketamine-propofol combination to perform lumbar puncture.

Similarly Figure 2 highlights the need of intraoperative boluses that was also significantly higher in KPS group as compared to KPF group (p = 0.006)

Overall the Heart Rate showed a decrease from baseline value in both the groups(Figure 3). This decrease in Heart Rate was significant in KPF group from T20 to T30 as the p value was 0.041, 0.034 and 0.048 at T20, T25 and T30 respectively.

The mean mean arterial pressure was 72.52±8.95mmHg and 72.48±9.5mmHg in KPF and KPS group respectively (Figure 4). A decrease from baseline values was seen in both the groups but this difference was statistically insignificant.

The Modified Aldrete score was comparable in both groups and no statistically significant difference was seen among the two groups. The average time required to achieve a Modified Aldrete Score of 9/10 was also statistically similar in both groups

The total dose of Propofol required was 1265.52 ±250.22 mcg/kg body weight in KPF group and 1772.16 ±261.51mcg/kg body weight in KPS group (p<0.001). The total dose of Ketamine was 304.38± 67.16 mcg/kg body weight and 411.04± 97.18mcg/kg body weight in KPF and KPS group respectively (p<0.0001).

All patients were awake within 5 minutes of end surgery.

Spinal blockade was effective in all the patients and there were no perioperative complications.

Table 1: Demographic Paramteres

	KETAMINE PROPOFOL FENTANYL(KPF)	KETAMINE PROPOFOL SALINE (KPS)	P *value
AGE(YRS)	5.6	5.16	0.340
HEIGHT(CMS)	112.2	107.88	0.141
WEIGHT(KGS)	16.4	16.56	0.930
DURATION OF SURGERY(MINS)	30.8	28.6	0.446

Data are in mean. YRS=years CMS= centimeters KGS= kilograms MINS= minutes KPF= ketamine propofol fentanyl KPS= ketamine propofol saline
* p value insignificant (p >0.05)

Table 2: Mean time of achieving Modified Aldrete Score 9/10.

	KETAMINE PROPOFOL FENTANYL (KPF) IN MINS	KETAMINE PROPOFOL SALINE (KPS) IN MINS	P value
Time of achieving 9 in aldrete score	12.6± 3.85	11.2±2.99	0.160

Presented values are in mean ± SD in minutes. KPF= ketamine propofol fentanyl KPS= ketamine propofol saline. p value insignificant.

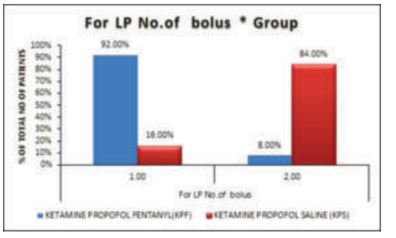

Figure 1: Comparison Of No. Of Bolus Required For LP Among KPF And KPS Group,

Data are in percentage KPF= ketamine propofol fentanyl KPS= ketamine propofol saline LP= lumbar puncture
*p value (0.001) significant

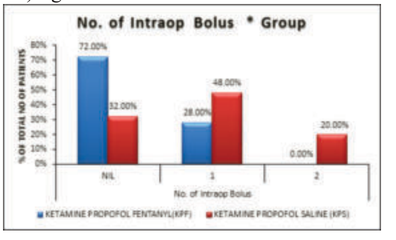

Figure 2: Comparison of requirement of No. of intraoperative ketaine-propofol bolus to maintain sedation score among KPF and KPS group.

Data are in percentage. KPF= ketamine propofol fentanyl KPS= ketamine propofol saline
*p value (0.006) significant.

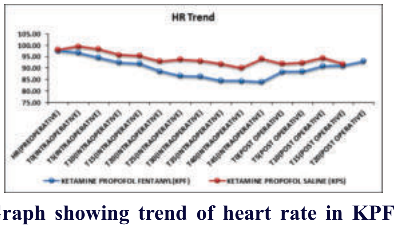

Figure 3:Graph showing trend of heart rate in KPF and KPS group,

KPF= ketamine propofol fentanyl KPS= ketamine propofol saline T= time in minutes
*p value was 0.041, 0.034 and 0.048 at T20, T25 and T30 respectively, significant.

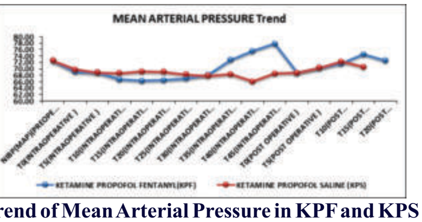

Figure 4 Trend of Mean Arterial Pressure in KPF and KPS group.

KPF= ketamine propofol fentanyl KPS= ketamine propofol saline Mean arterial pressure is in mmhg.
* p value insignificant.

The mean mean arterial pressure was 72.52±8.95mmHg and 72.48±9.5mmHg in KPF and KPS group respectively (Figure 4). A decrease from baseline values was seen in both the groups but this difference was statistically insignificant.

DISCUSSION

The last few years have witnessed a renewed interest in spinal anaesthesia in paediatric patients. Besides being a cheaper alternative, it causes minimum cardiorespiratory disturbances and blunts the neuroendocrine stress response to surgery.[12] Paediatric patients are usually anxious and hence sedation becomes necessary for performance of neuraxial block per se as well as for intraoperative period.

We observed that giving fentanyl prior to combination of propofol-ketamine (4:1ratio) provides better intraoperative sedation without any complications as compared to giving propofol-ketamine only. This is evident by the increased bolus requirement for performance of spinal block and intra operative maintenance in KPS group as compared to KPF group (p<0.05).

Dabiass et al compared propofol-ketamine in 1:1and 4:1 ratio. They encountered complications like significant hypotension, arterial desaturation after bolus administration, hypercarbia, apnea, hypoxia, airway obstruction in propofol-ketamine (4:1) group. Rabinder et al also observed 5% incidence of airway complications in propofol-ketamine (4:1) group.We did not observe any haemodynamic disturbances or airway complications in any of the groups.This could be due to much lower dose of propofol-ketamine combination used in our study that made it a safer option. Also, the addition of fentanyl to the PK combination did not lead to any undesirable side effects.

The use of fentanyl prior to PK combination did not prolong the recovery in our study. This could be attributed to the duration of surgery which lasted for about 30 minutes in our study and this corresponds to the duration of action of fentanyl.[13]

Time to achieve Modified Aldrete score 9/10 was comparable in both our groups and all children were awake within 5 minutes after sugery. Our recovery profile is similar to that observed by Rabinder et al where they also encountered quick recovery.

Use of ketamine comes with the concern of psychomimetic side effects and post operative nausea vomiting (PONV). At the doses used in our study, the incidence psychomimetic effects was nil in our patients. Similar to our finding Rabinder et al also did not observe any such side effects.

The addition of fentanyl did not affect the incidence of PONV in our patients. Aydin et al used PFK for sedation in interventional radiological procedure.[14] They also did not find any episode of PONV in their patients.

CONCLUSION

We conclude that the addition of fentanyl to low dose PK combination during spinal anaesthesia in paediatric patients provide may provide better quality of sedation and quick recovery without any haemodynamic or respiratory compromise.

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