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Original Research Paper

Anesthesiology

A COMPARATIVE STUDY OF PROPOFOL-KETAMINE AND PROPOFOL-FENTANYL FOR TOTAL INTRAVENOUS ANAESTHESIA FOR SHORT SURGICAL CASES IN PAEDIATRIC PATIENTS

Dr Virendra Singh Raghuvanshi Assistant Professor Department of Anaesthesiology Chirayu Medical College & Hospital Bhopal

Dr. Sasmita Panda* Assistant Professor Department of Anaesthesiology Chirayu Medical College & Hospital Bhopal *Corresponding Author

ABSTRACT

Aims and objective : To compare combinations of Propofol-Ketamine and Propofol-Fentanyl for total intravenous anesthesia in short surgical cases in pediatric patients. The study also compared recovery characteristics and the incidence of side effects / complications in the groups.

Methodology: The patients were randomly divided into two groups depending upon the drug combination used for Total Intravenous Anaesthesia.

Group I : 30 patients were given i.v. Ketamine followed by Propofol.

Group II: 30 patients were given i.v. Fentanyl followed by Propofol

Recovery characteristics were compared and the incidence of side effects and complications in two groups were noted.

Results: The pulse rate and blood pressure remained near to preinduction value in group I, while in group II these values decreased. After induction RR increased in group I but decreased in group II at 1,3%5 min after induction.None of the patients in both groups were observed to have nausea, vomiting and respiratory depression. . A significant no. of the patients in group II were observed to have either pain on injection site or restlessness.

Conclusion: Propofol-Ketamine and Propofol-Fentanyl combinations provide satisfactory surgical conditions for minor surgical procedures in paediatric patients, but the Propofol-Ketamine combination gives better hemodynamic stability and less restlessness during induction and maintenance of anaesthesia.

KEYWORDS : Propofol,Ketamine ,Fentanyl , Hemodynamic stability

INTRODUCTION

The choice of anaesthesia for short surgical cases in paediatric patients have always been matter of discussion. The requirements for anaesthesia for short surgical cases are those of general anaesthesia i. e. rapid painless induction, profound analgesia with minimum changes in cardiovascular and repiratory systems; rapid smooth recovery with post-operative analgesia with least side effects.

Earlier anesthesia even for short surgical cases in children was given by inhalational agents for induction as well as for maintenance. This method of anaesthesia was an unpleasant experience causing resistance of the patients for putting face mask and volatile inhalational agents which caused stage of excitation associated with post-operative nausea, vomiting and emergence delirium.In the early 1970s, the concept of total intravenous anaesthesia has evolved from administration of intravenous agents for induction as well as for maintenance of anesthesia for short surgical cases.Many intravenous anesthetic agents like methohexital, etomidate, ketamine, midazolam have been used to provide total intravenous anaesthesia. All these agents themselves did not provide stable and satisfactory conditions for the surgery.

In recent years the development of new hypnotic sedative drugs like Propofol were found to offer better condition given intravenously, than those offered by the agents used earlier. This has renewed interest in total intravenous anaesthesia to provide satisfactory condition for short surgical cases in paediatric patients. It provides rapid induction and smooth emergence with minimal physiological changes.

Propofol (2, 6 di-isoprophyl phenol) synthesized in 1977 is a potent sedative-hypnotic agent with excellent recovery characteristics but lacks analgesic properties. Potent intravenous drugs with analgesic properties such as ketamine & opioid derivatives such as Fentanyl have been tried in combination with Propofol to obtain stable and satisfactory operative conditions of the patients.These analgesic drugs could be combined with Propofol for their synergistic action to produce rapid inductin smooth recovery and good post-operative analgesia.

Thus, the present study is therefore carried out to compare Propofol-ketamine and Propofol-fentanyl combinations in their paediatric dose range in terms of efficacy, hemodynamic stability, recovery profile, side effects and complications in short surgical cases for paediatric age group.

METHODOLOGY

The present study entitled "A comparative study of Propofol-Ketamine and Propofol-Fentanyl for total intravenous Anaesthesia for short surgical cases in paediatric patients" was carried out in Department of Anaesthesiology, Chirayu Medical College Hospital Bhopal (M.P.). The study was carried out in 60 patients of ASA grade I and II scheduled for various minor surgical procedure like circumcision, skin grafting, suprapubic cystolithotomy, heriotomy, post burn contracture release, closed manual reduction, incision and drainage etc. The patients considered for the study were between the age group of 3 to 14 years of either sex.

Exclusion criteria were as follows: Patients with history of cardiovascular disease, respiratory disease, liver or renal dysfunction, psychiatric illness, preoperative pain, having any analgesic or narcotic in the preceding 48 hrs were excluded from the present study.

Through pre-anesthetic checkup of all the patients were carried out, routine and special investigations were carried out, routine and special investigations were advised as required. Details of the procedure were explained to the attendants of the patients and informed consents were obtained. All the patients kept nil orally as required as per the age.

The patients were randomly divided into two groups depending upon the drug combination used for Total Intravenous Anaesthesial.
Group I : 30 patients were given i.v. Ketamine followed by Propofol.
Group II: 30 patients were given i.v. Fentanyl followed by Propofol.

Method:

The patients were taken on operation table and then pulse rate, blood pressure, respiratory rate, SPO2, degree of sedation were recorded. A 22 gauze intravenous cannula was established and connected to the infusion of a crystalloid solution.

Premedication was done uniformly to all the patients with intravenous Glycopyrolate 0.01 mg/kg and were pre oxygenated. The patients of group I were administered i.v. Ketamine 1 mg/kg followed by Propofol one minute later till the loss of eye lash reflex was noted.The patients of group II were administered i.v. Fentanly 2 mcg/kg followed by Propofol one minute later till the loss of eye lash reflex was noted.

Induction dose requirement of Propofol, hemodynamic and respiratory parameters were recorded. Reactions of patients on surgical stimulation were noted. Then surgeon was asked to start the procedure. Supplementary dose of Propofol 0.5 mg/kg was given when the patients became light (lacrimation, body movements and/or increase in blood pressure or pulse rate). Supplementary dose of Propofol also recorded.The vital parameters like pulse rate, blood pressure, respiratory rate, SPO2, degree of sedation were recorded intraoperatively. The time duration from start of induction to end of surgery was recorded.Degree of sedation assessed intra-operatively and at the end of the surgery.

At the end of the surgery patients were observed for any undue side effects such as –nausea, vomiting, pain on injection, bradycardia, hypotension, respiratory depression (RR<10/min), laryngospasm and hallucination).Recovery time was recorded from the administration of last dose of anaesthetic agent to when patient could open their eye on command.The time was recorded when discharge criteria met i.e. when patients were fully conscious and oriented, able to walk without assistance, without post operative nausea and vomiting, and were hemodynamically stable.

OBSERVATION TABLES

The comparison of Propofol-Ketamine and Propofol-Fentanyl for total intravenous anaesthesia for short surgical cases in paediatric patients a clinical study was carried out in 60 patients, who were divided into two groups of 30 each.

TABLE NO.-1 AGE WISE DISTRIBUTION CASES

S. No.	Age (years)	Group I		Group II	
		No.	%	No.	%
1	3-6	13	43.0	13	43.0
2	7-10	9	30.0	10	33.0
3	11-14	8	27.0	7	24.0

The above table shows that the maximum number of patients were in the age groups of 3-6 years and found to be 13 (43.0%) and also 13 (43.0%) in group I and II. The mean age of the patients in both the group is almost equal i.e. 7.76 years in group I and 7.56 years in Group II.

TABLE NO. 2 DISTRIBUTION OF VARIOUS MINOR SURGICAL PROCEDURES

S. No.	Operative Procedure	Group I	Group II
1	Incision and Drainage	9	6
2	Suprapubic cystolithotomy	6	10
3	Herniotomy	2	3
4	Circumcision	1	3
5	Contracture release and skin grafting	3	1
6	Lipoma excision	0	2
7	Rectal polypectomy	1	1
8	Closed manual reduction and hip spica	8	4

Above table shows distribution of various minor surgical procedures in both groups. All types of procedure were divided in both groups so that they were comparable to each other.

TABLE NO. 3 MEAN PULSE RATE AT VARIOUS TIME INTERVALS

S. No.	Time	Group I	Group II
		Mean ±SD	Mean ±SD
1	Before induction	91.46±10.37	89.63±9.34
2	1 minute after induction	90.83±10.76	85.03±11.75
3	3 minute after induction	89.26±9.82	84.90±8.76
4	5 minute after induction	88.63±9.76	85.16±8.56
5	15 minute after induction	91.60±9.42	90.36±8.40
6	30 minute after induction	92.70±9.86	89.28±10.76

Above table shows the changes in mean PR at various time intervals before and after induction. The mean PR remained near to preinduction value in group I, while in group II it decreased at 1,3 % 5 min after induction. This decrease in PR in group II was statistically significant.

TABLE NO. 4 SBP AT VARIOUS TIME INTERVALS

S. No.	Time	Group I	Group II
		Mean ±SD	Mean ±SD
1	Before induction	104.96±12.79	105.53±13.08
2	1 minute after induction	101.46±10.49	97.43±9.46
3	3 minute after induction	100.63±10.20	96.96±9.23
4	5 minute after induction	99.80±11.13	98.2±9.78
5	15 minute after induction	102±13.22	103.86±13.29
6	30 minute after induction	103±13.37	105.71±13.14

Above table shows mean SBP at various time intervals before and after induction. The mean SBP remained near at per induction value in group I while in group II it decreased at 1,3&5 min after induction. The decrease in SBP in group II was statistically significant.

TABLE NO. 5 MEAN RESPIRATORY RATE AT VARIOUS TIME INTERVALS.

S. No.	Time	Group I	Group II
		Mean ±SD	Mean ±SD
1	Before induction	22.4±5.56	22.36±4.29
2	1 minute after induction	23.93±5.45	18.96±5.39
3	3 minute after induction	24.90±5.67	19.46±5.45
4	5 minute after induction	25.70±6.89	19.50±6.96
5	15 minute after induction	24.20±5.45	23.04±5.23
6	30 minute after induction	22.30±5.09	22.78±5.34

Above table shows the mean RR at various time intervals. After induction RR increases in group I but decrease in group II at 1,3%5 min after induction. The change are statistically significant in group II.

TABLE NO. 6 -SIDE EFFECTS OBSERVED

S. No.	Complication	Group –I		Group –II	
		No. of patients	% of patients	No. of patients	% of patients
1	Nausea and vomiting	0	0	0	0
2	Bradycardia	0	0	2	6.66
3	Hypotension	1	3.33	3	10
4	Pain on injection	0	0	8	26.66
5	Restlessness	1	3.33	7	23.33
6	Laryngo spasm	1	3.33	0	0
7	Hallucination	3	10	1	3.33
8	Respiratory depress	0	0	0	0
9	Others	0	0	0	0

Above table shows the side effects observed. None of the patients in both groups were observed to have nausea, vomiting and respiratory depression. Few of the patient in group II were observed to have bradycardia & Hypotension but a significant no. of the patients in group II were observed to have either pain on injection site or restlessness. 10% of the patients in group I reported to have hallucinations.

RESULTS

The mean PR remained near to preinduction value in group I, while in group II it decreased at 1,3 % 5 min after induction. This decrease in PR in group II was statistically significant. The mean SBP remained near at pre induction value in group I while in group II it decreased at 1,3&5 min after induction. The decrease in SBP in group II was statistically significant. After induction RR increases in group I but decrease in group II at 1,3%5 min after induction. The change are statistically significant in group II.None of the patients in both groups were observed to have nausea, vomiting and respiratory depression. Few of the patient in group II were observed to have bradycardia & Hypotension but a significant no. of the patients in group II were observed to have either pain on injection site or restlessness. 10% of the patients in group I reported to have hallucinations.

Statistical analysis: Statistical analysis was done using Stata 11 software. A descriptive analysis was done on all variables to obtain a frequency distribution. The mean + SD and ranges were calculated for quantitative variables. For continuous variables descriptive statistics (mean and standard deviations) were computed. Continuous variables were compared by the Student t test. Proportions were analyzed with the chi-square test. .Demographic characteristics, hemodynamic parameters data was analyzed statistically. For categorical data chi-square test was applied. A P value of 0.05 or less was considered statistically significant.

DISCUSSION

The present study entitled "A comparative study of Propofol-Ketamine and Propofol-Fentanyl for total Intravenous Anaesthesia for short surgical in pediatric patients", (A clinical study) was carried out in 60 patients of ASA grade I and II scheduled for various minor surgical procedures to be done under general Anaesthesia. The patients taken for study were of either sex, between 3-14 years of age. Patients were divided into two groups of 30 each. The patient in Propofol-Ketamine group received fixed dose of i.v. Ketamine 1 mg/kg b.w. followed by i.v. Propofol till the end point of induction was reached. The patient in Propofol Fentanyl group received fixed dose of i.v. Fentanyl 2mcg/kg b.w. followed by i.v. Propofol till the end point of induction was reached. After induction procedure was started and anaesthesia was further supplemented if needed, by i.v. Propofol 0.5 mg/kg b.w. in both the groups.

The observations were made in terms of the induction dose of Propofol, total dose of Propofol, pulse rate, systolic and diastolic blood pressure, respiratory rate, SPO2, recovery profile, side effects and complications.

Several similar studies are done on anaesthesia in children and which agentsare safeand what combinations would be suitable . We usually face a common problem dealing with pediatric patients due to their high levels of anxiety and fear, associated with various surgical procedures. Such children are usually managed by various pharmacological methods.Krauss B, Green SM et al did their study on sedation and analgesia for procedures in children. Quality assurance data were collected for all patients, including anesthetic technique, dosage, and the occurrence of specific adverse events during anesthesia and recovery periods. [1]

McDowall RH, Scher CS et al gave total intravenous anesthesia to children undergoing brief diagnostic or therapeutic procedures. They compared the quality of anesthesia with propofol, ketamine, or etomidate in retrospective study of 971 pediatric oncology patients undergoing brief diagnostic or therapeutic procedures outside the operating room during a one-year period.Total intravenous anesthesia was administered primarily with ketamine, etomidate, or propofol for oncology-related procedures such as bone marrow aspiration, lumbar puncture, radiologic imaging, and radiation therapy. Anesthesia with propofol, ketamine, or etomidate is safe and efficacious for children undergoing brief procedures. Propofol is associated with a decreased incidence of postanesthetic agitation and vomiting. Its association with respiratory depression is confirmed.[2]

Aydin Erden I, Gulsun Pamuk A et al did a comparison of propofol-fentanyl with propofol-fentanyl-ketamine combination in pediatric patients undergoing interventional radiology procedures.: With an increase in the frequency of interventional radiology procedures in pediatrics, there has been a corresponding increase in demand for procedural sedation to facilitate them. The purpose of their study was to compare the frequency of adverse effects, sedation level, patient recovery characteristics in pediatric patients receiving intravenous propofol fentanyl combination with or without ketamine for interventional radiology procedures. Their main hypothesis was that the addition of ketamine would decrease propofol/fentanyl associated desaturation. The authors concluded that addition of low dose ketamine to propofol-fentanyl combination decreased the risk of desaturation and it also decreased the need for supplemental propofol dosage in pediatric patients at interventional radiology procedures.[3]

In a similar study by Tosun Z, Esmaoglu A et al done with propofol–ketamine vs propofol–fentanyl combinations for deep sedation and analgesia in pediatric patients undergoing burn dressing changes The aim of this study was to compare propofol–ketamine (PK) and propofol–fentanyl (PF) combinations for deep sedation and analgesia in pediatric burn wound dressing changes. Asin ourstudy ,heart rate, systolic arterial pressure, peripheral oxygen saturation, respiratory rate and Ramsey sedation scores of all patients were recorded perioperatively. Patients were randomly assigned to receive either PK or PFThere were no significant differences in heart rate, systolic arterial pressure, peripheral oxygen saturation, respiratory rate and sedation scores during the procedure between the groups. Restlessness during the procedure was seen in seven (47%) patients in Group PF and one (5.9%) patient in Group PK (P = 0.013).Conclusion was that both propofol–ketamine and propofol–fentanyl combinations provided effective sedation and analgesia during dressing changes in pediatric burn patients. But propofol–ketamine combination was superior to propofol–fentanyl combination because of more restlessness in patients given propofol–fentanyl.[4]

Khutia SK, Mandal MC et al did their study on intravenous infusion of ketamine-propofol. They studied if it can be an alternative to intravenous infusion of fentanyl-propofol for deep sedation and analgesia in paediatric patients undergoing emergency short surgical procedures. Singh R, Batra YK, Bharti N et al did a randomized clinical trial of efficacy and safety . Theydid comparison of propofol versus propofol-ketamine combination for sedation during spinal anesthesia in children.This study was designed to compare the efficacy and safety of propofol vs propofol-ketamine combination for sedation during pediatric spinal anesthesia.The infusion rate was titrated to keep the child sedated at University of Michigan Sedation Score of 3. The heart rate, blood pressure, respiratory rate and oxygen saturation were recorded every 5 min. The episodes of spontaneous body movements and requirement of supplemental sedation were recorded. The postoperative recovery was assessed by modified Aldrette score.The recovery time was similar in both groups. None of the patient had postoperative nausea/vomiting or psychomimetic reactions. They also concluded that propofol-ketamine combination provided better quality of sedation with lesser complications than propofol alone and thus can be a good option for sedation during spinal anesthesia in children.Resultswere comparable with our study.[5,6]

Alletag MJ, Auerbach MA et al compared ketamine, propofol, and ketofol use for pediatric sedation The use of a combination of ketamine and propofol (ketofol) for procedural sedation and analgesia in the emergency department setting shows promise as an agent that may minimize adverse effects of ketamine or propofol as single agents. This article provides a summary of current literature regarding ketofol. It also reviews the comparative pharmaco kinetics, adverse effects, and dosing of ketamine, propofol, and ketofol as agents for procedural sedation and analgesia.[7]

Weatherall A, Venclovas R et al shared their experience with a

propofol–ketamine mixture for sedation during pediatric orthopedic surgery.Various combinations of propofol and ketofol have been described for the provision of procedural sedation in both adults and children.During an orthopedic aid trip, a 1:1 mixture of propofol and ketamine (200 mg of each drawn up to 22 ml) was utilized to provide deep sedation or general anesthesia as an adjunct to regional analgesia for lower limb surgery. Details for 18 patients having a total of 19 procedures were recorded with a record of intraoperative and postoperative parameters including initial bolus doses and infusion rates of ketofol required to produce deep sedation. Ketofol successfully produced deep sedation for prolonged pediatric orthopedic procedures in conjunction with regional analgesia.[8]

Other authorslike Goel S, Bhardwaj N et al studied efficacy of ketamine and midazolam as co-induction agents with propofol for laryngeal mask insertion in children.Use of midazolam and ketamine lowers the induction dose of propofol (co-induction) producing hemodynamic stability. Large doses of propofol needed for induction and laryngeal mask (LM) insertion in children may be associated with hemodynamic and respiratory effects. Co-induction has the advantage of reducing dose and therefore maintaining hemodynamic stability. In children, the combination of propofol with ketamine or midazolam produces stable hemodynamics and improved LM insertion conditions but is associated with delayed recovery.[9]

Another study on co induction was done by Rai K, Hegde A, Goel K. in sedation in uncooperative children undergoing dental procedures .This was a comparative evaluation of midazolam, propofol and ketamine. Dentists usually face a common problem dealing with pediatric patients due to their high levels of anxiety and fear, associated with dental procedures. Such children are usually managed by various pharmacological methods. The efficacy and safety of conscious sedation, using intravenous short acting group of drugs (midazolam, propofol and ketamine) in uncooperative children, requiring oral rehabilitation was thus evaluated in this study. A total of 30 uncooperative children, aged 3-6 years, belonging to ASA I, II category formed the study group. The efficacy of the three group of drugs was evaluated on the basis of the onset of sedation, duration of action, side effects encountered, and the overall cooperative behavior of the child throughout the course of the procedure, after obtaining parental consent. Results showed that propofol was highly effective in terms of onset of sedation, although increased body movements and crying, pain on injection and intermittent cough was observed as the main side effects of the drug. Midazolam showed the longest duration of action, but was not very effective in terms of treatment completion due to increased movements and crying. Maximum cooperation during the procedure was obtained with ketamine and no adverse effects were encountered. Theauthors preferred ketamine from the results of study and recommended ketamine in combination with other sedatives.[10]

In our study also , the mean age of patients in Propofol-Ketamine group was 7.76 years and in Propofol-Fentanyl group, 7.56 years. The maximum number of patients was in the age group of 3-6 years in both the groups. Male patients in Propofol-Ketamine group and Propofol-Fentanyl group were 21 and 24 respectively. Thus, the two study groups were comparable to each other in terms of age and sex.Similar results were derived by us when compare to similar studies above. From the present study, it can be infered that Propofol-Ketamine and Propofol-Fentanyl combinations provide satisfactory surgical conditions for minor surgical procedures in paediatric patients, but the Propofol-Ketamine combination gives better hemodynamic stability and less restlessness during induction and maintenance of anaesthesia.

CONCLUSION

1. Propofol ,the main component in both the combinations has rapid onset of action and brief half life, making it a suitable induction drug for use in short duration surgery.
2. Average induction dose of Propofol was 1.86 mg/kg and total propofol requirement (induction + maintenance) was 2.52 mg/kg and total Propofol requirement was 3.48 mg/kg in group II. These dose were less in Propofol-Ketamine group.
3. Recovery was smooth and earlier with Propofol-Fentanyl as compared to Propofol-Ketamine.
4. There were more incidence of hypotension and bradycardia seen in Propofol-Fentanyl group, which could be attributed to the cumulative cardio depressant effect of Propofol and Fentanyl.
5. There was no pain on injection and less intropeative restlessness in Propofol-Ketamine group as compared to Propofol-Fentanyl group.

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