

Research Article

Two different concentrations of propofol and ketamine combinations in pediatric patients under intrathecal injection of chemotherapy drugs

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ABSTRACT

Background: Intrathecal injection of chemotherapy drugs in leukemic children is a painful procedure that needs sedation and analgesia. Different combinations of ketamine and propofol (ketofol) are used for this purpose. In this study we compared two different concentrations of ketofol (combination of 1/3 and 1/5 of ketamine and propofol).

Methods: In this randomized double blinded controlled clinical trial, 80 Children were studied in two groups. Group 1 received a combination of 1/3 of ketamine and propofol and group 2 received a combination of 1/5 for procedure of Intrathecal injection of chemotherapy drugs. Hemodynamic parameters, recovery time, and drug side effects were compared between two groups.

Results: In this study 80 children age 4-12 years old underwent Intrathecal injection of chemotherapy drugs were studied. There were no significant differences in age, weight between groups. Recovery time was significantly shorter in group 2 ($p = 0.001$). Also heart rate was lower in group 2 significantly ($p = 0.001$), but mean arterial pressure was not different between two groups ($p = 0.287$). SPO₂ was $> 95\%$ in all the children during the procedure ($p = 0.74$).

Conclusions: Combination of 1/5 of ketamine and propofol (ketofol) for sedation in the children undergoing intrathecal injection of chemotherapy drugs is better than a combination of 1/3 because of shorter recovery time and lower heart rate.

Keywords: Propofol, Ketamine, Ketofol, Chemotherapy drugs.

INTRODUCTION

Invasive procedures such as Intrathecal injection of chemotherapeutic drugs and lumbar puncture are painful procedures that are often repeated at regular intervals in leukemic patients. Especially in children these procedures need sufficient sedation and analgesia.¹ Propofol is an agent with rapid onset and short duration of action. Its uses include the induction and maintenance of general anesthesia, procedural sedation and sedation for

mechanically ventilated adults. Adverse effects include dose-related cardiovascular and respiratory depression and bradycardia.² Propofol is known to be amnestic but not analgesic, which for some clinicians is a potential concern when performing painful procedures.³ Ketamine is a phencyclidine anesthetic that produces intense analgesia, sympathetic nervous system stimulation, and increased blood pressure and heart rate. Unlike propofol, ketamine causes minimal cardiovascular and respiratory depression, and patients maintain protective airway

reflexes as well as spontaneous respiration. A major drawback of ketamine is the incidence of emergence reactions at increasing doses, which may include nightmares or vivid hallucinations.¹ Other ketamine uses include analgesia, treatment of bronchospasm, and sedation in intensive care.⁵ Administering ketamine and propofol mixed in the same syringe (ketofol) has been shown to be efficacious in the operating room, ambulatory settings and emergency departments.^{6,7} Various combinations of propofol and ketofol have been described in the provision of procedural sedation in adults and children. This study was designed to evaluate the use of ketofol "ketamine/propofol mixtures" in two different ratios (1:3 and 1:5) for sedation and analgesia for Intrathecal injection of chemotherapy drugs in leukemic children.

METHODS

This study was randomized double blinded clinical trial was done after approval by the Ethical Committee of Yazd University of Medical Sciences, Iran and written informed consent from October 2012 to Mars 2013. In these study 80 leukemic children aged 4_12 years old underwent Intrathecal injection were evaluated. Sample size was done with simple randomization. Patients with a history of allergy to ketamine or propofol, Albumen, Soya, hemodynamic instability or elevated intracranial pressure excluded from the study. According to random-number table patients assigned two groups of 40. In this study, intrathecal injection of chemical drugs was done by a pediatric oncology specialty and sedation was performed by an anesthesiologist. Pediatric assistant, anesthesia assistant, and pediatric nurse were present during process. The patient was constantly under monitoring including pulse oximetry, NIBP, and HR from beginning to end of procedure. Ketofol was prepared by anesthesia nurse as 1-3 (one part of Ketamine and three parts of Propofol) and 1-5 (one part of Ketamine and five parts of Propofol) and the syringes are encoded in a way that the injector is not aware of the drug. Group 1 (40 Patients) received ketofol (1/3) and group 2 received ketofol (1/5) for sedation before Intrathecal injection of chemotherapy drugs to achieve near Ramsay score = 5 sedation level. Electrocardiograms, pulse oximetry and non-invasive blood pressure monitored during the procedure. During the procedure, if the child is an awake, additional dose of ketofol is injected intravenously to reach ramsay score = 5. After surgery, nausea and vomiting, hallucination, respiratory depression, HR, MAP, Ramsay score, duration of recovery, respiratory rate, and ketamine/propofol doses recorded in a questionnaire during recovery time. All data analyzed by SPSS software version 15 and statistical tests. P. Values <0.05 was considered significant.

RESULTS

In this study 80 children age 4-12 years old with ALL that underwent Intrathecal injection of chemotherapy drugs were studied. The patients were assigned into two groups of 30: group 1(ketofol: 1/3) and group 2 (ketofol: 1/5).

Analyzed data showed that demographic features they were similar in two groups and there was no significant in age ($p = 0.704$), weight ($p = 0.157$) between two groups (Table 1).

The mean of heart rate in group 1 (109.43 ± 6.65) was greater in group 2 (100.73 ± 8.26) and it was significant between two groups ($p = 0.0001$), but mean of mean arterial blood pressure were not significant in both groups ($p = 0.287$).

Table 1: Mean of age, weight between two groups.

Group Variable	Ketofol 1/3		Ketofol 1/5		P value*
	Mean	SD	Mean	SD	
Age (year)	6.29	2.89	6	2.93	0.704
Weight (Kg)	16.87	6.72	20.2	10.76	0.157

*: t-test

Table 2: Mean of HR, RR, MAP, So₂, RS, and recovery time between two groups.

Group Variable	Ketofol 1/3		Ketofol 1/5		P value*
	Mean	SD	Mean	SD	
RR (b/min)	19.47	1.69	16.87	2.2	0.0001
HR (b/min)	109.43	6.65	100.73	8.26	0.0001
MAP (mmHg)	58.4	7.6	60.3	5.99	0.287
So _{2(s)}	96.97	1.18	96.87	1.13	0.74
RS	4.17	0.64	3.87	0.57	0.062
Recovery time	8.03	0.89	5.3	1.51	0.0001

*: t-test

RR: respiratory rate. HR: heart rate. MAP: mean arterial pressure. So₂: O₂ saturation. RS: Ramsay score

This study showed that the mean of respiratory rate in group 1 (19.47 ± 1.69) was greater in group 2 (16.87 ± 2.2) and there were significant differences in respiratory rate in both groups ($p = 0.0001$). Recovery time in group 1 (8.03 ± 0.89) was longer in group 2 (5.3 ± 1.51) and there were significant differences in recovery time between two groups ($p = 0.0001$), also there were significant differences in ketamine/propofol doses ($p = 0.002$) between two groups. This study demonstrated there were no significant differences in So₂ ($p = 0.74$) and Ramsay

score ($p = 0.62$) between two groups (Table 2) also there were no significant difference in adverse effects (Nausea and vomiting, hallucination and respiratory depression) between two groups ($p = 0.137$) (Table 2).

DISCUSSION

Intrathecal injection of chemotherapy drugs are invasive procedures that cause moderate to severe pain and anxiety so adequate analgesia and sedation are required when these procedures is planned especially in leukemic children. The goals of procedural sedation are to provide an adequate level of sedation while minimizing pain, stable cardiovascular and respiratory status.⁸ Propofol used for the induction and maintenance of general anesthesia as a short-acting intravenous sedative agent. Ketamine is a phencyclidine anesthetic that produces intense analgesia.⁸ The combination of ketamine with propofol produces favorable adverse event and recovery time profiles.⁹ This study was designed to evaluate the use of ketofol ketamine/ propofol mixtures in two different ratios (1:3 and 1:5) for sedation and analgesia for intrathecal injection of chemotherapy drugs in leukemic children.

In this study showed that combination of 1/5 of ketamine and propofol (ketofol) for sedation in the children undergoing intrathecal injection of chemotherapy drugs is better than a combination of 1/3 because of shorter recovery time and lower heart rate that result in smaller dose of ketamine in ketofol combination (1.5) minimizes the psychomimetic side effects and shortens the recovery time. Similar to our study, Hashemi et al. reported that the adjunctive use of the smaller dose of ketamine in ketofol combination (1.2) minimizes the psychomimetic side effects and shortens the recovery time.¹⁰ In our study recovery time was significantly shorter in group 2 (1.5) too, but there was no significant difference in side effects between two groups. Also Davis et al. compared the quality of analgesia and side effects of two different concentrations of ketofol (1.1 and 1.4) in children undergoing procedural operation. They found an increase in postoperative nausea, psychomimetic side effects and delay in discharge times in the group with the largest ketamine dosage (1.1). So, according to their study smaller dose of ketamine in ketofol combination (1.4) shortens the recovery time¹¹ but in our study, there were no significant in postoperative nausea, psychomimetic side effects. Abdellatif et al. evaluated the use of ketofol in two different ratios (1:1 and 1:2) for sedation and analgesia for outpatient transrectal ultrasound prostate biopsy. Similar to our study time for home discharge was shorter in group 1 (1.2) compared to group 2 (1.1).¹² Yazdi et al. compared two different combinations of ketamine/propofol (1.2 and 1.3) to reach necessary sedation scale. In their study, recovery time and hallucination was significantly higher in group I (1.2), but in both groups hemodynamic were stable, amnesia was enough, and there was no respiratory depression. According to their study Lower doses of Ketamine in

these combinations have lower psychomimetic side effects, and shorter recovery time.¹³ According to this study Combination of 1/5 of ketofol for sedation in the children undergoing intrathecal injection of chemotherapy drugs is better than a combination of 1/3 because of shorter recovery time and lower heart rate.

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