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SCIENTIFIC ARTICLE

Ketamine–propofol sedation in circumcision

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KEYWORDS
Ketamine–propofol;
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Abstract
Background and objective: To compare the therapeutic effects of ketamine alone or ketamine plus propofol on analgesia, sedation, recovery time, side effects in premedicated children with midazolam–ketamine–atropin who are prepared circumcision operation.
Methods: 60 American Society of Anaesthesiologists physical status I–II children, aged between 3 and 9 years, undergoing circumcision operations under sedation were recruited according to a randomize and double-blind institutional review board-approved protocol. Patients were randomized into two groups via sealed envelope assignment. Both groups were administered a mixture of midazolam 0.05 mg/kg + ketamine 3 mg/kg + atropine 0.02 mg/kg intramuscularly in the presence of parents in the pre-operative holding area. Patients were induced with propofol–ketamine in Group I or ketamine alone in Group II.
Results: In the between-group comparisons, age, weight, initial systolic blood pressure, a difference in terms of the initial pulse rate was observed ($p > 0.050$). Initial diastolic blood pressure and subsequent serial measurements of 5, 10, 15, 20th min, systolic blood pressure, diastolic blood pressure and pulse rate in ketamine group were significantly higher ($p < 0.050$).
Conclusion: Propofol-ketamine (Ketofol) provided better sedation quality and hemodynamy than ketamine alone in pediatric circumcision operations. We did not observe significant complications during sedation in these two groups. Therefore, ketofol appears to be an effective and safe sedation method for circumcision operation.

PALAVRAS-CHAVE
Cetamina-propofol;
Sedação;
Circuncisão

Sedação com cetamina-propofol em circuncisão

Resumo
Justificativa e objetivo: Comparar os efeitos terapêuticos da cetamina isolada ou combinação de cetamina-propofol em analgesia, sedação, tempo de recuperação e efeitos colaterais em crianças pré-medicadas com midazolam-cetamina-atropina programadas para procedimentos de circuncisão.

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Métodos: Sessenta crianças, estado físico ASA I-II (de acordo com a classificação da Sociedade Americana de Anestesiologistas), com idades entre três e nove anos, submetidas a procedimentos de circuncisão sob sedação, foram recrutadas de acordo com um protocolo de randomização duplo-cego aprovado pelo Conselho de Revisão Institucional. Os pacientes foram randomizados e alocados em dois grupos com o uso do método de envelopes lacrados. Ambos os grupos receberam uma mistura de midazolam 0,05 mg kg^{-1} + cetamina 3 mg kg^{-1} + atropina 0,02 mg kg^{-1} por via intramuscular, na presença dos pais na área de intervenções pré-operatórias. A indução foi realizada com propofol-cetamina no Grupo I ou cetamina isolada no Grupo II.
Resultados: Nas comparações entre os grupos foram observadas a idade, o peso, a pressão arterial sistólica inicial e a diferença em relação à taxa de pulso inicial ($p > 0,050$). A pressão arterial diastólica inicial e as mensurações seriadas subsequentes nos minutos 5, 10, 15 e 20 da pressão arterial sistólica, pressão arterial diastólica e taxa de pulso do grupo cetamina foram significativamente maiores ($p < 0,050$).
Conclusão: Cetamina-propofol (cetofol) proporcionou melhor qualidade de sedação e estabilidade hemodinâmica que cetamina isolada em cirurgias pediátricas de circuncisão. Não foram observadas complicações significativas durante a sedação nos dois grupos. Portanto, cetofol parece ser um método de sedação eficaz e seguro para procedimentos de circuncisão.

Introduction

Circumcision is a painful and stressful outpatient procedure in children.[1] An ideal anesthetic agent for this operation should provide adequate analgesia, amnesia, sedation, immobility and short recovery time while should be avoid cardiovascular and respiratory depression, nausea-vomiting and agitation.

The combination of propofol and ketamine (ketofol) in the same syringe successfully produced adequate action for oncologic procedures,[2] interventional radiology,[3] cardiac catheterization,[4] hematological diseases[5] in children. Opiods, midazolam, ketamine, propofol and dexmedetomidine are the generally preferred sedoanalgesic agents.[6] Propofol, as an intravenous anesthetic, is applied as an intermittent infusion for sedation in spinal anesthesia.[7] If the long infusion duration is ignored, waking is provided at the time of terminating the infusion.[8] Nonetheless, the use of propofol may cause cardiovascular and respiratory system depression.[9] Ketamine may be considered effective with direct sympathetic stimulation and norepinephrine by reuptake inhibition from the postganglionic sympathetic system.[10] It also induces functional dissociation between the limbic and cortical system often referred to as 'dissociative anesthesia'. Protective airway reflexes are maintained during sedation and the high therapeutic index of ketamine makes this drug suitable for regional anesthesia.[11]

Ketofol is prepared as a 1:1 mixture of ketamine 10 mg/mL and propofol 10 mg/mL mixed in a 10 mL or 20 mL syringe and is constituted a solution which is 5 mg each of ketamine and propofol in each mililiters.

In this study we aimed to evaluate the effects of ketamine alone or ketamine plus propofol on analgesia, sedation, recovery time, and side effects in premedicated children with midazolam–ketamine–atropin who are undergoing circumcision operation.

Materials and methods

60 ASA physical status I–II children, aged between 3 and 9 years, undergoing circumcision operations under sedation were recruited according to a randomize and double-blind institutional review board-approved protocol. Patients with clinically significant neurological, respiratory, cardiovascular and psychiatric diseases were excluded from the study.

Patients were randomized into two groups via sealed envelope assignment. Both groups were administered a mixture of midazolam 0.05 mg/kg + ketamine 3 mg/kg + atropine 0.02 mg/kg intramuscularly in the presence of parents in the pre-operative holding area. After 5 min, children were included in the operating room. Monitoring for the procedure consisted of three lead ECG, SpO_2 with plethysmography and noninvasive blood pressure. After placement of an intravenous cannula, patients were induced with propofol–ketamine in Group I or ketamine alone in Group II. Medication dosages, administration times, total procedure time, vital signs (non-invasive blood pressure, oxygen saturation via pulse oxymetry, heart rate, respiration rate), side effects, and sedation scores were recorded by the same anesthesiologist at the beginning of the procedure and after induction at 5 min and then every 5 min until the end of the procedure. The sedation levels of the patients were assessed by Ramsay sedation score; induction and maintenance were applied to target score of 2 or 3. Prilocaine was injected for the dorsal penile nevre block by the surgeon and the procedure was started. Through the circumcision procedure, when the drug doses were not sufficient to achieve the targeted sedation scores or when

the patient moved, additional boluses of propofol–ketamine was administered in Group I or ketamine was administered in Group II. Supplemental drug requirements were noted. We also noted the adverse symptoms including desaturation (SpO_2 < %90), apnea (>15 s), rash, agitation, vomiting, and increased secretions. All patients received oxygen supplementation via nasal cannula or by blow-by with a gas flow rate of 2 L/min throughout the procedure. All operations were performed by the same surgeon.

The Ramsay sedation scale used to determine the response to sedation and analgesia is graded as 5, deep sedation: 1, patient awake: 6, patient asleep with no response to any stimuli.

When the procedure was complete, the patients were transferred to the recovery room and their levels of sedation, discharge time, and adverse events were assessed at 5 min intervals. Discharge criteria were as follows: airway patent with adequate oxygenation; awake or easily aroused (minimal tactile or vocal stimulation might be necessary); swallowing reflex present, demonstrating ability to swallow clear liquids while protecting the airway; presedation level of responsiveness achieved.

Statistical analysis was made using Statistical Package for the Social Sciences15.0 (SPSS 15.0, SPSS Inc., Chicago, IL) software. All quantitative data were analyzed with the Kolmogorov–Smirnov test to show distribution. Data with normal distribution were expressed as mean ± standard deviation and data with non-normal distribution as median (inter quartile range). According to the distribution status of quantitative data independent sampling *t*-test or Mann–Whitney *U*-test was used. The Chi-square test was used to compare categorical data. A confidence interval of 95% was defined and a value of $p < 0.05$ was accepted as statistically significant.

Results

In the between-group comparisons, age, weight, initial systolic blood pressure, a difference in terms of the initial pulse rate was observed ($p > 0.050$). Initial diastolic blood pressure and subsequent serial measurements of 5, 10, 15, 20th min, systolic blood pressure (Fig. 1), diastolic blood pressure (Fig. 2) and pulse rate (Fig. 3) in ketamine group were significantly higher ($p < 0.050$). Follow-up time in terms of the need for additional analgesic in ketofol group used

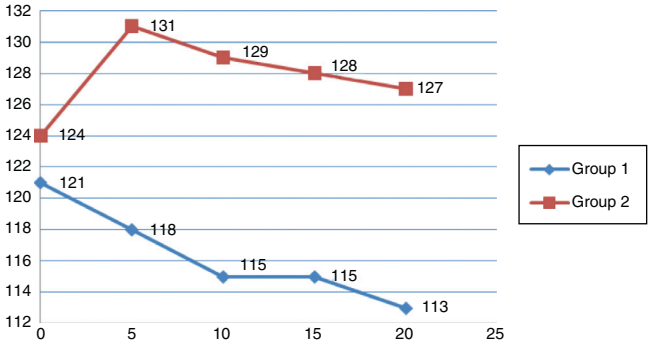

Figure 1 Comparison of systolic blood pressure levels between groups.

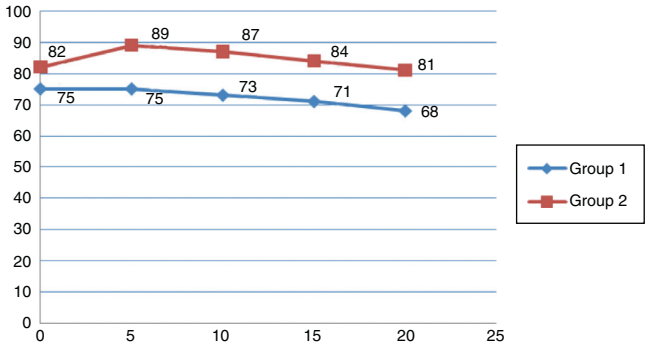

Figure 2 Comparison of diastolic blood pressure levels between groups.

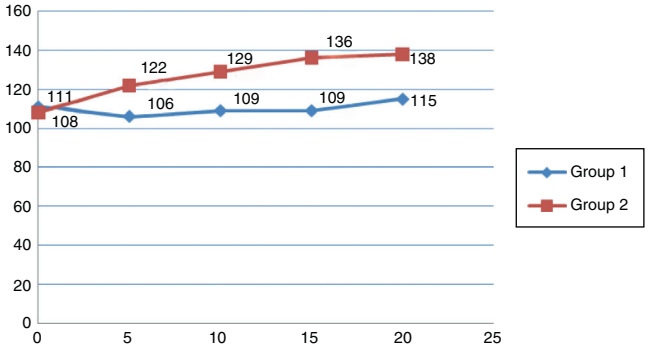

Figure 3 Comparison of heart rates between groups.

significantly fewer analgesics ($p < 0.050$). Both groups were similar in terms of complications ($p > 0.050$).

Discussion

According to American Society of Anaesthesiologists (ASA) data (2006), high doses of sedation have been reported to lead to respiratory depression and are an important reason for unexplained malpractice.[12] Anesthesia is a balance between the patient's state of wakefulness and the need for anesthetic medication. If an insufficient dose is administered, the patient's wakefulness increases while a high dose causes hemodynamic instability, prolonged time to waking and other complications.[13] In relation to the response to sedation and analgesia, it was decided to use the Ramsay scale in the current study because it is easy to apply.[14–16] The ideal sedative agent for regional anesthesia should have a rapid onset of action, produce a level of sedation sufficient for patient comfort, and have a short duration of action.[10] Generally, the intermittent intravenous application in sedation does not allow for the adjustment of the plasma concentration level of the medication and extends the time to waking.[17]

A pharmacological disadvantage of propofol is its relatively narrow therapeutic range. Unlike opioids and benzodiazepines, an antagonist is not available to reverse the effects. Despite its high potential to induce respiratory depression and cardiovascular instability, propofol has been routinely administered by anesthesiologist.[18]

In this prospective, randomized study, we compared the safety and efficacy of ketamine/propofol combination

(ketofol) and ketamine alone for circumcision operation under local anesthesia via penile block. Our study showed that ketofol supplied more effective and safety sedation than ketamine alone in children.

Circumcision is a painful operation and it usually is performed in children.[1] Many studies are performed on the method of anesthesia in this operation and most of them involved penile block and caudal block with or without sedation/general anesthesia.[11]

The clinical effects of propofol and ketamine are complementary. While propofol provides hypnosis, ketamine performs analgesia and stable hemodynamic activity,[19] the combination of ketamine and propofol is renamed ''ketofol'' and is currently popular agent for procedural sedation.[2–5]

David and Shipp[20] compared the frequency of respiratory depression during emergency department procedural sedation with ketamine plus propofol versus propofol alone. Ketamine was applied only one as a 0.5 mg/kg via intravenous route at the beginning procedure, not was prepared ketofol. And they arrived at the conclusion of ketamine/propofol did not reduce the incidence of respiratory depression but resulted in greater provider satisfaction, less propofol administration and perhaps better sedation quality. In a study by Shah et al.,[21] which compared with ketamine alone and the combination of ketamine and propofol for pediatric orthopedic reductions, it was shown that ketamine/propofol combination produced slightly faster recoveries while also demonstrating less vomiting, higher satisfaction scores and similar efficacy and airway complications. Both groups did not experience significant respiratory depression and ketofol group had better sedation levels than ketamine group in our study. We found that ketofol provided more acceptable hemodynamy than ketamine alone. But we did not study for the sedation or recovery time.

In conclusion, ketofol provided better sedation quality and hemodynamy than ketamine alone in pediatric circumcision operations. We did not observe significant complications during in these two groups. Ketofol obtained by mixing ketamine with propofol provided appropriate analgesia and sedation.

Our results indicate that intravenously administered ketofol produces faster recovery time and safe sedation.

Conflicts of interest

The authors declare no conflicts of interest.

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