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THE EFFECTS OF DIFFERENT DOSE KETAMINE ON PROPOFOL SEDATION FOR INFANTS AND CHILDREN UNDERGOING AMBULATORY MAGNETIC RESONANCE IMAGING

Bebek ve Çocuk Hastalarda Ambulatuar Manyetik Rezonans Görüntüleme Uygulamalarında Propofol Sedasyonuna Farklı Doz Ketamin Eklenmesinin Etkileri

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ABSTRACT

Objective: The aim of this study was to evaluate the efficiency and effectiveness of the sedation practice, recovery time, and adverse event profile and total propofol consumption combined propofol infusion plus bolus propofol with different doses of ketamine -propofol combinations for infants and children sedation undergoing ambulatory magnetic resonance imaging.

Methods: After obtaining approval from the University Ethics Committee, This double-blind, randomized trial enrolled American Society of Anesthesiology (ASA) Class I - III patients, aged 1 month to 12 years requiring MRI under deep sedation. One hundred and forty two patients were included in the study and were divided into 4 groups, prospectively. Premedication consisted of intranasal midazolam 0.5 mg/ kg over six month children. Group I received 1 mg/kg propofol intravenously (IV), bolus followed by a 100 µq/kg/min infusion. Group II, III, IV received IV ketamine bolus of 0.5mg/ kg, 1mg/kg and 1.5mg/kg respectively and then patients received an infusion of a solution containing propofol 100 µq/kg/min augmented with additional propofol boluses as needed. Blood pressure, heart rate, Ramsey sedation scores, oxygen saturation and end-tidal CO2 levels were recorded once every five minutes. Duration of the procedure, total amount of propofol used, time until Aldrete scores reached 9 and additional propofol doses needed were also recorded, as were complications like agitation, desaturation, bradycardia and hypotension.

Results: There were no differences between the demographic properties of the groups. Twenty-five, 65, 70 and 75th minute heart rates were higher in ketamine groups when compared to Group 1, the difference was significant ($p<0.05$). Systolic blood pressure levels at 5, 10, 15, 25, 30 and 35th minute were lower in group I. There were no statistically significant differences between diastolic blood pressures, end tidal carbondioxide levels, saturation levels and complications between the groups. More additional propofol needs and longer recovery duration were recorded in group I compared with Group IV.

Conclusion: We have found that 1.5mg/kg bolus ketamine doses added to propofol infusion resulted in lower additional propofol doses and shorter recovery times and is a good option in sedation of children during MRI.

Key Words: Propofol, ketamine, MRI sedation, children, outpatient (day-case).

ÖZET

Amaç: Çalışmanın amacı, manyetik rezonans görüntüleme uygulamalarında bebek ve çocuk hastalarda kombine propofol infüzyon + bolus propofol ile farklı doz ketamin-propofol kombinasyonunun, sedasyon uygulaması , derlenme süresi ve yan etki profili ile toplam propofol tüketimi, verimliliğini ve etkinliğini değerlendirmektir.

Yöntem: Çalışmaya etik kurul onayı alındıktan sonra anestezi altında manyetik rezonans görüntüleme işlemi yapılacak olan 1 ay – 12 yaş arası, ASA I-III 142 hasta dahil edildi ve 4 gruba ayrıldı. 6 aydan büyük çocuklara 0,5 mg/kg dan intranazal midazolam ile premedikasyon yapılmıştır. Grup 1 olgulara 1 mg/kg'dan bolus propofol uygulandıktan sonra100 µq/kg/dk dan propofol infüzyonu başlandı. Grup 2; 0,5 mg/kg dan bolus ketamin; Grup 3; 1 mg/kg'dan ketamin Grup 4; 1,5 mg/kg'dan bolus ketamin'i takiben da 100 µq/kg/dk dan propofol infüzyonu başlandı. Hastaların kalp atım hızı, sistoloik/diyastolik kan basıncı, oksijen satürasyonu, end-tidal karbondioksit değeri ve Ramsey sedasyon skoru 5'er dakikalık aralıklarla kaydedildi. İşlem süresi, kullanılan propofol miktarı, Aldrete skorları 9'a ulaşma zamanı, toplam ve gerekli ek propofol dozları kaydedildi. Ajitasyon, desatürasyon, bradikardi ve hipotansiyon gibi yan etkiler kaydedildi.

Bulgular: Grupların demografik özellikleri arasında anlamlı bir farklılık saptanmadı. Grup 1

Table 1: Additional propofol doses and discharge times of groups.

	Group I	Group II	Group III	Group IV	P value
Additional propofol doses	1.3 ± 0.8	2.2 ± 1.5	1.3 ± 0.5	1.4 ± 0.6	0.026*
Recovery time (min)	20 ± 5	17 ± 4	20 ± 8	16 ± 4	0.006*

Table 2: Distribution of complications.

	Group I	Group II	Group III	Group IV	P value
Convulsion	0	0	0	1	0.175
Halusination	1	0	0	0	0.157
Agitation	0	1	0	3	0.196
Myoclonus	0	3	4	3	0.157
Nistagmus	0	2	0	1	0.828
Apnea	0	0	0	1	0.175
Bradycardia	0	0	1	1	0.204
Desaturation	7	10	6	10	0.791

ile karşılaştırıldığında kalp atım hızı ketamin alan gruplarda 25., 65., 70. ve 75. dakikalarda daha yüksekti (p <0.05). Grup 1 olgularda diğer gruplara göre istatistiksel olarak anlamlı ek propofol gereksinimi , daha uzun derlenme süresi saptandı.

Sonuç: 1.5mg/kg ketamin bolus + propofol infüzyonu olan grupta ek propofol gereksinim dozları ve derlenme süreleri daha kısa bulundu, bu dozların MRG sırasında çocukların sedasyonu için iyi bir seçenek olduğu kanısına vardık.

Anahtar Kelimeler: Propofol, ketamin, MRG sedasyon, çocuklar, ayaktan (günlük vaka).

INTRODUCTION

Many children increasingly need effective sedation or anaesthesia for painful or distressing diagnostic or therapeutic procedures in sites apart from operating rooms such as magnetic resonance imaging (MRI) or computed tomography (CT) sections. This need has become apparent in children hospitals in which case numbers in sites apart from operating rooms have become closer to those in operating rooms (1).

There are two main reasons of this increase. First of them is the rapid increase of technical developments in radiology (2,3). Radiologists prefer to perform MRI under anesthesia because of better image quality. Invasive procedure rates are decreasing due to detailed information from these improvements (4). Secondly, anesthesiologists who work in pediatric MRI or CT centers are experiencing that their presence helps to be obtained good outcomes. Radiologists also recognize this truth and they demand a continuous anesthesia service (3).

Propofol, a short-acting hypnotic, is the most common used agent in radiological procedures (5). Its short recovery time is the reason of choice. However some dose-depended hemodynamic and respiratory side effects can be seen. Although ketamine has amnestic and analgesic effects, it has no important respiratory and cardiovascular side effects (6). On the other hand, it has some undesirable side effects such as hallucinations and nausea (7).

The aim of this study was to evaluate the efficiency and effectiveness of the sedation practice, recovery time, adverse event profile and total propofol consumption combined propofol infusion plus bolus propofol with different doses of ketamine - propofol combinations for infants and children sedation undergoing ambulatory MRI.

MATERIALS AND METHODS

Patients and Procedure

142 ASA I-III patients (minimum-maximum age: 1 month-12 years) who underwent MRI (1.5 Tesla Siemens, Germany) were included to the study as double-blinded design with The University ethical committee approval (ethical committee number : LUT 09/162-14 Date: 22.04.2010). All the patients were included to the study by taken informed consent from their parents. Patients were divided into four groups. In all the groups, children older than 6 mounts were performed premedication by 0.5 mg/kg intranasal midazolam before appliance of vascular access. After appliance of vascular access, 100 µq/kg/min propofol infusion was started after 1mg/kg bolus propofol in group 1, 0.5 mg/kg bolus ketamine in group 2, 1mg/kg bolus ketamine in group 3 and 1.5mg/kg bolus ketamine in group 4. 0.5 mg/kg bolus propofol administration was planned in the case of patient movement or being awake during procedure. Additional propofol doses were noted as " the need of additional doses of propofol". Ramsey score was aimed to achieve 5 during the procedures (8). Propofol infusion doses were decreased to 50 µq/kg/min at the time Ramsey scores achieve to 5. Propofol infusion was stopped at the end of the procedure and total dose of propofol was calculated and recorded. Although total propofol doses consist of sum of bolus doses, infusion amounts and additional doses in group 1, it was equal to sum of infusion amounts and additional doses in group 2, 3 and 4.

Basal parameters were recorded before procedure, during procedure, heart rate, systolic and diastolic blood pressure, oxygen saturation, end-dial carbon dioxide level and Ramsey sedation scores were calculated in per 5 minutes periods. In this study, during and after the procedure, patients were given 2lt/min nasal oxygen support and decrease of oxygen saturation under 95% was accepted significant. In this case, jaw suspension, airway appliance or mask ventilation were the choice of interventions. Complications were noted to the patient follow-up forms. These complications were described as seizure, hallucinations, nausea, vomiting, delirium, diplopia, agitation, myoclonus, nystagmus, apnea, bradycardia, decrease in oxygen saturation, hypotension and other.

After completion of procedure, patients were followed-up in recovery room after stopping propofol infusion. Period between completion of propofol infusion and and the tıme until modified adrete score reaches 9 or above was recorded as recovery time. When modified aldrete score reached 9, patients were sent to daily service or home (9).

Statistical Analysis

Statistical analysis of the study was performed by using SPSS version 13.0. Normal distribution of data was checked by Kolmogorov – Smirnov test. For non-normal distributed data, Kruskal – Wallis was used for four group and Mann – Whitney U test for two group comparisons. For normal distributed data, ANOVA was used for four group and t-test for two group comparisons. Pearson Chi-Square test and Fisher's Exact Chi-Square tests were used for analysis of categorical data. Paired t-test and Wilcoxon test were performed for interval comparison. Statistically significance was described as p value under 0.05.

RESULTS

142 ASA I-III patients (minimum-maximum age: 1 month-12 years) who underwent MRI were included to the study. There was

no statistically significant difference between four groups according to age, body weight and gender (p>0.05).
73 (51%), 32 (22.7%), 10 (7.1%), 4 (2.8%), 3 (2.1%), 3 (2.1.%) and 17 (12.1%) out of 142 patients were underwent cranial MRI, cranial MRI+spectroscopy, cranial MRI+ other (pituitary, lumbal MRI etc…), extremity MRI, abdomen MRI, cardiac MRI, others (pituitary, orbita MRI etc…), respectively. There was no statistically significant difference between distribution and durations of procedures of groups (p > 0.05) (Figure 1).
No significant difference was found between the total propofol consumption doses of the four groups. Although difference did not reach to significant level, total propofol doses of group 1 was higher than others as predicted (Figure 2).
A statistically significant difference was found between additional propofol dose numbers and discharge times (Table 1). The need of additional doses was higher in group 2 than others. However total propofol consumption doses of this group did not reach to those of group 1 (p < 0.05). In regards of duration of the procedure, no statistically significant difference was found (p > 0.05)
Complications were not seen in 74 (52.4%) out of 142 patients. Statistically significant difference was not seen between the complication rates of groups. Details of complications for each group were demonstrated in table 2.
In the comparison of basal values, there was not a statistically significant difference between peripheral oxygen saturation and heart rates of four groups (p >0.05). In the intra-group comparison of heart rates, increase in the 15th minute and decrease at the 5th, 10th, 20th, 25th, 30th, 35th, 40th, 45th, 50th, 55th and 65th minutes were found significant in group 1 (p<0.05).
Although it was not statistically significant, simultaneous increase in hearth rate and blood pressure in group 1 and administration of additional dosage during this time was evaluated in regards of patient wake-up periods. Change in systolic blood pressure of groups during procedures was demonstrated in figure 3.
The comparison of the four groups' diastolic blood pressure, end-tidal carbondioxide levels and Ramsey sedation scores did not yield a statistically significant (p>0.05) difference.
In regards of recovery time (Figure 4), the recovery time of 1.5mg/kg bolus ketamine administered group was significantly shorter (p>0.05).

DISCUSSION

Several different techniques can be performed during MRI procedures. General anesthesia supplies a safe airway, mean while improvements in sedation techniques reportedly allows use of sedation agents in small children (10,11). It should be kept in mind that deep sedation can cause the reduction of airway reflexes and suppression of respiration. On the other hand positive effects of propofol have been reported in several studies (12). Today, propofol is the first choice of agent in the sedation and anesthesia procedures outside the operating room. As seen in propofol sedation program of Srinivasan et al., propofol is not only being used by anesthesiologist, it is also in the daily practice of pediatricians (13). In our study, the effect of addition of different ketamine bolus doses to propofol infusion to adverse effects, recovery time and total propofol doses has been compared in children who underwent MRI. It was not seen any difference between groups according to demographic data and procedure durations.
In the study of Srinivasan et al., an increase was detected in the complication rate due to increase in propofol doses in older patients (13). Propofol might cause adverse effects such as hemodynamic instability, decrease in saturation rates and apnea (14). In this study we aimed to decrease total propofol doses and its adverse effects by adding different ketamine doses.
According to current literature, ketamine may cause adverse effects such as increase in secretions, respiratory complications, prolonged recovery times and hallucinations (15). Guite et al. has been reported that combined usage of ketamine and propofol is effective to decrease adverse effects of ketamine (16). Mortero et al. reported that application of low dose ketamine might positively affect to shorten of recovery times (17). Results of our study support this data. Although no statistical significant difference was detected between complication rates of groups, there is an increase in paradoxical reaction rate with increase in ketamine doses.
Tomatır et al. have found an statistically significant difference in hearth rates between the groups that received propofol (2.5 mg/kg bolus propofol and 100 µq/kg/min propofol infusion) and the groups that received propofol plus ketamine ketamin (0.5 mg/kg ketamine plus 1.5 mg/kg-1 propofol and 75 µq/kg/min propofol infusion) (14). In our study, a significant difference in heart rates between pre-sedation and pre-procedure and some parameters during procedure was found, all the parameters were in the normal limits. Tomatır at al. have been reported a significance in intra and intergroup evaluation of systolic blood pressure between propofol and ketamine groups, in their patients who underwent sedation during MRI (14). In our study, we have found a significant difference between systolic blood pressure of group 1 and others. Also, in group 1, we have found a significant decrease in blood pressure during procedure. These results are similar to other studies and current literature (18). Unlike other studies, in our study, there was no difference in diastolic blood pressure of 4 groups (14, 19). Ketamine might have inhibited propofol depended blood pressure decrease.
In our study, 2 lt/min oxygen was given to all the patients in the time span from beginning of the procedure until entrance to recovery room. Administration of oxygen to all sedated patients is the standard protocol in our center. Compared to other ketamine

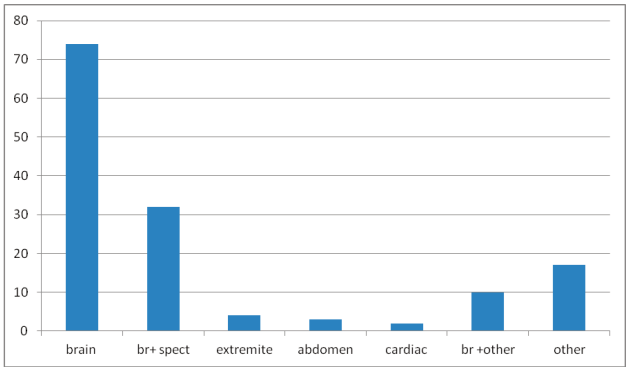

Figure 1: Distribution of procedures in entire patient groups.

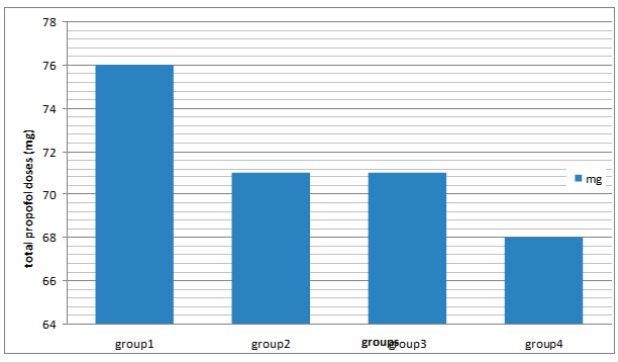

Figure 2: Total propofol doses of groups.

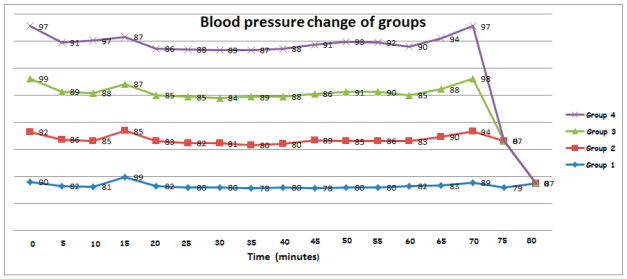

Figure 3: Changes in systolic blood pressure of groups during procedures.

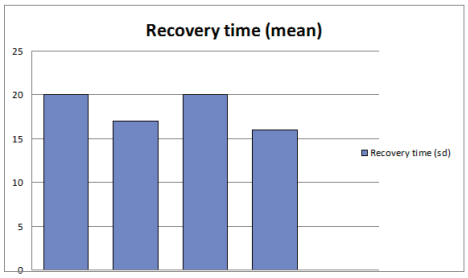

Figure 4: Recovery times of groups.

groups, an insignificant decrease has been seen in peripheral oxygen saturation of group 1. Also continuous end-tidal carbondioxide measurements have been done in case continuous oxygen provision hides a possible respiratory depression. There was no significant difference in peripheral oxygen saturations of groups. It is a proof to show the sufficiency of respiration in all groups.

It has not been possible to completely remove additional doses of propofol. As a result no difference was found between total propofol dosage. Although it was not significant, decrease in propofol doses in high dose ketamine (1.5mg/kg) group was accompanied with shortening in recovery times. Especially when used with midazolam premedication, even relatively high doses of ketamine did not lead to the feared complications.

In this study, we have not found significant difference in total propofol doses of groups. However, maximum difference was alculated between group I and IV. In parallel with this finding, a shortening has been detected in discharge times of group IV in comparison with group I. In contrast with our results, Tomatır et al have found shortening in discharge times of ketamine plus propofol group over propofol group (14).

A significant difference in additional propofol doses between group I and II was shown. The detection of significant difference between group II and other ketamine groups (III, IV) has demonstrated the insufficiency of 0.5 mg/kg ketamine appliance to supply qualified sedation during MRI. Ozdamar et al have compared propofol and ketamine and they have not found significant difference in need of additional doses (18). Reducing the need for additional dosage aims to increase the continuity of the MRI procedure and minimize the difference between procedure time and time spent sedating the patient (time spent during the administrationof the sedatives by the anesthesiologist/ other qualified stuff in the MR room)

Mason et al. had used dexmedotomidine in their study for sedation during MRI procedure (20). They had given 1mcq/kg/h dexmedotomidine by infusion following a bolus of 3mcg/kg dexmedotomidine to 279 patients. They had seen hypotension in 33% of patients. Additional bolus dose of dexmedotomidine and additional doses of pentobarbital had been needed in 48 and 13 patients, respectively. This study revealed that alternative agents to widely accepted propofol might have similar adverse effects. Rate of additional dose administrations by interrupting the procedure and the need of combination with other agents are similar in current studies (14,20).

CONCLUSION

This study demonstrated that 1.5mg/kg bolus ketamine combination is a safe and effective option to decrease the complication of propofol in MRI unites as a practice area apart from surgery rooms. Thus, prevention of possible complications and shortening of discharge times by decreasing total and additional doses of propofol, supply continuity of procedure and completion of procedure as soon as possible and with the best image quality are predicted. However, new studies are needed to describe ideal application time, dose and cost by trying different protocols in different procedures.

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