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ORIGINAL ARTICLE

Evaluation of clinical effectiveness of three different sedation protocols (intravenous propofol vs. ketamine vs. ketofol) in anxious children

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ABSTRACT

Aim: The aim of this prospective randomized blinded study was to evaluate clinical effectiveness of three different sedation protocols (intravenous propofol vs. ketamine vs ketofol) in children scheduled for dental treatment.

Methodology: Seventy five ASA I patients were enrolled; were randomly selected from 6-12 years aged children with documented high anxiety level and were randomly divided into 3 groups: ketamine treated group (Group K) – received a priming dose of 1 mg/kg, followed by continuous infusion dose of 50-60 µg/kg/min, propofol treated group (Group P) – received priming dose of 2 mg/kg, followed by continuous infusion dose of 70-90 µg/kg/min, and ketamine plus propofol treated group (ketofol) (Group KP) - which received priming dose of 0.6 mg/kg, followed by continuous infusion dose of 40-60 µg/kg/min. During the study period, vital signs of children, the level of sedation using BIS monitor and time interval needed for full recovery were recorded every 5 min. The levels of changing anxiety were measured using Children's Fear Survey Schedule – Dental Subscale (CFSS-DS) and face version of the Modified Child Dental Anxiety Scale (MCDASf).

Results: A higher complication rate was noted in ketamine treated group ($p < 0.05$). Also mean time of recovery was found statistically longer in ketamine treated group ($p < 0.05$). Both in KP and P groups we found similar associations between BIS values and sedation levels. In contrast there was no correlation between BIS values and sedation levels in ketamine treated group. Children's anxiety levels were significantly decreased in propofol and ketofol treated groups compared with ketamine treated group ($p < 0.05$).

Conclusion: During the study period no serious complication noted in both of three different sedation protocols. We found that ketamine plus propofol treatment is associated with lower complication and higher satisfaction rates in pediatric patients undergoing dental treatment.

Key words: Intravenous sedation; Ketofol; Ketamine; Propofol; Anxiety; CFSS-DS; children's dental anxiety; $MCDAS_f$

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INTRODUCTION

Dental anxiety and fear is a common entity that causes treatment difficulties for both, the dentists and the patients, especially in case of children.[1,2] Oosterink et al.[3] reported that dental anxiety has fourth place after snake phobia, fear of heights and physical injury. Prevalence of dental anxiety and fear changes between 6%-52%, in accordance with type of evaluation method used, population, the prevalent culture and the country.[2,4,6] Several factors identified as risk factors for dental anxiety include age, female gender, traumatic medical or dental experiences, education level and socio-economic class of the family.[7,8]

Procedural sedation for dental treatments of children offers safe and comfortable environment with decreased anxiety levels. In this manner intravenous sedation, with combined sedative agents such as midazolam, ketamine, propofol, fentanyl, provides various sedation levels between conscious to unconscious sedation. Propofol and ketamine combination is relatively new and promising sedation option with decreased respiratory and hemodynamic complications.[9,10] It is thought that the unique pharmacological features of these two agents reduce the side effects of each other and thus provide comfortable and safe sedation.

In this study we investigated the effects of three different sedation techniques, e.g. ketamine alone, propofol alone and ketamine plus propofol (ketofol) on children anxiety. Also clinical effectiveness of these procedures was evaluated via BIS monitoring, Observer's Assessment of Alertness/Sedation (OAAS) and Ramsay Sedation Scales (RSS) scores.

METHODOLOGY

After obtaining ethical committee approval we enrolled 75 children, aged 6 to 12, American Society of Anesthesiologists (ASA) class I, with high level of dental anxiety [Frankl Behavioral Scale (FDS) ≤ 2], referred to Gazi University Faculty of Dentistry, Department of Pedodontics. All the patients had failed to start dental treatment despite behavioral guidance techniques. Healthy subjects with no mental or motor disability, no sedation/general anesthesia history and requiring at least two sessions of dental treatment were included. Exclusion criteria were history of sensitization or allergic reaction to propofol, ketamine, soy or egg products; increased intracranial or intraocular pressure; use of drugs known to interact with either study agent, administration of medication due to upper and/or lower respiratory tract infection during 48 hours before sedation. Written, informed consent was obtained from parents of all patients. None of the patients received premedication in order to achieve objective results.

Patients were randomized using closed envelope method to one of the three study groups;

Group K: (n = 25) Patients received IV ketamine (Ketalar® 50 mg/mL Pfizer/Turkey). 4 ml ketamine diluted with normal saline to make a total volume of 20 ml, 1 mg/kg bolus dose followed by 50-60 μg/kg/min continuous infusion via infusion device (Injectomat MC Agilia® Fresenius Kabi-France)

Group P: (n = 25) Patients received IV propofol (Propofol® 1% Fresenius 10 mg/ml, Fresenius Kabı/Sweden) (total volume was 20 ml, 2 mg/kg bolus dose followed by 70-90 μg/kg/min continuous infusion via infusion device.

Group KP: (n = 25) A mixture in a ratio of 1:1 was prepared using 200 mg propofol (20 ml) combined with 200 mg ketamine (4 ml). Patients received 0.6 mg/kg bolus dose followed by 40-60 μg/kg/min continuous infusion via infusion device.

Prilocaine containing cream (Emla®) was applied to children hands 1 h before cannulation. Preoperative anxiety levels of patients were measured using face version of the Modified Child Dental Anxiety Scale (MCDASf) and Children's Fear Survey Schedule – Dental Subscale (CFSS-DS). In order to investigate economical and education levels of parents, all parents completed a questionnaire.

Respiratory rate (RR), heart rate (HR), systolic, diastolic and mean arterial pressure (SAP, DAP and MAP) and oxygen saturation (SpO2) were recorded at the beginning of study and then every 5 min during all procedures.

Loading dose was injected for 2 min followed by maintenance infusion. All patients were oxygenated with 4 L/min O2 via nasal cannula. An experienced anesthetist, who was blinded to the study drugs performed sedation procedure. An anesthesia assistant who was blinded to study groups recorded all parameters.

Depth of sedation was measured with BIS monitoring (BİS® XP, Aspect) for every 5 min during operation. RSS and OAAS were noted every 5 min during the procedure.

Topical anesthetic (Xylocaine®-Pump spray) was applied to oral mucosa and then local anesthesia with articaine hydrochloride (Ultracaine D-S Forte® -Aventis) was given.

Modified Vancouver Sedation Recovery Scale (MVSDS) was used in order to evaluate patients at postoperative period. Patients with a MVSDS score of 1 were discharged. After being fully recovered, the patients were questioned with MCDASf and CFSS-D again.

Table 1: Comparison of pre and postoperative CFSS-DS, MCDASf scores [Mean ± SD]

Scale	Group P (n = 25)	Group K (n = 25)	Group KP (n = 25)	p
CFSS-DS preoperative	41,32 ± 7,41	40.12 ± 6,37	39,56 ± 6,17	0.637
CFSS-DS postoperative	32,60 ± 6,92*, +	39,36 ± 6,30	34,40 ± 5,62*, +	0.001
MCDASf preoperative	31,76 ± 5,62	30.32 ± 5,60	29,32 ± 7,38	0.387
MCDASf postoperative	23,68 ± 5,67*, +	29,60 ± 5,55	25,04 ± 7,15*, +	0.003

*p < 0.05: Compared to Group K
+ p < 0.05:Compared to preoperative scores

Side effects and complications during perioperative period were recorded.

Statistical Analysis:

In order to achieve a difference level of at least 1.8 value with 85% confidence interval (CI) and 5% (0.05) alpha error between two groups in terms of changes in CFSS-DS levels at preoperative period versus postoperative period; we decided that the minimal sample size in each group had to be at least 23 patients. We used NCSS & PASS 2000 (NCSS LLC, Kaysville, Utah, USA) statistical package in order to determine sample size. Also we used SPSS 17.0 statistical package programme for statistical analysis. We presented statistical data as mean ± standard deviation (Min-Max) or n (%)]. Shapiro–Wilk test was used to evaluate the convenience of numerical data and normal range; parametric tests were used to compare the variables which showed normal range and non-parametric tests were used to compare variables which did not show normal range. One way analysis of variance (ANOVA) was used to compare normally distributed categorical variables between independent groups. Bonferroni test was used for significant differences found in ANOVA test. Kruskal Wallis test was used for non-parametric variables. Significant differences between groups were compared using Mann Whitney U test. Repeated measures variance analysis were used in order to evaluate significant differences between intragroup pulse rate, systolic blood pressure, diastolic blood pressure SpO2, BIS, RSS, and OAAS values. Preoperative versus postoperative CFSS-DS and MCDASf values were compared using paired t-test. Sex, economic status, education level of parents, satisfaction rates of anesthesiologist and dentist, complication rates were evaluated with Chi-square or Fisher's exact Chi-square tests. Pearson correlation analysis was used for assocations between BIS values and OAAS/RSS, also between preoperative CFSS-DS, MCDASf and other parameters. $p < 0.05$ was considered statistically significant.

RESULTS

There were no significant differences between the groups with respect to demographic data ($p > 0.05$).

Mean CFSS-DS and MCDASf scores after dental treatment in Group P and Group KP were significantly lower than that in Group K ($p = 0.001$, $p = 0.021$ and $p = 0.003$; $p = 0.033$ respectively) (Table 1).

Mean CFSS-DS and MCDASf scores of girls at preoperative period were significantly higher than those measured for boys ($p = 0.049$; $p = 0.01$)

We found negative correlation between patients' age and preoperative CFSS-DS score while no correlation was found between CFSS-DS, education level and economic status of family ($r = -0.650$; $p < 0.0001$, $p > 0.05$ respectively). Similar results were found for preoperative MCDASf scores and patients' age, education level and economic status of parents ($r = -0.735$; $p < 0.0001$and $p > 0.05$ respectively).

We found strong positive correlation between preoperative CFSS-DS and MCDASf scores ($r = 0.794$; $p < 0.0001$).

Vital Parameters

Mean systolic artery pressure (SAP) and diastolic artery pressure (DAP) levels after drug administration in Group P and Group KP were significantly lower than those in Group K ($p < 0.0001$ and $p < 0.05$ at all time points) (Table 2). Additionally mean SAP and DAP levels in Group P at 5th minutes of operation was significantly lower than that measured in Group KP ($p < 0.0001$ and $p = 0.013$).

Mean heart rate (HR) levels in Group P at all time points were statistically lower than those in Group K ($p < 0.0001$; $p < 0.0001$; $p < 0.0001$; $p < 0.0001$; $p = 0.002$). Similar results were found –except HR at 25th minutes- in Group KP when compared to GroupK ($p < 0.0001$; $p < 0.0001$; $p < 0.0001$; $p = 0.002$). Additionally mean HR levels in Group P at 5th and 10th minutes were significantly lower than those in

Table 2: Comparison of mean SAP (mmHg), DAP (mmHg) and HR values between groups [Mean ± SD]

Time	Group P (n = 25)	Group K (n = 25)	Group KP (n = 25)	p
0 min	100.29 ± 7.88 74.40 ± 4.81 112.36 ± 7.60	101.28 ± 6.27 70.68 ± 11.46 108.44 ± 15.44	99.24 ± 6.06 74.20 ± 4.93 114.88 ± 9.52	0.571 0.144 0.137
5th min	77.12 ± 4.30*+ 61.96 ± 4.88*+ 79.68 ± 3.53*+	119.52 ± 9.61+ 75.92 ± 11.94 115.08 ± 12.96+	94.48 ± 6.77*& 68.96 ± 3.69*&+ 96.56 ± 8.88*&+	< 0.0001 < 0.0001 < 0.0001
10th min	88.56 ± 4.37*+ 63.88 ± 4.90*+ 83.68 ± 3.48*+	124.72 ± 8.82+ 76.56 ± 10.64 120.00 ± 15.46+	92.80 ± 6.39* 67.48 ± 3.56*+ 94.80 ± 8.96*&+	< 0.0001 < 0.0001 < 0.0001
15th min	92.52 ± 5.87* 68.04 ± 3.99*+ 85.96 ± 6.28*+	119.32 ± 9.19+ 77.92 ± 11.76+ 111.96 ± 13.08	94.32 ± 6.05* 69.44 ± 3.00*+ 92.36 ± 8.22*+	< 0.0001 < 0.0001 < 0.0001
20th min	93.90 ± 3.95* 69.29 ± 3.05*+ 89.90 ± 6.46*+	111.61 ± 11.19+ 81.78 ± 9.12 100.13 ± 12.11	94.35 ± 5.02* 68.83 ± 2.90*+ 90.65 ± 5.64*+	< 0.0001 < 0.0001 < 0.0001
25th min	93.31 ± 4.55* 69.29 ± 3.05*+ 90.00 ± 4.96*	110.71 ± 17.56 76.17 ± 11.16 102.38 ± 11.70	95.00 ± 5.30* 69.57 ± 3.03*+ 93.88 ± 8.82	< 0.0001 0.020 0.011

*p < 0.05: Compared to Group K
&p < 0.05: Compared to Group P
+p < 0.05: Compared to 0th minute

Table 3: Comparison of BIS values [Mean ± SD]

Time	Group P (n = 25)	Group K (n = 25)	Group KP (n = 25)	p
0 min	97.20 ± 1.69	96.32 ± 1.91	97.28 ± 1.10	0.066
5th min	66.76 ± 4.47*+	87.60 ± 4.55+	76.24 ± 2.28*&+	< 0.0001
10th min	69.40 ± 4.12*+	87.76 ± 5.46+	74.84 ± 2.10*&+	< 0.0001
15th min	66.44 ± 3.37*+	89.72 ± 6.76	74.96 ± 1.90*&+	< 0.0001
20th min	68.10 ± 3.53*+	89.74 ± 5.38	77.10 ± 2.36*&+	< 0.0001
25th min	67.00 ± 1.73*+	89.13 ± 4.26	75.73 ± 1.62*&+	< 0.0001

*p < 0.05: Compared to Group K
&p < 0.05: Compared to Group P
+p < 0.05: Compared to values at 0th minute

Group KP (p = 0.018; p = 0.005). (Table 2)

Sedation Levels and BIS Scores

Mean BIS scores at all time points after drug administration in Group P and KP were significantly lower than those in Group K (p < 0.0001, all time points). Additionally mean BIS scores at all time points after drug administration in Group P were significantly lower than those in Group KP (p < 0.0001, all time points).

Mean BIS levels at all time points in Group P and KP were significantly lower than those in same groups before drug administration (p < 0.0001, all time points) (Table 3).

In Group K mean BIS values at 5th and 10th minutes were significantly lower than that measured at zero time point (p < 0.0001 and p < 0.0001 respectively).

Mean Ramsay Sedation Scale (RSS) scores in Group P at all time points –except 25th minutes- were significantly lower than those in Group K (p < 0.0001; p = 0.001; p < 0.0001; p < 0.0001) while in Group KP mean RSS scores at 10th, 15th and 20th minutes were significantly lower than those in Group K (p = 0.003; p = 0.002; p = 0.007). We found significant difference between mean RSS scores in Group KP and Group P only at 5th minutes time point of intervention (p = 0.007).

We found negative correlation between RSS and BIS values at all time points in Group P and Group KP after drug administration while no correlation was found in Group K.

Mean OAAS scores in Group P at all time points –except 5th minutes- and in Group KP –except 5th and 10th minutes- were significantly higher than those in Group K (p < 0.0001; p = 0.002; p < 0.0001; p < 0.0001 and p = 0.016; p < 0.0001; p < 0.0001 respectively). When Group P and Group KP compared, we found that mean OASS score only at 10th minutes was significantly higher than that in Group P (p = 0.019).

We found strong positive correlation between OAAS and BİS values in Group P for all time points. Similarly positive correlation in Group KP for all time points was found. In contrast we couldn't find

any correlation in Group K.

Complication Rates

Complication rates in Group P and Group KP were significantly lower than those in Group K ($p < 0.0001$; $p < 0.0001$). Complication rates were similar in Group P and Group KP ($p = 0.480$) (Table 4).

Cough, hallucination, hypersalivation rates were significantly higher in Group K than those in Group P and Group KP ($p = 0.009$; $p = 0.033$; $p = 0.033$ and $p = 0.001$; $p = 0.033$; $p = 0.033$ respectively). Nausea and vomiting rates were higher in Group K than those in Group P (0.011) (Table 4).

Table 4: Comparison of complication rates [Data presented as n (%)]

Complications	Group P (n = 25)	Group K (n = 25)	Group KP (n = 25)	p
Pain at injection site	2(8)	0(0)	0(0)	$X^2 = 4.110$ 0.128
Spontaneous movement	2(8)	0(0)	0(0)	$X^2 = 4.110$ 0.128
Hiccups	2(8)	0(0)	0(0)	$X^2 = 4.110$ 0.128
Cough	0(0)	6(24)	0(0)	$X^2 = 14.261.0.001$
Nausea-Vomiting	0(0)	5(20)	2(8)	$X^2 = 7.569$ 0.023
Hallucination	0(0)	3(12)	0(0)	$X^2 = 6.845$ 0.033
Agitation	0(0)	3(12)	2(8)	$X^2 = 3.000$ 0.223
Hypersalivation	0(0)	3(12)	0(0)	$X^2 = 6.845$ 0.033
Diplopia	0(0)	3(12)	2(8)	$X^2 = 3.000$ 0.223
Total	6(24)	17(68))	4(16))	$X^2 = 22.641$ < 0.0001

*p < 0.05: Compared to Group K
&p < 0.05: Compared to Group P
+p < 0.05: Compared to 0th minute

Satisfaction Scores of Parents', Dentists' and Anesthesiologists'

Parents' of patients in Group P and Group KP had higher satisfaction rates than those in Group K ($p = 0.018$; $p < 0.0001$) while similar satisfaction rates were found in parents of patients in Group P and Group KP ($p = 0.110$) (Table 5).

Table 5. Duration of intervention. recorvery / satisfaction rates of parents. dentists and anesthesiologists [Data presented as mean ± SD or n]

Variable	Group P (n = 25)	Group K (n = 25)	Group KP (n = 25)	p
Duration of intervention (min)	21.36 ± 4.27	23.24 ± 4.24	22.64 ± 3.83	0.26
Duration of recovery (min)	9.72 ± 3.41*	19.44 ± 5.48	11.96 ± 2.32*	< 0.0001
Parents satisfaction (Very satisfied/ satisfied/dis satisfied)	25/0/0*	14/08/03	21/4/0*	X2 = 20.901 < 0.0001
Anesthesiologist (Very satisfied/ satisfied/dis satisfied)	4/15/6	4/17/4	24/1/0*&	X2 = 51.053 < 0.0001
Dentist (Very satisfied/satisfied/dis satisfied)	4/15/6	1/21/3	24/1/0*&	X2 = 63.572 < 0.0001

*p < 0.05: Compared to Group K
&p < 0.05:Compared to Group P

Anesthesiologists' and the dentists' satisfaction rates were higher for Group KP than those in Group K and Group P ($p < 0.0001$; $p < 0.0001$). Anesthesiologist and dentist satisfaction rates were similar for Group P and Group K ($p = 0.150$ and $p = 0.769$) (Table 5).

Mean Operation Time and Duration of Recovery

Mean duration of operation were similar in three groups ($p = 0.263$) (Table 5). Mean duration of recovery in Group K was significantly longer than those in Group P and Group KP ($p < 0.0001$ and $p < 0.001$, respectively). Mean duration of recovery in Group P and Group KP were found statistically insignificant ($p = 0.148$) (Table 5).

DISCUSSION

Dental anxiety is prevalent among children and reported incidence varies between 6% and 52%.[11-14] Dental anxiety in children may influence future dentist visits and so can result in poor dental and oral hygiene.[15-18] Sedation protocols in dentistry offers

comfortable treatment environment especially for children. Several studies reported that deep sedation via intravenous route is the safest and most effective sedation protocol.[19,20]

Previous studies showed decreased side effect profile and complication rates with ketamine propofol combination when compared each agent alone.[9,21-24] There is no consensus about certain ketamine propofol mixtures ratios however various studies showed that mixtures in ratios of 1:1 were related with lower respiratory depression with appropriate hemodynamically responses compared to ratios of 3:1 and 2:1.[25-27] We chose mixture in ratios of 1:1 and bolus dose of 0.6 mg/kg followed by 40-60 μg/kg/min continuous infusion protocol which was effectively used by Dabbaiss et al.[28] previously – with an infusion dose of 100 μg/kg/min.

Various studies reported hypotension, bradycardia, desaturation and/or apnea free sedation sessions with ketofol usage and they concluded that contrary effects of ketamine and propofol on autonomic nervous system lead these desired effects.[9,29,30] Similarly ketofol sedation provided decreased ratio of respiratory depression between 0.9% and 15% during dental treatment of children.[24,29,31] In our study we reported insignificant hypotension and bradycardia periods in Group KP and we conclude that decreased propofol dosage combined with ketamine –a symphatomimetic agent- provided more stable cardiovascular hemodynamics.

Andolfatto et al.[22] reported higher involuntary movements in propofol group than that in ketofol group. They explained this difference with analgesic property of ketamine used in ketofol procedure. Similarly we reported higher involuntary movement ratio in propofol group (8% vs 0%) and so we suggest that propofol has to be combined with an analgesic agent during painful procedures such as dental treatments.

Postoperative nausea and vomiting is a well-known side effect of ketamine and different PONV incidence ratios have been reported. Green et al.[32] reported a PONV incidence of 8.4% underwent ketamine sedation while Wathen et al.[33] reported a PONV incidence of 19.4% in patients younger than 10 years. In contrast findings of ketofol studies are promising. Daabiss et al.[28] reported 2% PONV ratio with mixture in ratios of 1:1 while no PONV was determined with ratios of 1:4 (ketamine: propofol). Shah et al.[9] reported higher nausea and vomiting incidence with ketamine compared to ketofol (2% versus 12%) in 136 patients aged between 2-17 years. Similarly several studies investigating effects of ketofol sedation reported PONV free recovery periods with ketofol usage.[22,30,34] We found higher PONV rates in Group K than that in Group KP (20% versus 8%) and we suggest that anti-emetic property of propofol limits emetogenic effects of ketamine when used in combination.

Psychotomimetic effects of ketamine include hallucination, agitation decrease when combined with propofol.[22,31,35] da Silva et al.[30] showed extremely small numbers of patients experienced hallucination and diplopia (1 and 2 patient(s)) in a study investigating effects of ketofol sedation in patients aged between 4-12 years. Shah et al.[9] reported lower postoperative agitation rates with ketofol sedation compared to ketamine alone (8% versus 13%). Andolfatto and Willman31 reported an agitation ratio of 0.9% in 219 patients aged between 1-20 years during ketofol sedation. We found higher hallucination, agitation and diplopia ratios in ketamine group when compared to ketamine plus propofol group (12%, 12% and 12% versus 8%, 8% and 0% respectively). We suggest that anxiolytic property of propofol provides comfortable recovery period when combined with ketamine.

The overall risk of pain from propofol injection was about 70% and various reports indicates decreased pain when combined with ketamine.[9,36-38] In our study none of patients in Group K and Group KP experienced any injection pain while in Group P we noted injection pain in 8% of patients. We explain this result with preventive effect of ketamine on releasing pain mediators. Also we applied prilocaine containing cream on dorsum of hands 1 hour before cannulation and thus this precaution might decrease the intensity of possible injection pain.

We investigated whether a positive correlation between dental anxiety scales and found positive correlation between CFSS-DS and MCDASf ($r = 0.794$; $p < 0.0001$). There are controversial findings in previous studies in terms of correlation between these two scales. Several studies show positive correlation between these two while some of which reported negative correlation.[39,40] We suggest that consideration of patients' age when choosing the type of scale, has been provided positive correlation that we found.

Alexopoulos et al.[41] investigated changes in dental anxiety of 76 patients aged between 5-16 years using CFSS-DS and MCDASf scales during propofol

versus nitrous oxide/oxygen mixture sedation. They concluded that both sedation methods provided decreased anxiety levels in children. Girdler et al.[42] showed decreased anxiety levels with propofol sedation. McDowall et al.[43] compared dental anxiety levels in children underwent dental treatment under propofol, etomidate or ketamine sedation and they found that propofol sedation was significantly related with decreased anxiety levels. In contrast to studies above, Mizrak et al.[44] found lower anxiety levels with ketamine sedation than that in propofol sedation and they discussed that low dose fentanyl combined to ketamine provided their results. In our study we found significantly decreased anxiety levels in Group P and Group KP ($p = 0.001$; $p = 0.003$ respectively) while in Group K we found decreased anxiety levels numerically however statistically significancy level of this finding was considered as insufficient ($p > 0.05$). We suggest that anxiolytic effect of propofol plays important role on decreased anxiety levels we found in ketofol group.

Many authors consider that gender is a determinant factor for dental anxiety and female gender is accepted as highly anxious.[7,14,45,46] In contrast there are many studies that couldn't indicate any relationship between gender and anxiety levels.[2,8,47,48] In our study we showed that girls have higher anxiety levels than boys have and this conclusion was valid with both of two scales we used ($p < 0.05$). Also we found negative correlation between increased age and anxiety levels with two scales we used. This finding was compatible with many previous studies.[8,46,47,49] Social economic status and education level of parents are other two factors studied previously. Also there are different findings related with social economic status and education level of parents.[46,50,51] Folayan et al.[8] couldn't find any significant relationship between dental anxiety and social economic status of parents and they concluded that dental anxiety should not be evaluated using only one way parameters. Similar with Folayan et al.8 we couldn't find any significant correlation between dental anxiety and social economic status or education level of parents.

Sadhasivam et al.[52] showed positive correlation between BIS values and OAAS in children under sedation. Overly et al.[53] found strong positive correlation between BIS values and clinical scoring systems such as OAAS and RSS in children underwent dental treatments under sedation and they suggested that BIS monitoring can be helpful in determining depth of sedation in children. In contrast to propofol sedation various studies reported higher BIS values and negative correlation between sedation levels and BIS values during ketamine sedation despite achieved appropriate clinical sedation levels.[54-56] Ketamine blocks responsiveness of patients however may not decrease BIS values. Additionally when ketamine combined with propofol BIS values are not affected but deep levels of sedation can be achieved.[56,57] Cillo et al.[58] reported different BIS values with propofol alone and combinations with ketamine at different ratios during intra-orally surgery. They reported higher BIS values with increased ketamine doses combined with same propofol dose (propofol alone 63.2, 10:1 (propofol : ketamine) 69.6, 5:1-71.8 and 3:1-72.1). In our study -similar to previous studies- BIS values were highest in Group K while lowest in Group P. RSS and OAAS scores were similar for all study groups. We found positive correlation between RSS/BIS and OAAS/BIS parameters after drug administration at all time points while we couldn't find any correlation in Group K.

Parents and physician satisfaction scores were high in studies investigating effects of ketofol sedation on satisfaction rates.[9,22,24,30,31] Similarly we found higher satisfaction rates for dentists and anesthesiologists for Group KP while we couldn't find significant difference for parents satisfaction rates in Group P and Group KP although lower rates were noted in Group K. We suggest that several factors, including higher complication rates of hallucinations, nausea, vomiting and prolonged recovery period seen after ketamine sedation, significantly affect parents' satisfaction scores. On the other hand more comfortable and safe environment provided by ketofol results in higher dentist and anesthesiologist satisfaction rates.

Ketofol induces shortening recovery time which was reported between 6.5 and 23 min in children.[9,21,29,30] However longer recovery periods such as 25-103 min for ketamine sedation33,59,60 and 8-93 min for propofol sedation were reported.[61-63] We found shorter recovery periods with propofol alone and ketofol than ketamine alone (9.72 ± 3.41 min and $11,96 \pm 2.32$ min vs 19.44 ± 5.48 min). Lower ketamine doses combined with propofol for ketofol sedation provides shorter recovery time than ketamine alone but longer than propofol alone.

CONCLUSION

In conclusion we can state that during dental treatments of children propofol and ketofol provide

effective sedation levels without serious perioperative complications. However, ketofol, with more stable cardiovascular hemodynamics, less side effect profile, shorter recovery time than ketamine alone, higher patient and physician satisfaction rates and decreased patient anxiety level, can be safely used in children aged between 6-12 years undergoing dental treatments.

Conflict of interest: None declared by the authors

Authors' contribution:

GY – writing the manuscript

NO - conduction of the study work

GK - conduction of the study work and manuscript editing

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