Osmangazi Tıp Dergisi
Osmangazi Journal of Medicine 2020; 42 (5):466-473

Research Article / Araştırma Makalesi

Evaluation of Advanced Behavior Guidance Techniques Used in Dentistry: Sedation and General Anesthesia

Diş Hekimliğinde Kullanılan İleri Davranış Yönlendirme Tekniklerinin Değerlendirilmesi: Sedasyon ve Genel Anestezi

[1]Hande Gurbuz Aytuluk

[1]Derince Training and Research Hospital, Department of Anesthesiology and Reanimation, Kocaeli, Turkey

Abstract: Although most of the dental procedures can be held in the office setting, sedation or general anesthesia is required in some of the patients. The aim of this study was to review patients who underwent dental procedures under anesthesia with the emphasis on patient characteristics, procedural and anesthetic properties, and to consider this issue from various aspects. Medical records of 362 patients who underwent dental procedures under sedation or general anesthesia were analyzed. Demographic data, the reasons for treatment under anesthesia, anesthetic, and procedural characteristics were recorded. Patients were evaluated under three groups according to their ages (<10years: children; n=159, 10-24 years: young people; n=113, ≥25 years; n=90: adults). Noncompliance was the main reason for dental surgery under anesthesia in children (76.1%) and young people (41.6%). Mental retardation (26.7%) and extreme dental phobia (24.4%) were found to be the most frequent reasons for dental surgery under anesthesia in adults. For the reversal of rocuronium, while neostigmine was the primary choice in pediatric patients, sugammadex was the most preferred reversal agent in adults. Patients undergoing dental procedures under anesthesia constitute a specialized patient group (e.g. pediatric patients and patients with special needs). Therefore, implementing nonsurgical interventions and postponing elective surgeries to an appropriate time must be taken into consideration. For the safety and the quality of the dental procedure, the choice of anesthesia technique must be made according to the risk and benefit analysis.

Keywords: anesthetics; child; dental anesthesia; general anesthesia; outpatients

Özet: Dental işlemlerin çoğu ofis ortamında yapılabilmesine rağmen, bazı hastalarda sedasyon veya genel anestezi gereklidir. Bu çalışmanın amacı, anestezi altında dental prosedür uygulanan hastaları hasta özellikleri, işlemsel ve anestezi özellikleri vurgulanarak gözden geçirmek ve bu konuyu farklı açılardan ele almaktır. Sedasyon veya genel anestezi altında dental prosedür uygulanan 362 hastanın tıbbi kayıtları incelendi. Demografik veriler, anestezi altında tedavi nedenleri, anestezi ve prosedür özellikleri kaydedildi. Hastalar yaşlarına göre üç grup altında değerlendirildi (<10 yaş: çocuklar; n = 159, 10-24 yaş: gençler; n = 113, ≥25 yaş; n = 90: yetişkinler). Çocuklarda (76.1%) ve gençlerde (41.6%) anestezi altında diş cerrahisinin temel nedeni uyumsuzluktu. Mental retardasyon (26.7%) ve aşırı diş fobisi (24.4%) yetişkinlerde anestezi altında diş cerrahisinin en sık nedenleri olarak bulundu. Roküronyumun geri çevrilmesi için çocuk hastalarda neostigmin birincil seçenek iken, sugammadeks yetişkinlerde en çok tercih edilen ilaçtı. Anestezi altında diş tedavisi gören hastalar özel bir hasta grubu oluşturmaktadır (örneğin pediyatrik hastalar ve özel ihtiyaçları olan hastalar). Bu nedenle cerrahi olmayan müdahalelerin uygulanması ve elektif ameliyatların uygun bir zamana ertelenmesi dikkate alınmalıdır. Dental prosedürün güvenliği ve kalitesi için, risk ve fayda analizine göre anestezi tekniği seçimi yapılmalıdır.

Anahtar Kelimeler: anestezikler; ayaktan hastalar; çocuk; dental anestezi; genel anestezi

ORCID ID of the author: H.G.A 0000-0002-3562-9517

Received 22.04.2020 ***Accepted*** 14.05.2020 ***Online published*** 22.06.2020

Correspondence: Hande Gürbüz AYTULUK - Derince Training and Research Hospital, Department of Anesthesiology and Reanimation, Kocaeli, Turkey e-mail: handegrbz@gmail.com

Cite this article as:
Aytuluk HG, Evaluation of Advanced Behavior Guidance Techniques Used in Dentistry: Sedation and General Anesthesia, Osmangazi Journal of Medicine, 2020;42(5):466-473 ***Doi:*** *10.20515/otd.725531*

1. Introduction

Dentistry is usually performed as an outpatient procedure in the office setting with or without local anesthesia by dentists. A good level of communication between the dentist and the patient is required for an uneventful dental procedure. While most of the patients can be managed effectively using basic behavior guidance (for example tell-show-do, ask-tell-ask, voice control, distraction, etc.), some noncompliant patients (including pediatric patients, and patients with special health care needs) require more advanced techniques (for example protective stabilization, sedation, general anesthesia) (1). Sedation or general anesthesia facilitates the work of the dentist by providing optimum conditions for invasive dental interventions in prolonged and complicated procedures, especially in full mouth dental caries. However, dental anesthesia is a real challenge for anesthesiologists because of the comorbidities and anatomical abnormalities of these patients. Additionally, factors like loss of preventive upper airway reflexes during deep sedation and sharing of the airway with the surgeon pose additional risks for the management of patients undergoing dental anesthesia. Because of this reason, dental interventions under anesthesia requires specialized equipment and trained professionals for the management of perioperative complications and must be performed at the hospital setting.

The aim of this study was to review patients who underwent dental procedures under anesthesia with the emphasis on patient characteristics, procedural and anesthetic properties, and to consider this issue from various aspects.

2. Material and Methods

After the approval of the local ethical committee (Derince Training and Research Hospital, decree 2019/206), this retrospective descriptive study was conducted by analyzing the medical records of patients who underwent dental procedures under sedation or general anesthesia. The data was collected through cluster sampling from the records of the patients who were operated in Alikahya Obstetrics-Gynecology and Children's Hospital (Derince Training and Research Hospital) between January 2017 and June 2019. Demographic data, the reasons for treatment under anesthesia, anesthetic, and procedural characteristics were recorded. Patients were evaluated under three groups according to their ages (<10years: children, 10-24 years: young people, ≥25 years: adults) defined by the World Health Organization (2).

All of the patients were evaluated on a preoperative anesthesia visit and discussed in a multidisciplinary consultation if needed. Mallampati scores were not taken into analysis due to a lack of proper preoperative evaluation and documentation in many of the noncompliant patients. On the surgery day following premedication, routine monitorization of heart rate, non-invasive blood pressure, and peripheral oxygen saturation were established in the operating theatre. After the operation, patients were evaluated in the post-anesthesia care unit until the modified Aldrete scores were >8 and then transferred to the surgical ward. Patients were followed-up for possible postoperative complications (nausea and vomiting, bleeding, etc.) in the surgical ward. Patients who fulfilled discharge criteria for ambulatory anesthesia by the late afternoon or the evening of the day of the operation were discharged with a responsible adult (3).

Statistics

Statistical analyses were performed using computerized statistical software: IBM SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp.). The normality of the distribution of the data was analyzed using the Shapiro-Wilk test. The Pearson chi-square test was used to compare the categorical variables. The Mann Whitney-U test was used for intergroup comparison, and Kruskal Wallis test was used for intragroup comparison of the procedural times. Dunn's post hoc method was used for pair wise comparisons following a significant Kruskal-Wallis test. Wilcoxon sum rank test was used

to compare pre-postoperative heart rate measurements. Continuous data are presented as mean ± standard deviation, and median (interquartile range 25-75), and categorical data are expressed as counts and percentages. An alpha value of <0.05 was considered as statistically significant.

3. Results

A total of 362 patients who underwent the dental procedure under sedation or general anesthesia were evaluated under three groups: children (n=159), young people (n=113), and adults (n=90).The demographic characteristics of the patients are presented in Table-1.

Table 1. Demographic characteristics of the patients.

Patient characteristics	Children (2-9 years) (n=159)	Young people (10-24 years) (n=113)	Adult (>25 years) (n=90)
Age (*years*)	6.18±1.74	15.01±4.11	35.1± 9.24
Weight (*kg*)	21.46±5.62	49.75±16.62	72.11±13.16
Female	57 (35.85)	52 (46.02)	46 (51.11)
ASA I	106 (66.67)	36 (31.86)	35 (38.89)

Data are presented as mean ± standard deviation or number (%).

Among the reasons for dental treatment under anesthesia, there was a statistically significant difference between children, young people, and adults in all variables, except cerebral palsy and down syndrome. All results of paired comparisons of the subgroups showed a statistical significance, except young people-adults binary comparisons for mental retardation and schizophrenia, and children-young people comparison for autism (Table-2). Noncompliance was the main reason for dental surgery under anesthesia in children (76.1%) and young people (41.6%). Mental retardation (26.7%) and extreme dental phobia (24.4%) were the most frequent reasons for dental surgery under anesthesia in adults.

Table 2. Clinical characteristics of the patients and the reasons for treatment under anesthesia.

	Children (n=159)	Young people (n=113)	Adult (n=90)	p	Paired comparisons		
					C-Y	**C-A**	**Y-A**
Noncompliance	121 (76.1)	47 (41.6)	9 (10.0)	<0.001*	<0,001	<0,001	<0,001
Cerebral palsy	9 (5.7)	11 (9.7)	6 (6.7)	0.429			
Mental Retardation	8 (5.0)	18 (15.9)	24 (26.7)	<0.001*	0,003	<0,001	0,061
Schizophrenia	- (-)	7 (6.2)	13 (14.4)	<0.001*	0,001	<0,001	0,051
Autism	15 (9.4)	9 (8.0)	1 (1.1)	0.039	0,674	0,010	0,025
Down Syndrome	6 (3.8)	5 (4.4)	4 (4.4)	0.952			
Extreme phobia	- (-)	12 (10.6)	22 (24.4)	<0.001*	<0,001	<0,001	0,009
Severe gag reflex	- (-)	4 (3.5)	11 (12.2)	<0.001*	0,017	<0,001	0,019

Data are presented as number (%).
***C:** children; **Y:** young; **A:** adult.*

Preoperative and postoperative mean heart rate values of children, young people, and adults were 119.31±14.85 and 120.50±15.30, 100.26±16.27 and 104.79±15.43, 87.77±16.58 and 88.56±11.69, respectively. There was no statistically significant difference between pre-postoperative mean heart rate values of the patients (data were not presented). Adults required tooth extraction statistically significantly lower than children and young people. Adults required fillings statistically significantly higher than children and young people. Children required both tooth extraction and filling procedure statistically significantly higher than young people and adults ($p<0.05$) (Table-3). There was no statistically significant difference between children, young people, and adults for sedation or general anesthesia. While procedural times for sedation or general

anesthesia did not differ significantly between the three groups, procedural times for sedation were significantly shorter than general anesthesia in all three groups ($p<0.05$). There was no statistically significant difference between groups for the laryngeal mask airway (LMA), orotracheal intubation, and nasotracheal intubation. (Table-3). All patients were able to be intubated, at least at the first attempt.

Table 3. Procedural features.

	Children (n=159)	Young people (n=113)	Adults (n=90)	p	Paired comparisons		
					C-Y	C-A	Y-A
Dental procedure							
Extraction	48 (30.2)	23 (20.4)	9 (10)	0.001	0,069	0,000	0,044
Filling	73 (45.9)	79 (69.9)	75 (83.3)	0.000	0,000	0,000	0,026
Extraction & Filling	38 (23.9)	11 (9.7)	6 (6.7)	0.000	0,003	0,001	0,433
Procedural time (minutes)							
Sedation	15 (10.0-18.8)	10 (10-17.5)	15 (10-15)	0,578[K]			
General anesthesia	40 (30-55)	45 (35-60)	40 (30-55)	0,489[K]			
Procedural properties							
Sedation	50 (31.5)	39 (34.5)	26 (28.9)	0.689			
General anesthesia	109 (68.6)	74 (65.5)	64 (71.1)				
Airway during GA							
LMA	24 (22.0)	9 (12.2)	7 (10.9)	0.086			
OTI	66 (60.6)	42 (56.8)	41 (64.1)	0.681			
NTI	19 (17.4)	23 (31.1)	16 (25.0)	0.096			
Drugs used for sedation and general anesthesia							
Midazolam	145 (91,2)	97 (85,8)	62 (68,9)	0,000	0,165	0,000	0,004
Propofol	136 (85,5)	107 (94,7)	84 (93,3)	0,023	0,016	0,065	0,684
Ketamine	54 (34)	23 (20,4)	8 (8,9)	0,000	0,014	0,000	0,024
Fentanyl	26 (16,4)	15 (13,3)	43 (47,8)	0,000	0,484	0,000	0,000
Rocuronium	94 (59,1)	71 (62,8)	63 (70)	0,232	0,537	0,087	0,284
Sugammadex	18 (11,3)	41 (36,3)	49 (54,4)	0,000	0,000	0,000	0,010
Neostigmine	78 (49,1)	34 (30,1)	15 (16,7)	0,000	0,002	0,000	0,026
Analgesia							
Infiltration	114 (71.7)	90 (79.7)	68 (75.6)	0.326			
Infiltration + Paracetamol or Dexketoprofen	16 (10.1)	9 (8.0)	9 (10.0)	0.821			
Infiltration + Paracetamol or Dexketoprofen + Tramadol	- (-)	2 (1.8)	4 (4.4)	0.031			
No analgesia	29 (18.2)	12 (10.6)	9 (10.0)	0.096			

Data are presented as median (IQR 25-75) or number (%), $p<0.05$.
***C:** children; **Y:** young people; **A:** adults; **GA:** general anesthesia; **LMA:** laryngeal mask airway; **OTI:** orotracheal intubation; **NTI:** nasotracheal intubation; **IQR:** interquartile range.*
[K]: Kruskal Wallis H analysis

Laryngospasm at various degrees and durations occurred in 31 pediatric (4 sedation, 27 general anesthesia), 12 young (1 sedation, 11 general anesthesia), and six adult (6 general anesthesia) patients. The symptoms of laryngospasm were recognized immediately and treated successfully in all patients. No other major complications were observed during dental procedures. All patients were discharged on the day of the surgery.

Midazolam was the most used agent for premedication before the dental procedures. Propofol was more frequently used for sedation and general anesthesia than ketamine and fentanyl. Ketamine was preferred more frequently in pediatric patients than young people and adults, while fentanyl was more frequently used in adults than in young people and pediatric patients. Rocuronium was used as a muscle relaxant for the intubation of the patients. For the reversal of rocuronium, while neostigmine was the main choice in pediatric patients, sugammadex was the most preferred reversal agent in adults (Table-3) (Figure-1).

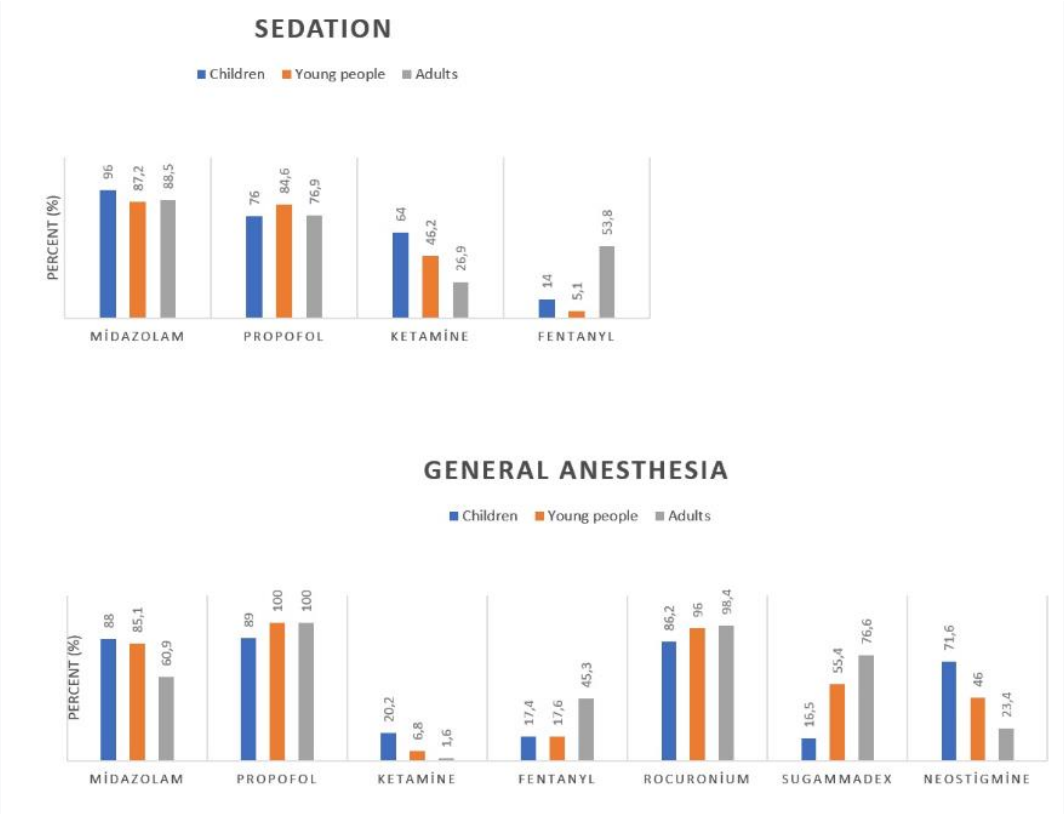

Figure 1. The distribution of the participants according to the drugs used for their sedation *(Figure 1A) and general anesthesia (Figure 1B).*

4. Discussion

Demand for anesthesia for the treatment of dental disorders (including fillings and extraction) is increasing directly proportional to the increase in the quality of patient care in medicine. The patient safety movement has raised awareness for the prevention of complications and deaths in hospitals by paying careful attention to system factors (4). Thus, the patient safety issue has gained great importance. The field of anesthesia is the leading one in patient safety. Many measurements have been developed for the management and safety of patients who receive day-case anesthesia guidelines that have been put into practice. Although many dental procedures can be performed in the office setting, these interventions can be challenging, especially in young children who do not have sufficient emotional and psychological maturity, and in patients who are mentally or physically disabled. If the patients make sudden and undesirable movements during the procedure, the procedure may not be sufficient, and worse; the patients may harm themselves. Therefore, non-pharmacological or pharmacological behavior guidance techniques can be used to improve compliance with patients. Dentists can apply non-pharmacological -basic- behavior guidance techniques in the office setting. However, it is a necessity for patient safety to use these pharmacological -advanced- behavior guidance techniques in the office with optimum conditions, or (and best) in the hospital setting by a professional team (5-8).

After finding out the exposure of developing animals to commonly used anesthetics can cause neurotoxicity, the relevance of this information to children has become the main concern (9,10). Accordingly, an interdisciplinary team of investigators developed the Pediatric Anesthesia NeuroDevelopment Assessment (PANDA) project to provide evidence to address this issue (11). Following that, conflicting results have been reported in different studies.

Although it was emphasized in some clinical studies that even a single exposure to anesthesia is associated with impaired neurodevelopment, other studies have reported an association with multiple exposures to anesthesia, or no association with anesthesia (12). In 2016, the results of a study which was supported by US Food and Drug Administration (FDA) showed there were no significant differences in IQ scores in children aged 8 to 15 years who were exposed to a single administration of anesthesia before the age of 36 months in comparison with children with no anesthesia exposure (13). Following these results, the FDA announced a drug safety warning about a potential risk for detrimental effects of 11 frequently used anesthetics on neurodevelopment, when used in the third trimester of pregnancy and children under the age of 3 years (14). However, it was also stated that more research is needed to provide evidence about the safe use of these medications in early childhood and pregnancy (15). Accordingly, the most recent studies support the relevance of early childhood anesthesia exposure to language and cognitive deficits (16-18). Additionally, the children who received anesthesia at an early age were found to require attention deficit/hyperactivity disorder medications more likely than unexposed children (19). The FDA has been researching the possible consequences of anesthetic drugs on the developing brain since the first animal study, and the PANDA symposium has been a leading forum for clinicians regarding this issue (20). In the present study, midazolam and ketamine were used for sedation in short-term interventions (10-20 minutes) for three of the 3-year-old patients; different combinations of midazolam, ketamine, propofol, and sevoflurane were used for general anesthesia in one of the 2-year-old and five of the 3-year-old patients for maximum 65-minute procedures. Additionally, 159 of 362 patients were under the age of 10 years.

Dental care is necessary to prevent and treat oral infections, cavities, and toothache. Poor oral hygiene is one of the public health problems which majorly affect children and patients with mental disorders and physical disabilities (21). Thus, there is now more emphasis on active surveillance and prevention of caries (1,22). When taking into consideration the possible risks of anesthesia, especially in children and patients who have an anticipated difficult airway, it was also recommended in dental surgeries to implement nonsurgical interventions and to postpone elective surgeries where possible (5,22). In this present report, it was found that the majority of the patients comprised of healthy but noncompliant children. Among the patients with special needs, the diagnosis of autism spectrum disorder was significantly high in the children group, and the diagnoses of mental retardation and schizophrenia were significantly high in the adult group. Extreme phobia and severe gag reflex were the primary diagnoses in healthy adults.

Dental procedures are commonly performed as day-care surgeries. The young age of the patients, accompanying central nervous diseases in patients with special needs, and a high incidence of maxillofacial anatomic abnormalities, these patients are more prone to perioperative complications (23,24). Oropharyngeal interventions in which airway have to be shared between anesthetists and surgeons would lead to intraoperative and postoperative complications (e.g., inadvertent extubation, aspiration, hypoxia, laryngospasm…etc.). Because of this reason, these procedures often result in anxiety among anesthesia staff, and they have to be alert for possible complications. Securing the airway with an endotracheal tube during these procedures would protect the patient from aspiration. Nasotracheal intubation is usually preferred for providing a large playground for the surgeon to work. However, in selected cases, an orotracheal tube, and even a laryngeal airway mask can be placed. Additionally, in some short and basic interventions, non-intubated anesthesia can be preferred (25). But in this case, to keep excellent cooperation between the dentist and anesthesiologist is mandatory to prevent disappointing results. Thus, the selection of anesthetic methods must be tailored to the properties of the individual patient and the skills of the anesthesiologist. In the present study, nasal cannula and/or mask ventilation

was preferred in 115 patients for different levels of sedation. General anesthesia was performed for longer interventions. Orotracheal intubation was the most frequently performed airway management technique. There were no patients who cannot be intubated.

For dental procedures, local infiltration anesthesia usually provides adequate analgesia. However, additional analgesics are needed for long and complex surgeries. It was found in the present study that, 272 patients had sufficient pain relief with buccal anesthesia with local anesthetics, 34 patients required paracetamol or non-steroid anti-inflammatory drugs in addition to local anesthesia, six patients needed opioids in addition to local anesthesia and paracetamol/NSAIDs, and no any analgesic methods were administered to 49 patients.

It was found in this study that, midazolam, ketamine, propofol, fentanyl, sevoflurane, rocuronium, sugammadex, and neostigmine were used in various combinations for sedation or general anesthesia in day-case dental surgeries in our institute. It must be pointed out that, midazolam, ketamine, propofol, and sevoflurane (which were the most frequently used anesthetic drugs) are some of the 11 anesthetic drugs that the FDA has issued safety warnings (14).

Laryngospasm at various degrees and durations occurred in 31 pediatric (4 sedation, 27 general anesthesia), 12 young (1 sedation, 11 general anesthesia), and six adult (6 general anesthesia) patients. These results seem to be significantly higher in comparison with previously reported incidence rates (26). However, it is known that the incidence of laryngospasm increases inversely proportional to age, and the risk is higher in oropharyngeal interventions, during the recovery from general anesthesia, and in patients with a previous history of asthma. Therefore, the results of this study may be related to the surgical procedure, anesthesia type, and young ages of the patients. Another possible reason may be the additional diseases of these patients. Additionally, it was reported that sugammadex might be associated with laryngospasm (27). Laryngospasm was also experienced in two patients (aged 9 and 16) after the administration of sugammadex in this study. Although it was a precise observation that laryngospasm occurred just after applying sugammadex, it cannot be concluded that sugammadex was the exact and the only reason for the laryngospasm in these two patients.

5. Conclusion

It should be kept in mind that each additional intervention performed brings its risks. Most of the patients undergoing dental procedures constitute a specialized patient group, which includes pediatric patients, and patients with additional diseases who require special needs. Therefore, implementing nonsurgical interventions and postponing elective surgeries to an appropriate time must be taken into consideration. For the safety and the quality of the dental procedure, the choice of sedation or general anesthesia must be made according to the risk and benefit analysis.

Etik kuruş onayı alınmıştır. Derince Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu.No:2019-106

REFERENCES

1. American Academy of Paediatric Dentistry. Guideline on behavior guidance for the paediatric dental patient. *Pediatr Dent.* 2017;39:246-59.
2. World Health Organization, Commonwealth Medical Association Trust and UNICEF. Orientation Programme on Adolescent Health for Health-care Providers; 2006. Available from: https://www.who.int/maternal_child_adolescent/documents/pdfs/9241591269_op_handout.pdf
3. Turkish Anesthesiology and Reanimation Association Anesthesia Practice Guides. General Anesthesia and Sedation Applications in Dentistry (in Turkish), 2016. Available from: http://www.tard.org.tr/akademi/?p=kilavuz-detay&bID=13&session=12295985635616-24591971271232
4. Foundation NPS. Free from Harm: Accelerating Patient Safety Improvement Fifteen Years After "To Err is Human". Boston, MA: National Patient

Safety Foundation; 2015. Available from: https://www.aig.com/content/dam/aig/america-canada/us/documents/brochure/free-from-harm-final-report.pdf
5. American Academy of Pediatric Dentistry. Guideline on use of anesthesia personnel in the administration of office-based deep sedation/general anesthesia to the pediatric dental patient. *Pediatr Dent*. 2016;38:246-9.
6. Coté CJ, Wilson S; American Academy of Pediatrics; American Academy of Pediatric Dentistry. Guidelines for monitoring and management of pediatric patients before, during, and after sedation for diagnostic and therapeutic procedures. *Pediatrics*. 2019;143
7. Lee H, Milgrom P, Huebner CE, et al. Ethics rounds: death after pediatric dental anesthesia: an avoidable tragedy?. *Pediatrics*. 2017;140.
8. Giovannitti JA Jr. Anesthesia for off-floor dental and oral surgery. *Curr Opin Anaesthesiol*. 2016;29:519-25.
9. Bosnjak ZJ, Logan S, Liu Y, et al. Recent insights into molecular mechanisms of propofol-induced developmental neurotoxicity: implications for the protective strategies. *Anesth Analg*. 2016;123:1286-96.
10. Wu J, Bie B, Naguib M. Epigenetic manipulation of brain-derived neurotrophic factor improves memory deficiency induced by neonatal anesthesia in rats. Anesthesiology. 2016;124:624-40.
11. Sun LS. Introduction to "anesthesia and neurodevelopment in children": a supplement from the sixth pediatric anesthesia neurodevelopmental assessment (PANDA) symposium. *J Neurosurg Anesthesiol*. 2019;31:101-2.
12. Backeljauw B, Holland SK, Altaye M, et al. Cognition and brain structure following early childhood surgery with anesthesia. Pediatrics. 2015;136:2014-3526.
13. Sun LS, Li G, Miller TL, et al. Association between a single general anesthesia exposure before age 36 months and neurocognitive outcomes in later childhood. *JAMA*. 2016;315:2312-20.
14. U.S. Food and Drug Administration. FDA Drug Safety Communication: FDA review results in new warnings about using general anesthetics and sedation drugs in young children and pregnant women; 2016. Available from: *https://www.fda.gov/media*/101937/download
15. SmartTots. Consensus Statement of the Use of Anesthetic and Sedative Drugs in Infants and Toddlers; 2015. Available from: *http://www.pedsanesthesia.org/wp-content/uploads*/2015/12/ConsensusStatement.pdf.
16. Ing C, Wall MM, DiMaggio CJ, et al. Latent class analysis of neurodevelopmental deficit after exposure to anesthesia in early childhood. *J Neurosurg Anesthesiol*. 2017;29:264-73.
17. Talpos JC, Chelonis JJ, Li M, et al. Early life exposure to extended general anesthesia with isoflurane and nitrous oxide reduces responsivity on a cognitive test battery in the nonhuman primate. *Neurotoxicology*. 2019;70:80-90.
18. Cabrera OH, Gulvezan T, Symmes B, et al. Sex differences in neurodevelopmental abnormalities caused by early-life anaesthesia exposure: a narrative review. *Br J Anaesth*. 2020;124:e81-e91.
19. Ing C, Ma X, Sun M, et al. Exposure to surgery and anesthesia in early childhood and subsequent use of attention deficit hyperactivity disorder medications. *Anesth Analg*. 2020.
20. Lee JJ, Sun LS, Levy RJ. Report on the sixth pediatric anesthesia neurodevelopmental assessment (PANDA) symposium, "Anesthesia and Neurodevelopment in Children*". J Neurosurg Anesthesiol*. 2019;31:103-7.
21. Brailo V, Janković B, Lozić M, et al. Dental treatment under general anesthesia in a day care surgery setting. *Acta Stomatol Croat*. 2019;53:64-71.
22. American Academy of Pediatric Dentistry. Policy on early childhood caries (ECC): unique challenges and treatment options. *Pediatr Dent*. 2016;38(6):55–6.
23. Özkan AS, Erdoğan MA, Şanlı M, et al. Retrospective evaluation of dental treatment under general anaesthesia. Turk J Anaesthesiol Reanim. 2015;43:332-6.
24. Akpinar H. Evaluation of general anesthesia and sedation during dental treatment in patients with special needs: a retrospective study. *J Dent Anesth Pain Med.* 2019;19:191-9.
25. Şimşek T, Yılmaz M. retrospective comparison of general anesthesia and sedation unused in pediatric patients during dental procedures. *Kocaeli Medical J*. 2017;6:59-62.
26. Landsman IS, Hays SR, Karsanac CJ, et al. Pediatric Anesthesia. Editors: Coran AG, Adzick NS, Caldamone AA, et al. Pediatric Surgery (7th Ed). Philadelphia: Elsevier BV; 2012.p.201-26.
27. Wu TS, Tseng WC, Lai HC, et al. Sugammadex and laryngospasm. *J Clin Anesth*. 2019;56:52.