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Analysis of Different Sedation Approaches for Epileptic Patients in Dentistry: A Retrospective Study

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Abstract

Few clinical studies have been reported on the use of sedation in epileptic patients receiving dental treatments. The aim of this study was to perform a retrospective analysis of epileptic patients who underwent dental treatments under sedation. The medical records of 212 epileptic patients treated under sedation were reviewed retrospectively. Demographic data, ASA classification, comorbid diseases, medications, sedation duration, sedation agents, oral disorders, dental treatments, and complications were recorded. The mean age of the patients was 24.2±9.1 years. One hundred ninety-four patients were classified as ASA II (91.5%) and 18 (8.5%) as ASA III. Mental retardation was identified in 117 (55.2%) patients. Midazolam (n=204 patients, 96.2%) and ketamine (n=168, 79.2%) were the most frequently used sedation agents. Dental caries (n=192, 79.2%) and periodontal diseases (n=31, 14.6%) were the most common oral disorders. The surgical, periodontal, restorative and prosthodontic treatments were performed. Epileptic seizures (n=2), vomiting and desaturation (n=2) and haemorrhage (n=1) were observed. It was concluded that sedation can be effectively and safely used for providing dental care in epileptic patients. Cooperative work of experienced anesthesia and dental team is of great importance to provide a safe and comfortable treatment for epileptic patients requiring a specific treatment approach.

1. Introduction

Epilepsy is a common neurological disorder, with approximately half of the cases beginning in childhood or adolescence (Yeung, Wong, McGrath, Yiu, Lee, 2019). Epileptic patients are frequently seen in dental practice (Subki, Mukhtar, Saggaf, Ali, Khalifa, Al-Lulu, Alsallum, Bokhary, Baabdullah, Kassar, Jan, Hindi, Jan, 2018). The disease may affect the oral health of patients. Patients with seizure disorders tend to have less than ideal oral health, with higher numbers of decayed and missing teeth. They also tend to receive less dental procedures, with significantly fewer restored and replaced teeth than the general population (Chellathurai, Thiagarajan, Jayakumaran, Devadoss, Elavazhagan, 2016). The seizures themselves can contribute to the development of dental problems such as trauma or poor oral hygiene. Patients with epilepsy may experince more frequent dental trauma during epileptic seizures. However, some antiepileptic drugs (AEDs) may induce the formation of carries and gingival overgrowth (Yeung et al., 2019). The most common dental complication for AEDs is gingival hyperplasia, which have been encountered in patients taking phenytoin. Phenobarbital, valproic acid, or carbamazepine, can also cause gingival enlargement. AEDs that induce hepatic cytochromes can reduce vitamin D levels and cause alveolar bone loss (Devinsky, Boyce, Robbins, Pressler, 2020).

Dental treatments may be challenging in patients with epilepsy. Local anesthetics may lower the seizure threshold. Indeed, stress and anxiety may increase the risk of a seizure (Schöpper, Ludolph, Fauser, 2016). In addition, epileptic patients with mental disabilities may not cooperate at the desired level and dentists cannot provide effective treatment (Akpınar, 2019). During dental treatment, a possible seizure development can be prevented by means of sedation (Yaltırık, Özer, Tonguç, Kocaelli, 2012). In these patients, sedation provides optimized treatment outcomes (Schnabl, Guarda, Guarda, von Spreckelsen, Riedmann, Steiner, Dumfahrt, 2019).

It is important not to trigger an epileptic attack during dental procedures, and to preserve airway and swallowing reflexes during sedation. Therefore, these patients require a specific approach. Limited data are available in the literature regarding the management of dental treatment procedures for people with epilepsy. The use of sedation for dental care in epileptic patients is poorly documented. The present study was designed to conduct a detailed retrospective analysis of epileptic patients receiving dental treatment under sedation.

2. Materials and Methods

This retrospective study included 212 epileptic patients receiving dental treatment under sedation at Gazi University, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery between 2012 and 2017. All dental treatments were performed in the sedation unit of oral and maxillofacial surgery department by the anesthesia and dental team. Data were obtained by medical records from the patient files. Patients with incomplete data and informed consent were excluded from the study. Physical examinations were carried out prior to sedation by the anesthesiologist. Demographic data including age and gender, ASA classification, comorbid systemic diseases, and related medications were

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recorded on the patient files. Duration of epilepsy, seizure frequency, antiepileptic, antipsychotic and/or antidepressant drug use were also noted. Depending on the patient's medical condition, laboratory tests and consultations were obtained if necessary. The dental, clinical and radiological examinations of the patients were also performed prior to sedation. Dental treatments included tooth extraction, restorative, periodontal and prosthetic treatments, temporomandibular joint (TMJ) arthrocentesis, cyst operation, and implant surgery. Preoperative and postoperative instructions were given before the procedure (Table 1) (Practice guidelines, 2017).

Table 1: Preoperative and postoperative patient instructions

Preoperative
1. Take your regular prescription medications unless instructed by your dentist or physician.
2. Do not eat or drink for 8 hours prior to the appointment.
3. Patient must arrive at the hospital by a responsible adult.
4. Do not smoke or drink alcohol for 8 hours prior to the appointment.
5. Sedative medications must be taken according to the dentists' instructions.
Postoperative
1. Take all regular or prescribed medications as prescribed by physician or dentist.
2. Do not take any alcohol for 12 hours postoperatively
3. Do not drive for 12 hours postoperatively.
4. Do not drive or operate machinery for 12 hours postoperatively.
5. Must have a responsible adult drive patient home and remain with the patient.
6. Be sure to provide a phone number where dentist can be reached.

The dental treatments were performed after a fasting period of at least 6 hours. An IV line was inserted in cooperative patients, for uncooperative patiens sevoflurane induction was performed for securing the IV line. Electrocardiography (ECG) monitorization, oxygen saturation (SpO_2), and non-invasive blood pressure monitorization were performed throughout dental treatment and the recovery period according to the ASA guidelines (ASA guidelines, 2021). Type and amount of the sedative agents used, duration of anesthesia, complications related to sedation and/or dental treatments were recorded.

The statistical package for the Social Sciences (SPSS Inc., Chicago, IL, USA) 13.0 software was utilized for statistical analysis. Values of numbers, percentages, means, and standard deviations were used in defining the data.

3. Results

Medical records of 212 epileptic patients (106 males, 106 females) were retrospectively analyzed. Patients' characteristics, dental procedures, and clinical findings are shown in Table 2. The mean age of the patients was 24.2±9.1 years (range 8 to 57). Of these patients, 194 were classified as ASA II and 18 as ASA III. The most common comorbid diseases were endocrinological and psychiatric diseases. All the comorbid diseases are shown in Table 2. Mental retardation (autism, MMR, cerebral palsy etc.) was observed in 117 patients.

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Table 2 : Demographic data of the patients

Age, M ± SD*	24.2±9.1
Gender, N(%)	
Female	106 (50)
Male	106 (50)
ASA† score, N (%)	
ASA I	-
ASA II	194 (91.5)
ASA III	18 (8.5)
Comorbid diseases, N (%)	
Cardiovascular disease	6 (2.8)
Respiratory disease	6 (2.8)
Endocrinologic disease	14 (6.6)
Hematological disease	1 (0.5)
Oncologic disease	3 (1.4)
Central nervous system disease	5 (2.4)
Psychiatric disease	7 (3.3)
Liver disease	1 (0.5)
Others	18 (8.5)
Mental retardation	117 (55.2)

*M ± SD- Mean, Standard Deviation.
†ASA- American Society of Anesthesiologists

Table 3: Epilepsy characteristics

Duration of epilepsy (yr*), M ± SD†	17.40±11.89
Frequency of seizures, N (%)	
Everyday	2 (0.9)
Once a week	11 (5.2)
Once a month	10 (4.7)
Less than once a month	20 (9.4)
Seizure free for 1-5 years	31 (14.6)
Seizure free for more than 5 years	15 (7)
Not known	123 (58)
Antiepileptic drug use, N(%)	
Single	91 (42.9)
Combined	84 (39.6)
No drug use	28 (13.2)
Not known	9 (4.2)
Antipsychotic drug use	36 (17)
Antidepressant drug use	25 (11.8)

*Yr-Year
†M± SD-Mean, Standard Deviation

The mean disease duration for epilepsy was 17.40±11.89 years. Of the patients, 2 patients had seizures every day, 11 had seizures once a week, 10 had seizures once a month and 20 had seizures less than once a month. Thirty-one patients were seizure free for 1 to 5 years and 15 patients for more than 5 years. In the remaining patients, exact information regarding the frequency of seizures could not be provided by the families (Table 3).

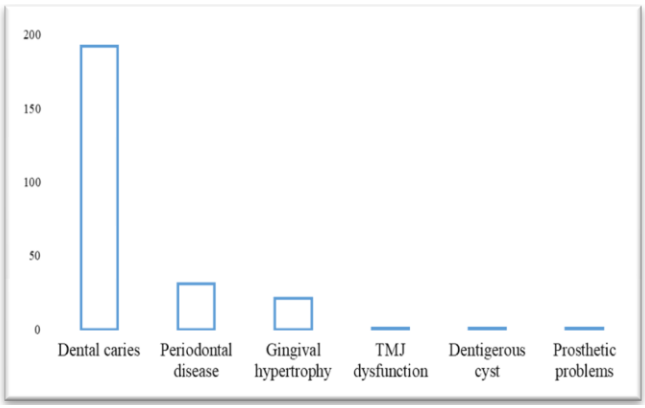

Figure 1: Oral disorders of the patients

Concerning the AEDs use in this study, the patients received phenytoine, valproate, topiramate, lacosamide, oxycarbazepine, zonisamid, carbamazepine, levetiracetam, lamotrigine, clobazam, clonazepam, and pyrimidone. The drugs were used as a single or combined therapy. Among these patients, 36 received antipscyhotic and 25 received antidepressant medications in addition to AEDs (Table 3).

The distribution of oral disorders is shown in Figure 1. Dental caries was the most common oral disorder, occurring in 192 patients (90.6%). Periodontal diseases were found in 31 patients (14.6%) and 21 patients (9.9%) had gingival hypertrophy.

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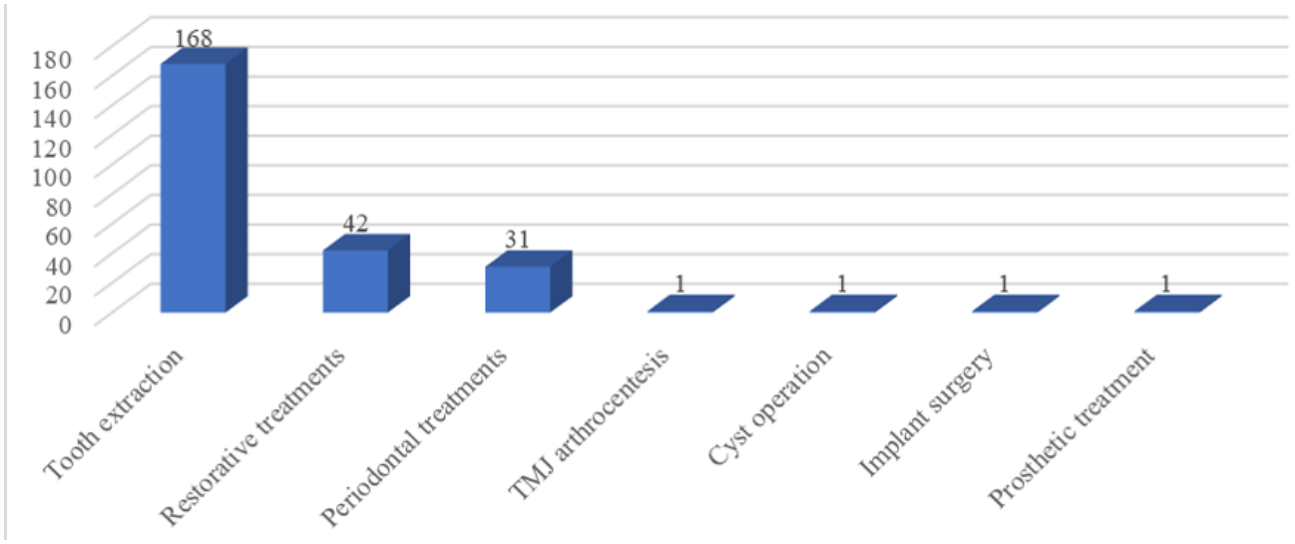

Figure 2: Dental treatments

The treatment needs of the patients are shown in Figure 2. The most common treatment was determined as tooth extraction, performed in 168 patients (79.2%). Forty-two patients (19.8%) required restorative treatments (fillings and root treatment). Periodontal treatments (scaling, root planing, and gingivoplasty) were performed in 31 patients (14.6%). In addition, 1 patient (0.5%) received arthrocentesis for TMJ dysfunction, 1 patient (0.5%) underwent cyst operation for dentigerous cyst, and 1 patient (0.5%) had implant surgery for tooth loss. Three patients (1.4%) were examined intraorally.

The mean anesthesia time from the start of the procedure to the end of the treatment was 40±16 minutes. Midazolam, ketamine, propofol, and fentanyl were used as intravenous and, nitrous oxide and sevoflurane were used as inhalation anesthesic agents. These agents were used alone or in combination with other agents. The doses of the agents used are shown in Table 4. Midazolam was the most commonly used sedation agent. Nitrous oxide and sevoflurane were also used in 18 and 34 patients, respectively (Figure 3).

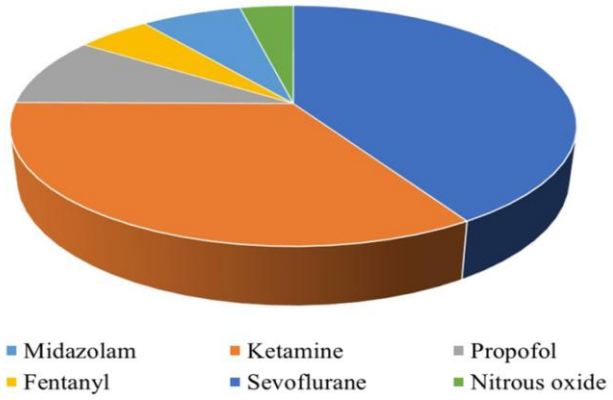

Figure 3: Sedation agents used in patients

Local anesthesia was performed in all patients using articaine with 0.006 mg or 0.012 mg epinephrine (Maxicaine DS-Forte, VEM İlaç San. Ve Tic. A.Ş, Ankara).

Regarding complications, vomiting with desaturation was observed in 2 patients while performing dental treatment. One patient had convulsions intraoperatively. One patient had a seizure 10 minutes prior to the dental procedure. One patient

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had intraoperative haemorrhage. No postoperative complications were observed in the recovery period.

Table 4: Amount of agents utilized during sedation

	Midazolam Use	Ketamine Use	Propofol Use
Midazolam Ketamine Group	0.24±0.05 mg/kg	0.14±0.08 mg/kg	-
Midazolam Ketamine Propofol Group	0.014±0.04 mg/kg	0.07±0.06 mg/kg	25Mcg/kg/min

4. Discussion

Epilepsy is defined as a chronic neurological disorder and the most common comorbid condition which is characterized by recurrent unprovoked seizures. The estimated prevalence of epilepsy ranges from 0.5% to 0.9% in the general population (Subki et al., 2018).

The mental disability has been reported to range from 5% to 83%, and physical disability from 23% to 54% among epileptic patients (Mielnik-Błaszczak, Skawińska-Bednarczyk, Michałowski, Błaszczak, 2018). These problems contribute to the development of poor oral health (Subki et al., 2018). In addition, AEDs can also have side effects intraorally (Devinsky et al., 2020). Phenytoin, for example, causes gingival hyperplasia in up to 60% of patients. Xerostomia is a side effect of a multi anti-epileptic drugs (e.g. carbamazepine, oxcarbazepine, levetiracetam, gabapentine and lamotrigine) and increases the risk of caries. In addition, bone mass density has been reported to reduce in patients taking phenobarbital, phenytoin, primidone, carbamazepine, and valproic acid (Schöpper et al., 2016).

In the present study, 212 epileptic patients received dental treatment under sedation. Some patients received multiple dental procedures in the same treatment session. The results demonstrated that sedation was mostly performed for surgical treatments.

Dental treatment plan may be modified according to the comorbidity and related medication of the patient, and sometimes medical consultation may be required (Walia, Bhatia, Singh, Kaur, Duggal, Ajaypal, 2017). In this study, endocrinologic diseases were the most encountered comorbitidies followed by psychiatric, cardiovascular, and respiratory diseases. The selection and dosage of the appropriate anesthetic agent were determined by considering the drugs used in these patients with medical consultations as well as the type of dental treatment. Dental anxiety is a frequent situation resulting with the avoidance of dental treatment as well as increased medical and surgical complications. It is also one of the critical factors which complicates dental treatment (Melini, Forni, Cavallin, Parotto, Zanette, 2020). Dental procedures carry an innate risk of triggering seizures (Chellathurai et al., 2016; Subki et al., 2018). Seizures have been reported as the third most common type of adverse medical event in patients in dental practice (Ransford, Soryal, McCorry, Sander, Duncan, Huggins, 2014). The factors that may trigger stress should be eliminated prior to the beginning of the procedure. The appointment should be in the early hours, treatment sessions should be kept short, and sudden stimulants such as shimmering bright lights, and extreme noise should be avoided (Yaltırık et al., 2012). In the present study, dental treatments were performed in line with these recommendations. Apart from fear and anxiety, local anesthetics used during dental treatments lower the seizure threshold in epilepsy patients. Local anesthetics administered in therapeutic dosages do not have an interaction

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with antiepileptic drugs. However, generalized tonic-clonic convulsions may occur in case of a critical overdose of local anesthetics. It has been also stated that adrenaline in local anesthetics has a potential effect of epileptic inducing epileptic attacks by means of intravenous injection (Yaltırık et al., 2012). In the present study, the local anesthetic was administered in therapeutic dosages. No adverse outcome was noted with local anesthetic agent.

Dentally compromised patients include not only medically disabled patients with limited ability to cooperate or tolerate, but also those with severe dental phobia and young children with poor communication (Seok, Ji, Yoo, Kim, Kim, Kim, 2016). In addition, local anaesthetics, antibiotics and analgesics have been reported to lower the seizure thresold. Stress and anxiety may increase the risk of seizure (Schöpper et al., 2016). For patients who are difficult to manage with conventional strategies, behavior management by means of drugs can be considered. Drug-induced sedation can help managing anxiety, phobias, and pain; since it can relax the muscles, it is used to provide safe, high-quality dental treatments (Seok et al., 2016). In case of treating epileptic patients with mental disabilities, sedation also provides comfortable environment as well as eliminating any unexpected movement or response during treatment (Schöpper et al., 2016).

Patients undergoing sedation are asked to fast preoperatively. Before elective procedures, a fasting time of 6-8 hours is recommended after their meals. Oral nutrition is started after 2 hours following IV sedation (Practice guidelines 2017; ASA, 2021). In our study, the fasting and oral nutrition procedures were applied in line with this guideline above. The patients were followed up at least 4 hours postoperatively and discharged on the same day. Patients requiring more recovery time were followed-up for a longer period of time.

In comparison to general anesthesia, IV sedation is advantageous in terms of rapid recovery following treatment with fewer complaints of nausea and vomiting since the dosage can be titrated as needed, and less respiratory complications are seen since intubation is not required. However, considering the health expenses associated with general anesthesia, sedation is preferable, facilitating dental treatment, and reducing the duration of hospital time (Seok et al., 2016).

This study showed that IV sedation on epileptic patients were safe and effective. The effectiveness was mainly based on the appropriate usage of sedation drugs and the prediction of the patient difficulties. The low complication rate (2.3%) has shown that sedation may be an alternative option to general anesthesia for epileptic patients. Only 5 complications including epileptic seizures, vomiting followed by desaturation and haemorrhage were recorded. All the complications were observed in mentally retarded patients. Among these complications, the haemorrhage was related with technical difficulties of third molar extraction. Haemorrhage was controlled with local measures. In patients with nausea and vomiting, the procedure was stopped, the foreign bodies in the mouth were cleaned by placing the patients on their side, and the continuation of the airway opening was ensured by pulling the tongue forward, the patients were monitorized and followed up with oxygen.

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Hypoxia, which precipitate convulsion, has to be avoided during the sedation. Thus, the oxygen status of these patients' was monitorized continuously using pulse oximeter, and supplement oxygen was provided as a standby; to be used in case of emergency (Chellathurai et al., 2016).

Although the anesthetic effect starts rapidly in intravenous sedation, the time required for dental treatment is short. Therefore, it is suitable for treatments less than 2 hours (Seok et al., 2016). In the present study, the mean duration of anesthesia was 40±16 minutes.

Current sedation agents used in epileptic patients include propofol, thiopental, dexmedetomidine, midazolam, cloral hydrate, ketamine, and inhalation agents including nitrous oxide and sevoflurane. Most sedative hypnotics have an effect on brain electroencephalography (EEG), which is not optimal when evaluating for seizure or interictal activity (Ransford et al., 2014). In the present study, midazolam, ketamine, propofol, fentanyl, nitrous oxide, and sevoflurane were the preferred agents. Regarding drug choice, no ideal anesthetic regime has been reported. Seizure-like activity is normal during the induction of and emergence from anesthesia, and most anaesthetic drugs possess convulsant and anticonvulsant properties. Seizure susceptibility also depends on the innate individual variation. Epileptic patients may take antidepressants or antipsychotics, which may lower the seizure threshold (Ransford et al., 2014). These drugs produce a higher sensitivity to sedative agents. In fact, the antiepileptic drugs have been shown to diminish hepatic metabolism (Salinas Salmeron, Kim, Seo, 2019). In case of other comorbidities, the doses and type of the sedative agents are of big concern. In this study, the sedation agent and the doses were determined based on the patient's general condition, comorbidity, and medications as well as the type of dental procedure and the amount of time needed for dental treatment.

In our study, midazolam, ketamine, and propofol were the most commonly used intravenous sedation agents. For people who are anxious and have stress-induced seizures, benzodiazepines can be used because of anxiolytic and anticonvulsive properties. Midazolam is the most preferred benzodiazepine with its short duration of action. However, midazolam have some disadvantages for epileptic patients. IV midazolam is reduced by benzodiazepines tolerance and people may require larger doses midazolam if they are taking liver cytochrome P450 enzyme-inducing agents such as carbamazepine, phenytoin, or barbiturates. On the other hand, reversal of sedation with flumazenil may trigger a seizure in poorly controlled epileptic patients and those taking oral benzodiazepines therapy (Ransford et al., 2014).

The relationship between anesthesia and epilepsy is complex and further research is needed. The effect of propofol is dose-dependent and, low dose propofol is epileptogenic. A high dose of propofol is antiepileptic and has been recommended as third line in status epilepticus (SE) rescue and the first line treatment in refractory SE related to anesthesia (Lu, Xiong, Zhang, Xiao, Zhou, 2019).

Ketamine alone or in combination of other anesthetics has been safely and effectively used for sedation. In fact, the use of ketamine in epileptic patients is debated. Some studies report that ketamine

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will activate epileptogenic foci in patients with known seizure disorders (Jolly & McLean, 2012). In addition, ketamine has also demonstrated anticonvulsant properties and has a recognised analgesic property which is very beneficial for dental sedation (Wood, Manley, Bezzina, Hassan, 2015). It differs from other sedatives in its ability to preserve cardiovascular stability, spontaneous respiration, and protective airway reflexes, making it attractive for emergencies (Jolly & Mclean, 2012). Unique among anaesthetic agents, ketamine is able to preserve the functional residual capacity of the lungs during sedation and decreases the chances of intra-operative hypoxemia. Patients will breathe spontaneously, even in a fully anaesthetised state, as they would in their awake state with the minute volume being maintained (Wood, Manley, Bezzina, Hassan, 2015). Preservation of laryngeal reflexes and airway protection is vital when performing dental treatments under sedation (Jolly & Mclean, 2012). Both deep sedation and protection of airway reflexes are possible with the use of ketamine. Therefore, we used ketamine frequently in the present study. No epileptic attack due to ketamine was observed.

If the patient has severe and; poorly controlled epilepsy, a dental setting with special equipment is recommended. Many dental practitioners routinely treat these patients in hospital settings. It is generally accepted that preoperative evaluation is essential before sedation. Anesthesiologist may need additional data such as ECG, chest radiograph or laboratory study to obtain levels of AEDs. However, the dental team should be fully prepared to manage all possible attacks and related complications (Ransford et al., 2014).

5. Conclusion

The need for dental treatment in epileptic patients is higher than in the general healthy population. Sedation may be recommended as an alternative to general anesthesia in order to make dental treatments more comfortable and safe, to minimize possible attacks, and to ensure cooperation in patients with mental retardation. For this purpose, the combination of ketamine, propofol and ketamine-propofol are the agents that can be preferred in epileptic patients because of their short recovery time, lower complications such as nausea and vomiting, and its ability to allow the surgeon to work comfortably. However, there are very few clinical studies on the dental treatment of epileptic patients under sedation. More clinical studies are needed on patients with epilepsy, which require a special approach in dentistry.

Statistical analysis

The statistical package for the Social Sciences (SPSS Inc., Chicago, IL, USA) 13.0 software was utilized for statistical analysis. Values of numbers, percentages, means, and standard deviations were used in defining the data.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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