

# Assessment of the Knowledge Levels and Attitudes of Physicians Regarding the Management of Acute Seizures in Pediatric Patients

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#### **ABSTRACT**

Aim: To evaluate the knowledge levels and attitudes of physicians regarding acute management of seizures in pediatric patients.

Materials and Methods: A self-administered questionnaire was distributed electronically to physicians. The participants were divided into 3 groups according to the estimated number of patients managed by the physician due to acute seizures per year; i) group 1: ≤10, ii) group 2: 11-50, iii) group 3: ≥51. Also, the participants were categorized whether they were pediatricians or not. Demographical features, and administration details regarding first- and second-line therapy were questioned. Rates of correct answers were compared between the groups.

**Results:** A total of 400 physicians responded to the questionnaire. Precisely, 74.5% of participants were pediatricians. The time point  $t_1$  for tonic clonic status epilepticus (SE) and focal SE with impaired consciousness were the least known details. Rates of correct answers to questions of the maximum number of benzodiazepines in case of ongoing seizures (p<0.001), intravenous diazepam dose (p=0.017), and diazepam infusion time (p=0.034) were significantly higher in group 3. Also, there was a tendency to administer lower doses of levetiracetam (p=0.003) and phenytoin (p>0.001), and prefer longer durations for phenytoin (p=0.003) in group 1 and group 2. Rates of correct answers to questions regarding the approach to patients who presented during the postictal period (p<0.001), the time point  $t_1$  for tonic-clonic SE (p=0.07), the maximum number of benzodiazepines in case of ongoing seizures (p<0.001), diazepam infusion time (p<0.001), and co-administered liquid for phenytoin (p=0.043) were higher in pediatricians. Additionally, there was a significant tendency to administer lower doses of levetiracetam (p<0.001) and phenytoin (p<0.001), and prefer longer durations for levetiracetam (p<0.001) and phenytoin (p<0.001) in physicians other than pediatricians.

**Conclusion:** There is a wide variation in knowledge levels and attitudes among physicians. Post-graduation education programs focusing on the least-known and important details are needed.

Keywords: Seizure, acute management, children and adolescents, knowledge level, attitude

#### Introduction

A seizure is defined as "a transient occurrence of signs and symptoms owing to abnormally excessive or synchronous neuronal activity in the brain" (1). The estimated risk of experiencing any kind of seizure during the whole lifetime of an individual is approximately 8%

(2). Its prognosis is associated with age, etiology, and duration of the seizure (3,4). International League Against Epilepsy proposed two operational dimensions in 2015 as follows: the time point  $t_1$  (TP- $t_1$ ) indicates the time when pharmacological treatment should be initiated; the time point  $t_2$  (TP- $t_3$ ) indicates the time when long-

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term consequences may appear. The TP-t,s for tonicclonic status epilepticus (SE), focal SE with impaired consciousness, and absence SE are 5 minutes, 10 minutes, and 10-15 minutes, respectively. The TP-t, for tonic-clonic SE is 30 minutes, and the time point to for focal SE with impaired consciousness is 60 minutes. However, the TP-t<sub>3</sub> for absence SE is unknown (1). The first-line therapy consists of benzodiazepines. Intravenous administrations of levetiracetam, phenytoin, phenobarbital, and valproic acid are the options for the second-line therapy. Since the rapid termination of the seizure is crucial, physicians must have the adequate knowledge of the seizure management (5). However, there are not many studies investigating the knowledge level of the physicians about the acute seizures (6-9). To perform postgraduate programs, it is important to reveal their knowledge levels. Herein, we aimed to evaluate the knowledge level and attitudes of the physicians regarding the management of acute seizures in pediatric patients.

#### **Materials and Methods**

We have obtained the approval of the Aydın Adnan Menderes University Faculty of Medicine Clinical Research Ethics Committee (date: 20/01/2022; approval no: 2021/200) outlined in the Second Revision of WMA Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects. A self-administered questionnaire was written in Turkish with a cover letter, and reviewed by two independent pediatric neurologists and a pediatrician (Appendix 1). Afterwards, the questionnaires were distributed electronically to physician WhatsApp groups in Turkey. Informed consent was taken from the participants. We aimed to reach physicians who had a high possibility to treat children with acute seizures (practicing in speciality/subspecialities of pediatrics, general medicine, specialites of family medicine, neurology, neurosurgery, anesthesiology and reanimation). Physicians who agreed to respond to the items of the questionnaire were included in the survey. Data about demographic features including age, gender, and years of experience were collected. The participants were divided into three groups according to the estimated annual number of pediatric patients with acute seizures they treated as follows: i) group 1: ≤10, ii) group 2: 11-50, and iii) group 3: >50. Also, the participants were categorized whether they were pediatricians or not. The self-confidence of the physicians, administration details of the medications in the first-, and the secondline therapies were questioned. The correct answers to the questions regarding the durations of TP-t, for tonicclonic SE and focal SE with impaired consciousness were accepted as 5 minutes, and 10 minutes, respectively. The correct answers to the questions relating to the "approach to the patients who presented during the postictal period", and "who started to seize in the hospital" were "investigating the etiology after initial stabilization steps", and "initial stabilization steps", respectively (1,5). The appropriate choice for the firstline therapy is benzodiazepines. In the first-line therapy, benzodiazepines can not be administered more than twice. The appropriate dose, maximum intravenous dose, and infusion rate for diazepam should be 0.15-0.2 mg/ kg/dose, 10 mg/dose, and 5 mg/min, respectively. The appropriate dose, minimum infusion time, and suitable administration solution for phenytoin should be 20 mg/kg/dose, 20 minutes, and 0.9% sodium chloride, respectively (5,10,11). The appropriate loading IV infusion dose of levetiracetam is 40-60 mg/kg/dose and it should be administered within 15-20 minutes (5,12).

#### **Statistical Analysis**

Statistical analysis was performed using SPSS version 22 (IBM Corporation, Armonk, NY, USA). The sample size was calculated as three hundred eighty four by using stat calc (Epi Info) at p=0.5 d:0.05 and within 95% confidence interval. Descriptive variables were expressed as percentages (%), the means ± standard deviation, or medians with maximum and minimum values in parentheses. A chi-squared or Fisher's exact test was used for categorical variables, and the Mann-Whitney U test and Kruskal-Wallis H test were followed by a Dunn's post-hoc test for quantitative data after normality of distribution was assessed using the Kolmogorov-Smirnov test. A p-value <0.05 was considered to indicate statistical significance.

#### Results

A total of four hundred participants including 234 (58.5%) male, and 166 (41.5%) female physicians responded to the questionnaire. Precisely, 84.5% of the responders were pediatricians who remarked that they had self-confidence (Table I). Tables II, III and Figure 1 present the rates of answers to the questions. Details about the TP-t<sub>1</sub> for tonic-clonic SE (32.3%) and for focal SE with impaired consciousness (6.8%) were least known. The rates of correct answers to the questions of the maximum number of benzodiazepine administrations in case of ongoing seizures (p<0.001), intravenous

Table I. Demographical features of the physicians			
	n/mean ± SD	%/median (minmax.)	
Gender			
• Female	166	41.5	
• Male	234	58.5	
Age	36.1±8.2	35.0 (24.0-67.0)	
Experience in years	11.3±8.6	10.0 (0.1-42.0)	
Speciality			
• Pediatrics	298	74.5	
Emergency medicine	20	5.0	
• Family medicine	12	3.0	
General medicine	57	14.3	
• Other	13	3.3	
Having self-confidence regarding the management of acute seizures			
• Yes	338	84.5	
• No	10	2.5	
• Unsure	52	13.0	
Estimated annual number of patients with acute seizures managed by the physician			
• <b>≤</b> 10	120	30.0	
• 11-50	121	30.3	
• ≥51	159	39.8	

Descriptive variables are expressed as percentages (%), the means ± standard deviation, or medians with maximum and minimum values in parentheses SD: Standard deviation, min.: Minimum, max.: Maximum

	n	%
Approach to the patient who presented during the postictal period after a 2-3 minutes lasting seizure Investigating the etiology after initial stabilization steps (supports of the airway, breathing, and circulating) Intravenous administration of levetiracetam (loading and maintainence) Intravenous administration of phenytoin (loading and maintainence doses) Rectal diazepam	<b>387</b> 8 4 1	<b>96.8</b> 2.0 1.0 0.3
Approach to the patients who started to seize in the hospital (the first step should be chosen) • Rectal diazepam • Initial stabilization steps (supports of the airway, breathing, and circulating) • Blood glucose sampling • Establishing an intravenous route	11 <b>383</b> 3	2.8 <b>95.8</b> 0.8 0.8
The time point t <sub>1</sub> for tonic-clonic SE (initiation of pharmacological threapy) As soon as possible Within 2-3 min following the initial stabilization steps At 5. min following the initial stabilization steps At 10. min following the initial stabilization steps	80 189 <b>129</b> 2	20 47.3 <b>32.3</b> 0.5
The time point t <sub>1</sub> for focal SE with impaired consciousness (initiation of pharmacological threapy) As soon as possible Within 2-3 min following the initial stabilization steps At 5. min following the initial stabilization steps At 10. min following the initial stabilization steps	176 110 87 <b>27</b>	44.0 27.5 21.8 <b>6.8</b>
The appropriate medication in the first-line therapy Benzodiazepin (intravenous/buccal/intranasal/rectal) Intravenous administration of levetiracetam (loading and maintainence doses) Intravenous administration of phenytoin (loading and maintainence doses) Phenobarbital (by nasogastric tube)	<b>346</b> 37 16	<b>86.5</b> 9.3 4.0 0.3
The maximum number of benzodiazepine administrations that can used in case of ongoing seizure in the first-line therapy One Two Three	16 <b>223</b> 161	4.0 <b>55.8</b> 40.3

diazepam dose (p=0.017), and diazepam infusion time (p=0.034) were significantly higher in group 3 than in the other groups. Also, there was a significant tendency to administer lower doses of levetiracetam (p=0.003), and phenytoin (p>0.001), and to infuse IV phenytoin for longer periods of time (p=0.003) in group 3 than in the other groups (Table IV). The rates of correct answers to the questions regarding the approach to the patients who presented during the postictal period (p<0.001), the TP-t<sub>1</sub> for tonic-clonic SE (p=0.07), the maximum number of benzodiazepine administrations

in case of ongoing seizures (p<0.001), infusion times for diazepam (p<0.001), and levetiracetam (p<0.001), suitable administration solution for phenytoin (p=0.043) were significantly higher among pediatricians than non-pediatricians (Table V). Additionally, there was a significant tendency to administer lower doses of levetiracetam (p<0.001), and phenytoin (p<0.001), and administer phenytoin with a longer infusion time at a dose of 20 mg/kg (p<0.001) among physicians other than pediatricians.

Fable III. The rates of answers to the details regarding the knowledge of pha			
	n	%	
ntravenous doses of diazepam (per kilogram) 0.15-0.2 mg/kg/dose 0.5 mg/kg/dose 1 mg/kg/dose	<b>322</b> 69 9	<b>80.5</b> 17.3 2.3	
Maximum dose of intravenous diazepam (adult dose) 5 mg/dose 10 mg/dose 20 mg/dose	158 <b>213</b> 29	39.5 <b>53.3</b> 7.3	
ntravenous infusion rate of diazepam Rapid enjection (bolus) 5 mg/min infusion 30 min infusion	142 <b>214</b> 44	35.5 <b>53.5</b> 11.0	
ntravenous levetiracetam loading dose 10 mg/kg/dose 20 mg/kg/dose 40-60 mg/kg/dose	60 185 <b>155</b>	15.0 46.3 <b>38.8</b>	
Levetiracetam infusion time Rapid enjection (bolus) 15-20 min infusion 30 min infusion	51 <b>202</b> 147	12.8 <b>50.5</b> 36.8	
ntravenous phenytoin dose 10-15 mg/kg/dose 20 mg/kg/dose 40 mg/kg/dose	316 <b>80</b> 4	79.0 <b>20.0</b> 1.0	
Minimum infusion time for phenytoin dose of 20 mg/kg 10 min 20 min 30 min	50 <b>159</b> 191	12.5 <b>39.8</b> 47.8	
Suitable diluent administration solution for intravenous phenytoin  Dextrose + ringer lactate  0.9% sodium chloride  5% dextrose in water  10% dextrose in water	6 <b>325</b> 66 3	1.5 <b>81.3</b> 16.5 0.8	

**Table IV.** Comparison of rates of correct answers to the questions regarding the management of acute seizures according to the estimated annual number of patients with acute seizures managed by physicians

	Group 1 ≤10 (n=120) n (%)	Group 2 11-50 (n=121) n (%)	Group 3 ≥51 (n=159) n (%)	p-value
Approach to the patient who presented during the postictal period	115 (95.8)	115 (95.8)	157 (98.7)	0.178
Approach to the patient whose seizure initiated in the hospital	113 (94.2)	115 (95.0)	155 (97.5)	0.356
The time point $t_1$ for tonic clonic seizures	29 (24.2)	40 (33.1)	60 (37.7)	0.055
The time point t <sub>1</sub> for focal seizures with impaired consciousness	7 (5.8)	5 (4.1)	15 (9.4)	0.192
The appropriate medications in the first-line therapy	104 (86.7)	102 (84.3)	140 (88.1)	0.659
The maximum number of benzodiazepines in case of ongoing seizures	55 (45.8)	60 (49.6)	108 (67.9)	<0.0001
Knowledge level regarding intravenous diazepam administration  • Appropriate intravenous dose  • Maximum dose  • Infusion time	87 (72.5) 55 (45.8) 53(44.2)	98 (81.0) 64 (52.9) 66 (54.5)	137 (86.2) 94 (59.1) 95 (59.7)	0.017 0.088 0.034
Knowledge level regarding levetiracetam administration • Appropriate intravenous dose • Infusion time	35 (29.2) 56 (46.7)	43 (35.5) 56 (46.3)	77 (48.4) 90 (56.6)	<b>0.003</b> 0.140
Knowledge level regarding pheniytoin administration  • Appropriate intravenous dose  • Suitable administration solution  • Minimum Infusion time	57 (47.5) 92 (76.7) 37 (30.8)	69 (57.0) 98 (81.0) 43 (35.5)	116 (73.0) 135 (84.9) 79 (49.7)	<0.0001 0.217 0.003

Kruskal-Wallis H test were followed by a Dunn's post-hoc test for quantitative data following an assessment of normality in the Kolmogorov-Smirnov test

Table V. Comparison of rates of correct answers to the questions regarding the management of acute seizures according to the speciality			
	Pediatricians (n=298) n (%)	Physicians other than pediatricians (n=102) n (%)	p-value
Approach to the patient who presented during the postictal period	295 (99.0)	92 (90.2)	<0.001
Approach to the patient whose seizure initiated in the hospital	288 (96.6)	95 (93.1)	0.130
The time point t <sub>1</sub> for tonic-clonic SE	107 (35.9)	22 (21.6)	0.007
The time point t <sub>1</sub> for focal SE with impaired consciousness	18 (6.0)	9 (8.8)	0.334
The appropriate medication in the first-line therapy	258 (86.6)	88 (86.3)	0.938
The maximum number of benzodiazepines in case of ongoing seizures in the first-line therapy	182 (61.1)	41 (40.2)	<0.001
Knowledge level regarding intravenous diazepam administration  • Appropriate intravenous dose  • Maximum dose  • Infusion time	245 (82.2) 166 (55.7) 166 (59.1)	77 (75.5) 47 (46.1) 38 (37.3)	0.139 0.093 <b>&lt;0.001</b>
Knowledge level regarding levetiracetam administration  • Appropriate intravenous dose  • Infusion time	131 (44) 164 (55.4)	24 (23.5) 37 (36.3)	<0.001 <0.001
Knowledge level regarding phenytoin administration  • Appropriate intravenous dose  • Suitable administration solution  • Infusion time	209 (70.1) 249 (83.6) 138 (46.3)	33 (32.4) 76 (74.5) 21 (20.6)	<0.001 0.043 <0.001
Mann-Whitney U test for quantitative data following an assessment of normality in the Kolmogorov-S	, ,	21 (20.0)	\0.0

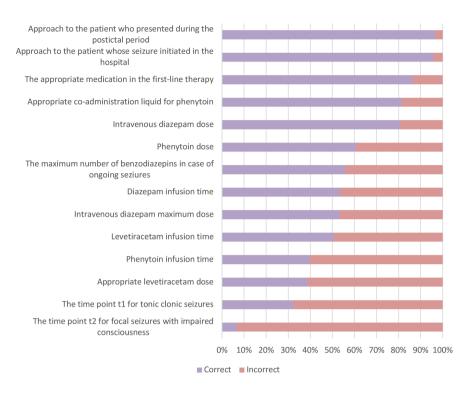


Figure 1. Rates of correct and incorrect answers to the questions regarding the management of acute seizures in pediatric patients

#### Discussion

The major findings in the current study were as follows; i) the details of the TP-t<sub>1</sub> for tonic-clonic SE (32.3%) and focal SE with impaired consciousness (6.8%) were the least known, ii) 40.5% of the participants wrongly stated that benzodiazepine should be administered at most three doses in case of ongoing seizures, iii) there was a tendency to administer lower doses of levetiracetam, and phenytoin, and use longer infusion time for phenytoin, iv) there was a wide distribution in knowledge levels and attitudes between the groups and between pediatricians and non-pediatricians.

The current study is the first study that evaluated the knowledge level of physicians regarding the time points. We demonstrated that details regarding Tp-t<sub>1</sub> for tonic-clonic SE (32.3%) and focal SE with impaired consciousness (6.8%) were the least known, and there were no significant differences between the groups in terms of knowledge levels of these questions. The rate of correct answers to the question of TP-t<sub>1</sub> for tonic-clonic SE was significantly higher among pediatricians. Most of the incorrect answers to both questions were related to the earlier initiation of pharmacological treatment. Although earlier onset of pharmacological therapy may not lead to poor outcomes compared to delay in treatment, it may

increase adverse effects such as respiratory depression (13-18). After examining the efficacy of initial pharmacological treatment in 26 randomized controlled trials, intravenous administrations of lorazepam and diazepam were proposed as the efficacious options (level A evidence). Also, non-intravenous benzodiazepines (rectal diazepam, intramuscular midazolam, and buccal midazolam) were suggested as probably effective medications (level B evidence) (5). Experimental models have proposed that inhibitory GABA<sub>A</sub> receptors that are located on the postsynaptic membrane move into clathrin-coated vesicles, and N-methyl-D-aspartate (NMDA) receptors are mobilized into the membrane in case of seizure. Therefore, it has been proposed that benzodiazepines are effective in the early minutes (within 5-20 minutes) of SE (19,20).

Intravenous lorazepam and diazepam can be administrated twice, in case of ongoing seizures (5). In the current study, 86.5% of the participants responded correctly to the question inquiring the appropriate medication to be administered in the first-line therapy. There were no significant differences between the three groups, and also between pediatricians and non-pediatricians in terms of correct response rates concerning this question. Since the inadequate knowledge level of physicians regarding this emergency situation may lead to failure of seizure

control, the rate of correct answers should be raised to maximum. The question regarding the maximum number of benzodiazepine administrations in case of ongoing seizures was responded correctly by 55.8% of the participants and 40.2% of the participants responded incorrectly as "three times". However, the effects of benzodiazepines may diminish in the later stages of SE, and an overdose of benzodiazepines may lead to respiratory depression (21).

In the current study, 80.5% of the participants responded correctly to the question related to the appropriate dose for intravenous diazepam. The rate of correct answers was higher in group 3. Most of the incorrect answers were related to higher doses that may lead to respiratory depression. Non-intravenous benzodiazepines are also effective and it is suggested especially if an intravenous line is not available (level B evidence) (5). Rectal diazepam administration (0.5 mg/kg/dose) may be easier to remember. Rectal tubes containing 5 mg, and 10 mg diazepam are appropriate for an infant weighing <10 kg, and a child weighing ≥10 kg, respectively (5). Ease of remembering may lead to a preference for rectal diazepam, especially in physicians who managed pediatric patients with acute seizures more infrequently. Precisely, 53.2% of the participants responded correctly to the question of appropriate maximum dose of diazepam and most of the incorrect answers were stated as 5 mg/dose (39.5%). There were no significant differences between the three groups, and between pediatricians and non-pediatricians in terms of response rates related to this question. However, the administration of lower doses of diazepam may fail to control seizures (5,22). In the current study, 53.5% of the participants responded correctly to the question related to appropriate diazepam infusion time. The rate of correct answers was significantly higher in group 3 and among pediatricians. Precisely, 35.5% of the participants have chosen the "rapid injection (bolus)" option which may lead to respiratory depression (23-25).

The second-line therapy should be initiated when the seizure persists up to 20 minutes. Intravenous fosphenytoin/phenytoin (level U evidence), valproic acid (level B evidence), and intravenous levetiracetam (level U evidence) are the recommended options (5). There have been studies comparing the effectiveness of phenytoin/fosphenytoin and levetiracetam in the second-line therapy. According to the results of the "Emergency treatment with Levetiracetam or Phenytoin in convulsive SE in children" trial, levetiracetam (40 mg/kg) was not significantly superior to phenytoin (20 mg/

kg) in terms of cessation rate of convulsive seizures, the time taken to terminate convulsive seizures or adverse effects (26). Also, in Convulsive SE Paediatric Trial, there were no significant differences between levetiracetam (40 mg/kg, over 5 min) and phenytoin (20 mg/kg), in terms of intubation rates, length of intensive care unit, and hospital stay, and termination of the seizure (27). In the study of the Established SE Treatment Trial, the efficacy and safety of levetiracetam (60 mg/kg), fosphenytoin (20 mg/kg), and valproic acid (40 mg/kg) were compared. According to the results of this trial, any of the three drugs had no superiority over each other in the second-line therapy (17). However, due to some serious adverse effects such as acute hepatotoxicity or acute hepatic failure after administration of valproic acid may occur, utilization of valproic acid is limited especially in children <2 years old, and in the presence of a higher risk of inborn error of metabolism (28,29). Thus, we questioned the administration details of phenytoin and levetiracetam in pediatric patients. In the current study, 38.8% of the participants responded correctly to the question of appropriate levetiracetam dose. Most of the incorrect answers consist of lower doses. The rate of correct answers was significantly higher in group 3 and among pediatricians. However, since higher doses of levetiracetam (40-60 mg/kg) were proposed in the previous trials, administration of lower doses may lead to failure of the treatment (17,26,27). Precisely, 50.5% of the participants answered correctly to the question of levetiracetam infusion time and the rate of the correct answers was significantly higher among pediatricians. Since 36.8% of the participants have preferred a longer duration of infusion (30 min), some patients may not benefit from the advantage of rapid achievement of high serum levels. The rates of correct answers to the questions of "maximum loading dose per kilogram" and "infusion time of fosphenytoin/phenytoin" were 20.0% and 39.8%, respectively. Additionally, the rates of correct answers to both questions were significantly higher in group 3 and also among pediatricians. Among all participants, there was a significant tendency to administer lower doses of phenytoin (10-15 mg/kg) and prefer longer durations of infusion (30 min). Although these tendencies do not increase the risk of adverse effects, the possibility of rapidly terminating seizure may decrease. Most (81.3%) of the participants responded correctly to the question of suitable administration solution and the relevant knowledge level was significantly higher among pediatricians. Since phenytoin becomes unstable with

liquids containing dextrose (11), incorrect administration of phenytoin may lead to the poor seizure control.

There are few studies evaluating the knowledge level and attitudes of physicians regarding asthma, SE, and febrile seizures. Mikhaeil-Demo et al. (9) evaluated the improvement of the knowledge level of neurology residents regarding SE after using a stimulation-based mastery learning curriculum. According to the results, after the intervention, significant improvements were observed in evaluating the relevant medical history, stabilizing patients, ordering first- and second-line treatments correctly, evaluating the necessity of neuroimaging, and re-evaluating the case (9). Yilmaz et al. (30) suggested that recommending a prophylactic treatment for febrile seizures (intermittent/long-term) differed even within the same speciality. Similarly, Bashiri et al. (31) demonstrated that there was a wide variation in knowledge levels and attitudes regarding febrile seizures in different specialities. Additionally, they proposed that a significant number of physicians should receive further education on this issue (31). Also, it was proposed that education is necessary concerning the management of asthma (32). Similarly, the results of the current study indicate the necessity for postgraduate education programs regarding the acute management of seizures.

#### **Study Limitations**

This is the first study that questioned the knowledge level of physicians regarding the acute management of seizures in children. However, our study had some limitations. First, the majority of the responders were pediatricians that may erroneously lead to yielding results indicating a higher knowledge level. Second, we were only able to provide estimates, as information on the annual number of pediatric patients managed by physicians was obtained based on their own reports. Third, the level of knowledge regarding the administration of benzodiazepines other than midazolam was not obtained. This may result in the study not fully reflect the level of knowledge for all benzodiazepines (e.g., diazepam). In addition, since the number of studies evaluating the level of knowledge on this subject is limited, we compared studies examining the knowledge levels of physicians on different subjects. These studies may not be fully comparable with our study in some aspects.

#### Conclusion

In conclusion, there is a wide variation in knowledge levels and attitudes among physicians. Organizing

education programs focusing on the least known and/or important details for physicians is necessary for the acute management of seizures in pediatric patients.

#### **Ethics**

**Ethics Committee Approval:** We have obtained the approval of the Aydın Adnan Menderes University Faculty of Medicine Clinical Research Ethics Committee (date: 20/01/2022; approval no: 2021/200).

**Informed Consent:** Informed consent was taken from the participants.

**Peer-review:** Externally peer-reviewed.

#### **Authorship Contributions**

Design: M.A., S.Ö., A.T., Data Collection and/or Processing: M.A., Analysis and/or Interpretation: S.Ö., Literature Search: A.T., Writing: M.A.

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#### References

- Trinka E, Cock H, Hesdorffer D, et al. A definition and classification of status epilepticus-Report of the ILAE Task Forse on Claeeification of Status Epilepticus. Epilepsia 2015; 56:1515.
- Hauser WA. The prevalence and incidence of convulsive disorders in children. Epilepsia 1994; 35:S1-S6.
- Zhang R, Gao C, Liu J, Zhao M, Wu Y. Children's Neurological Status Epilepticus and Poor Prognostic Factors through Electroencephalogram Image under Composite Domain Analysis Algorithm. J Healthc Eng 2021; 2021;8201363.
- Selvan T, Nagaraj M, Saravanan P, Tudu MN. A study of the etiology and short term outcome of status epilepticus in children. International Journal of Contemporary Pediatrics 2017; 4:878.
- 5. Glauser T, Shinnar S, Gloss D, et al. Evidence-based guideline: treatment of convulsive status epilepticus in children and adults: report of the Guideline Committee of the American Epilepsy Society. Epilepsy Curr 2016; 16:48-61.
- Kanjo M, Najjar A, Bokhari AY, Alqarni GA, Darwesh EA, Alqarni GS. Knowledge of epilepsy and seizure first aid among teachers in Jeddah, Saudi Arabia. Epilepsy & Behavior Reports 2021;16:100475.
- 7. Yang K, He Y, Xiao B, Wang J, Feng L. Knowledge, attitudes and practice towards epilepsy among medical staff in Southern China: does the level of hospitals make a difference? Seizure 2019; 69:221-7.
- 8. Zhao T, Gao Y, Zhu X, et al. Awareness, attitudes toward epilepsy, and first aid knowledge of seizures of hospital staff in Henan, China. Epilepsy Behav 2017; 74:144-8.
- Mikhaeil-Demo Y, Barsuk JH, Culler GW, et al. Use of a simulation-based mastery learning curriculum for neurology

- residents to improve the identification and management of status epilepticus. Epilepsy Behav 2020; 111:107247.
- Prasad M, Shenton P, Dietz S, Saroha V, Whitehouse WP. What is the easier and more reliable dose calculation for ivPhenytoin in children at risk of developing convulsive status epilepticus, 18 mg/kg or 20 mg/kg? BMC pediatrics 2013;13:1-5.
- Bauman JL, Siepler JK, Fitzloff J. Phenytoin crystallization in intravenous fluids. Drug Intelligence & Clinical Pharmacy 1977; 11:646-9.
- Ramael S, Daoust A, Otoul C, et al. Levetiracetam intravenous infusion: a randomized, placebo-controlled safety and pharmacokinetic study. Epilepsia 2006; 47:1128-35.
- Talukdar B, Chakrabarty B. Efficacy of buccal midazolam compared to intravenous diazepam in controlling convulsions in children: a randomized controlled trial. Brain Dev 2009; 31:744-9.
- 14. Shah I, Deshmukh C. Intramuscular midazolam vs intravenous diazepam for acute seizures. Indian J Pediatr 2005; 72:667-70.
- Mahmoudian T, Zadeh MM. Comparison of intranasal midazolam with intravenous diazepam for treating acute seizures in children. Epilepsy Behav 2004; 5:253-5.
- Fişgin T, Gurer Y, Tezic T, et al. Effects of intranasal midazolam and rectal diazepam on acute convulsions in children: prospective randomized study. J Child Neurol 2002; 17:123-6.
- Chamberlain JM, Kapur J, Shinnar S, et al. Efficacy of levetiracetam, fosphenytoin, and valproate for established status epilepticus by age group (ESETT): a double-blind, responsive-adaptive, randomised controlled trial. The Lancet 2020; 395:1217-24.
- Ashrafi MR, Khosroshahi N, Karimi P, et al. Efficacy and usability of buccal midazolam in controlling acute prolonged convulsive seizures in children. Eur J Paediatr Neurol 2010; 14:434-8.
- Wasterlain CG, Chen JW. Mechanistic and pharmacologic aspects of status epilepticus and its treatment with new antiepileptic drugs. Epilepsia 2008; 49:63-73.
- 20. Naylor DE. Glutamate and GABA in the balance: convergent pathways sustain seizures during status epilepticus. Epilepsia 2010; 51:106-9.

- Norris E, Marzouk O, Nunn A, McIntyre J, Choonara I. Respiratory depression in children receiving diazepam for acute seizures: a prospective study. Dev Med Child Neurol 1999; 41:340-3.
- Brophy GM, Bell R, Claassen J, et al. Guidelines for the evaluation and management of status epilepticus. Neurocrit Care 2012; 17:3-23.
- 23. Gross JB, Smith L, Smith TC. Time course of ventilatory response to carbon dioxide after intravenous diazepam. Anesthesiology 1982; 57:18-21.
- 24. Alexander CM, Gross JB. Sedative doses of midazolam depress hypoxic ventilatory responses in humans. Anesth Analg 1988; 67:377-82.
- 25. Del Vecchio P. Apnea after intravenous diazepam administration. JAMA 1978; 239:614.
- 26. Lyttle MD, Rainford NE, Gamble C, et al. Levetiracetam versus phenytoin for second-line treatment of paediatric convulsive status epilepticus (EcLiPSE): a multicentre, open-label, randomised trial. Lancet 2019; 393:2125-34.
- Dalziel SR, Borland ML, Furyk J, et al. Levetiracetam versus phenytoin for second-line treatment of convulsive status epilepticus in children (ConSEPT): an open-label, multicentre, randomised controlled trial. Lancet 2019;393:2135-45.
- 28. Afzal RM, Lund AM, Skovby F. The impact of consanguinity on the frequency of inborn errors of metabolism. Mol Genet Metab Rep 2018; 15:6-10.
- 29. Guo HL, Jing X, Sun JY, et al. Valproic acid and the liver injury in patients with epilepsy: an update. Curr Pharm Des 2019; 25:343-51.
- Yilmaz D, Arhan E, Yuksel D, et al. Attitudes of parents and physicians toward febrile seizures. Clin Pediatr (Phila) 2008; 47:856-60.
- 31. Bashiri FA, Al Shalawi AA, Hamad MH, et al. Assessment of physicians' knowledge and attitudes in the management of febrile seizures. Neurosciences (Riyadh) 2018; 23:314-9.
- 32. Dahmash EZ. Physicians' Knowledge and Practices Regarding Asthma in Jordan: A Cross-Sectional Study. Front Public Health 2021; 9:712255.

#### Appendix 1: English version of the questionnaire

Assessment of the knowledge level and attitudes of physicians regarding the management of acute seizures in pediatric patients

Dear participants;

We aimed to evaluate the knowledge level of physicians regarding the acute management of seizures in pediatric patients. The targeted speciality groups consist of pediatrics, emergency medicine, family medicine, general medicine, neurology, neurosurgery, anesthesia and reanimation. According to the study results, postgraduation education programs are going to be organized. Your answers to the questionnaire will be anonymous and will not be known to us. Answering the questionnaire takes ten minutes. We appreciate your participation.

#### 1. If you want to participate in this study, please click yes, and continue.\*

- Yes
- No
- 2. Age\* .....
- 3. Gender \*
- Female
- Male
- 4. How many years have you been working as a physician?

#### 5. In which speciality do you work or study?

- General medicine
- Pediatrics
- Emergency medicine
- Anesthesia and reanimation
- Neurology
- Neurosurgery
- Familiy medicine

#### 6. Approximately, how many children presenting with acute seizures do you treat per year?

#### 7. Do you have the self-confidence regarding the management of acute seizures?

- Yes
- No
- Unsure

#### 8. How would be your approach to the patient who presented during the postictal period after a 2-3 minutes lasting seizure?

- Investigating the etiology after initial stabilization steps (supports of the airway, breathing, and circulating)
- Intravenous administration of levetiracetam (loading and maintainence)
- Intravenous administration of phenytoin (loading and maintainence doses)
- Rectal diazepam

#### 9. How would your approach to the patients who started to seize in the hospital (The first step should be chosen)

- Rectal diazepam
- Initial stabilization steps (supports of the airway, breathing, and circulating)
- Blood glucose sampling
- Establishing an intravenous route

#### 10. When would you initiate pharmacological therapy in a seizing child (tonic-clonic)? (The time point t1 for tonic-clonic SE)

- As soon as possible
- Within 2-3 min following the initial stabilization steps
- At 5. min following the initial stabilization steps
- At 10. min following the initial stabilization steps

## 11. When would you initiate pharmacological therapy in a seizing child (focal SE with impaired consciousness)? (The time point t1 for focal SE with impaired consciousness)

- As soon as possible
- Within 2-3 min following the initial stabilization steps
- At 5. min following the initial stabilization steps
- At 10. min following the initial stabilization steps

### Appendix 1: Continued 12. Which anticonvusant would you chose in the first-line therapy? • Benzodiazepin (intravenous/buccal/intranasal/rectal) • Intravenous administration of levetiracetam (loading and maintainence doses) • Intravenous administration of phenytoin (loading and maintainence doses) • Phenobarbital (by nasogastric tube) 13. What is the appropriate dose for intravenous diazepam? • 0.15-0.2 mg/kg/dose • 0.5 mg/kg/dose • 1 mg/kg/dose What is the maximum dose (adult dose) of intravenous diazepam? • Maximum 5 mg/dose • Maximum 10 mg/dose • Maximum 20 mg/dose What is the appropriate infusion time for intravenous diazepam? • Rapid enjection (bolus) • 5 mg/min • 30 dk iv infusion 14. How many doses of benzodiazepines would you administer in the first-line therapy in case of ongoing seizure? • One • Two • Three What is the appropriate intravenous phenytoin, in case of ongoing seizure? • 10-15 mg/kg/dose • 20 mg/kg/dose • 40 mg/kg/dose What is the minimum infusion time for a dose of 20 mg/kg phenytoin? • Minimum 10 minutes • Minimum 20 minutes • Minimum 30 minutes What is the suitable diluent solution for intravenous phenytoin? • Dextrose + ringer lactate • 0.9% sodium chloride • 5% dextrose in water • 10% dextrose in water 15. What dose do you administer intravenous levetiracetam, in case of ongoing seizure? • 10 mg/kg/dose • 20 mg/kg/dose • 40-60 mg/kg/dose What is the appropriate infusion time for intravenous levetiracetam • Rapid enjection (bolus)

• 15-20 min infusion
• 30 min infusion