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Emergency Physicians' Knowledge and Attitudes Towards Childhood Traumatic Tooth Avulsion in Turkey: A Multicenter Questionnaire-Based Cross-Sectional Study

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Abstract

Aim: In children presenting to the emergency room with traumatic tooth avulsion (TTA), the immediate replantation of the avulsed permanent tooth is required. We study aimed to investigate the knowledge and attitude of emergency physicians (ER) regarding emergency management of avulsed teeth

Methods: This multi-center cross-sectional survey study was conducted from October to December 2020. A self-administered questionnaire that had been designed in the Internet environment was sent to directors of ER facilities in hospitals regarding physicians at the emergency room in the hospitals. A total of 381 physicians participated by filling out the questionnaire.

Results: Data revealed that 92.1 % of the participants did not find prior knowledge sufficient about avulsion and only 8.9% would replant the tooth by themselves. 56.2% of the physicians did not know the importance of tetanus prophylaxis. Only 48% of the participants selected the best transport media for an avulsed tooth. Experienced physicians and the emergency specialist had significantly better knowledge about the management of avulsed teeth ($p=0.005$ and $p<0.001$, respectively).

Conclusion: The knowledge of avulsed teeth among emergency physicians in Turkey ranges from low to moderate, which highlights the need to improve the knowledge of the management of traumatic dental injuries among emergency physicians.

Keywords: Surveys and questionnaires, tetanus, emergency service, tooth avulsion, specialization, general practitioners

Introduction

The prevalence of childhood traumatic dental injuries (TDIs) has been increasing in recent years, and studies in this field in literature estimate that TDIs will in time come to exceed tooth decay and periodontal disease in terms of prevalence (1). According to epidemiological studies, oral region traumas account for 5% of all body traumas across all age groups, and this rate increases to 18% in preschool children (2). Avulsion, as one form of TDI, is defined as the complete displacement of a tooth from its socket due to trauma (3). Avulsion injuries are more common in primary teeth than in permanent teeth, with previous studies reporting the prevalence of avulsion injuries to be 0.5-16% in permanent teeth and 7-21% in primary teeth (4). It has further been reported that 75% of avulsion traumas to primary tooth also cause damage to the developing permanent tooth (3). Avulsions occur more frequently during permanent dentition, and especially in those age 7-9 years, at the time when the anterior teeth are still erupting, due to the weakness of the periodontal tissue surrounding the teeth. While fighting and sports injuries are frequently involved in the etiology of avulsion injuries in permanent teeth, avulsions involving the primary teeth mainly result from falls on hard surfaces (5). In general, only one tooth is affected in avulsion cases, and the most commonly avulsed teeth

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among both the primary and permanent teeth are the maxillary central incisors (6).

Today, even though considerable steps have been taken as a result of the investments made by the Ministry of Health into Oral and Dental Health, it may be difficult to directly access dental centers, due especially to socioeconomic reasons (7). In rural areas in particular, where the full integration of dental services with the social security institution is lacking, physicians inevitably perform emergency dental interventions in cases presenting to the emergency rooms (ER) of hospitals and primary healthcare centers with such injuries. A study conducted in Chile found the emergency room of hospitals to be the most common first stop for the treatment of TDIs, since dental services may not always be convenient or accessible (8). Although the literature contains publications examining the knowledge and attitudes toward such topics as the early detection of caries, fluoride applications and nutritional problems, due to their effects on oral and dental health in children, there is a lack of publications examining the knowledge of, and attitudes toward, tooth avulsion injuries that may be caused by TDIs among emergency physicians (9,10).

The present study evaluates the attitudes and knowledge levels of emergency physicians in Turkey related to traumatic tooth avulsion (TTA).

Methods

Study Design

Approval for the study was obtained from the Istanbul Medipol University Non-invasive Clinical Research Ethics Committee (decision no: 10840098-604.01.01-E65339, date: 18 December 2019). This multicenter cross-sectional questionnaire-based study was conducted between October and December 2020. A link to the questionnaire that had been designed in the Internet environment. was sent via a mailing database list to emergency physicians employed at the different hospitals (public, university or private hospitals) in Turkey. Emergency medicine specialists emergency medicine assistant doctors, and general practitioners working in hospitals that did not have a dental emergency service room were included in the study. All participants gave written informed consent. After filling out the questionnaire, the respondent sent it back to the database, and it was checked for any missing parts before being included in the evaluation. Incomplete questionnaires were returned to the relevant respondent with a request that they complete the missing parts.

Questionnaire Evaluation

The questionnaires included questions that had been used previously and tested for validity and reliability in similar studies published in the literature (11-13). The section part of the three-part questionnaire garnered data on the respondents' age, gender, specialization (if any), years of professional experience and the type of healthcare institution. The second section included questions about physicians' previous experience with TTA; prior knowledge on this subject; the source of prior knowledge, if any; and attitudes in the event of coming across such cases. The third and final section was aimed at establishing the knowledge level of emergency physicians as regards to TTA, for which questions were asked about the definition of an avulsed tooth, its prognosis, the time from avulsion of the tooth to admission to the healthcare institution for intervention, and the required storage conditions of the avulsed tooth during this period. Additionally, the knowledge of the respondents related to such issues as the importance of the tooth type (permanent or primary tooth) for replantation; the appropriate part of the tooth for handling; and the method of cleaning the tooth if contaminated, were examined. The knowledge level of the participants was based on their scores from the third section of the questionnaire, with 1 point given for each correct answer.

Statistical Analysis

All statistical analyses were made using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY). Descriptive analyses were presented using mean, standard deviation, median, frequency and percentage values, where appropriate. Shapiro-Wilk test was used to control whether the variables were normally distributed. Chi-square and Fisher's Exact test were used for categorical data. The student's t-test was used for the comparison of normally distributed parametric variables. Intergroup comparisons were performed using Kruskal-Wallis test and One-Way ANOVA. Bonferroni-Dunn test was used as a post-hoc test for significant cases while with post-hoc Tukey HSD test was used for parametric variables. The statistical significance level was taken as 0.05 in all tests

Results

The questionnaire was completed by a total of 381 emergency physicians. The distribution of physicians participating in the study by gender, age, institution status, professional experience and position in the hospital, garnered from the first section of the questionnaire, is presented in Table 1.

The responses of the physicians to the second part of the questionnaire, examining their attitudes toward traumatic tooth avulsion, are presented in Table 2. A vast majority (92.1%) of the respondents stated that they did not think they had adequate knowledge of TTA and the number of those stating that they had received knowledge

Table 1. Demographic data and knowledge level of the participants

Demographic data			Knowledge level		
		N(%)	Mean (SD)	Median (range)	p
Gender	Female	135 (35.6%)	4.49 (2.0)	5 (0-8)	0.280*
	Male	244 (64.4%)	4.26 (1.98)	4 (0-8)	-
Age	20-30	166 (43.6%)	4 (2.11)	4 (0-8)[a]	**0.004**†
	31-40	171 (44.9%)	4.44 (1.91)	5 (0-8)[ab]	-
	41-50	39 (10.2%)	5.33 (1.42)	5 (2-8)[b]	-
	> 50	5 (1.3%)	4.4 (1.82)	5 (2-6)[ab]	-
The status of the health institution	Public university hospital	40 (10.5%)	5.15 (1.53)	5 (1-8)	0.067
	Training and research hospital	230 (60.4%)	4.8 (2.49)	5 (1-7)	-
	Public hospital	97 (25.5%)	4.3 (2.01)	5 (0-8)	-
	Private hospital	9 (2.3%)	4.14 (2.07)	4 (0-8)	-
	Private university hospital	5 (1.3%)	3.67 (1.12)	4 (2-5)	-
Specialty	General practitioner	97 (25.5%)	3.84 (1.98)[a]	4 (0-8)	**<0.001**‡
	Emergency medicine assistant doctor	126 (33.1%)	4.18 (2.06)[a]	4 (0-8)	-
	Emergency medicine specialist	158 (41.4%)	4.91 (1.73)[b]	5 (1-8)	-
Professional experience	0-5	175 (45.9%)	3.98 (2.07)[a]	4 (0-8)	**0.005**†
	6-10	109 (28.6%)	4.41 (1.87)[a b]	4 (1-8)	-
	11-15	68 (17.8%)	4.82 (1.97)[b]	5 (0-8)	-
	16-20	19 (5%)	5.11 (1.49)[b]	5 (2-8)	-
	> 20	10 (2.6%)	5.2 (1.23)[b]	5.5 (3-7)	-

Student's t-test, † Kruskal-Wallis test, ‡ANOVA. Different lowercase letters in a column indicate the statistically significant difference between group

on TTA during vocational courses was quite low (n=14). Of the physicians, 91.1% stated that they needed more training in the management of tooth avulsion following trauma.

In a question on the medical treatment to be administered to patients presenting with TTA, the majority (67.7%) of respondents marked the correct answer, which is the use of antibiotics, anti-inflammatory and analgesic agents and 43.8% of the respondents stated that they would administer tetanus prophylaxis after TTA. The ratio of physicians who stated that they would refer the patient to another center for the necessary treatment was high (84.2%), while those who stated that they could do the intervention themselves accounted for 8.9% of the total. Regarding the referral center, 32.5% of the respondents stated that they would refer pediatric patients to a pediatric dentist.

The responses of the participants to the third section of the questionnaire, measuring the level of the knowledge related to TTA, are presented in Table 3. Although the majority (56.4%) of physicians correctly understood the definition of an avulsed tooth, a considerable number did not. Of the physicians who participated in the study, only 36.5% chose the response "If the avulsed tooth is a permanent tooth, it appropriate for replanting" regarding the effect of the type of avulsed tooth on treatment. The ratio of physicians who chose the correct responses to questions of how to clean an avulsed tooth after contamination, which is rinsing under running water, and the appropriate part of the tooth for handling during this procedure, which is holding from the crown, were 51.4% and 52%, respectively. Of the respondents, 82.7% expressed the importance of the elapsed time for the success of the treatment of the avulsed tooth, whereas the rate of those who knew the best time for replantation was 18.1%. Regarding the storage of an avulsed tooth when replantation is not immediately possible, 48.0% of the respondents gave the optimal answer, while 24.9% stated that the tooth could be carried in dry cotton or gauze and 4% in alcohol.

A comparison of the knowledge scores inquired in the third section of the questionnaire according to the demographic characteristics of the participants revealed no difference between genders (p=0.280) or institution types (p=0.067), while the knowledge scores were lower among those aged 20-30 in terms of the age factor (p=0.004) (Figure 1). Regarding professional experience, the participants with 0-5 years of professional experience

Table 2. Previous experience and attitudes of participants toward dental avulsion		
Questions	**Options**	**N (%)**
What is your medical approach to a patient presenting with avulse dental trauma?	If the patient has no special condition, I do not prescribe antibiotics, I prescribe anti-inflammatory and analgesic.	111 (29.1%)
	I prescribe antibiotics, anti-inflammatory, and analgesic	258 (67.7%)
	I add topical antibiotics	14 (3.7%)
	Tetanus prophylaxis should be administered	167 (43.8%)
Have you ever come across a patient with an avulsed tooth?	Never	164 (43%)
	1-5	164 (43%)
	6-10	26 (6.8%)
	> 10	27 (7.1%)
Do you have any prior knowledge about the management of avulsed teeth?	No	253 (66.4%)
	Yes	128 (33.6%)
If your answer is yes, what was your source of information?	In-service course	14 (10.9%)
	National-international congress	3 (2.3%)
	Medical books	60 (46.9%)
	Other	51 (39.8%)
Do you find your knowledge about teeth avulsed after trauma sufficient?	No	349 (92.1%)
	Yes	32 (7.9%)
In your opinion, learning about traumatic dental injuries is	Not important	12 (3.1%)
	Somewhat important	126 (33.1%)
	Important	186 (48.8%)
	Very important	57 (15%)
Would you like to receive more information to properly manage traumatic dental injuries?	No	34 (8.9%)
	Yes	347 (91.1%)
What do you do for the replantation of the avulsed tooth?	I do it myself	34 (8.9%)
	I refer to any dentist	197 (51.7%)
	I refer to the pediatric dentist	124 (32.5%)
	No idea	26 (6.8%)

had lower knowledge scores than the other groups (p=0.005) (Figure 2), while the total scores of general practitioners and emergency medicine residents were lower than those of the emergency medicine specialists (p<0.001) (Figure 3).

Table 4 presents the results of a statistical comparison of emergency medicine specialists, emergency medicine residents and general practitioners based on their responses to the third section of the questionnaire. The rate of correct responses to the question "What is the definition of tooth avulsion after trauma?" was higher among the participants who were working as emergency medicine specialists than those working as general practitioners and emergency medicine residents, and the difference was significant (p=0.003). To the question "What is your opinion of the prognosis of an avulsed tooth?", the highest rate of correct responses was among the emergency medicine specialists, while the lowest rate was among the general practitioners (p<0.001). The rate of correct responses to the question of cleaning a contaminated tooth after trauma was higher among the emergency medicine specialists than the general practitioners (p=0.001). To the question "Does the time from trauma to intervention effect the success of intervention to the avulsed tooth?", the rate of correct responses were given by the emergency medicine specialists was higher than that of the emergency medicine residents (p=0.025). The rate of correct responses to the question "How much time do you think should elapse for increased the success of replantation?" was lower among emergency medicine residents than emergency medicine specialists and general practitioners (p<0.001) (Table 4).

Discussion

Traumatic tooth avulsions account for approximately 16% of all dental injuries, and the loss of an anterior tooth can lead to esthetic, social and psychological problems (14,15). The majority of maxillofacial traumas in particular lead to tooth avulsion in children (16). In cases

Table 3. Participants knowledge about traumatic dental avulsion		
Questions	**Options**	**N (%)**
What is the definition of a tooth avulsion?	No idea	33 (8.7%)
	Total dislodgement of intact tooth out of its socket due to any trauma†	215 (56.4%)
	Dislodgement of fractured segment of the tooth due to any trauma	99 (26.0%)
	Tooth fracture due to any trauma	34 (8.9%)
What is your opinion about the prognosis of an avulsion tooth?	Recoverable †	260 (68.2%)
	Unrecoverable	24 (6.3%)
	No idea	97 (25.5%)
What are the possible options after an avulsed tooth is replanted?	It will not help; the tooth will fall off again	24 (6.3%)
	There is a risk of infection spreading throughout the body	85 (22.3%)
	Implanted teeth may be rejected as foreign bodies †	14 (3.7%)
	Replantation can damage adjacent teeth	57 (15.0%)
	No idea	201 (52.8%)
Which of the following is true about the replantation of a tooth with avulsion?	It must be guaranteed to be the primary tooth. Permanent teeth should not be placed	15 (3.9%)
	It must be guaranteed to be a permanent tooth. Primary teeth should not be placed †	139 (36.5%)
	There is no need to define the tooth type. Need to relocate both	120 (31.5%)
	No idea	107 (28.1%)
If the tooth you are replanting has fallen to the ground and is dirty, what would you do?	I used to gently brush the tooth with a toothbrush	41 (10.8%)
	I gently wipe the dirt stuck on the tooth with my hand	13 (3.4%)
	I used to rinse the tooth under running water †	196 (51.4%)
	I clean the tooth with disinfectant	35 (9.2%)
	No idea	96 (25.2%)
How to hold an avulsed tooth?	The crown part of the tooth (outside the alveolus) †	198 (52.0%)
	From the root part of the tooth (the part remaining in the alveoli)	26 (6.8%)
	No crown or root	11 (2.9%)
	No idea	146 (38.3%)
Does extra-oral time affect the prognosis of an avulsed tooth?	No	10 (2.6%)
	Yes †	315 (82.7%)
	No idea	56 (14.7%)
What is the best time for an avulsed tooth replacement?	First 15 minutes †	69 (18.1%)
	First 1 hour	121 (31.8%)
	first 12 hours	64 (16.8%)
	First 24 hours	46 (12.1%)
	No idea	81 (21.3%)
In pediatric cases, If you did not replant the tooth, which one is the most appropriate media to carry the tooth to the dentist?(24)	Childs' sublingual	94 (25.2%)
	Saliva	133 (35.7%)
	Dry cotton or gauze	93 (24.9%)
	Ice water	73 (19.6%)
	Saline †	179 (48%)
	Alcohol	15 (4%)
† Correct answers		

of TTA, there are several critical points that should be taken into account, such as which tooth requires the intervention, who should perform the intervention, the condition and storage of the avulsed tooth before the intervention, and the time from the occurrence of the trauma to the moment of intervention (6). It is believed that increasing the knowledge of emergency physicians in this area will contribute positively to the success of treatment, as healthcare professionals who inevitably come across dental injuries resulting from trauma in ER

that provide emergency medical services 24 hours a day (17-20).

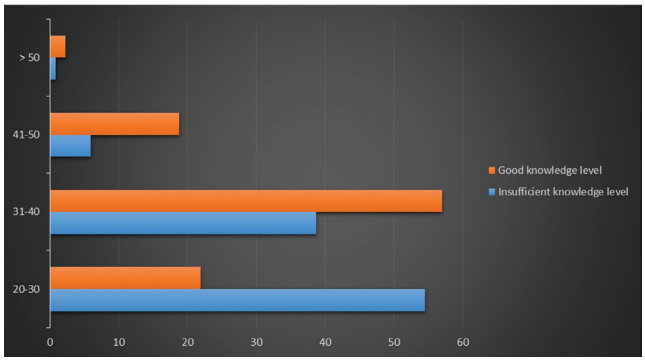

Figure 1. Percentage of knowledge level according to age

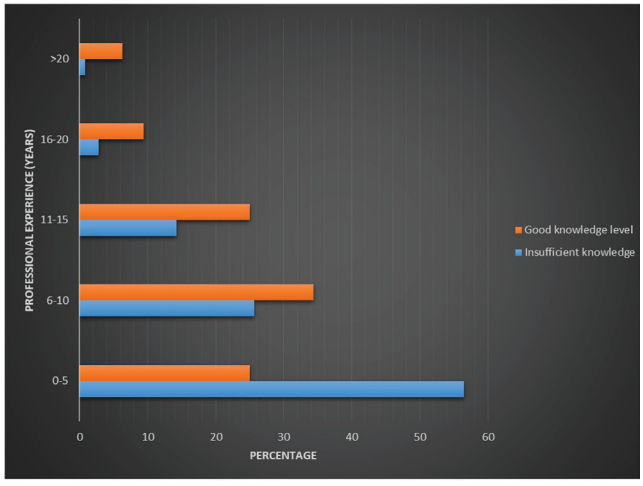

Figure 2. Percentage of knowledge level according to professional experience

In children presenting to the emergency room with TTA, the immediate replantation of the avulsed permanent tooth is required, while replantation is considered inappropriate in avulsions of primary teeth. Previous studies have revealed that the number of physicians who believe that permanent teeth should be replanted is not as high as expected, with a rate of 15.9% noted in a study by Ulusoy et al. (13) and 10.32% in another study by Aren et al. (19). In the present study, 36.5% of the physicians believed that the tooth should be replanted if it is a permanent tooth. These rates reveal that the majority of emergency physicians lack sufficient knowledge of the replantation of permanent teeth.

In two studies conducted in Turkey involving emergency physicians, it was established that the rate of exposure to TTA at least once during the professional lives of the respondent physicians was 55.56% and 68.1% (13,19). These two studies further reported that the number of respondents who gave the answer "a dentist should perform the procedure" to the question "who should perform the intervention" was 73.9% and

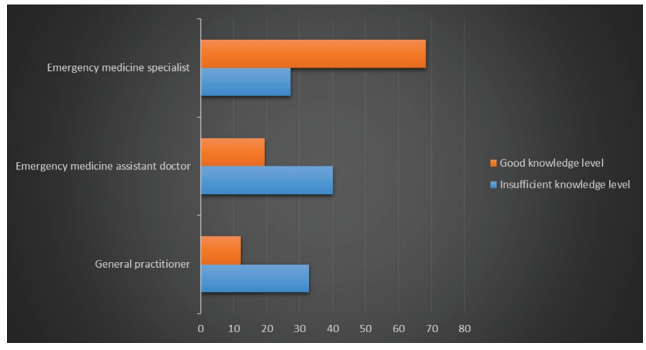

Figure 3. Percentage of knowledge level according to specialty

Table 4. Emergency physicians' right response about traumatic dental avulsion according to their specialties

Questions	General practitioner (n=91) N(%)	Emergency medicine assistant doctor (n=117) N(%)	Emergency medicine specialist (n=147) N(%)	p
What is the definition of a tooth avulsion?	43 (47.3%)[a]	61 (52.1%)[a]	100 (68%)[b]	**0.003***
What is your opinion about the prognosis of an avulsion tooth?	43 (47.3%)[a]	80 (68.4%)[b]	122 (83%)[c]	**<0.001†**
What are the possible options after an avulsed tooth is replanted?	4 (4.4%)	3 (2.6%)	5 (3.4%)	0.763
Which of the following is true about the replantation of teeth with avulsion?	35 (38.5%)	47 (40.2%)	51 (34.7%)	0.642
If the tooth you are replanting has fallen to the ground and is dirty, what would you do	35 (38.5%)[a]	57 (48.7%)[a b]	93 (63.3%)[b]	**0.001***
How to hold an avulsed tooth?	39 (42.9%)	64 (54.7%)	85 (57.8%)	0.072
Does extra-oral time affect the prognosis of avulsed tooth?	73 (80.2%)[a b]	90 (76.9%)[a]	131 (89.1%)[b]	**0.025***
What is the best time for an avulsed tooth replacement?	24 (26.4%)[a]	8 (6.8%)[b]	34 (23.1%)[a]	**<0.001***
In pediatric cases, if you did not replant the tooth, how would you carry the tooth to the dentist?	53 (58.2%)	79 (67.5%)	101 (68.7%)	0.223

Data are presented as n (%). *Chi-square test, †Fisher's Exact test. Different lowercase letters in a row indicate the statistically significant difference between groups.

7.94%, respectively. The studies also reported a low rate of recommended referral to a pediatric dentist (18.8% and 1.59%, respectively). Studies of emergency physicians by Holan and Shmueli, and Subhashraj identified a tendency to refer the patient to a dentist of 96% and 94.5%, respectively, suggesting that emergency physicians abroad consider the treatment of TTA to be a technical issue (21,22).

In the present study, 56.9% of physicians reported encountering to avulsed dental injury at least once during their professional life and 7.9% of physicians reported having sufficient knowledge to undertake an intervention, while in the study by Ulusoy et al. (13) 14.5% of physicians believed they had sufficient knowledge to treat this type of trauma. Some 51.7% stated that they would turn to dentists for professional support in this area, while 32.5% stated a preference for pediatric dentists in this regard (13). While the findings of the present study concur with Ulusoy et al. (13) they differ considerably from those established by Aren et al. (19). The findings of the present study suggest that the respondents do not consider themselves trained in TTA, leading them to avoid intervention, due mainly to the fact that there are physicians who are specialists or residents in this field.

The questions included in the third section of the questionnaire aimed to measure the level of the knowledge level of emergency physicians regarding TTA management. For the medical treatment of children presenting to the emergency department with an avulsed tooth after trauma, 67.7% of the respondent emergency physicians in the present study stated that they would prescribe an antibiotic, anti-inflammatory and analgesic combination, which is the correct answer, while in the study by Aren et al. this rate was 80.96% (19). The present study, unlike other studies on this subject in literature, also established the level of the knowledge of the physicians regarding post-traumatic tetanus prophylaxis, with 43.8% of the respondents stating that they would administer tetanus prophylaxis (14). While these rates determined in the study reveal that emergency physicians have sufficient knowledge of the potential for infection and inflammation following TTA, the rates indicate that they do not have the same level of the knowledge about tetanus prophylaxis.

The studies also differ in the level of knowledge among the respondents of the correct handling of an avulsed tooth and the appropriate method of cleaning if contamination is present. In the study by Aren et al. (19) 48.41% of the physicians knew the correct handling approach, and 50.79% correctly answered what to do in the event of the avulsed tooth being contaminated. These rates were 34.3% and 33.3%, respectively, in the study by Ulusoy et al. (13) and 51.6% and 48.4%, respectively, in the study by Bahammam (23). In the present study, 51.4% knew the correct approach to cleaning a contaminated tooth, which is washing gently with water, while those who knew the tooth should be held by the crown amounted to 52%.

The question about the critical time for intervention in TTA was correctly answered by 26.19% of the participants in the study by Aren et al. (19) while this rate was 10.1% in the study by Ulusoy et al. (13) falling short of the desired rate. In the studies by Subhashraj (22) and Bahammam (23) this rate was reported as 52% and 54%, respectively. The present study found that the rate of physicians who expressed the time from the occurrence of the trauma to the required intervention as the first 15 minutes was 18.1%, indicating that the majority of the respondents lacked sufficient knowledge of timing.

In previous studies in the literature, correct answers to the question of the most appropriate method of transportation vary between 31.1% and 31.9% among physicians, although Aren et al. (19) recently reported a rate of 94.3% in a study conducted again with emergency physicians. In the present study, 48% of the participants gave the correct answer to the question to emergency physicians about the appropriate media for storage (24). It is believed that the vast difference between the findings of Aren et al.'s (19) study and those of other studies may result from the greater number of appropriate storage media provided to the participants.

Previous studies have examined the effects of demographic factors on knowledge of TTA, comparing the effects of age, specialty and professional experience on knowledge levels. The study by Bahammam (23) found that demographic factors had an effect on knowledge levels, while both Aren et al. (19) and Ulusoy et al. (13) found that the knowledge scores from the section of their questionnaires measuring the level of the knowledge did not statistically significantly differ based on demographic factors. That said, the study by Ulusoy et al. (13) found physicians working in the ER of public hospitals to be better informed about the appropriate emergency management of an avulsed tooth, and that getting professional help would be more appropriate compared to the physicians working in the same departments of universities ($p<0.05$). In the present study, an examination of the relationship between demographic factors and knowledge scores revealed no significant difference between genders and the type of institution in which the respondent was employed, while the level of the knowledge was found to increase with increasing years of professional experience and with increasing age, which concurs with the findings of Bahamman's (23) study ($p<0.001$ for both). Furthermore, an analysis of the position of the respondents in the institution revealed specialist emergency physicians to

have more accurate knowledge of TTA than emergency residents and general practitioners ($p<0.001$).

Study Limitations

Since the involvement of participants in the survey studies such as this is on a voluntary basis, it is believed that emergency physicians with an interest in dental traumas may increase the rate of correct responses to the posed questions. That said, the present study has some prominent characteristics, such as being one of the few studies conducted into TTA in Turkey involving emergency physicians, and including those working in the peripheral regions outside big cities, by conducting the questionnaire online throughout Turkey. The study also benefits from having the highest number of participants among those conducted to date into TTA.

Conclusion

It can be concluded from the present study that emergency physicians lack sufficient knowledge and experience of TTA, which can be attributed to shortfalls in their education and post-specialty training programs. It is therefore believed that it would be appropriate to include dental trauma training in specialist training programs due to the potential for frequent exposure to this condition during and after medical education.

Authorship Contributions

Concept: B.K.E., Design: B.K.E., B.G.Y., Data Collection or Processing: B.G.Y., Analysis or Interpretation: B.K.E., Literature Search: B.K.E., Writing: B.K.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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