

Original Article



Residents and interns in the 3 university hospitals: their knowledge of and attitudes to drug allergy

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ABSTRACT

Background: Previous studies revealed there are many gaps in the awareness and knowledge regarding the diagnosis and management of drug allergy (DA) among various health-care professionals.


Objective: To assess the knowledge, attitudes, and practices towards DA among residents and interns of 3 university hospitals in the region of Trakya (Thrace), Turkey.

Methods: A cross-sectional survey was conducted at university hospitals of 3 cities in the Trakya region: 1. Trakya University Medical Faculty, Edirne (n = 405), 2. Namik Kemal University Medical Faculty, Tekirdag (n = 114), and 3. Canakkale 18 Mart University Medical Faculty, Canakkale (n = 111). A Turkish questionnaire was developed based on previous published studies.

Results: The majority of participants (67%) had not received education on DA as a separate subject during their medical education. Less than a third (28.3%) of all respondents were satisfied with their knowledge concerning patients with clinical signs of DA. Of the 6 knowledge questions on DA, the average score for the study was 3.51 out of 6 (58.5%). Residents had a higher knowledge score (3.93 ± 1.1) compared with interns (3.05 ± 1.2) ($p < 0.001$). The lowest percentage of correct answers were in response to questions on laboratory confirmation of drug-related anaphylaxis (14.5%) and the possibility of penicillin toleration in patients with a history of penicillin allergy (11.8%). The majority of participants (92%) believe that medical doctors should be educated in DA. There were no significant correlations between taking DA histories and the frequency during daily practice of encountering patients.

Conclusion: Our study revealed that DA knowledge and attitudes are not at satisfactory level among respondents, and we concluded the importance and necessity of reinforcement of DA education in pre- and postgraduate education of medical doctors.

Keywords: Drug allergy; Knowledge; Awareness; Interns; Residents; Medical education

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Conflict of Interest

The authors have no financial conflicts of interest.

Author Contributions

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INTRODUCTION

Hypersensitivity reactions represent about one-third of all adverse drug reactions. Adverse drug reactions affect 10%–20% of hospitalized patients and more than 7% of the general population [1]. Drug allergy (DA) reactions are immunologically mediated drug-hypersensitivity reactions and they are typically unpredictable. They can be life-threatening, may require or prolong hospitalization, and may be associated with changes in subsequent therapy. Under- and overdiagnosis of DA is worsening the problem [2, 3]. Proper management of DA is imperative and crucial for patients. Patients are commonly labeled as being drug allergic as a consequence of vague symptoms that do not correspond to true allergic reactions [4]. Thus, diagnosis and proper management of DA is an important challenge for physicians and the unmet needs of patients. Previous studies revealed there are many gaps in the awareness and knowledge regarding the diagnosis and management of DA among various health-care professionals [4–7]. Some of these previous studies were performed in our country, they were regarding DA knowledge and attitudes among pediatric residents and family physicians [6, 7]. Residents and interns are front-line practitioners. To our knowledge, there is no study in our country regarding their DA knowledge, attitudes, and practices. Our aim in this study was to assess the knowledge, attitudes, and practice patterns towards DA among residents training in all clinical branches and interns at 3 university hospital in the Trakya (Thrace) region of Turkey.

MATERIALS AND METHODS

Study design and study population

A cross-sectional survey was conducted at university hospitals in 3 cities in the Trakya region, Turkey: 1. Trakya University Medical Faculty, Edirne; 2. Namik Kemal University Medical Faculty, Tekirdag; and 3. Canakkale 18 Mart University medical Faculty, Canakkale. The study was performed during the 2017–2018 academic year and was approved by Trakya University's ethical committee (approval number TÛTF-BAEK 2017/139). Sixth-grade medical students (interns) and all residents working in clinical branches were involved in the study at each study center. The authors visited departments where interns and residents were working and explained the purpose of the study. Data were collected from respondents using a self-administered questionnaire distributed as hard copies by the authors at each study center. Those willing to participate anonymously filled in the questionnaire forms. Each form took approximate 15–20 minutes to complete. Verbal informed consent was obtained from all participants before being included in the study.

Data collection instrument

Turkish questionnaire was developed. Questions modified from previously published studies [4, 5]. There were 3 open-ended (age, specialty, and practical experience time) and 16 multiple-choice questions. The survey comprised 3 domains:

- (1) Eight questions were related to the demographic characteristics of the participants.
- (2) Six questions were related to participants' knowledge of clinical features, diagnosis, and the management of DA. Knowledge scores were calculated between 0 and 6 according to true answers to 6 questions on the knowledge domain of the questionnaire.
- (3) Five questions were related to their attitudes and practice patterns concerning DA.

Statistical analysis

Descriptive parameters, such as means and standard deviations for normally distributed continuous data, frequencies, and percentages for categorical data were calculated. Normality

distribution of the numerical variables was tested by the Shapiro-Wilk test. Comparison of the knowledge scores between elements comprised of 2 categories was performed by the Student *t* test for normally distributed data and by the Mann-Whitney *U* test for nonnormally distributed data. Spearman correlation analysis was used to determine the relationship between experience time and knowledge scores. All tests were 2-tailed, and $p < 0.05$ was considered statistically significant. IBM SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA) was used for statistical analysis.

RESULTS

Characteristics of the study population

The final number of respondents who completed the survey was 630, with a response rate of 76% (total number of respondents from all centers was 829 but 630 of them answered the all questions). Distribution of respondents between study centers; as (intern/resident/total number of participants) were (192/213/405) for Trakya University Medical Faculty, (49/65/114) for Namik Kemal University Medical Faculty, and (51/60/111) for Canakkale 18 Mart University Medical Faculty. The majority of participants (67%) had not received education in DA as a separate subject during their medical education. The mean number of years in practice of residents was 2.5 ± 1.5 years, and 81% of them had less than 3 years' experience. The demographic characteristics of participants are summarized in **Table 1**.

Assessment of knowledge domain

Of the 6 knowledge questions on DA, the average score for the study was 3.51 out of 6 (58.5%). Residents had a higher knowledge score (3.93 ± 1.1) compared with interns (3.05 ± 1.2) ($p < 0.001$). There was no difference between the knowledge scores of participants in terms of age ($r = 0.20$, $p < 0.001$), sex ($p = 0.522$), and experience for residents ($r = -0.14$, $p = 0.012$).

Table 1. Demographic characteristics of participants (n = 630)

Characteristic	Value
Age (yr)	26.1 (21–38)
Sex	
Female	352 (56)
Male	278 (44)
Education status	
Intern	292 (46)
Resident	338 (54)
Year in practice (for residents)	
<3	273 (81)
≥3	65 (19)
Specialty group (residents)	
Internal branches	209 (62)
Surgical branches	129 (38)
Receiving education in drug allergy as a separate subject during medical education	
Yes	208 (33)
No	422 (67)
Weekly frequency of encountering with the patient who states (he/she) has drug allergy	
Less than 5% in a week	346 (55)
More than 5% in a week	284 (45)
Participation or observation to any drug provocation test before	
Yes	32 (5)
No	598 (95)

Values are presented as median (range) or number (%).

Table 2. Comparison of knowledge scores of respondents according to their different properties (n = 630)

Variable	Knowledge score	p value
Sex		0.522
Female	3.53 ± 1.31	
Male	3.49 ± 1.22	
Experience		0.012 (r = -0.14)
0-1 yr	4.11 ± 1.04	
1-2 yr	3.75 ± 1.01	
2-3 yr	3.94 ± 1.27	
3-4 yr	3.89 ± 0.97	
4-5 yr	3.69 ± 1.11	
Centers		0.007*
Trakya University	3.42 ± 1.25	
Canakkale 18 Mart University	3.85 ± 1.10	
Namik Kemal University	3.57 ± 1.26	
Education status		<0.001
Intern	3.05 ± 1.2	
Resident	3.93 ± 1.1	
Receiving or not education about drug allergies during medical school		0.026
Yes	3.68 ± 1.21	
No	3.43 ± 1.28	
Branches (residents)		0.003
Internal	4.07 ± 1.1	
Surgery	3.68 ± 1.08	
Satisfaction with their knowledge in the case of a patient who has clinical signs of drug allergy		<0.001
Satisfied	4.0 ± 1.1	
Unsatisfied	3.3 ± 1.2	

Values are presented as mean ± standard deviation.

*Namik Kemal University- Canakkale 18 Mart University ($p = 0.136$), Namik Kemal University-Trakya University ($p = 0.223$), Canakkale 18 Mart University-Trakya University ($p = 0.002$).

When the knowledge scores of participants compared among cities; there was a difference ($p = 0.007$). Comparison of knowledge scores of respondents according to their different properties are summarized in **Table 2**. Residents working in internal branches scored more highly in knowledge than those in surgical branches ($p = 0.003$). Most of the participants gave correct answers to the questions on the most common manifestations of DA and the treatment of drug-induced anaphylaxis (85.1% and 84.7%, respectively). Questions related to desensitization procedures and to skin tests were correctly answered 63.1% and 75.6% of the time, respectively. The lowest correct-answer percentages were in response to the questions on laboratory confirmation of drug-related anaphylaxis (14.5%) and the possibility of penicillin toleration in patients with a history of penicillin allergy (11.8%) (**Table 3**).

Attitudes and practices of the respondents in DA

The majority of the participants (92%) believe that physicians should be educated in DA. Less than one-third (28.3%) were satisfied with their knowledge of patients with clinical signs of DA. Those residents working in internal branches were more satisfied with their knowledge than those in surgical branches ($p = 0.032$). There were no significant correlations between taking DA histories and the frequency during daily practice of encountering patients with DA ($p = 0.086$). Answers to the questions assessing the respondents' attitudes to and practice of DA are summarized in **Table 4**.

Table 3. Knowledge of respondents regarding drug allergy (n = 630)

Question/choices	Correct answers, n (%)
Which one should be first choice in the treatment of drug-related anaphylaxis? (A) Systemic antihistaminics (B) Systemic glucocorticoids (C) Epinephrine (D) Dopamine	533 (84.7)
Which one is the most common manifestation of drug allergy? (A) Elevated transaminases (B) Skin rash (C) Serum disease (D) Anaphylaxis	535 (85.1)
A desensitization procedure can be used for patient treatment in which of the following drug reaction? (check all that apply) (A) Phenytoin induced toxic epidermal necrolysis (B) Cotrimoxazole induced Stevens-Johnson syndrome (C) Meropenem induced anaphylaxis (D) Shortness of breath, wheezing and nasal obstruction due to the use of aspirin in the patient with asthma and nasal polyps	361 (63.1)
If an anaphylactic reaction to a drug is suspected, which of the following tests may be ordered for confirmation of anaphylaxis? (A) Plasma histamine (B) Serum specific IgE level (C) Serum total tryptase (D) C1q binding assay (E) I don't know	90 (14.5)
What percentage of patients with a history of penicillin allergy can tolerate penicillin? (A) >75% (B) 51%–75% (C) 26%–50% (D) 16%–25% (E) 0%–15%	74 (11.8)
Skin tests can be used for evaluation in which of the following drug reaction? Check all that apply (A) Digoxin induced cardiac arrhythmia (B) Vaginal candidiasis due to ciprofloxacin (C) Morbilliform rash due to amoxicillin clavulanate (D) Electrolyte imbalance due to furosemide	465 (75.6)

Correct answers were shown as bold.

Table 4. Attitudes and practices of participants about drug allergy (n = 630)

Question/options	Answers, n (%)
Education of medical doctors about drug allergy is absolutely essential. I agree. 579 (92) I don't agree. 13 (2) I am not sure. 38 (6)	
I definitely know what should I do in the case of a patient who has clinical signs of drug allergy (satisfaction with their knowledge in the case of a patient who has clinical signs of drug allergy). I agree. (satisfied) 178 (28.3) I don't agree. (unsatisfied) 108 (17.1) I am not sure. (unsatisfied) 344 (54.6)	
I think it is necessary to determine drug allergy by <i>in-vitro</i> or <i>in-vivo</i> tests, before administering any medication to any patient. I agree. 240 (38) I don't agree. 233 (37) I am not sure. 157 (25)	
I take drug allergy history when prescribing any medication. No, I have no time. 22 (3.5) Sometimes 91 (14.5) Usually 252 (40) Always 265 (42)	
If one of your patients reports a drug allergy and you do not believe that the patient is truly allergic to that medication, do you still give the medication? Yes 67 (10.7) No 410 (65) Sometimes 153 (24.3)	

DISCUSSION

In this study, we surveyed DA knowledge and the attitudes and practices of interns and of residents at the outset of their professional career. To our knowledge, this is the first study performed among residents training in all clinical branches and sixth-grade medical students to assess DA knowledge in our country. Our study revealed that there are many gaps regarding DA among respondents, and consequently they were not satisfied with their knowledge level. Of the 6 knowledge questions on DA, the average score for the study was 3.51 out of 6 (58.5%), slightly lower than previously reported by Sturm and Temprano [4] and Wang et al. [5] (66.6% and 59.8%, respectively). In our study, more than 90% of respondents reported that they thought the education of physicians in DA is absolutely essential, although 67% reported that they had not taken separate lessons on DA during medical school. In a survey ascertaining baseline drug-allergy knowledge before the implementation of a clinical allergy guideline, Blumenthal et al. [8] found that 2 out of 5 inpatient practitioners reported no prior drug-allergy education.

In our survey, only 28.3% were satisfied with their knowledge of patients with clinical signs of DA. The knowledge scores of participants who had taken no DA lessons and who were not satisfied with their knowledge were lower than the other participants. When considering our study and previous studies in Turkey [6, 7], we believe DA education is not satisfactory in our country. Learning the classification and the pathophysiology of drug-related hypersensitivity reactions is part of preclinical medical education in the United States and has been recommended as clinical medical education for medical students by the American College of Allergy, Asthma, and Immunology [9]. We believe that if such a regulation is made in our country, physicians' DA knowledge levels will increase.

Residents had higher knowledge scores compared with interns, as expected. Wang et al. [5] also reported higher knowledge scores of physicians compared with medical students and nurses. Interestingly, there was no difference between the knowledge scores of residents according to their experience time. This finding suggests that periodic postgraduate education may be beneficial. Residents working in internal branches had higher knowledge scores than those in surgical branches. Similarly, previous studies have revealed physicians with internal medical training and residents in pediatrics had higher knowledge levels compared with others [4, 6].

Eighty-five percent of the participants knew that skin eruption is the most common manifestation of DA. Being familiar with DA manifestations is important in the cessation of the responsible drug(s) and to prevent severe reactions. Epinephrine was picked out by 84.7% of respondents as the first choice among treatment options in drug-related anaphylaxis. Drugs are the most frequent cause of anaphylaxis in hospitalized patients, and thus it is essential to know about the treatment of such life-threatening reactions triggered by drugs [10]. Two previous studies conducted with family physicians in Turkey reported lower correct response rate than our result to questions on the treatment of anaphylaxis of 31.7% and 12.8% [7, 11].

Again interestingly, in our study, the percentage of respondents reporting that they always take patients' DA history was much higher than in another study in Turkey by Guvenir et al. [6] (42% vs. 24.4%). But there was no significant correlation between taking DA histories and the frequency during daily practice of encountering patients with DA in both studies. Wang et

al. [5] reported 59.1% of respondents always take the DA history before drug administration. Results from other studies performed in Turkey, though, indicate that this habit may not be adequately common among Turkish medical doctors.

Only 38% of respondents disagreed with the statement, “it is necessary to determine DA by *in-vitro* or *in-vivo* tests before administering any medication to any patient.” It is impossible and is unnecessary, to perform these tests without any previous DA history. Furthermore, the patient can be sensitized during *in-vivo* tests. Taking a careful history is the most important step in getting information about a patient's DA. Only 10.7% of respondents stated that they would administer the culprit drug if the patient's history was not compatible with DA—although immune-mediated drug reactions may constitute 6%–10% of adverse drug reactions, making a decision only based on history risky in some situations (e.g., a long period after reaction, using more than one drug during reaction, etc.) [12].

Eighty-five percent of the participants were unaware of relationship between serum total tryptase level and anaphylaxis. Diagnosis of anaphylaxis and decision about epinephrine treatment should be based on clinical manifestations. On the other hand, despite the fact that the positive predictive value of an elevated serum tryptase is high and the negative predictive value is low, serum tryptase level can be helpful in some cases to exclude other conditions. Serum tryptase levels reach peak values at the end of the first hour and return to baseline levels within 4 hours following an anaphylactic reaction [13], and thus being familiar with this fact may allow taking blood samples within true time period during drug-related anaphylaxis.

Questions on indications of desensitization procedures and on skin tests were correctly answered 63.1% and 75.6%, respectively, revealing a lower level of knowledge than previously reported [4]. This result suggests a significant number of residents and interns included our study were unaware which patients should be referred to an allergy specialist for detailed evaluation and appropriate treatment.

Our study reveals the low level of knowledge of true incidences of confirmed penicillin allergy. Only 11.8% of participants correctly answered the question on what percentage of patients with a history of penicillin allergy can tolerate penicillin. A history of penicillin allergy can lead to an increase in health-care costs. Fewer than 5% of patients with a history of penicillin allergy have actually been confirmed as being allergic to penicillin, but physicians often prefer to prescribe a different class of antibiotics [4, 14-17]. Patients may attribute nonallergic rashes during viral illness or symptoms not related to hypersensitivity reactions to penicillin allergy. DA knowledge is important for medical doctors to distinguish nonallergic signs and symptoms from the truly allergic.

There are 2 main limitations of our study. First, the survey may not represent actual knowledge, attitudes, and the clinical practices of the respondents. Most of the questions were multiple choice; it must be acknowledged that it is easier to make a choice on paper than it is to take action in real life. Secondly, this study was carried out in only 3 university hospitals, and thus our results cannot be generalized to all medical schools in Turkey or internationally.

In conclusion, our study reveals that most of the respondents did not receive adequate DA education during medical school and consequently, they were not satisfied with their knowledge levels and believe in the importance and necessity of such education. We think such training should be added to the pre- and postgraduate education of medical doctors. A beneficial next

step would be to perform an intervention study to attempt to improve interns' and residents' DA knowledge and to prevent future drug-allergy-related morbidity and mortality.

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