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# Adrenaline auto-injector prescription profiles and clinical features of adult patients: A study from Malatya Province



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**Abstract**
Aim: Adrenaline auto-injectors (AAIs) are frequently prescribed to patients who have had previous anaphylaxis or conditions with a risk of anaphylaxis. We aimed to evaluate the clinical characteristics of patients who were prescribed AAI, the prescription indications for AAI, and the carriage and usage rates of AAI.
Material and Methods: Patients who were prescribed AAIs between August 2017 and April 2022 in our outpatient clinic were enrolled in the study. Demographic and clinical features of patients, AAI prescription indications, the carriage rate of the AAI, and the reasons for not carrying the device, experience of anaphylaxis after AAI prescription, and patients' anaphylaxis management methods were recorded.
Results: A total of 191 patients were enrolled (51.8% female) and the mean age of the patients was 40.8±12.6 years. Venom allergy (72.3%) was identified as the most common trigger. The most common symptoms were mucocutaneous manifestations among patients who had experienced anaphylaxis. The carriage rate of AAI was found to be 57.5%, and the most common reason expressed for not carrying AAI was the belief that it was not necessary (51.6%). Nineteen (13%) patients experienced anaphylaxis after the AAI prescription, and 47.4% of these patients used AAI at the time of anaphylaxis.
Discussion: Our findings provide information among the adult population in the eastern region of Turkey regarding the etiological and clinical features of anaphylaxis and patients' AAI carriage and usage attitudes. Patient education should be repeated at each clinical visit to improve the carriage and usage rates of AAI.

**Keywords**
Adrenaline Auto-Injector, Anaphylaxis, Etiology, Carriage, Usage

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## Introduction

Anaphylaxis is an acute-onset, life-threatening reaction that affects different organ systems and requires immediate treatment [1]. The prevalence of anaphylaxis is estimated to be 0.3–5.1%, although it varies depending on geographic regions, populations, and study methodology [2-4]. The increasing incidence of anaphylaxis in recent years causes high economic costs [4]. Mortality, hospitalization, and biphasic reactions can be prevented by immediate intramuscular adrenaline administration [5-7]. National and international guidelines recommend prescribing adrenaline auto-injectors (AAIs) to patients at an increased risk of anaphylaxis [8-9]. However, studies have reported that the rate of AAI prescriptions is low and some patients experiencing anaphylaxis are not prescribed at all [10-12].

Anaphylaxis triggers are generally considered similar according to age groups. In children and young adults, foods, followed by venom and drugs, were reported as the most common triggers. However, in adults and the elderly, venom and drugs are more common. Idiopathic anaphylaxis is also more common in adults and the elderly than in children [13-15].

In this study, we aimed to evaluate the clinical characteristics of patients who were prescribed AAI, the prescription indications for AAI, and the carriage and usage rates of AAI in Malatya Province.

## Material and Methods

This study was conducted at the adult allergy and immunology outpatient clinic. We retrospectively reviewed the medical files of patients, and included adult patients in the study who were prescribed AAI for any reason between August 2017 and April 2022. At the prescription visit, patients were trained about how to and when to use AAI by the same allergy specialist and were given an informative brochure. Data on demographic features, clinical history of patients, accompanying diseases (asthma, allergic rhinitis, eczema), AAI prescription indications and prescription date were recorded from the medical files of patients. Data on the carriage rate of the AAI, if they did not carry it on, the reasons for not carrying the AAI, whether the patients experienced anaphylaxis after the AAI prescription, and patients' anaphylaxis management methods were collected from patients by a short telephone interview. A total of 191 eligible patients were included in the study. The diagnosis of anaphylaxis was established based on the European Academy of Allergy and Clinical Immunology Anaphylaxis guideline [9]. An individual was counted only once during the entire study period, even if they were prescribed AAI more than once. The Turkish Ministry of Health provides all prescribed AAIs, and Penepin (Vem Ilac Sanayi ve Tic. LTD STI, Istanbul, Turkey) has been used as an AAI in our country since November 2016.

Informed consent was obtained from all patients. The study was approved by the ethics committee (2022/90).

*Statistical Analysis*

All statistical analyses were performed using SPSS for Windows, version 21.0 (IBM Corp., Armonk, N.Y., USA). Quantitative variables were expressed as mean±SD and as medians with IQRs. For categorical variables, frequencies and proportions were used to describe patient characteristics.

## Results

Overall, 191 patients who had been previously prescribed AAI were included in our study. Of these, 99 (51.8%) were females. The mean age in the study population was 40.8±12.6 years (min-max: 19-70). An AAI had been prescribed to 140 (73.3%) patients with a compatible history of anaphylaxis and 51 (26.7%) patients who had a condition with a risk of anaphylaxis (such as food allergy or generalized cutaneous reactions due to venom allergy) but had never experienced it. When all patients were evaluated, venom allergy (n=138, 72.3%) was identified as the most common indication for AAI prescription. Other indications were food allergy (n=24, 12.6%), idiopathic (n=11, 5.8%), drug allergy (n=9, 4.7%), and latex allergy (n=2, 1%). The median time elapsed was 2 (min-max: 0.25-4.5) years after the prescription of AAI. General characteristics of the study population are shown in Table 1.

Among 140 patients who had experienced anaphylaxis before the AAI prescription, the most commonly identified causes were venom (73.6%) and foods (11.4%), while 5.7% of the cases were idiopathic. The median number of anaphylaxis that patients experienced was 2 (min-max: 1-8). The most common symptoms were mucocutaneous manifestations in 116 patients (82.9%), followed by cardiovascular manifestations in 98 patients (70%), respiratory manifestations in 73 patients (52.1%), and gastrointestinal manifestations in 35 patients (25%). General characteristics of the patients with a history of

**Table 1.** General characteristics of the study population (n=191)

| Parameters | |
|---|---|
| Sex, n (%) | |
| Female | 99 (51.8%) |
| Male | 92 (48.2%) |
| Current age (year) mean±SD | 40.8 ± 12.6 |
| Age at the first episode mean±SD | 34.4 ± 14.4 |
| Index reaction, n (%) | |
| Anaphylaxis | 140 (73.3%) |
| Condition with a risk of anaphylaxis | 51 (26.7%) |
| Indication for AAI, n=191 | |
| Venom | 138 (72.2%) |
| Food | 24 (12.6%) |
| Idiopathic | 11 (5.8%) |
| Drug | 9 (4.7%) |
| Latex | 2 (1%) |
| Others* | 7 (3.7%) |
| Concomitant diseases, n=183 | |
| Asthma | 16 (8.7%) |
| Allergic rhinitis | 51 (27.9%) |
| Eczema | 6 (3.3%) |
| Education level, n=155 | |
| Primary school | 52 (33.5%) |
| High school | 35 (22.6%) |
| University | 68 (43.9%) |
| Location, n=157 | |
| Urban | 101 (64.3%) |
| Rural | 56 (35.7%) |
| After prescription of AAI, median time elapsed, years, (min-max) | 2 (0.25-4.5) |

* mastocytosis (n=1), exercise induced anaphylaxis (n=1), hydatid cyst (n=2), insect (n=2), formol (n=1). AAI; adrenaline auto-injector.

anaphylaxis are shown in Table 2.

We were able to interview 146 patients (76.4%) by phone, but were unable to do so with 45 (23.6%). One hundred and twenty-six (126/146, 86.3%) patients obtained AAI after prescription. Eighty-four patients (84/146, 57.5%) responded that they had the AAI with them (60/84, 71.4% at all times; 24/84, 28.6% only where they considered it risky), while 62 patients (62/146, 42.5%) did not. The most common reason expressed for not carrying AAI was the belief that it was not necessary (32/62, 51.6%). Nineteen (13%) patients experienced anaphylaxis after the AAI prescription (hymenoptera sting (n=12, 63.1%), food (n=5, 26.3%), drug (n=1, 5.3%), and idiopathic (n=1, 5.3%)). Nine (47.4%) of these patients used AAI alone or with oral steroids and antihistamines at the time of anaphylaxis. There was no need for a second dose of adrenaline in any of these patients, and no fatal reactions were reported. Characteristics of patients who were interviewed by phone are shown in Table 3.

**Table 2.** General characteristics of the patients with a history of anaphylaxis (n=140)

| Parameters | |
|---|---|
| Sex, n (%) | |
| Female | 70 (50%) |
| Male | 70 (50%) |
| Age (year) mean±SD | 41.1±12.5 |
| Age at the first episode mean±SD | 34.9±14.8 |
| Indication for AAI, n (%) | |
| Venom | 103 (73.6%) |
| Food | 16 (11.4%) |
| Idiopathic | 8 (5.7%) |
| Drug | 4 (2.9%) |
| Latex | 2 (1.4%) |
| Others* | 7 (5%) |
| Median number of anaphylaxis (min—max) | 2 (1-8) |
| Symptoms, n (%) | |
| Mucocutaneous symptoms | 116 (83%) |
| Cardiovascular symptoms | 98 (70%) |
| Respiratory symptoms | 73 (52%) |
| Gastrointestinal symptoms | 35 (25%) |

* mastocytosis (n=1), exercise induced anaphylaxis (n=1), hydatid cyst (n=2), insect (n=2), formol (n=1). AAI; adrenaline auto-injector.

**Table 3.** Characteristics of patients who were interviewed by phone (n=146).

| Parameters | |
|---|---|
| Prescription obtaining data, n (%) | |
| Patients who obtained AAI | 126 (86.3%) |
| Patients who did not obtain AAI | 20 (13.7%) |
| AAI carriage rate, n (%) | 84 (57.5%) |
| Reasons for not carrying an AAI, (n=62) | |
| I did not think it was necessary | 32 (51.6%) |
| I took it once. After that, I did not renew the device report | 8 (12.9%) |
| I did not get it because it was difficult to obtain | 7 (11.3%) |
| I did not carry it because it was difficult due to its physical features | 5 (8.1%) |
| I did not get it because of fear | 4 (6.4%) |
| Other | 6 (9.7%) |
| Experience of anaphylaxis after AAI prescription, n (%) | 19 (13%) |
| Anaphylaxis management, (n=19) | |
| Self-administration of AAI | 6 (31.6%) |
| Self-administration of AAI+ usage of oral medications | 3 (15.8%) |
| Usage of only oral medications | 4 (21%) |
| Treated in an emergency department | 6 (31.6%) |

oral medications; oral steroid and antihistamines. AAI; adrenaline auto-injector.

## Discussion

This study reported the etiology, clinical features, and the AAI carriage and usage rates of patients with anaphylaxis or conditions at risk of anaphylaxis in Malatya Province, which is located in the eastern region of Turkey. According to the results of this study, venom allergy was found to be the most common AAI prescription indication, and mucocutaneous manifestations were found to be the most common symptoms. The carriage and usage rates were found to be 57.5% and 47.4%, respectively. The most common reason expressed for not carrying an AAI was the belief that it was not necessary (51.6%).

Anaphylaxis in children and adults has various allergic triggers. These triggers may vary according to different geographic areas. In a study from Japan, food was the most common trigger of anaphylaxis, followed by drugs, in patients older than 15 years old [16]. Medications were found to be the leading cause of anaphylaxis in China [17]. In our study, the most common cause of anaphylaxis was venom. This high rate of venom allergy may be related to the common presence of beekeeping in this geographical region.

It has been reported that in patients experiencing anaphylaxis, cutaneous symptoms occur most frequently (> 90% of cases), followed by respiratory and cardiovascular system symptoms (> 50%) [9]. In our patient population, we found that cutaneous manifestations were the most common symptoms, followed by cardiovascular system and respiratory system signs, in accordance with previous studies.

In the treatment of anaphylaxis, intramuscular adrenaline administration is the first-line intervention [9]. Patients should carry AAI with them at all times because rapid intervention can be life-saving at the onset of anaphylaxis. The main problem with AAI administration is that patients do not always carry the device with them. In our study, 86.3% of patients obtained their AAI after prescription, and this rate was consistent with a previous study [18]. However, eleven (8.7%) of these patients reported that they never carried an AAI with them. In our study, AAI carriage rate was found to be 57.5%. In previous studies, this rate was reported to range from 23% to 79.7% [19,20]. There are studies investigating the factors that affect the carriage of AAI. Unclear physician advice, insufficient patient training, and poor physical features of the device were reported as the most common barriers to carry AAI [21,22]. In our study "the thought that adrenaline is unnecessary" was found to be the most common reason for not carrying the device all the time.

There is limited information regarding medical follow-up after an AAI prescription, and there are few studies that investigate the recurrence rate of anaphylaxis in adults. A study of adult and pediatric patients found that 3% of the whole cohort had a repeat anaphylaxis-related emergency department visit within

1 year after the index reaction, and this rate was 2.8% among adults [23]. In pediatric cases, O'Keefe et al. found a 17.6% annual recurrence rate of anaphylaxis [24]. In the present study, 19 of 146 (13%) patients had experienced anaphylaxis after the AAI prescription. AAI use at the time of anaphylaxis was reported as 47.4%, and this rate was similar to a previous study [25]. However, this usage rate (9/146, 6.2%) is still low when evaluated according to 146 patients. The European Anaphylaxis Registry reported that 12% of patients administered AAI before presenting to the emergency department [14].

*Conclusion*

Our findings provide information among the adult population in the eastern region of Turkey regarding the etiological and clinical features of anaphylaxis and patients' AAI carriage and usage attitudes. Patient education about the importance of AAI with clear physician advice should be repeated at every opportunity and at each clinical visit to improve the carriage and usage rates of AAI.

***Scientific Responsibility Statement***

*The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.*

***Animal and human rights statement***

*All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.*

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***Conflict of interest***

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