

ORIGINAL PAPER/PRACA ORYGINALNA

Details and effects of pre-hospital pharmacotherapy in pediatric population patients with anaphylactic or severe allergic symptoms – a single-center study

Charakterystyka farmakoterapii w postępowaniu przedszpitalnym w przypadkach ciężkich reakcji alergicznych i anafilaksji u pacjentów pediatrycznych – badanie jednośrodkowe

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ABSTRACT

Introduction: Anaphylaxis is an acute, potentially life-threatening, systemic hypersensitivity reaction. Its prevalence in pediatric population is constantly increasing. Adrenaline is a first-line treatment in every case of anaphylaxis.

Aim: To examine the details of anaphylaxis treatment in the pre-hospital setting in a pediatric population. We wanted to determine whether there is a correlation between pharmacotherapy being implemented during the Emergency Medical Services (EMS) interventions and subsequent admission to the hospital.

Material and methods: In our retrospective study, we collected 2444 copies of the patients' documents transferred by the EMS to the Emergency Department (ED) in the Pediatric Hospital in Warsaw throughout the calendar year 2020. The documents included demographic data, details of the given prehospital medication, and the initial diagnosis, among other information. Moreover, complementary data from the stay at the ED were added.

Results: Forty patients met the inclusion criteria, which was 1.64% of all the patients transported to the ED. Twenty-three (58%) patients received pharmacotherapy during pre-hospital emergency care (group A) while 17 (42%) did not receive it (group B). There was no significant difference in gender distribution between the groups. In group A there were 5 hospitalizations and in group B, 2 patients were admitted to the hospital ($p > 0.05$). The most common allergen was the food component ($n = 22$; 55%). Hydrocortisone was the most frequently used drug in pre-hospital care, being administered to 11 (48%) patients, with intramuscular adrenaline being given only 3 times (13%).

Conclusions: The gender of the patient did not influence the decision of whether pharmacotherapy should be implemented. Adrenaline is being underused in the prehospital treatment of severe allergic reactions. No correlation between the implementation of prehospital pharmacotherapy and subsequent hospitalization was found.

KEY WORDS

emergency department, drug therapy, anaphylaxis, emergency medical technicians, emergency medical services, emergencies, adrenaline, ambulances, emergency treatment, allergy.

STRESZCZENIE

Wprowadzenie: Anafilaksja to nagła, potencjalnie zagrażająca życiu, uogólniona reakcja nadwrażliwości. Jej częstość w populacji pediatrycznej stale wzrasta. Adrenalina to lek pierwszego rzutu w każdym przypadku anafilaksji.

Cel: Poznanie charakterystyki postępowania przedszpitalnego w przypadkach anafilaksji i ciężkiej reakcji alergicznej u pacjentów pediatrycznych. Poszukiwano korelacji pomiędzy wdrożeniem farmakoterapii podczas czynności zespołów ratownictwa medycznego a decyzją o przyjęciu do szpitala.

Materiał i metody: Wykonano retrospektywną analizę, która objęła dokumentację medyczną 2444 pacjentów przywiezionych przez zespoły ratownictwa medycznego do Szpitalnego Oddziału Ratunkowego Dziecięcego Szpitala Klinicznego w Warszawie w 2020 roku. Dokumentacja zawierała między innymi: dane demograficzne, informacje o podjętej farmakoterapii oraz wstępne rozpoznanie. Kryterium włączenia było wystąpienie ciężkiej reakcji alergicznej.

Wyniki: Czerdziestu pacjentów spełniło kryterium włączenia, co stanowiło 1,64% wszystkich pacjentów z badanego okresu. Wśród nich 23 (58%) zostało poddanych farmakoterapii w ramach przedszpitalnych czynności ratunkowych (grupa A), a 17 (42%) nie otrzymało żadnego leku (grupa B). Nie zaobserwowano istotnej różnicy w rozkładzie płci między grupami A i B. W grupie A 5 pacjentów zostało przyjętych do szpitala, a w grupie B – 2 pacjentów. Różnica ta nie była istotna statystycznie ($p > 0,05$). Najczęstszy alergen stanowił pokarm ($n = 22$; 55%). Najczęściej używanym lekiem był hydrokortyzon – otrzymało go 11 pacjentów. Adrenalina w postaci domięśniowej została podana 3 pacjentom.

Wnioski: Płeć pacjenta nie wpływała na decyzję o podjęciu leczenia farmakologicznego. Adrenalina jest stosowana rzadko w przedszpitalnej terapii reakcji anafilaktycznych. Nie stwierdzono korelacji pomiędzy wdrożeniem farmakoterapii w czynnościach przedszpitalnych a decyzją o przyjęciu pacjenta do szpitala.

SŁOWA KLUCZOWE

szpitalny oddział ratunkowy, farmakoterapia, anafilaksja, ratownik medyczny, ratownictwo medyczne, zespoły ratownictwa medycznego, adrenalina, ambulans, medycyna ratunkowa, alergja.

ADDRESS FOR CORRESPONDENCE

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INTRODUCTION

Anaphylaxis is an ever-growing problem in the pediatric population [1, 2]. It is an acute, severe, systemic hypersensitivity reaction, which can manifest itself by dermatological, respiratory, cardiovascular, gastrointestinal, or neurological symptoms [3]. Although its prevalence is relatively low, it is constantly increasing [4]. The fact that each severe allergic reaction is potentially life-threatening makes anaphylaxis a relevant problem. Its mechanism can be either immunologic or non-immunologic. The former

term most commonly describes IgE-dependent reactions, where cross-linking of two or more FcεRI–IgE complexes with an allergen molecule causes mast cells and basophils to degranulate and release mediators (e.g. histamine) which are responsible for the symptoms of anaphylaxis. Less common and less discovered are the non-IgE-dependent mechanisms of degranulation of the mast cells and basophils, for example, those mediated by IgG antibodies or by the complement system [5, 6].

The most common cause of anaphylaxis in children is a food allergy. Many studies show that food allergy is

becoming more and more frequent in many countries, regardless of their development [7]. Young children are at the highest risk, as admissions to hospitals due to food-related anaphylaxis occur more often in this group. Gender distribution in anaphylaxis changes with the patient's age [8].

Although proper recognition of anaphylaxis-related reactions can be difficult, especially for non-healthcare professionals, it is very important to identify them as quickly as possible. Such a reaction can have a very rapid onset, and the only well-documented treatment is to administer intramuscular epinephrine (adrenaline) as soon as an anaphylactic reaction is suspected [6]. Therefore, proper education of patients (or parents of children) at risk of developing anaphylaxis is very important, so that they can call for professional help quicker. Apart from the paramedics or doctors, who are often the first responders, people at risk or their relatives can also help with self-administered epinephrine. Unfortunately, some studies show that intramuscular adrenaline is underused by health care professionals, and patients at risk often lack a prescription or proper instruction on how to use it [9]. Other treatment methods include intravenous fluid therapy, inhaled β 2-mimetics, and oxygen. Antihistamines (H_1 and H_2 antagonists) and steroids are also commonly used.

In the Polish health care system, Emergency Medical Service teams can be either a specialized team (SEMS – specialist emergency medical service) or a basic team (BEMS – basic emergency medical service). The first term describes an ambulance with at least one physician on board, while the second describes an ambulance without a physician on board. Paramedics in BEMS can perform a limited number of medical activities and administer a limited number of medications (47 medications are available). These include epinephrine, clemastine, steroids (hydrocortisone and dexamethasone), and salbutamol. Physicians in SEMS can additionally administer some intensive care drugs such as dopaminum hydrochloricum 4%, etomidat or propofol 2% [10]. Every EMS team is also obliged to fill in a Medical Emergency Card which contains information about the treated patient. Apart from the personal data, it also consists of the list of medications that had been used, abbreviated medical history, and the initial diagnosis. EMS, if they find indications for transport to the hospital, transfer patients to the Emergency Department, which is a specialized ward established to save people's health and life in emergency situations [11].

AIM

The aim of our study was to determine the details of anaphylaxis treatment in the prehospital setting and

especially whether there is an association between such treatment and hospitalization. We were interested in what kind of pharmacotherapy is most common, what the demographic characteristics are, and how they influence the later treatment of patients admitted with severe allergic reactions. To our knowledge, this is the only research in Poland that collected data involving pediatric patients with severe allergy or anaphylactic presentations in the pre-hospital setting. We hope that this insight into the pediatric population will help to treat and recognize anaphylaxis better.

MATERIAL AND METHODS

MATERIAL

This is a retrospective study of all interventions of the Emergency Medical Services (EMS) that resulted in transportation to the Emergency Department in the Pediatric Teaching Clinical Hospital of the University Clinical Center of the Medical University of Warsaw in the period between January 1, 2020, and December 31, 2020.

We analyzed all of the 2444 Emergency Medical Card copies of the patients transferred by the EMS to our Emergency Department in 2020. Then, we collected all of the data mentioned before as well as the GCS scale and pain severity. Information on the type of team providing help was also gathered.

METHODS

In order to collect the data about patients suffering from a serious allergic reaction, we included all of the patients whose initial diagnosis was within the following ICD10 codes: T78, Z88, and L50. We excluded all of the cases in which the documentation was not complete (e.g., it lacked the age of the patient, did not specify the ICD10 code or the documentation was illegible). In order to assess some more information about the patients' treatment, we collected some information from the Emergency Department as well. This included information such as whether the patient was hospitalized and, if so, for how many days, whether additional pharmacotherapy was implemented within the ED as well as additional medical history, including, for example, questions about the possible allergen being the cause of the allergic reaction.

ETHICS APPROVAL OF RESEARCH

Ethics committee written approval was received for this study from the Ethics Committee of the Medical University of Warsaw – decision number AKBE/109/2021.

STATISTICAL ANALYSIS

The χ^2 statistical test was used and the threshold of statistical significance was considered to be $p < 0.05$. The statistical work was performed with IBM SPSS Statistics 27 software.

RESULTS

Out of the group of 2444 patients who were transported to the Emergency Department (ED) by the Emergency Medical Services (EMS) in 2020, only 40 cases (1.64% of all of the patients received in the ED) met the inclusion criteria and therefore could be defined as serious allergic reactions.

Twenty-three (58%) patients received pharmacotherapy during the pre-hospital emergency care and transportation to the hospital (later referred to as group A), while 17 (42%) patients did not receive any pharmacotherapy whatsoever (later referred to as group B). Among all of the 40 patients, 16 of them were girls (40% of all patients), and 24 of them were boys (60% of all patients). In group A there were 11 boys (48% of group A) and 12 girls (52% of group A) and in group B there were 13 boys (76% of group B) and only 4 girls (24% of group B). This difference in the gender distribution was statistically insignificant, which was confirmed using the chi-square test ($p = 0.068$) – presented in Table 1. The average age in group A was 5.2 years, and 3.12 years in group B. Out of the 40 EMS interventions, 33 were interventions of BEMS teams (18 in group A, 15 in group B), and 7 interventions were performed by SEMS teams (5 in group A, 2 in group B). We found no correlation between the type of the EMS team (either a specialized or a basic team) and the decision to implement pharmacotherapy or the need for hospitalization ($p > 0.05$).

In the case of 5 patients from group A, a decision of hospitalization was made, and it took 15 h, 24 h, 6 days, 9 days, and 11 days. In group B only 2 such decisions were made, and both were 24 h long. There was no statistically

significant correlation between the number of hospitalizations and gender or pharmacotherapy.

In our group of patients, the most common allergen, according to the medical history, was food or a component of food ($n = 22$; 55%). In 12 (30%) cases it was impossible to establish the probable allergen. Additionally, the causes of those allergic reactions also included medications ($n = 5$; 12.5%) and cosmetics ($n = 1$; 2.5%) (Table 2).

The most used medication in pre-hospital care was hydrocortisone. It was administered to 11 patients from group A (48%). The second one was dexamethasone ($n = 9$; 39% – administered intramuscularly or intravenously), and then clemastine ($n = 5$; 22%), 0.9% NaCl (saline) ($n = 5$; 22%), adrenaline – both intramuscular and nebulized were used 3 times each (13% of the patients each), paracetamol ($n = 2$; 9%), salbutamol ($n = 2$; 9%) and oxygen, midazolam, cetirizine and glucose (in each case, $n = 1$; 4%) (Figure 1).

DISCUSSION

The aim of this study was to obtain information about how often the EMS teams are confronted with severe allergic reactions/anaphylaxis and the details of such interventions. To our knowledge, it is the first research with such an objective in Poland. Because of the fact that the EMS interventions are emergency situations requiring a quick response, the documentation obtained from the EMS is usually limited and it is not possible to precisely assess how the patient presented him or herself and how the symptoms appeared initially. Therefore, we assumed that all of the allergic reactions that were severe enough to call an ambulance could be described as severe allergic reactions and could possibly be associated with anaphylaxis.

Heterogeneous clinical presentation of anaphylaxis with its acute onset makes correct diagnosis challenging in the pre-hospital interventions [12]. The gold standard of anaphylaxis treatment is intramuscular administra-

TABLE 1. Relationship between gender and pharmacotherapy

Parameter	Pharmacotherapy		Total
	Not present	Present	
Gender – female	4	12	16
Gender – male	13	11	24
Total	17	23	40

TABLE 2. The frequency of suspected allergens

Suspected allergen	Food	Drug	Cosmetic	Not enough information
Number of patients	22	5	1	12
Percent of patients	55%	12.5%	2.5%	30%

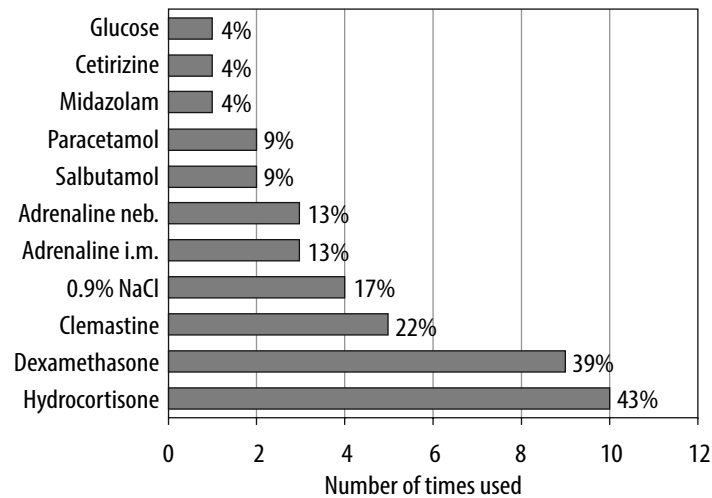


FIGURE 1. Frequency of individual drugs used by Emergency Medical Services in the pharmacotherapy group

tion of adrenaline, with the dose being dependent on the patient's weight. In our study, almost 60% of patients received emergency pharmacological treatment, but intramuscular adrenaline was only the fifth most popular choice in such cases. This is consistent with some other evidence showing that adrenaline is underused in anaphylaxis treatment in children [13, 14].

The reason for that could potentially be the difficulties in diagnosing anaphylaxis, as there are no 100% specific algorithms or tests. Many recommendations vary to some extent, for example in terms of the number of organs affected by the symptoms. The World Allergy Organization (WAO) has recently published guidelines that suggest diagnosing anaphylaxis when at least one of the following criteria are met:

- 1) acute onset of symptoms including skin, mucosal tissue, or both (pruritus, generalized hives, or flushing) with at least one of the following:
 - a) respiratory compromise,
 - b) reduced blood pressure or associated symptoms of end-organ dysfunction,
 - c) severe gastrointestinal symptoms, for example, repetitive vomiting or crampy abdominal pain;
- 2) acute onset of bronchospasm or laryngeal involvement or hypotension after being exposed to a known or to a highly probable allergen (this does not require typical skin symptoms to occur).

What can also make the decision harder for the healthcare professionals is the fact that clinical presentation of anaphylaxis can be similar to those in aspiration of a foreign body, vasovagal episodes, panic attacks or asthma [15, 16]. Another fact that makes proper treatment of severe allergic reactions even more difficult is the fact that patients frequently are not sufficiently aware of what causes them, how to prevent such reactions, and what steps should be taken in case of a life-threatening exacerbation [9].

It seems impossible to predict the progression of anaphylaxis symptoms after exposure to an allergen [12, 17], so many authors recommend using intramuscular adrenaline in all cases of anaphylaxis in order to reduce the risk of severe complications and death [15, 17]. Such recommendations are also supported by the fact that many studies have shown that adverse cardiovascular events after administration of intramuscular adrenaline are rare, especially when the dose and way of administration are correct [13, 18–20].

Despite adrenaline being the first-line treatment in anaphylaxis-related presentations [21], our study showed that many other medications were used more frequently. Administration of other medications, such as antihistamines or glucocorticoids, has been widely researched, but to date, there are no significant, randomized trials showing that the use of these medications in the initial management of the anaphylaxis improves the outcome of the treatment and should always be a part of the anaphylaxis management [22, 23]. Furthermore, the doses used in such interventions are often extrapolated from the use of these medications in other diseases but not from the data related to anaphylaxis. On the other hand, there seem to be no data showing that these medications can worsen the outcome, so many authors agree that after administration of intramuscular adrenaline, the use of other medications can be considered [22, 24, 25].

In recent years, an increase in the prevalence of pre-hospital pediatric anaphylaxis has been observed [1]. There is good evidence for this especially in the so-called western countries, for example, Australia, the United Kingdom, and the United States of America [1, 26]. The European anaphylaxis registry from 2014 revealed that 1 in 4 cases of anaphylaxis occurred in pediatric patients [27]. Polish studies indicate a slightly lower incidence of anaphylaxis in children, estimating it at 13.1% [28]. To

our knowledge, there has not been any research on the frequency of EMS interventions related to anaphylaxis in the Polish pediatric population yet. Our results in that matter seem to be similar to another study from Australia, where, out of all patients attended by EMS teams, 3.2% had allergic presentations [1]. Place of living seems to have a significant impact on the anaphylaxis prevalence, as one large-scale study conducted in Poland, based on the data obtained from the Polish National Health Fund statistics, showed that there was a large, sixteen-fold difference between anaphylaxis prevalence in urban and rural areas (urban areas being more affected) [29].

The most common triggers of anaphylaxis vary significantly depending on the age of the patients. While many sources indicate that stinging insects' venom is the leading cause in adult patients, the most common allergens in pediatric anaphylaxis are food-related, which our study confirmed as well, as food was the most common trigger [7]. In western countries, peanuts are widely considered the most frequent cause of food-induced anaphylaxis [30, 31]. Other frequent allergens include eggs, dairy, seafood and chocolate [1, 32, 33]. The prevalence of food allergies is highest in early childhood, then it falls as age increases [34]. The most recent guidelines formed as a consensus between the American Academy of Allergy, Asthma, and Immunology and other American associations state that introducing eggs and peanuts to the diet of a newborn around the 6th month of life decreases the risk of developing an allergy to them in later years of life (but they should not be given before the 4th month of life) [35]. According to our study and many others, apart from food-related allergens, medications and cosmetics are also relevant triggers of anaphylaxis [36]. Interestingly, although insects' venom is also mentioned as an important cause of severe allergic reactions, there was not a single such case in our research. It is worth noting, however, that there is one Polish study pointing to completely different main causes of anaphylaxis in children – Hymenoptera venom (over 40%), drugs (almost 30%), and food (only about 15%). Our research work presents results much more similar to foreign data (food represents 55% of the causes, and medications 12.5%, with no cases of anaphylaxis caused by Hymenoptera venom) [37].

The incidence of anaphylaxis, regardless of the cause, is almost 3 times higher in children aged 0–4 than in other age groups [26]. As regards gender, one large study showed that anaphylaxis is more likely to occur in male newborns (around 70% of cases), but the ratio changes with the age, and in the group of children aged 12–16, the majority of those affected were female (around 60%) [1]. Overall, our study shows a greater number of male patients, which is also reflected in other studies [1, 12]. In the adult population of western countries, women are more likely to experience an anaphylactic event than men [38, 39]. Because of the differences between the prevalen-

ce of anaphylaxis in prepubertal and reproductive age, it is suggested that female sex hormones can play some role in the occurrence of anaphylaxis and could possibly be a risk factor [39, 40]. Our study showed that the decision on whether pharmacotherapy should be implemented does not differ significantly between the genders.

LIMITATIONS OF THE STUDY

Even though the initial number of Emergency Medical Cards analyzed was large, our study was not able to gather a large group of patients with anaphylactic reactions, due to the relative rarity of this condition. In order to provide further insight into this topic, a multi-center study with the same aims is needed. Moreover, the nature of the EMS interventions makes it difficult to precisely assess the symptoms and vital signs in patients with a severe allergic or anaphylactic reaction. The symptoms of anaphylactic reactions vary; they may be similar to and may imitate some other diseases. Therefore, some patients with real anaphylactic reactions were probably initially diagnosed with other diseases (by the EMS) and hence were not included in our study. Moreover, anaphylactic events are inevitably highly stressful both for the child and for the relatives. Therefore, we were not able to determine the appropriateness of the treatment in every patient, or whether some patients who were not administered adrenaline should have received such pharmacotherapy.

CONCLUSIONS

Anaphylaxis or a severe allergic reaction is a rare event – it concerned only 1.64% of patients brought to the pediatric emergency department by emergency medical teams. There was no correlation between the use of pre-hospital pharmacotherapy and the need for hospitalization of a pediatric patient. No statistically significant differences were found between the fate of the patient and emergency medical teams with or without a doctor. No correlation was found between gender and the frequency of pre-hospital drug administration in pediatric patients. Emergency medical teams in children with anaphylactic reactions are more likely to decide to administer pre-hospital medications than not. Epinephrine is a drug rarely administered in the pediatric population with anaphylaxis. Steroids are the most commonly used drugs in pediatric cases of anaphylaxis and severe allergic reactions. Food was the leading cause of severe allergic reactions in children.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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