REVISTA CHILENA DE PEDIATRÍA
www.revistachilenadepediatria.cl
www.scielo.cl

Rev Chil Pediatr. 2019;90(1):44-51
DOI: 10.32641/rchped.v90i1.839

ORIGINAL ARTICLE

Detection and management of Anaphylaxis in children

Reconocimiento y manejo de la Anafilaxia en pediatría

Fustiñana Ana Laura[a], Rino Pedro B.[a], Kohn-Loncarica Guillermo A.[a]

[a]Unidad de Emergencias del Hospital de Pediatría Prof. Dr. Juan P. Garrahan. Argentina.

Recibido: 17-7-2018; Aceptado: 23-10-2018

Abstract

Introduction: Anaphylaxis is an emergency condition. According to the latest international guidelines, early recognition and treatment with intramuscular epinephrine are associated with increased survival. **Objective:** To determine the level of knowledge of pediatricians in a tertiary Pediatric Hospital about the diagnostic criteria and treatment of anaphylaxis. **Material and Method:** A cross-sectional descriptive study was conducted, designing, applying, and validating an anonymous survey to physicians with complete residency in pediatrics who are on call at a third level hospital. The statistical analysis was made using the SPSS v.21 software, presenting measures of central tendency (median, range, and frequency table) and Chi-square test for comparison. A value of $p < 0.05$ was considered significant. **Results:** 71 physicians completed the survey with a median of three years after the end of residency.35% of them identified all clinical criteria, 99% (70) indicated epinephrine, 73% chose the intramuscular route, and 55% indicated the correct dose. Only 48% of responders chose the dose and administration route correctly. In general, 21% recognized anaphylaxis and used epinephrine correctly. Physicians with less than five years of experience performed better in the intramuscular administration of epinephrine (83% vs 52% $p = 0.005$) and in the detection of gastrointestinal symptoms (60% vs 35% $p = 0.043$). **Conclusions:** There are difficulties in the identification and proper management of anaphylaxis by pediatricians of a tertiary Pediatric Hospital in a theoretical clinical setting. Although most of pediatricians chose epinephrine as a first-line drug, half of them did not indicate it correctly, and only one-third recognized anaphylaxis in all scenarios.

Keywords:
Anaphylaxis;
epinephrine;
emergency treatment;
early diagnosis

Correspondence:
Ana Fustiñana
anafusti@hotmail.com

How to cite this article: Rev Chil Pediatr 2019;90(1):44-51. DOI: 10.32641/rchped.v90i1.839

Introduction

Anaphylaxis is an emergency in which early recognition and management save lives. The clinical criteria recognition (table 1) defined in 2005 during an expert meeting of the U.S. National Institutes of Health (NIH)[3] and the intramuscular epinephrine as the drug of choice and first treatment action are key in reversing symptoms according to the latest recommendations[4-7].

In the last 15 years, it has been observed an anaphylaxis incidence increase in the USA and Europe[8,9]. Between 2008 and 2014, consultations due to anaphylaxis increased by 147%[10] in the US pediatric emergency departments (PEDS), in addition to an increase in food allergies in children between 1997 and 2007[11].

PEDS are often the first place of anaphylaxis care. Despite the increase in the number of cases, there are still difficulties in the recognition and proper management of the condition[12-16]. Faced with this reality, we decided to conduct a survey to pediatricians who assist emergencies in a tertiary Pediatric Hospital in order to evaluate the knowledge about the latest recommendations[4-7] on anaphylaxis management and recognition.

Material and Method

Descriptive cross-sectional study, conducted through the survey design and implementation on August 24, 2016 at the Hospital de Pediatría "Prof. Dr. Juan P. Garrahan", a tertiary, 534-bed Pediatric hospital (Ciudad Autónoma de Buenos Aires (CABA), Argentina), with about 90,000 Pediatric Emergency Department visits (PED) per year and 300 Intermediate and Moderate Care (IMC) beds. *Population:* Pediatricians (physicians with complete pediatric residency) who do shifts* in the IMC and PED units. Those physicians who were on medical leave at the time of the survey as well as PED fellows and staff physicians** were excluded. The number of service years after completing the pediatric residency was recorded.

The *survey* (Figure 1) was self-administered and anonymous. In order to avoid consultations with other colleagues or bibliographic sources, surveys were conducted under direct observation by the same operator. The survey was elaborated based on other published surveys[17,18] and was adapted to our objective. The design was carried out by senior PED physicians. In order to validate it, four physicians with experience in caring for patients in emergency situations, who did not participate in the study, received the survey and their suggestions led to the final version (*face validity*) which consists of nine items of multiple-choice and short answer questions. The items comprise three dimensions, operator experience (two items), pharmacological management (three items), and clinical picture identification (four items). Informed consent was requested.

The study was conducted on a single day for eight consecutive hours in order to prevent dissemination of the content. It was given in a sealed envelope to ensure anonymity. Consent was recorded on a separate sheet to ensure confidentiality. In order to reduce information bias and to improve the instrument reliability, a single operator was responsible for administering the survey. For statistical analysis, the SPSSv.21 statistical software was used; for numerical and categorical variables, measures of central tendency were used (median, range, and frequencies table), and for their comparison, Chi-square test was used. A $p-< 0.05$ value was considered statistically significant.

Results

At the "Prof. Dr. Juan P. Garrahan" pediatric hospital, 100 physicians with complete pediatric residency perform shifts in the IMC and PED units. 71 physicians were surveyed and 29 were excluded (18 were on medical leave, three were unavailable, five were PED staff physicians, and three were PEDs fellows). 67 out of 71 answered the survey completely. The median of years since the end of residence was three years (0.1-24 years). 69% (49) reported having ever witnessed an anaphylaxis episode in their daily practice.

Four questions were asked to assess knowledge of the diagnostic criteria published in 2005 by NIH[1] (table 2). Only 35% (25) recognized all anaphylaxis criteria.

Although 99% (70) choose epinephrine as the first-choice drug for treatment (table 3), only 73% (52) indicated it by the recommended route (intramuscular), and 55% (39) at the appropriate dose (0.01 mg/kg). When we fully analyzed the epinephrine indication (choice, dose, and route), we observed that 48% (34) answered correctly.

When analyzing globally, both the clinical recognition of anaphylaxis and the correct choice and use of epinephrine, we noticed that only 21% (15) of the respondents answered adequately.

Finally, when we compare anaphylaxis management according to the respondent experience (table 4),

* At Juan P. Garrahan Hospital, on-call shifts are from 16 to 8 hours on weekdays and 24 hours on non-working days. During this period the medical work is performed by staff doctors who once a week extend their schedule.

** Pediatricians who perform their duties Monday through Friday from 8 a.m. to 4 p.m. in a Unit or Service of the institution.

Table 1. Clinical criteria for the diagnosis of anaphylaxis and its differences with urticaria and hereditary angiedema

Clínical Condition	Definition	physiopathology	Diagnosis	First-line treatment
Urticaria[1]	Development of hives, angioedema or both	Degranulation of mast cells	Clinical diagnosis	Second generation histamine H1 blockers
Hereditary angioedema[2]	Vascular reaction of the dermis or mucosal/submucosal tissue resulting in edema that can cause asphyxia	Vascular reaction secondary to the production of bradykinins due to deficiency or dysfunction of the C1 inhibitor (C1-INH)	Is suspect if: 1. Family History 2. Onset in childhood or adolescence 3. Recurrent abdominal pain 4. Upper respiratory tract swelling 5. Lack of response to treatment with antihistamines, corticosteroid or epinephrine 6. Prodromal symptoms 7. Absence of urticaria Diagnosis: Low dosaje of C4 and low dosaje or dysfunction of C1-INH	Plasma derived human C1-Inhibidor concentrate C1-INH recombinant concentrate Prophylaxis should be done in some procedures (odontogenic, endoscopic)
Anaphylaxis[3]	A serious, life-threatening generalized or systemic hypersensitivity reaction" and "a serious allergic reaction that is rapid in onset and might cause death"	IgE-mediated reaction or immune complexes mediated	Anaphylaxis is highly likely when any one of the following three criteria is fulfilled: 1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both And at least one of the following: a. Respiratory compromise b. Reduced blood pressure or associated symptoms of end-organ dysfunction (eg. hypotonia [collapse], syncope, incontinence) OR 2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours): a. Involvement of the skin-mucosal tissue b. Respiratory compromise c. Reduced blood pressure or associated symptoms (eg, hypotonia [collapse], syncope, incontinence) d. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting) OR 3. Reduced blood pressure after exposure to known allergen for that patient (minutes to several hours) a. Infants and children: low systolic blood pressure (age-specific) or greater than 30% decrease in systolic blood pressure b. Adults: systolic blood pressure of less than 90 mm Hg or greater than 30% decrease from that person's baseline	Inject epinephrine intramuscularly in the mid-anterolateral aspect of the thigh, 0.01 mg/kg of a 1:1,000 (1 mg/mL) solution, to a maximum of 0.5 mg (adult) or 0.3 mg (child) Place patient on the back, or in a position of comfort if there is respiratory distress and/or vomiting Give high flow supplemental oxygen by face mask If cardiovascular system is involve give rapidly fluid (fluid bolus of 20 ml/kg of cristalloid)

SBP= systolic blood pressure. Low systolic blood pressure for children is defined as less than 70 mmHg from 1 month to 1 year, less than (70 mm Hg + (2 x age]) from 1 to 10 years, and less than 90 mmHg from 11 to 17 years.

1. How many years/months have you been working since you completed your residency in pediatrics? _____ years or _____months
2. Have you ever treated a patient with anaphylaxis? YES ( ) NO ( )
3. Which is the first line drug for the treatment of anaphylaxis? _____ (fill in the blank with a single drug)
   3.a) What is the route of administration for this drug ?: Oral ( ) IV ( ) IM ( ) SC ( ) (Mark with a cross the one that corresponds)
   3.b) What is the appropriate dose for the drug? (mg/kg): _____ (fill in the blank with a dose)
4. Which of the following symptoms do you consider to be in the presence of anaphylaxis? (Mark with a cross the option or options that you consider correct or leave the box empty)
   A. Acute urticara and bronchospasm
   B. Sudden onset after exposure to an allergen of an itching generalized rash and persistent vomiting
   C. Acute onset of itch-flush
   D. Syncope and bradycardia the minutes after the infusion of a drug by IV route

Figure 1. Survey on the management and treatment of anaphylaxis answered by surveyed doctors. Oral = oral route; IV = intravenous route; IM = intramuscular route; SC = subcutaneous route.

Table 2. Recognition of clinical criteria for the diagnosis of anaphylaxis

Clinical criteria	n = 71(%)
Mucocutaneous + respiratory	60 (85)
Mucocutaneous + gastrointestinal	37 (52)
Neurological + cardiovascular	60 (85)
Mucocutaneous*	10 (14)

Clinical criteria for the diagnosis of anaphylaxis by NIH. *The isolate mucocutaneous compromise is not a clinical criteria.

Table 3. Dose and route of epinephrine administration

Epinephrine		n 70, (%)
Route of administration	IM	52 (74)
	SC	5 (7)
	IV	13 (19)
Dose	0.01 mg/kg	39 (56)
	0.1 mg/kg	25 (36)
	1 mg/kg	2 (3)
	0.001 mg/kg	1 (1)
	DR	3 (4)

IM = intramuscular, SC = subcutaneous IV = intravenous, DR = Don´t response. There was one respondent who did not choose epinephrine as a first-line drug.

Table 4. Comparison between respondents with less or more than 5 years in practice in the recognition and management of anaphylaxis

Recognition and treatment		Years in practice < 5 years n 48, (%)	Years in practice > 5 years n 23, (%)	p*
Recognition of anaphylaxis clinical criteria n (71)	Respiratory + Skin/mucosal	41 (85)	19 (83)	0.76
	Skin/mucosal + Gastrointestinal	29 (60)	8 (35)	0.043
	Nervous system + Cardiovascular	39 (81)	21 (91)	0.27
	Isolated skin compromise**	8 (17)	2 (9)	0.37
	Recognition of all the anaphylaxis clinical criteria	20 (42)	5 (22)	0.1
Treatment with epinephrine n (70)	Epinephrine by IM route	40 (83)	12 (52)	0.006
	Epinephrine dose of 0.01 mg/kg	31 (65)	8 (35)	0.1
	Appropriate administration of epinephrine (epinephrine by IM route + dose 0,01 mg/kg)	28 (58)	6 (26)	0.024

NIH clinical criteria: Skin/mucosal = involvement of the skin, mucosal tissue o both; Respiratory = respiratory compromise; Gastrointestinal = persistent gastrointestinal symptoms, nervous system=neurologic symptoms; Cardiovascular = Reduce blood pressure or associated symptoms; IM = intramuscular route; Epinephrine appropriate administration = 0,01 mg/kg of epinephrine by intramuscular route. *p = chi2 tests. **Is not a NIH criteria.

we observe that those with less than five years in practice more frequently recognize the association of persistent gastrointestinal symptoms and mucocutaneous symptoms (60% vs 35% p = 0.043), and administer epinephrine intramuscularly more frequently (83% vs 52% p = 0.006).

Discussion

A study published by Campbell et al.[26] in 2012 showed that the diagnostic criteria established in 2005 by the National Institute of Allergy and Infectious Diseases and the Food Allergy and Anaphylaxis Network (NIAID/FAAN) have 96.5% of diagnostic sensitivity and 82.4% of specificity. However, gaps in the anaphylaxis recognition are still a global problem today.

Currently, the WHO International Classification of Diseases (ICD-9 and ICD-10) for anaphylaxis generates confusion among users since it considers hypotension or shock in its definition and does not include other NIH criteria, thus contributing to the underdiagnosis[27,28]. Possibly, this situation changes soon after the ICD-11 publication which has a new section on "Allergic and hypersensitivity conditions" within the chapter on "Immune system disorders" which recognizes anaphylaxis as a clinical condition for the first time[29,30].

Another frequent obstacle to recognition is the use of anaphylactic shock and anaphylaxis as synonyms. It should be considered that hypotension in children is rare as shown by retrospective studies in pediatric PEDS. Alvarez-Perea et al.[13] described a series of 133 children with anaphylaxis in which only 7% had shock, and Goetz et al.[14] observed that, among 211 children with anaphylaxis, only 2% had hypotension associated with other symptoms and none of them had isolated hypotension associated with allergen (NIH criterion 3).

Most surveys conducted worldwide (table 5) emphasize more the choice and appropriate administration of epinephrine than the clinical picture recognition, which leads to its administration. Our results, coinciding with the surveys conducted by Wang et al.[12] and Jacobsen et al.[31], showed that classical presentations with skin and/or mucosa involvement, respiratory symptoms, and shock were more easily recognized than those less frequent cases with gastrointestinal involvement. When there is no skin involvement (10-20%)[32], Jacobsen et al.[31] and Wang et al.[12] observed that only 3% and 50% of respondents, respectively, recognized the condition.

Reviewing clinical records of children treated in the PED, Alvarez Perea et al.[13] found that anaphylaxis was recognized only in 53% of cases. The remaining patients were admitted with diagnosis of urticaria, angioedema, or allergic reaction, and did not receive adequate treatment.

The use of a standardized definition, key to recognition, is scarce. In Brazil, Russell et al.[33] reported that 90% of PEDs do not use standardized criteria.

The many barriers to the proper and timely identification of anaphylaxis is still a universal public health concern. The observed results in our survey reinforce the need to increase all the necessary measures to enhance the dissemination of clinical criteria in order to improve the recognition of the condition and give way to treatment.

Another assessed aspect of the survey was the internationally recommended first-line treatment[4-7]. When we compare our results regarding the choice of epinephrine as a first-line drug with other surveys on physicians (table 5), the outcomes are similar (between 85-95%). But when we observe the clinical condition management according to the data provided by retrospective studies in pediatric PEDs, Álvarez-Perea et al.[13], Goetz et al.[14], Wright et al.[15], and Robinson et al.[16] report that epinephrine is administered in children only between 32% and 68% of anaphylaxis episodes. On the other hand, Álvarez-Perea et al.[13] and Wright et al.[15] described high use of corticosteroids (81% and 51%, respectively), and antihistamines (63% and 62%, respectively) as first-choice drugs. Wright et al.[15] justified this discrepancy due to the lack of anaphylaxis management protocols in PEDs, poor knowledge of treatment guidelines, and misconceptions about the safety of intramuscular epinephrine in its management.

In our study, the intramuscular route selection (73%) and the dose of 0.01 mg/kg (55%) were similar to the analyzed surveys and higher in some cases (table 5). However, we noticed that in our results 18% chose the intravenous route and 35% administered higher doses than recommended. Cardona et al.[34] described that the intravenous epinephrine administration and the use of higher doses than recommended were associated with a higher frequency of adverse effects but did not observe higher morbidity and mortality.

Finally, we decided to evaluate whether the professional years in practice are related to adequate recognition and treatment according to the latest recommendations[4-7]. As Coletti et al.[17], we found that physicians with fewer years in practice indicate in greater proportion intramuscular epinephrine. Conversely, Grossman et al.[18] did not find an association with the years in practice but did with those who had carried out residency programs. Our analysis also shows that physicians with fewer years in practice recognized gastrointestinal symptoms better. These differences could be due to an increase in the number of publications on

Table 5. Summary of surveys that evaluate the recognition and treatment of anaphylaxis by physicians and nurses

Publication	Survey population/ Modality[1]	Use of epinephrine[2]			Recognized clinical criteria[3]			
		EP 1ra %	IM %	Dose %	Skin + Mucous %	Skin + Resp %	Skin + Low BP %	Low BP + Allergen %
Jose et al 2007[19]	95 Resident, P author presence	94	58	-	-	-	-	-
Grossman et al 2013[18]	620 PEM web	94	67	-	-	-	-	-
Baççioğlu et al 2013[20]	1172 P, N, M Stu, PM e mail	45	29	29	-	-	-	-
De Solé et al 2013[21]	350 A 160 M not A web	70 (M no A) 90 (A)	24 (M no A) 78 (A)	-	-	-	-	-
Ibrahim et al 2014[22]	190 N,P author presence and anonymous	T: 53 M (89) E (40)	T: 57 M (85) E (47)	T: 58 M (73) E (50)	T: 73 M (42) E (84)	T: 89 M (94) E (87)	T: 93 M (98) E (91)	T: 85 M (93) E (82)
Wang et al 2014[12]	7822 Medscape members web	95	-	-	5	85	-	57
Plumb et al 2015[23]	68 P autor presence anonymous	100	74	-	21	100	-	-
Altman et al 2015[24]	318 P by telephone	81-98	-	-	-	-	-	-
Colleti Junior et al 2016[17]	43 P PICU author presence	84	42	-	-	-	-	-
Drupad et al 2015[25]	265 M Stu. N Stu. N Medical interns	57	16,5	26	-	-	-	-

1) In population column: P = physician; N = nurse; Stu = student; A = allergist; PEM = pediatric emergency physician; PM = paramedic; M = medical; PICU = pediatric intensive care unit. 2) In use of epinephrine column: EP 1ra = epinephrine as first line drug; T = total percentage; IM = Epinephrine by intramuscular route; Dose = correct dose (0,01mg/kg) of epinephrine. 3) In recognized clinical criteria column: Skin and mocous = concomitant skin and mocous symptoms (is not one of the three clinical NIH criteria); skin + resp = Concomitant skin and/or mocous and respiratory symptoms (first criteria of NIH); Skin + Low BP = Concomitant skin and/or mucous plus low blood pressure (second criteria of NIH); Low BP + allergen= Low blod pressure ans allergen exposition (third NIH criteria).

the subject in recent years[30], to a more recent training, to the incorporation of the subject in the latest emergency congresses in the region, and in the curriculum of residents.

There are certain limitations in our study; surveys do not always reflect action in real situations, and the answers to multiple-choice surveys on a specific topic can be biased. However, the survey results have allowed us to take educational and training measures aimed at the institution's health personnel.

Conclusion

There are difficulties in the anaphylaxis identification and appropriate management by pediatricians from a tertiary hospital in a theoretical setting. Only one-third of respondents (35%) were able to recognize all clinical criteria for anaphylaxis, which could imply the existence of anaphylaxis underdiagnosis. Although most of the respondents chose epinephrine as first-line drug, more than half of them used it incorrectly, with

the risks involved (undertreatment and/or adverse effects). Finally, only 21% identified and treated adequately the condition. These results suggest the development of educational strategies and clinical care protocols to optimize the management of this type of events that require urgent action.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Financial Disclosure

Authors state that no economic support has been associated with the present study.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Aknowledgments

The authors thank Dra. Susana Rodriguez, for providing statistical analysis for this manuscript.

References

1. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA(2) LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. Allergy. 2014;69:868-87.
2. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema -The 2017revision and update. Allergy. 2018; 73:1575-96.
3. Sampson HA, Muñoz-Furlong A, Campbell RL, et al. Second symposium on the definition management of anaphylaxis: summary report-Second National Institute of and Infectious Disease/Food Allergy Anaphylaxis Network symposium. J Allergy Clin Immunol. 2006;117:391-7.
4. Muraro A, Roberts G, Worm M, et al. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. Allergy. 2014;69:1026-45.
5. Lieberman P, Nicklas RA, Randolph C, Oppenheimer J, Bernstein D, Bernstein J. Anaphylaxis: a practice parameter update 2015. Annals of Allergy, Asthma & Immunology. 2015;115:341-84.
6. Campbell RL, Li J, Nicklas RA, Sadosty M. Emergency department diagnosis and treatment of anaphylaxis. 2013. Ann Allergy Asthma Immunol. 2014;113:599-608.
7. Comité Nacional de Alergia. Actualización en las recomendaciones del tratamiento del choque anafiláctico: novedades sobre el uso de adrenalina. Arch Argent Pediatr. 2015;113:81-7.
8. Moneret-Vautrin DA, Morisset M, Flabbee J, Beaudouin E, Kanny G. Epidemiology of life-threatening and lethal anaphylaxis: a review. Allergy. 2005; 60:443-51.
9. Panesar SS, Javad S, de Silva D, et al. The epidemiology of anaphylaxis in Europe: a systematic review. Allergy. 2013;68:1353-1361.
10. Michelson KA, Hudgins JD, Burke LG, et al. Trends in Severe Pediatric Emergency Conditions in a National Cohort, 2008 to 2014. Pediatr Emer Care 2018;00:00-00.
11. Branum AM, Lukacs SL. Food Allergy Among Children in the United States. Pediatrics. 2009;124:1549-55.
12. Wang J, Young MC, Nowak-Wegrzyn A. International survey of knowledge of food-induced anaphylaxis. Pediatr Allergi Immunol. 2104;25:644-50.
13. Alvarez-Perea A, Ameiro B, Morales C, et al. Anaphylaxis in the Pediatric Emergency Department: Anaphylaxis of 133 Cases After and Allergy Workup. J Allergy Clin Inmunol Pract. 2017;5:1256-1263.
14. Goetz VL, Kim K, Stang AS. Pediatric anaphylaxis in the Emergency Department. Clinical Presentation, Quality of care, and Reliability of Consensus Criteria. Pediatr Emer Care. 2017;11:00-00.
15. Wright CD, Longiohn M, Lieberman PL, Lieberman JA. An analysis of anaphylaxis cases at a single pediatric emergency department during a 1-year period. Ann Allergy Asthma Immunol. 2017;118:461-4.
16. Robinson M, Greenhawt M, Stukus DR. Factors Associated with epinephrine administration for anaphylaxis in children before arrival to the emergency department: Ann Allergy Asthma Immonol. 2017;119:164-9.
17. Colleti J, de Carvalho WB. Anaphylaxis Knowledge Among Pediatric Intensivists in Brazil: A Multicenter Survey. J Intensive Care Med. 2017;32:593-6.
18. Grossman SL, Baumann BM, García Peña BM, Linares MY, Greenberg B, Hernandez-Trujillo VP. Anaphylaxis knowledge and practice of pediatric emergency medicine physicians: A national survey. J Pediatr. 2013;163: 841-6.
19. Jose R, Clesham GJ. Survey of the use of epinephrine (adrenaline) for anaphylaxis by junior hospital doctors. Postgrad Med J. 2007;83:610-611.
20. Baççıoğlu A, Yılmazel Uçar E. Level of knowledge about anaphylaxis among health care providers. Tuberk Toraks 2013;61:140-6.
21. Sole D, Ivancevich JC, Cardona V. Knowledge of anaphylaxis among Ibero-American physicians: Results of the Ibero-American online survey for physicians on the management and treatment of anaphylaxis (IOSPTA)- Latin American Society of Allergy, Asthma & Immunology (LASAAI). J Investig Allergol Clin Immunol 2013;23:441-3.
22. Ibrahim I, Chew BL, Zaw WW, Van Bever HP. Knowledge of anaphylaxis among emergency department staff. Asia Pac

Allergy. 2014;4:164-71.
23. Plumb B, Bright P, Gompels MM, Unsworth DJ. Correct recognition and management of anaphylaxis: not much change over a decade. Postgrad Med J. 2015;91:3-7.
24. Altman A, Camargo CA Jr, Simons FE, et al. Anaphylaxis in America: A national physician survey. J Allergy Immunol. 2015;135:830-3.
25. Drupad HS, Nagabushan H. Level of knowledge about anaphylaxis and its management among health care providers. Indian J Crit Care Med. 2015;19:412-5.
26. Campbell RL, Hagan JB, Manivannan V, et al. Evaluation of National Institute of Allergy and Infectious Diseases/ Food Allergy and Anaphylaxis Network criteria for the diagnosis of anaphylaxis in emergency department patients. J. Allergy Clin Inmunol. 2012;129:748-52.
27. Simons FE, Sampson HA. Anaphylaxis epidemic: Fact or fiction? J Allergy Clin Immunol. 2008;122:1166-8.
28. Tanno LK, Ganem F, Demoly P, Toscano CM, Bierrenbach AL. Undernotification of anaphylaxis deaths in Brazil due to difficult coding under the ICD-10. Allergy 2012;67:783-9.
29. Kase Tanno L, Bierrenbach AL, Simons FER, et al. Critical view of anaphylaxis epidemiology: open questions and new perspectives. Allergy Asthma Clin Immunol. 2018;14:12
30. Kase Tanno L, Chalmers RJG, Calderón MA, Aymé S, Demoly P, on behalf the Joint Allergy Academies (2017). Reaching multidisciplinary consensus on classification of anaphylaxis for the eleventh revision of the World Health Organization's (WHO) International Classification of Diseases (ICD-11). Orphanet J Rare Dis. 2017; 12: 53.
31. Jacobsen RC, Toy S, Bonham AJ, Salomone JA 3rd, Ruthstrom J, Gratton M. Anaphylaxis knowledge among paramedics: results of a national survey. Prehosp Emerg Care. 2012;16:527-34.
32. Lieberman P, Nicklas RA, Oppenheimer J, et al. The diagnosis and management of anaphylaxis practice parameter: 2010 Update. J Allergy Clin Immunol. 2010;126:477-80.
33. Russell SW, Farrar JR, Nowak R, et al. Evaluating the management of anaphylaxis in US emergency departments: Guidelines vs. practice. World J Emerg Med 2013; 4:98-106.
34. Cardona V, Ferré-Ybarz L, Guilarte M, et al. Safety of Adrenaline Use in Anaphylaxis: A multicentre Register. Int Arch Allergy Immunol. 2017;173:171-7.