

Original Article



Physicians' knowledge regarding epinephrine underuse in anaphylaxis

Joaquin A. Pimentel-Hayashi *, Elsy M. Navarrete-Rodriguez ,
Oscar I. Moreno-Laflor , and Blanca E. Del Rio-Navarro

Department of Allergy and Immunology, WAO Center of Excellence, Hospital Infantil de México Federico Gomez, Mexico City, Mexico.

OPEN ACCESS

Received: Sep 18, 2020

Accepted: Oct 21, 2020

*Correspondence to

Joaquin A. Pimentel-Hayashi

Department of Allergy and Immunology,
WAO Center of Excellence, Hospital Infantil
de Mexico Federico Gomez, Dr. Marquez 162,
Doctores, Mexico City, Mexico.
Tel: +52-55-5228-9917
E-mail: joacopim22@msn.com

Copyright © 2020. Asia Pacific Association of Allergy, Asthma and Clinical Immunology. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Joaquin A. Pimentel-Hayashi
<https://orcid.org/0000-0001-7130-5969>
Elsy M. Navarrete-Rodriguez
<https://orcid.org/0000-0001-9876-3206>
Oscar I. Moreno-Laflor
<https://orcid.org/0000-0003-3287-7002>
Blanca E. Del Rio-Navarro
<https://orcid.org/0000-0001-6441-8869>

Conflict of Interest

The authors have no financial conflicts of interest.

Author Contributions

Conceptualization: Joaquin A. Pimentel-Hayashi, Elsy M. Navarrete-Rodriguez. Data curation: Joaquin A. Pimentel-Hayashi, Oscar

ABSTRACT

Background: Anaphylaxis is a life-threatening hypersensitivity reaction. Epinephrine underuse in patients with anaphylaxis could lead to poor outcomes. There is evidence that the epinephrine use in such patients could be as low as 8%.

Objective: To assess the percentage of physicians who know that epinephrine is the first-line treatment in anaphylaxis. The secondary objective was to assess knowledge gaps regarding anaphylaxis diagnosis and treatment that could lead to epinephrine underuse.

Methods: We performed an online survey for physicians in Mexico City, using a 10-item questionnaire assessing anaphylaxis knowledge. We obtained measures of central tendency for statistical analysis, such as frequency, 95% confidence interval, as well as the chi-square test for comparing the groups.

Results: A total of 196 surveys were considered for analysis. Of all the participants, 96.44% were able to correctly diagnose an anaphylaxis case with cutaneous, respiratory, and cardiovascular symptoms. Fifty-two percent correctly diagnosed anaphylaxis without cutaneous symptoms. The 72.4% of the respondents chose epinephrine as the first-line treatment, 42.3% correctly answered that there is no absolute contraindication to giving epinephrine, and 20.9% ignored whether there was any contraindication for its use. Only 38.3% of participants answered that during discharge they would prescribe an autoinjector. Regarding the administration route, 63.4% answered that the first dose of epinephrine is applied intramuscularly and 50% of the participants chose the correct dose of epinephrine. Only 2.6% of the participants answered all 10 questions correctly.

Conclusion: There is still some difficulty recognizing anaphylaxis without cutaneous symptoms. Even though two-thirds of physicians identified that epinephrine is the treatment of choice, only 49.5% would have used intramuscular epinephrine as first-line treatment. We found a low percentage of epinephrine ampule prescription and knowledge of the correct dose. These findings can account for epinephrine underuse when dealing with anaphylaxis in the real clinical practice.

Keywords: Anaphylaxis; Epinephrine; Surveys and questionnaires; Knowledge; Attitudes

I. Moreno-Laflo. Formal analysis: Elsy M. Navarrete-Rodriguez., Oscar I. Moreno-Laflo. Methodology: Elsy M. Navarrete-Rodriguez, Joaquin A. Pimentel-Hayashi. Project administration: Elsy M. Navarrete-Rodriguez, Blanca E. Del Rio-Navarro. Visualization: Blanca E. Del Rio-Navarro, Elsy M. Navarrete-Rodriguez. Writing - original draft: Joaquin A. Pimentel-Hayashi, Elsy M. Navarrete-Rodriguez. Writing - review & editing: Joaquin A. Pimentel-Hayashi, Blanca E. Del Rio-Navarro.

INTRODUCTION

Anaphylaxis is a life-threatening hypersensitivity reaction, with fast onset and with variable symptoms [1]. Epinephrine is the first-line therapy for patients with anaphylaxis [2]; and so far, there is no absolute contraindication for its use [3]. Currently, the recommendation is the use of intramuscular (IM) epinephrine with repetitive dosing every 5 to 15 minutes depending on response. Additionally, in case the blood pressure does not improve after multiple dosing, an intravenous (IV) infusion is recommended [2, 4].

Epinephrine is a catecholamine that exerts its mechanism of action on the alpha and beta-adrenergic receptors, causing multiple effects such as vasoconstriction (alpha-1 receptors), increase in heart rate, myocardial contractility, renin release (beta-1 receptors), and bronchodilation (beta-2 receptors) [2].

The use of epinephrine in anaphylaxis treatment is seldom frequent, both in the Emergency Department (ED) and in ambulatory care, in spite of the clear indication of its benefit. Percentages of use as low as 24% have been reported in pediatric populations, especially in those under 7 years of age, and up to 36.9% in adults [5]. Ninchoji et al. [6] reported that epinephrine use in hospitals was scarcely 8% and that the use of epinephrine before the patients' arrival to the ED was 0% due to the lack of prescription of an autoinjector.

There is no clear evidence regarding the reasons why lead doctors choose not to use epinephrine in patients with anaphylaxis. Therefore, it is crucial to gather evidence to increase its prescription.

The aim of this study was to assess anaphylaxis knowledge, the frequency of epinephrine use by physicians who work in large hospitals in Mexico City, as well as the route of administration, and the possible causes of lack of use of this medication in patients with anaphylaxis.

MATERIALS AND METHODS

The following research was a transversal, comparative study based on performing an online questionnaire to pediatrics residents, pediatricians, internal medicine physicians, cardiologists, emergency medicine doctors, general surgeons, anesthesiologists, and gynecologists. The online questionnaire consisted of questions relating to the diagnosis of anaphylaxis, epinephrine use, dosage, route of administration, and main causes to avoid its use.

We followed accepted guidelines for survey development in medical research [7-9]. The questionnaire was elaborated by 3 pediatric allergists and reviewed by a panel of 6 experts in anaphylaxis, who evaluated the objective of each of the 10 questions in the survey using the Likert scale. When answers regarding the adequacy of questions were "neutral," "in disagreement," or "totally in disagreement," the reviewers were asked to provide ways of modifying each item so they could fulfill its objective. Three rounds were required to reach consensus, in which all the experts agreed with all the included questions.

Concerning the formulation of questions, the use of negatives and ambiguous words were avoided; correct medical terminology was selected, and the questions and answers were ordered so as to avoid predisposing the responders to choose a determined option. Five

answers were provided to each question in the survey, from which only one option was correct. In order to deter respondents from guessing, the option “I do not know” was always included.

The questions made reference to 2 clinical cases of anaphylaxis, 1 of them portraying cutaneous symptoms, and a second case without them. Participants were then questioned on the indication for the use of corticosteroids, antihistamines, and epinephrine, as well as the route of administration and the dose of epinephrine in both adults and children. It was also asked if they recognized any contraindication for the use of epinephrine. One question, in particular, was designed with the goal of knowing the percentage of respondents who would prescribe an autoinjector or its equivalent. The correct answers to the questionnaire were based on 4 anaphylaxis guidelines [1-4]. The survey was piloted with a representative group of residents and the study population was well defined.

The survey was sent through SurveyMonkey from May 1st to June 10th, 2020. The surveys included in the study were those with a response time of over 50 seconds but less than 15 minutes. We set up these response time exclusions based on pilot study insights, where we found that the mean time to answer each question was 3 minutes.

Microsoft Excel 2016 v16.0.6568.2036 (Microsoft Corp., Redmond, WA, USA) was used to arrange the collected data and IBM SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA) was selected to perform data analysis.

We obtained measures of central tendency for statistical analysis, such as frequency, 95% confidence interval, as well as the chi-square test for comparing the groups. We used a *p* value of 0.05 to determine statistical significance of analyses performed.

This study was approved by the Research Ethics Committee of Federico Gomez Children's Hospital of Mexico (HIM-2020-046). The questionnaire used for this study did not include physicians' personal details. Clinical data were deidentified and handled as linked anonymized data. Participation was voluntary and not subject to award of any benefit.

RESULTS

Two hundred and two questionnaires were received, 6 of which were discarded because the response time was longer than 15 minutes or less than 50 seconds. Therefore, a total of 196 surveys were considered for analysis. Overall, respondents were put into 3 groups. Group 1 (59.7%) included pediatricians and pediatric residents. Group 2 (28.1%) was constituted of internal medicine physicians, cardiologists, or anesthesiologists. Group 3 (12.2%) consisted of general surgeons, orthopedic doctors, and gynecologists.

The median of time to complete the survey was 201 seconds (51 seconds–14 minutes). There were no statistically significant differences among the 3 groups (*p* > 0.05).

Of all the participants, 96.44% were able to correctly diagnose the first anaphylaxis case, which presented cutaneous, respiratory, and cardiovascular symptoms. The second anaphylaxis case, which lacked cutaneous symptoms, was correctly diagnosed by 59.2% of the participants. Seventy-two percent of the respondents chose epinephrine as the first-line treatment; 42.3% of the participants correctly answered that there is no absolute

Table 1. Descriptive analysis: correct answers

Question	Group 1	Group 2	Group 3	Total (N = 196)
Anaphylaxis with cutaneous symptoms	114 (97.4)	52 (94.5)	23 (95.8)	189 (96.4)
Anaphylaxis without cutaneous symptoms	66 (56.4)	32 (58.2)	18 (75)	116 (59.2)
Epinephrine first-line treatment	85 (72.6)	39 (70.9)	18 (75)	142 (72.4)
Intramuscular epinephrine	73 (62.4)	35 (63.6)	18 (75)	126 (64.3)
Contraindication for epinephrine use	54 (46.2)	18 (32.7)	11 (45.8)	83 (42.3)
Correct dose of epinephrine	54 (46.2)	32 (58.2)	12 (50)	98 (50)
Autoinjector/epinephrine ampule prescription	50 (42.7)	19 (34.5)	6 (25)	75 (38.3)

Values are presented as number (%).

Group 1, pediatricians and pediatric residents; Group 2, internal medicine physicians, cardiologists, or anesthesiologists; Group 3, general surgeons, orthopedic doctors, and gynecologists.

contraindication to giving epinephrine in anaphylaxis, and 20.9% ignored whether there was any contraindication for epinephrine use. There were no statistically significant differences among the 3 groups ($p > 0.05$) (Table 1).

Thirty-eight percent of the participants answered that during discharge they would either prescribe an autoinjector or explain to the patient how to use an epinephrine ampule in case of an emergency. Regarding the route of administration, 63.4% answered that the first dose of epinephrine is applied intramuscularly, 22.4% subcutaneously, and 12.8% IV. Fifty percent of the participants chose the correct dose of epinephrine. The percentage of participants who chose the correct dose of epinephrine in each group is as follows: 46.2% in group 1, 58.2% in group 2, and 50% in group 3 (Table 1). There were no statistically significant differences among the 3 groups ($p > 0.05$).

Only 2.6% of the participants answered all 10 questions correctly; 39.3% answered 7 or more answers correctly. Forty-nine point five percent of the participants correctly indicated that epinephrine is the first-line therapy and that it is applied intramuscularly. Twenty percent of the respondents answered correctly the bundle of questions composed of epinephrine being the first-line treatment, IM route, the correct dose, and the accurate diagnosis of both anaphylaxis cases. However, only 7.1% of the participants answered the 5 previous questions correctly in addition to answering that there is no absolute contraindication for the use of epinephrine and that they would prescribe an autoinjector or an epinephrine ampule before discharging the patient (Fig. 1).

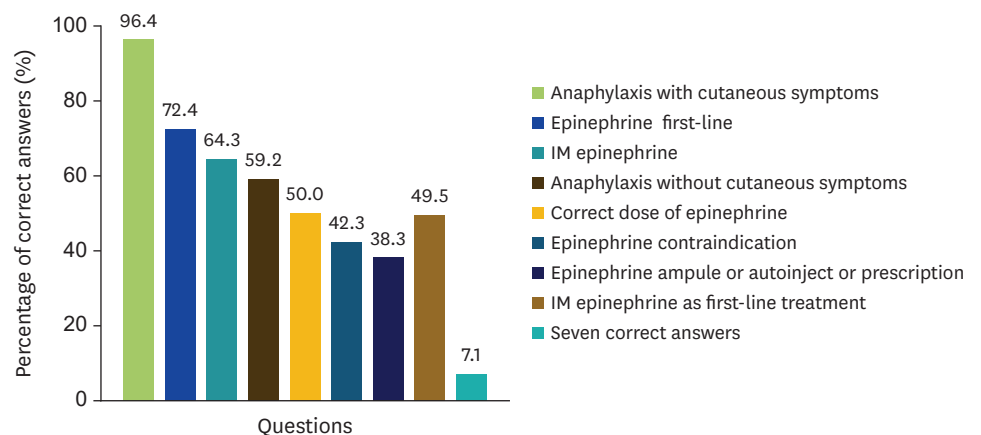


Fig. 1. Percentage of correct answers. Forty-nine percent of the respondents would prescribe intramuscular (IM) epinephrine as first-line treatment. Only 7.1% correctly identified both anaphylaxis cases, intramuscular epinephrine with the correct dosage as first-line treatment; and in addition, they would prescribe an autoinjector and knew that there is no contraindication for epinephrine use.

DISCUSSION

Mortality associated with anaphylaxis has decreased as time has gone by due to diverse reasons, mainly because of a more accurate diagnosis and better access to treatment. Currently, global mortality is reported as 0.5 to 1 case per million, in which food represents the most frequent trigger, and the pediatric population is the most affected group [10].

In spite of efforts to promote the use of IM epinephrine as first-line treatment in anaphylaxis, and the evidence of its safety when administered correctly [11, 12]; the percentage of its use is still low. Delayed application of epinephrine can lead to fatal outcomes [13]. Until now, there is no validated questionnaire for measuring physicians' knowledge about anaphylaxis. As far as we can tell, this is the first study in Mexico that has assessed healthcare workers' knowledge regarding the use of epinephrine in anaphylaxis. However, it is worth noting that Solé et al. [14] assessed epinephrine use in Ibero-American physicians.

It is important to promote the use of epinephrine in patients with anaphylaxis before their arrival to the ED among family members and nonmedical personnel. Robinson et al. [15] reported that only 36% of patients got epinephrine before their arrival to the ED and that this low percentage could be attributable to less than half the patients having a prescription for an autoinjector, with only two-thirds of them having it available at the onset of the symptoms.

Compared to other authors, we observed that the percentage of prescription of epinephrine ampules or autoinjectors was low. Grossman et al. [16] reported a prescription rate of 98%, although some studies found a percentage similar to ours [17, 18]. One of the possible causes of the low percentage we got is the scarce or nonexistent availability of autoinjectors in our country. Importantly, we emphasized in our questionnaire that participants had the option of prescribing an epinephrine ampule and explaining to the patient how to administer it in case of a new anaphylactic event. When it comes to Latin America, autoinjectors are only available in 2 countries, and Mexico is not one of them [19].

Regarding epinephrine use, Wang et al. [20] reported that only 59.5% of their participants used epinephrine and that it was administered as first-line therapy in just 74.1% of the patients. An interesting finding was that physicians are more likely to administer epinephrine in patients with respiratory symptoms.

There have been several studies performed to determine the causes of epinephrine underuse by physicians. We can only speculate this is due to physicians' lack of confidence in the diagnosis, or due to possible side effects of its administration [5].

The cardiovascular side effects associated with epinephrine use, are a consequence of wrong dosage and incorrect route of administration [21]. Campbell et al. [12] reported 8.3% of subcutaneous administration and 3.3% of IV administration; all the overdoses occurred in patients who had been administered IV epinephrine and only 1.3% of the patients with IM epinephrine had any cardiovascular side effects. We found that a large percentage (35.2%) of our participants would apply the first dose of epinephrine either IV or subcutaneously.

When it comes to pediatric patients, one of the possible explanations for the low use of epinephrine is that anaphylaxis can be underdiagnosed in this age group, since some

subjective symptoms are not verbalized properly. Crucially, pediatric age is when the first anaphylactic episode is most frequently observed [22].

The current evidence of physicians' underuse of epinephrine is limited to prospective studies and surveys measuring knowledge.

Grossman et al. [16] reported an important percentage of 93.5% use of epinephrine in a survey taken by pediatricians. Surveys taken by physicians report an epinephrine use higher than 75% [17, 18, 23-29]. Moreover, Plumb et al. [30] and Jose and Clesham [31] reported 100% and 94% use of epinephrine, respectively. Findings by Plumb et al. [30] are interesting because while even if 100% of their respondents would choose epinephrine administration, only 34% knew the correct dose and route of administration, which could lead to its underuse in real practice.

In our study, we found that 49.5% of the participants would use IM epinephrine as first-line therapy, but only 20.4% were able to diagnose anaphylaxis and would be able to use the right dose of IM epinephrine.

Krugman et al. [32] reported that 72% of their participants know epinephrine is the first-line treatment for anaphylaxis and Derinoz et al. [33] found that between 24.4% to 85.5% of their interviewed pediatricians and pediatric residents prescribe it. These results can be compared to ours, in which 72.4% answered that epinephrine is the first-line treatment.

The low percentage of epinephrine administration that we found could be justified by the percentage of physicians who answered that there was a contraindication to its use (36.7%). Furthermore, we need to consider that there were physicians who did not know whether there was a contraindication (20.9%) or did not know the right dose (50%).

As for the knowledge of the right dose, Olabbari et al. [18] reported a percentage of 81.6%, while Erkocoğlu et al. [17] reported a percentage as low as 16.6%. Our results are more in line with those of Fustiñana et al. [26] who reported a percentage of 55% correct answers regarding dosing; our result was 50%.

Another possible cause of the low percentage of use is unfamiliarity with the route of administration. Olabbari et al. [18] reported 92.6% of his participants correctly chose the IM route. However, we need to take into consideration that their survey was answered by emergency doctors. In research of Jose and Clesham [31], while 94% of physicians would use of epinephrine, only 57.9% would administer it intramuscularly. Our results indicated that 64.3% of physicians would administer epinephrine intramuscularly and are comparable to Grossman et al. [16]'s figures, who reported an IM administration in 66.9% of the participants. There are surveys with a percentage as low as 27.5% [34].

Several studies have reported the use of subcutaneous epinephrine as high as >18% [16, 25, 27, 33, 34]; our findings were similar, with 22.4%. This wrongful route of administration could lead to fatal outcomes in patients.

It is important to design protocols for the management of patients with anaphylaxis in order to improve the use of epinephrine in them. A study reported a 30% increase in the use of epinephrine by physicians and a decrease in corticosteroid monotherapy when a protocol

was installed in the ED [35]. Rueter et al. [36] reported a significant increase in treatment of anaphylaxis after 10 years of implementing training programs for physicians, in where 100% of participants would use IM epinephrine, and a significant decrease in the use of corticosteroids as first-line of treatment.

It is important to mention that globally speaking, 30% of the countries do not count with exclusive guidelines for anaphylaxis management [37]. Therefore, it is important for each country to perform big-scale studies to improve the treatment of anaphylaxis and to detect any knowledge deficiencies in the subject [38].

In our survey, we did not interrogate the participants about the in-hospital observation time of patients with anaphylaxis, adjuvant therapies such as supplemental oxygen, and the correct body position.

This study had some limitations, our results do not reflect the knowledge possessed by primary care physicians in a wide sense, since the survey was mostly answered by physicians working in the largest hospitals in Mexico City. Furthermore, the survey cannot inquire upon the kind of actions physicians would have taken in their real clinical practice. Finally, the survey that was used is not standardized.

In conclusion, our research indicates that there is still some difficulty recognizing anaphylaxis without cutaneous symptoms. While two-thirds of medical professionals identified that epinephrine is used as first-line treatment, only 49.5% of the participants would have used IM epinephrine as first-line treatment. Importantly, only 20.4% of respondents diagnosed both cases of anaphylaxis correctly and would have used IM epinephrine as first-line therapy with the correct dose. This crucial finding can account for epinephrine underuse when dealing with anaphylaxis. Another factor that could have an impact on epinephrine underuse is that a high percentage of physicians believe there are contraindications to epinephrine use. We also found a low percentage of prescription of autoinjectors. This figure can be due to the lack of availability of this technology in Mexico. However, physicians were also reluctant to prescribe epinephrine injections.

It is very important to promote strategies that allow physicians to recognize and treat anaphylaxis correctly. Additionally, it is of vital importance to highlight the evidence that there is no absolute contraindication for its use, as well as reinforcing the knowledge of anaphylaxis treatment not only in physicians but in all healthcare workers.

ACKNOWLEDGEMENTS

The authors would like to thank Axel Berber Del Rio, Dr. Carla Fabiola De Alba Navarro, Dr. Ricardo Baeza Bastarrachea, and Dr. Omar Saucedo Ramírez for their participation in this study.

REFERENCES

1. Atanaskovic-Markovic M, Gomes E, Cernadas JR, du Toit G, Kidon M, Kuyucu S, Mori F, Ponvert C, Terreehorst I, Caubet JC. Diagnosis and management of drug-induced anaphylaxis in children: an EAACI position paper. *Pediatr Allergy Immunol* 2019;30:269-76.

[PUBMED](#) | [CROSSREF](#)

2. Shaker MS, Wallace DV, Golden DBK, Oppenheimer J, Bernstein JA, Campbell RL, Dinakar C, Ellis A, Greenhawt M, Khan DA, Lang DM, Lang ES, Lieberman JA, Portnoy J, Rank MA, Stukus DR, Wang J. Anaphylaxis—a 2020 practice parameter update, systematic review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) analysis. *J Allergy Clin Immunol* 2020;145:1082-123. [PUBMED](#) | [CROSSREF](#)
3. Simons FER, Ebisawa M, Sanchez-Borges M, Thong BY, Worm M, Tanno LK, Lockey RF, El-Gamal YM, Brown SGA, Park HS, Sheikh A. 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. *World Allergy Organ J* 2015;8:1-16. [PUBMED](#) | [CROSSREF](#)
4. Muraro A, Roberts G, Worm M, Bilò MB, Brockow K, Fernández Rivas M, Santos AF, Zolkipli ZQ, Bellou A, Beyer K, Bindslev-Jensen C, Cardona V, Clark AT, Demoly P, Dubois AEJ, DunnGalvin A, Eigenmann P, Halken S, Harada L, Lack G, Jutel M, Niggemann B, Ruëff F, Timmermans F, Vlieg-Boerstra BJ, Werfel T, Dhimi S, Panesar S, Akdis CA, Sheikh A. Anaphylaxis: Guidelines from the European Academy of Allergy and Clinical Immunology. *Allergy Eur J Allergy Clin Immunol* 2014;69:1026-45. [CROSSREF](#)
5. Choi YJ, Kim J, Jung JY, Kwon H, Park JW. Underuse of epinephrine for pediatric anaphylaxis victims in the Emergency Department: a population-based study. *Allergy Asthma Immunol Res* 2019;11:529. [PUBMED](#) | [CROSSREF](#)
6. Ninchoji T, Iwatani S, Nishiyama M, Kamiyoshi N, Taniguchi-Ikeda M, Morisada N, Ishibashi K, Iijima K, Ishida A, Morioka I. Current situation of treatment for anaphylaxis in a Japanese Pediatric Emergency Center. *Pediatr Emerg Care* 2018;34:e64-7. [PUBMED](#) | [CROSSREF](#)
7. NHS England. Writing an effective questionnaire [Internet]. Wakefield (UK): NHS England; 2018 [cited 2020 Apr 14]. Available from: <https://www.england.nhs.uk/wp-content/uploads/2018/01/bitesize-guide-writing-an-effective-questionnaire.pdf>
8. Artino AR, La Rochelle JS, Dezee KJ, Gehlbach H. Developing questionnaires for educational research: AMEE Guide No. 87. *Med Teach* 2014;36:463-74. [PUBMED](#) | [CROSSREF](#)
9. Harrison C. Questionnaire design tip sheet [Internet]. Cambridge (MA): Harvard University Program Survey Research; 2007 [updated 2007 Nov. 17; cited 2020 Apr 15]. Available from: <http://psr.iq.harvard.edu/files/psr/files/PSRQuest>
10. Turner PJ, Campbell DE, Motosue MS, Campbell RL. Global trends in anaphylaxis epidemiology and clinical implications. *J Allergy Clin Immunol Pract* 2020;8:1169-76. [PUBMED](#) | [CROSSREF](#)
11. Fleming JT, Clark S, Camargo CA, Rudders SA. Early treatment of food-induced anaphylaxis with epinephrine is associated with a lower risk of hospitalization. *J Allergy Clin Immunol Pract* 2015;3:57-62. [PUBMED](#) | [CROSSREF](#)
12. Campbell RL, Bellolio MF, Knutson BD, Bellamkonda VR, Fedko MG, Nestler DM, Hess EP. Epinephrine in anaphylaxis: higher risk of cardiovascular complications and overdose after administration of intravenous bolus epinephrine compared with intramuscular epinephrine. *J Allergy Clin Immunol Pract* 2015;3:76-80. [PUBMED](#) | [CROSSREF](#)
13. Mullins RJ, Wainstein BK, Barnes EH, Liew WK, Campbell DE. Increases in anaphylaxis fatalities in Australia from 1997 to 2013. *Clin Exp Allergy* 2016;46:1099-110. [PUBMED](#) | [CROSSREF](#)
14. Solé 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. [PUBMED](#)
15. Robinson M, Greenhawt M, Stukus DR. Factors associated with epinephrine administration for anaphylaxis in children before arrival to the emergency department. *Ann Allergy Asthma Immunol* 2017;119:164-9. [PUBMED](#) | [CROSSREF](#)
16. Grossman SL, Baumann BM, Garcia Peña BM, Linares MYR, Greenberg B, Hernandez-Trujillo VP. Anaphylaxis knowledge and practice preferences of pediatric emergency medicine physicians: a national survey. *J Pediatr* 2013;163:841-6. [PUBMED](#) | [CROSSREF](#)

17. Erkoçoğlu M, Civelek E, Azkur D, Özcan C, Öztürk K, Kaya A, Metin A, Kocabaş CN. Knowledge and attitudes of primary care physicians regarding food allergy and anaphylaxis in Turkey. *Allergol Immunopathol* 2013;41:292-7.
[PUBMED](#) | [CROSSREF](#)
18. Olabbari M, Gonzalez-Peris S, Vázquez P, González-Posada A, Sanz N, Vinuesa A, Diez N, Benito J, Mintegi S. Management of anaphylaxis in Spain: pediatric emergency care providers' knowledge. *Eur J Emerg Med* 2019;26:163-7.
[PUBMED](#) | [CROSSREF](#)
19. Cardona V, Álvarez-Perea A, Ansotegui IJ, Arias-Cruz A, González-Díaz SN, Latour-Staffeld P, Ivancevich JC, Sánchez-Borges M, Serrano C, Solé D, Tanno LK. Management of anaphylaxis in Latin America: current situation. *Rev Alerg Mex* 2017;64:171-7.
[PUBMED](#) | [CROSSREF](#)
20. Wang J, Young MC, Nowak-Węgrzyn A. International survey of knowledge of food-induced anaphylaxis. *Pediatr Allergy Immunol* 2014;25:644-50.
[PUBMED](#) | [CROSSREF](#)
21. Prince BT, Mikhail I, Stukus DR. Underuse of epinephrine for the treatment of anaphylaxis: missed opportunities. *J Asthma Allergy* 2018;11:143-51.
[PUBMED](#) | [CROSSREF](#)
22. Simons FER. Anaphylaxis in infants: can recognition and management be improved? *J Allergy Clin Immunol* 2007;120:537-40.
[PUBMED](#) | [CROSSREF](#)
23. Redmond M, Pistiner M, Scherzer R, Stukus D, Twarog FJ, Lee J. Anaphylaxis knowledge in camp personnel. *J Allergy Clin Immunol Pract* 2018;6:2139-40.
[PUBMED](#) | [CROSSREF](#)
24. Altman AM, Camargo CA, Simons FER, Lieberman P, Sampson HA, Schwartz LB, Zitt FM, Collins C, Tringale M, Wilkinson M, Wood RA. Anaphylaxis in America: a national physician survey. *J Allergy Clin Immunol* 2015;135:830-3.
[PUBMED](#) | [CROSSREF](#)
25. Pinto ML, Rocha Felix MM, Bordalo C, Silva SH, Ferrão KDC, Pereira Bandeira De Mello MDB, Ribeiro J, Grinapel R, Bonorino A, Coser-Vianna J, Soares-De Souza M, Albuquerque-Garcês A. A survey study of medical knowledge about anaphylaxis [abstract]. *World Allergy Organ J* 2015;8:A229.
[CROSSREF](#)
26. Fustiñana AL, Rino PB, Kohn-Loncarica GA. Detection and management of anaphylaxis in children. *Rev Chil Pediatr* 2019;90:44-51.
[PUBMED](#)
27. Colleti Junior J, de Carvalho WB. Anaphylaxis knowledge among pediatric intensivists in Brazil: a multicenter survey. *J Intensive Care Med* 2017;32:593-6.
[PUBMED](#) | [CROSSREF](#)
28. Ibrahim I, Chew BL, Zaw WW, Van Bever HP. Knowledge of anaphylaxis among Emergency Department staff. *Asia Pac Allergy* 2014;4:164.
[PUBMED](#) | [CROSSREF](#)
29. Jain PD, Gupta RS, Chadha AS, Warren CM, Rao VV, Putcha UK. Knowledge, attitude, and practices of medical clinicians regarding food allergy and anaphylaxis in hyderabad, India. *Ann Allergy Asthma Immunol* 2020:S1081-1206(20)30440-3.
[PUBMED](#) | [CROSSREF](#)
30. 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.
[PUBMED](#) | [CROSSREF](#)
31. Jose R, Clesham GJ. Survey of the use of epinephrine (adrenaline) for anaphylaxis by junior hospital doctors. *Postgrad Med J* 2007;83:610-1.
[PUBMED](#) | [CROSSREF](#)
32. Krugman SD, Chiamonte DR, Matsui EC. Diagnosis and management of food-induced anaphylaxis: a national survey of pediatricians. *Pediatrics* 2006;118:e554-60.
[PUBMED](#) | [CROSSREF](#)
33. Derinoz O, Bakirtas A, Arga M, Catal F, Ergöcen S, Turktas I, Demirsoy MS. Pediatricians manage anaphylaxis poorly regardless of episode severity. *Pediatr Int* 2014;56:323-7.
[PUBMED](#) | [CROSSREF](#)
34. Adiga S, Nayak V, Bairy KL. Treatment of anaphylaxis in adults: a questionnaire survey. *Online J Health Allied Sci* 2008;7:6-9.

35. Arroabarren E, Lasa EM, Olaciregui I, Sarasqueta C, Muñoz JA, Pérez-Yarza EG. Improving anaphylaxis management in a pediatric emergency department. *Pediatr Allergy Immunol* 2011;22:708-14.
[PUBMED](#) | [CROSSREF](#)
36. Rueter K, Ta B, Bear N, Lucas M, Borland ML, Prescott SL. Increased use of adrenaline in the management of childhood anaphylaxis over the last decade. *J Allergy Clin Immunol Pract* 2018;6:1545-52.
[PUBMED](#) | [CROSSREF](#)
37. Simons FER. World Allergy Organization survey on global availability of essentials for the assessment and management of anaphylaxis by allergy-immunology specialists in health care settings. *Ann Allergy Asthma Immunol* 2010;104:405-12.
[PUBMED](#) | [CROSSREF](#)
38. Muraro A, Mendoza Hernandez DA. Managing food allergy and anaphylaxis: a new model for an integrated approach. *Allergol Int* 2020;69:19-27.
[PUBMED](#) | [CROSSREF](#)