Original Article

The Prescription Practices of Adrenaline Auto-injector for Children at Risk of Anaphylaxis

Ahmed Ali Elghoudi[1], Gary Stiefel[2], Judith Holloway[3]

[1]Department of Pediatrics, Al Ain Hospital, Al Ain, UAE, [2]Department of Pediatrics, University Hospitals of Leicester NHS Trust, Leicester Royal Infirmary, Leicester, [3]Clinical and Experimental Sciences Department, MSc Allergy Program, University of Southampton, Southampton, United Kingdom

Abstract

Background: Guidelines on indications for adrenaline auto-injector (AAI) exist. There is no consensus on the prescription criteria of AAI. However, the European Academy of Allergy and Clinical Immunology (EAACI) and the United Kingdom (UK) resuscitation council provide guidances on prescription practices. **Objectives:** This study aims to investigate prescription practices of AAIs prescribed by members of four regional pediatric allergy groups (PAGs) in the UK. **Materials and Methods:** An online questionnaire was e-mailed to the PAGs members. Scenarios of absolute and relative indications for AAI prescriptions (as per the EAACI guidelines) were presented to clinicians to establish whether they would prescribe an AAI. **Results:** One hundred and seventeen responses from members of PAGs working in four different regions were received. Practices were similar in scenarios of absolute indications for AAI. Intraregional (variations within the regions) as well as interregional (variations between the regions) variations were observed. There were statistically significant interregional differences in scenarios of relative indications for AAIs. For mild reaction to peanut (PN)/tree nut (TN), AAI would be prescribed more often by doctors from Wessex clinicians (67%) than those from Midlands (31%), London (24%), and Northern (20%) ($P < 0.05$). Whereas for a previous mild reaction to trace of PN/TN, Northern clinicians (47%) would prescribe AAI less often than those from the Midlands (78%), Wessex (82%) and London (79%) ($P < 0.05$). Intraregional differences were also observed. **Conclusions:** There is a consensus with absolute indications for AAI prescriptions across and within regions. There are intraregional and interregional differences in prescribing practices in scenarios where there is a relative indications for an AAI. Better intra- and interregional work could improve consistency or practice across the country are explain differences in practice.

Keywords: Adrenaline auto-injector/adrenaline auto-injectors, allergy, generalized hives and lips swelling, mild allergy, peanut, tree nuts

Address for correspondence: Dr. Ahmed Ali Elghoudi, Department of Pediatrics, Al Ain Hospital, Al Ain, UAE.
E-mail: aelghoudi@seha.ae

Submitted: 20-Apr-2020 **Revised:** 12-Jul-2020
Accepted: 21-Jul-2020 **Published:** 26-Sep-2020

Access this article online

Quick Response Code:

Website: www.ijmbs.org

DOI: 10.4103/ijmbs.ijmbs_34_20

How to cite this article: Elghoudi AA, Stiefel G, Holloway J. The prescription practices of adrenaline auto-injector for children at risk of anaphylaxis. Ibnosina J Med Biomed Sci 2020;12:169-76.

Introduction

Anaphylaxis is a serious, life-threatening systemic hypersensitivity reaction.[1,2] The condition is characterized by rapid onset with life-threatening manifestations affecting the airway, respiratory, and cardiovascular systems, and frequently associated with skin rashes.[3]

Anaphylaxis is very well described in pediatric populations and its incidence has increased.[4] It has been estimated that the incidence of anaphylaxis is 30/100,000 persons. The prevalence of anaphylaxis has been estimated at 5–15/100,000. In the United Kingdom (UK), the incidence of anaphylaxis has risen sevenfold from 1990 to 2003.[4] The highest rate has been observed in school-age children.[5] However, the exact figures of incidence and prevalence of anaphylaxis in Europe are difficult to calculate due to a number of factors. One of the challenges is the fact that there is no universal definition for anaphylaxis, which makes the diagnosis of the condition challenging and complex.[6] Anaphylaxis is a major public health concern. In children, it is very commonly linked to food. In a 3-year retrospective Australian pediatric emergency department chart review, it was found that food (e.g., peanut, tree nuts [PN/TN], egg, sesame seed, wheat, soya, and cow's milk) contributed to 56% of cases of anaphylaxis in children, whereas drugs such as beta-lactams, penicillin's, muscle relaxants, and insects were responsible for only 5% of anaphylaxis cases seen. The remaining 34% are thought to be idiopathic. In general, cases of anaphylaxis were greater in children than in adults.[7] Studies on severe morbidity and mortality due to anaphylaxis identified some risk factors such as a current attack of asthma, food allergies, especially nuts and shellfish allergies, previous reaction to trace of food, current use of beta-blockers, as well as a delay in administering intramuscular adrenaline auto-injector (AAI). Delay in administering AAIs remains the highest risk factor associated with severe and fatal cases.[7]

Despite the severity of the condition, there is still a considerable amount of ambiguity and variation: both in terms of making the diagnosis of the condition and in prescribing immediate treatment – the AAI.[6] To our knowledge, there is no consensus among clinicians as to which patients require an AAI and the number of AAIs that should be carried around at all times. The European Academy for Allergy and Clinical Immunology (EAACI) guidelines try to address this.[3] AAI device for on-the-spot use has been designed for 'immediate" emergency treatment of an anaphylactic shock. AAI is an injection device filled with adrenaline. It is designed to be used by patients or their parents or carers in emergency situations.[7] The intramuscular AAI device is available in three doses: 150 μg (0.15 mL) for children from 6 months to 6 years; 300 μg (0.3 mL) for children from 6 years to 12 years; and 500 μg (0.5 mL) for children more than 12 years.

The intramuscular route has a great margin of safety, does not require intravenous access, and it is easy to learn. The anatomical point of preference is on the anterolateral side of the thigh. Length of the needle is considered sufficient enough to ensure that adrenaline reaches the muscle.[8]

In terms of the guidelines for AAI indications, EEACI classified it into two types:[3] absolute and relative indications as follows: absolute indications include previous cardiovascular or respiratory reaction to a food, insect sting or latex, exercise-induced anaphylaxis, idiopathic anaphylaxis, and child with food allergy and coexistent asthma. The relative indications include any reaction to small amounts of a food (e.g., airborne food allergen or contact only via skin), history of only a previous mild reaction to PN/TN, remoteness of home from medical facilities, or food allergic reaction in a teenager as these age groups are described as risk-takers

In its published guidelines, the UK Resuscitation Council states that all patients at increased risk of idiopathic anaphylaxis and all those at continued risk of anaphylaxis such as venom stings and food-induced reactions should be given AAI unless the food is easy to avoid. The American Academy of Asthma, Allergy, and Immunology has different prescription criteria for those who have had a previous mild reaction. It recommends prescribing AAI to all individuals who have previously had a mild reaction. This is based on the fact that

initial symptoms of anaphylaxis can resemble those of mild reaction and that one cannot predict whether an episode of mild reaction will progress to anaphylaxis.[9] Johnson *et al*. suggest that the currently published UK guidelines – those of the Resuscitation Council, UK, and EAACI – both need more active implementation to help with improving the prescription practice of AAI.[6]

The variation in the practice of AAI prescription has been the subject of many studies.[5] Some clinicians attribute the inconsistency in the AAI prescription practices to the variation of the data obtained from different studies. A study on children with peanut allergy showed that children with previous mild reaction to peanut have shown a 5% annual rate of anaphylaxis compared to another study from the UK, which showed the anaphylaxis rate of a similar cohort is only 1%.[5]

Materials and Methods

Objectives

The aim of the project was to study the current practice and attitude of prescriptions of AAIs. The data were analyzed and compared to reference documents, primarily to the EAACI guidance on the prescription practice of AAI in anaphylaxis.

Two research questions were addressed: first, Are prescription practices of AAIs consistent with the EAACI and second, Are prescription practices of AAIs similar across regions in the UK.

Survey questionnaire

A web-based questionnaire (SurveyMonkey) designed to include 13 case scenarios based on AAI prescription in relation to the EAACI criteria on absolute and relative indications of AAI. A link to the survey was sent to members of different regional pediatric allergy groups (PAGs), namely the Midlands, Wessex, Northern, and London groups. Group members are typically pediatric allergists, general pediatricians with interest in allergy, allergy specialist nurses, and dieticians. They all see children with allergy in similar settings, i. e., pediatric allergy clinics. The project aimed to study the current practice and attitude of prescriptions of AAIs and to look for any intraregional and interregional variations. The data were analyzed by comparing it to reference documents the UK Resuscitation Council and the EAACI guidance.

Samples and testing

The questionnaire was sent to about 140 health-care professionals who were members of their regional PAGs and who ran allergy clinics in the Midlands, Wessex, Northern regions, and in London. The study was based in the Midlands regions, University Hospital Coventry. The database of the Midlands Pediatric Allergy Group (MPAG), Wessex allergy group, the Northern pediatrics allergy group, and London allergy group was used to identify participants. All participants had interest and expertise in pediatric allergy. All members of these groups were invited to participate in the study and there were no exclusion criteria. A general preliminary agreement for participation in the study was initially granted by the group administrators. Group members were briefed about the project's aims and objectives. A SurveyMonkey invitation e-mail was sent containing a link to the survey. Participants were informed that clicking on the link and answering the questionnaire implied their agreement to participate in the study. Participant's submissions were treated anonymously; however; information on their regions/areas of practice was requested to help identify variations in regional practice. Data were stored in an encrypted memory stick held by the researcher. SurveyMonkey account setting was altered by the researcher to disable tracking the IP addresses and e-mails of the participants.

Measurements

Participants were asked to complete an online questionnaire. Questions were straightforward, and no previous reading/preparation required. 5–8 min was enough to answer all the questions. Answers from the questionnaire were processed and analyzed to identify current practice in prescribing AAI. Invitations were sent by e-mail to the chair of the regional allergy groups mentioned with a request to disseminate it to their group members. Responses to the survey from the participants were collected the SurveyMonkey (www.surveymonkey) account made for the research group. Following data retrieval,

quantitative analysis used for closed-ended question and themes or specific categories drawn to allocate the open-ended questions answers and the comments made by the participants along with some answers, are grouped under certain themes accordingly.

Data management

A pilot study was performed in a small sample to assess the relevance, accuracy, and strengths of the survey questions. A paper copy of the questionnaire was distributed to a sample of health-care professionals, typically representative of the cohort. Feedback comments have been taken into account in further design. The data were kept safe in the researcher's encrypted memory stick and no information was disclosed to any third party. Data were then analyzed, and statistical tests such as percentages, *P* value, and Chi-squared test were used as appropriate to look at the statistical significance of intra-and interregional differences in the prescription practice of AAIs. When examining the statistical significance between the different groups, $P < 0.05$ was considered statistically significant.

Results

Characteristics of respondents

A total of 117 responses received from clinicians working in different regions including the Midlands (39), Wessex (22), London (19) Northern (20), and others (17). Respondents identified as general pediatricians with special interest in allergy were 61 (52%), pediatric allergists were 18 (15%), allergy specialist nurses were 18 (15%), junior doctors were 5 (4%), and others including adult physicians and general practitioners seeing children with allergy were 15 (13%).

Decisions to prescribe adrenaline auto-injector

Intra- and interregional practices were almost similar in scenarios of absolute indications, i. e., scenarios of previous or potentially imminent future anaphylaxis. When all the 117 participants initially pooled all together, 117 participants (100%) would prescribe AAI in the scenario of previous anaphylaxis to PN/TN), 112 (96%) would prescribe AAI for children with a previous mild allergic reaction to PN/TN but have poorly controlled asthma, 111 participants (95%) would prescribe AAI for idiopathic anaphylaxis, 109 (93%) for exercise induced anaphylaxis, 97 (83%) in case of previous anaphylaxis to egg, 95 (81%) in previous mild reaction but lives in a remote area, 79 (68%) in mild reaction to tract/airborne/skin contact to PN/TN, 70 (60%) would prescribe AAI in the scenario of mild reaction to egg where the child has poorly controlled asthma, and 35 (30%) of all the participants would prescribe AAI for children with previous mild allergy to egg with coexistent well controlled asthma. In the scenario of a mild reaction to an egg with well-controlled asthma, 35 (30%) would prescribe AAI and the figure doubles when asthma coexisted 70 (60%). Inconsistency in taking decisions on prescribing AAIs can be seen clearly in other scenarios [Table 1].

The scenario of a mild reaction to egg and poorly controlled asthma revealed intraregional and interregional variations in practice as 70 participants (60%) only would prescribe AAI and approximate figures witnessed at the group level [Figure 1b]: MPAG (19/39, 48.7%), WPAG (16/22, 72.7), London group (9/20, 47.4%), and Northern group (12/20, 60%). The majority of respondents would not recommend AAI in cases of previous mild reaction (generalized urticaria and lip swelling) to an egg with coexistent asthma (currently well controlled on Seretide 100 mcg/day) [Figure 1a]. Here, 18.3% of MPAG would prescribe AAI, versus 27.3% of WPAG, 44.4% of London, and 40% of the NPAG group. Only 16/117 participants commented on their practice. 62.5% would prescribe AAI if other risk factors such as asthma were present and 31% would prescribe AAI if the reaction was to well boiled/baked egg. In Figure 1b, The scenario of previous mild reaction (generalized urticaria and lip swelling) to egg, with coexistent asthma (specified as currently poorly controlled on Seretide 100 mcg/day), showed both intra -and interregional variations (70, 60%) would prescribe AAI and 46 (40%) would not. Junior doctors were the most likely to recommend it (80%). Regional practice varied with 48% of MPAG clinicians as compared to 73.7% of WPAG, 60% of London, and 20% of Northern clinicians prescribing AAIs in this scenario.

In Figure 1b of previous mild reaction to egg and poorly controlled asthma on Seretide, 40% (47/117)

Table 1: Responses on cases scenarios based on absolute and relative indications of adrenaline auto-injector, collected from different pediatric allergy groups in the United Kingdom

Cases scenarios	All (117)	Midlands (39)	Wessex (22)	London (19)	Northern (29)	Other (17)
1. Previous anaphylaxis to PN/TN (%)	100.0	100.0	100.0	100.0	100.0	100.0
2. Mild reaction to PN/TN* (%)	69.0	20.0	66.7	30.8	23.5	11.8
3. Mild reaction to PN/TN in well controlled asthma. (%)	71.0	86.4	82.3	65	64.9	76.5
4. Mild reaction to PN/TN and poorly controlled asthma (%)	96.0	92.3	100.0	100.0	95.0	94.1
5. Anaphylaxis to egg (%)	83.0	86.1	86.4	94.7	90.0	64.7
6. Mild reaction to egg and well controlled asthma (%)	30.0	18.4	27.3	44.4	40.0	40
7. Mild reaction to egg and poorly controlled asthma (%)	60.0	48.7	72.7	73.7	60.0	56.3
8. Mild reaction to trace/airborne/skin contact to PN/TN** (%)	68.0	78.0	81.8	78.9	47.4	47.1
9. Idiopathic anaphylaxes (%)	95.0	97.4	90.9	94.7	100	94.1
10. Exercise-induced anaphylaxis (%)	93.0	97.4	86.4	100	90.0	94.1
11. Previous mild reactions and lives in remote area (%)	81.0	82.0	81.8	84.2	75.0	82.3

The total number of regional group members may vary, when some members skip the question. * (P<0.05), **(P<0.005). PN/TN: Peanut/Tree nut

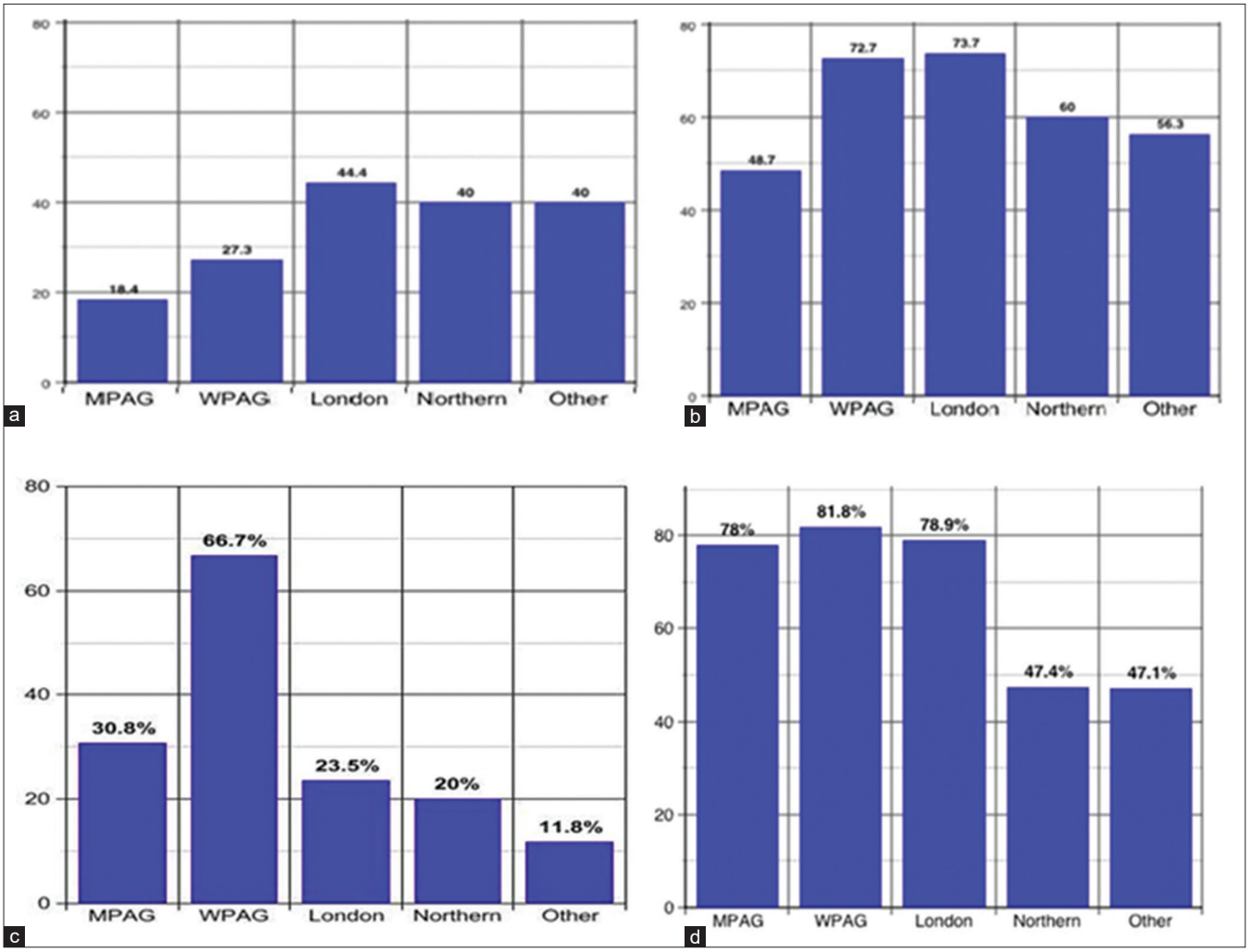

Figure 1: The relative frequency of participating respondents (from five different regions) who would prescribe AAI in four different scenarios namely, namely mild reaction to egg and well-controlled asthma (a), mild reaction to egg and poorly controlled asthma (b), previous mild reaction to peanut (c), and previous mild reaction to trace of PN/TN (d)

would not prescribe AAIs, 13% of this group stated that they would optimize asthma treatment first, 26% would do allergy testing, and 60% would only do so only for small children, i.e., nursery age, as these were thought most likely to grow out of it. There were much more marked intraregional differences

in cases with relative indications for AAIs. For a mild reaction to PN/TN [Figure 1c], it showed both inter and intraregional variations. Seventy-six (68%) of the responders would not prescribe AAIs versus 36 (32%) who would. General pediatricians were the most likely not to recommend AAIs (72.9%).

Interregional differences in practice

A statistically significant interregional difference in prescription practices was noted. AAI is prescribed more often by Wessex clinicians (67%) than Midlands (31%), London (24%), and Northern (20%) clinicians ($P < 0.01$). Factors influencing decision to prescribe AAI, in cases of mild reaction to PN/TN, 42 participants left supplementary comments. Thirty-eight (90%) would prescribe AAIs if there were other risk factors, mainly asthma and remoteness from nearest Accidents and Emergency Department. Six (10%) would look at test results, especially component testing, and if Ara h2 is positive, then they would definitely prescribe AAIs. For a previous mild reaction to traces of PN/TN [Figure 1C], a statistical significant interregional difference was observed. Northern clinicians (47%) would prescribe AAI less than those from the Midlands (78%), Wessex (82%), and London (79%) ($P < 0.05$). Figure 1d shows previous mild reaction (urticaria and lip swelling) to trace of air borne/skin contact to PN/TN. Here, the majority of responders (79.3%) would recommend AAI for mild reaction to PN/TN for those who live in remote areas [Table 1]. Pediatric allergists were more likely to recommend AAIs (83.3%) as compared to general pediatricians at 78%. No significant interregional variation was noted. One hundred and twelve (96%) would prescribe AAI to children with poorly controlled asthma if they have mild PN/TN allergy, but in the same time, only 70 (60%) would prescribe AAI if these children (with poorly controlled asthma) are mildly allergic to egg.

Discussion

The present study investigated the regional variation of AAI prescription in the UK. It demonstrated that there was a consensus in implementing the EAACI absolute indications of AAI prescriptions amongst clinicians across all the regions involved in the study. This is clearly evidenced through responses to cases 1, 5, 9, and 10 [Table 1]. However, there are fewer consensuses when it came to the case of previous anaphylaxis to egg. This clearly demonstrates some lack of knowledge and appreciation of the potential severe morbidity and possible mortality of the disease. Cases of relative indications of AAI clearly highlighted the inter- and intraregional variations. This could be explained by either lack of knowledge of the existing guidelines, i.e., EAACI, as shown in the study. However, still, there is a possibility that some clinicians are aware of the same but simply choosing to not implement it. The controversy seems more marked with the relative indications of AAI. It is understood that some individuals who previously had mild reactions may potentially develop anaphylaxis on further exposure.[3] While the proportion of these individuals are normally small, this recommendation could put pressure on clinicians and parents and result in unnecessary prescription of AAI. More research and data are needed to explore this area. Another interesting observation was noted from the pediatric allergist's responses. This group of clinicians would like to do allergy testing more than any other group to assist them in taking decisions of prescribing AAIs and to identify those at highest risk of developing anaphylaxis. In particular, they are keen on doing allergy molecular testing such as the component-resolved diagnostic (CRD) testing.[10] CRD utilizes purified native or recombinant allergens to detect immunoglobulin E sensitivity to individual allergen molecules.[10] The test is an advanced tool that can assist clinicians in making accurate diagnosis of allergy and it has the advantage of informing the clinicians about potential severity and cross-reactivity. When used by experts, it can predict the potential risk of anaphylaxis.[11] Such a useful test may find a place in the future guidelines for AAI prescription.

Factors influencing the decision to prescribe an AAI in our study were not different from those described in the literature.[12] Coexistence of asthma has strongly influenced decisions of AAI prescribing and had been mentioned in the vast majority of the

comments, especially in cases of a mild reaction. EAACI guidance recommends prescribing AAI to those with previous mild allergic reaction with coexistent asthma which is poorly controlled.[13] Overprescribing AAI to every child with food allergy with asthma may give clinicians the peace of mind, but it would increase the anxiety among children and their parents. In addition, the physical impact of carrying two AAI devices all time should not be overlooked.[14] Also, one can not ignore the financial burden on the health care provider ie National Health Services.

The amount of exposure has also been addressed in our and in previous studies as a risk factor which indicates AAI prescribing.[6] Our data on those requiring a second AAI due to misfired first AAI are not different from previous studies. Data showed that over a period of 2 years, 128 cases of accidental injections were reported. Incidents typically happen when people put pressure on the wrong end of the device, injecting the adrenaline into their thumb.[15] The systematic review examined the rate of occurrence of unintentional injections of adrenaline from AAI into fingers and found that the true rate of misfiring AAI into fingers is unknown, but it is increasing, and it was suggested that improvement of patient education and a better design of AAI might help.[15] This area needs further research, but in the interim, the issue could be managed intuitively by offering better education and training to patients and families on how to use the AAI device. This may be a better alternative to just prescribing additional AAIs, as studies have shown that parents and carers are sometimes poorly trained in the use of AAI. In addition, as some patients and parents do not carry a single AAI with them, it's worth encouraging parents to carry a single AAI first, instead of increasing the burden by asking them to carry a second AAI.[16] A second AAI was needed in some obese children more than 45 kg or if there was a previous reduced response to the first AAI. Some data show that a second AAI was given to up to 20% – during a study period of 5 years –of those seen in ER because of anaphylaxis.[5] Data from our and previous studies demonstrated that the percentage of those received a second AAI ranges from 0–15 to 32%–80% to over 80%;[3] hence, these figures should be considered and appreciated. Larger studies and research projects are required. Data from our study revealed that some obese children with >45 kg body weight have required a second AAI.

The methodology limitations were noted when participants answered the question on prescribing AAI to those with previous mild reactions to PN/TN. Although some participants answered "yes" and the rest answered "no", their comments on the answers revealed a similar prescription practice, i.e., they would prescribe AAI if the child has asthma or would not prescribe unless the child has asthma. It is probably the wording of the questions which caused ambiguity and difficulty in producing themes of answers and could have significantly affected the results. Another factor which may have limited the generalization of the results is that the responses collected are hypothetical and that responses in real-life prescribing situations, i.e., in allergy clinic, may be very different. Parental and school nurse anxiety, the type of allergenic food, and how easy to avoid it at home and in school and nursery may all affect the clinician's decision whether to prescribe an AAI or not. Also, the number of respondents was not equal from all the regions.

Conclusions

There is a need for more active implementation of the EAACI anaphylaxis guidelines or the BSACI guidance to improve the prescribing criteria and to ensure patient safety. More research is needed to study variation in different regions around the same country and even beyond. National professional bodies could play a role in educating and guiding clinicians to unify the practice of AAI prescription. Patient and family education and training on how to use AAI is also a key factor. Better education and awareness among clinicians with regard to the relative indications of AAI are required. CRD testing may find a place in future guidance of AAI prescription.

Acknowledgments

The authors are most grateful to all members of the Midlands, Wessex, London, and Northern

PAGs for sharing their expertise by completing the questionnaire.

Authors' contributions

The study was conceived by all authors, AAE conducted the survey and data collection, analysis and drafting of the manuscript. GS and JH provided expert guidance. All authors revised the manuscript and approved its final version.

Financial support and sponsorship

AAE received unconditional educational grant to cover the dissertation module fees from Mead Johnson and Danone Nutrition. The University of Southampton also contributed to the dissertation module costs.

Conflicts of interest

No conflicts of interest.

Compliance with ethical principles

The study was conducted according to the principles of the Declaration of Helsinki (2013). Ethical approval was granted by the University of Southampton ethics committee (Ref: 13842) and participants provided informed consent before they could access the questionnaire. Data were extracted and analyzed completely anonymously.

References

1. Simons FE, Ardusso LR, Bilo MB, El-Gamal YM, Ledford DK, Ring J, *et al*. World allergy organization guidelines for the assessment and management of anaphylaxis. J Allergy Clin Immunol 2011:127:587-93.
2. Johansson SG, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, *et al*. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. J Allergy Clin Immunol 2004;113:832-6.
3. Muraro A, Roberts G, Worm M, Bilò MB, Brockow K, Fernández Rivas M, *et al.* On behalf of the EAACI food allergy and anaphylaxis guidelines Group. Anaphylaxis: Guidelines from the European Academy of Allergy and Clinical Immunology. Allergy 2014;69:1026-45.
4. Macdougall CF, Cant AJ, Colver AF. How dangerous is food allergy in childhood? The incidence of severe and fatal allergic reactions across the UK and Ireland. Arch Dis Child 2002;86:236-9.
5. de Silva D, Roberts G, Worm M, Muraro A. EAACI Food Allergy and Anaphylaxis Guidelines Group. EAACI anaphylaxis guidelines: systematic review protocol. Clin Transl Allergy 2020;10:14.
6. Johnson MJ, Foote KD, Moyses HE, Roberts G. Practices in the prescription of adrenaline autoinjectors. Pediatr Allergy Immunol 2012;23:124-7.
7. Braganza SC, Acworth JP, Mckinnon DR, Peake JE, Brown AF. Pediatric emergency department anaphylaxis: Different patterns from adults. Arch Dis Child 2006;91:159-63.
8. Song TT, Nelson MR, Chang JH, Engler RJ, Chowdhury BA. Adequacy of the epinephrine autoinjector needle length in delivering epinephrine to the intramuscular tissues. Ann Allergy Asthma Immunol 2005;94:539-42.
9. Johnson, Roger F, Stokes Peebles R. Anaphylactic shock: Pathophysiology, recognition, and treatment. Seminars Respiratory Critical Care Med 2004;25:695-703.
10. Ebo DG. Component-resolved allergy diagnosis: a new era?. Verh K Acad Geneeskd Belg 2011;73:163179.
11. Cardona V, Ansotegui IJ. Component-resolved diagnosis in anaphylaxis. Curr Opin Allergy Clin Immunol 2016;16:244-9.
12. Simons FE, Ardusso LR, Bilo MB, Dimov V, Ebisawa M, El-Gamal YM, *et al*. 2012 update: World Allergy Organization Guidelines for the assessment and management of anaphylaxis. Curr Opin Allergy Clin Immunol 2012:12:389-99.
13. Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. The diagnosis and management of anaphylaxis: an updated practice parameter. J Allergy Clin Immunol. 2005;115(3 Suppl 2):S483-S523.
14. Soar J, Pumphrey R, Cant A, Clarke S, Corbett A, Dawson P, *et al*. Emergency treatment of anaphylactic reactions--guidelines for healthcare providers. Resuscitation 2008;77:157-69.
15. Simons FE, Lieberman PL, Read EJ Jr, Edwards ES. Hazards of unintentional injection of epinephrine from autoinjectors: a systematic review. Ann Allergy Asthma Immunol 2009;102:282-287.
16. Macadam C, Barnett J, Roberts G, Stiefel G, King R, Erlewyn-Lajeunesse M, *et al*. What factors affect the carriage of epinephrine auto-injectors by teenagers? Clin Transl Allergy 2012;2:3.