MMJ

Malta Medical Journal, 2024; 36(2)
http://mmsjournals.org/index.php/mmj/40

ORIGINAL ARTICLE

Knowledge on the use of adrenaline autoinjectors among healthcare professionals

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Background

Adrenaline auto-injectors are indicated in the emergency treatment of allergic reactions including anaphylaxis prescribed to patients at increased risk for anaphylaxis, intended for immediate self-administration as emergency supportive therapy only and not a substitute for immediate medical care. The objective of this audit was to study the knowledge of indications for prescription and administration, mode of administration and post-administration management of an adrenaline autoinjector among health care professionals at our local hospital.

Method

86 medical doctors across various working grades in the Department of Medicine and 16 pharmacists were asked to complete a questionnaire in the presence of the investigator in July 2018 at Mater Dei Hospital, Malta.

Results

The mean age was 27.5years and 57% were females. 21 participants had previously prescribed an EpipenÂ®. Questions answered correctly were as follows: dosage in adults 63% and children 54%; correct indication for prescription 73%; correct indication for administration 100%; correct injection end of autoinjector 79.4%; incorrect patient positioning for injection 13%; correct site of administration 99%; correct duration of injection 56.8%; common side effects 73.5%; referral to A&E post-administration 75%; timing of repeat injection 80%; contraindications 86.7%. 68.6% participants did not feel confident explaining to patients when to use it while 72.5% participants did not feel confident explaining how to use it.

Conclusion

It is evident that education is urgently needed among health care professions on the indications for prescription, mode of administration as well as post-administration management of this potentially life-saving medication.

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Adrenaline administration intramuscularly is the first-line, most important drug for the treatment of anaphylaxis,[1-4] and the only one with proven lifesaving properties if received in a correct and timely manner, while simultaneously discontinuing exposure to the potential trigger.[4] Anaphylaxis is defined as a 'severe, life-threatening systemic hypersensitivity reaction' characterized by its rapidity in onset with potentially life-threatening airway, breathing, or circulatory problems, usually but not always, associated with skin and mucosal changes[2] which is potentially fatal if left untreated.[4] Anaphylaxis is usually IgE-mediated, but other non-IgE mediated mechanisms are also said to play a role.[4] Diagnosis and management are challenging since reactions may be quick, often unexpected and severe, with no single test to diagnose anaphylaxis in routine clinical practice.[5] The most common triggers are food, insect stings, and drugs.[4] Despite the clinical importance of anaphylaxis and a recent increase in its occurrence, studies regarding epidemiology and risk factors are poorly described.[6] The results of 10 European studies suggest an incidence of 1.5 to 7.9 per 100,000 person-years[2] while United Kingdom report an annual incidence of 8.4 per 100,000.[7] Recent studies in the United Kingdom show an increase in admissions with anaphylaxis over the last couple of decades.[2]

Adrenaline is an emergency supportive therapy only, and not a substitute for immediate medical care. The safety profile of intramuscular adrenaline is excellent although some patients may experience transient pallor, palpitations, and headache. Once received, patients are expected to seek medical help as soon as possible after the event in view of a possible biphasic reaction a few hours later. Self-administered adrenaline is the main out-of-hospital treatment for anaphylaxis[8] and is usually available as a pre-filled syringe.[9] Rapid administration of the drug is of utmost importance since delayed administration has been associated with a poor prognosis.[10] The European Academy of Allergy and Clinical Immunology Taskforce on Anaphylaxis recommends that all healthcare professionals should be familiar with recognition and acute and ongoing management of anaphylaxis since it is a clinical emergency with potentially fatal consequences.[2,3,11]

It is widely recognized that education and training of how to use adrenaline auto-injectors is important for effective management of anaphylaxis[12]and preventing fatalities,[11] and training should be offered to all professionals dealing with patients at risk of anaphylaxis.[2] For this important medication to be administered timely and appropriately, patients and their relatives must also be educated on adrenaline auto-injector usage. Once prescribed, patients should be trained by the prescribing professional to learn promptly and correctly, use of the device[8] in case of anaphylaxis occurring in the absence of expert help.

Despite accurate training identified in an Italian survey, it is reported that many patients are still unable to use the adrenaline auto-injector properly.[8] Studies in the paediatric population have shown that both doctors and patients themselves may use the adrenaline auto-injector improperly and that usage skills are improved by training.[13]It is recommended that allergists should ensure that technique is reviewed and re-explained to the patients each time a renewal of the auto-injector is prescribed.[2,8] However, at our local hospital in the absence of an allergy service, the prescribing doctor should be responsible for this. Estimates of the incidence of anaphylaxis are not available locally and there is no data on adrenaline auto-injector prescribing rates either.

In a study in Toronto performed on medical convention's delegates and emergency department personnel as well as pharmacists of the target hospitals and retail pharmacists, only 25% of the study participants were able to demonstrate the steps of injection correctly.[14] In a study in Brussels, it was concluded that the low rate of doctors prescribing adrenaline auto-injectors in the emergency department setting underlines the need to train doctors in various fields on the management of anaphylaxis in close collaboration with allergologists.[15] Such studies demonstrate a lack of allergy knowledge in primary care, especially the recognition and treatment of anaphylaxis were problematic and that national guidelines are often not followed.[16]

The objective of this audit was to study the knowledge of indications for prescription and administration, mode of administration and post-administration management of an adrenaline autoinjector among health care professionals at our local hospital.

MATERIALS AND METHODS

Eighty-six random consecutive medical doctors across various working grades in various specialities in the Department of Medicine and 16 consecutive pharmacists who agreed to participate, were asked to complete a questionnaire during one month at Mater Dei Hospital, Malta. Acceptance rate to participate was 100%. Epipen® was the only adrenaline auto-

Table 1 *Questions answered for clinical indications for adrenaline auto-injector prescription (n=102)*

Clinical Indications	Correct	Incorrect	No answer
Adrenaline auto-injector is indicated following a first anaphylactic reaction, n(%)	90 (88.2)	12 (11.8)	0 (0)
Food allergy and chronic asthma, n(%)	45 (44.1)	55 (53.9)	2 (1.9)
Food allergy with trace amounts of food, n(%)	79 (69.6)	31(30.4)	0 (0)
Nut allergy, n(%)	94 (92.1)	8 (7.9)	0 (0)

injector available locally during the time of recruitment. Questions and their respective answers were therefore designed based on the Summary of Product Characteristics of the adult Epipen®.[17]

The questionnaire (Supplement File 1) was divided into the following sections: age, gender, working grade, whether the professional ever received training on adrenaline auto-injectors and whether the subject ever prescribed such treatment, indications for prescription, dosing regimen, mode of administration as well as how confident the professional felt about prescribing or explaining the use of adrenaline auto-injector to the patient.

The questionnaire was completed in the presence of the investigator so as to ensure that the participants did not search for the answers. The questionnaires were kept anonymous. Patient demographics and responses to the questionnaires were inputted and calculated using Microsoft Excel®.

RESULTS

Our cohort included a total of 102 participants, 86 medical doctors and 16 pharmacists. The mean age was 27.5years and 57% were females. Only 16.7% reported that they had been trained on how to administer an adrenaline auto-injector and 20.6% of doctors reported that they had ever prescribed an adrenaline autoinjector.

Table 1 shows the percentage of participants who answered the questions in the clinical indications for prescription section of the questionnaire. The majority of responders recognized the necessity for adrenaline in a first anaphylactic reaction and in nut allergy but not so frequently in the other indications.

Table 2 shows the percentage of participants who answered the questions for the prescription of an adrenaline auto-injector. The dosage for both adults and children was incorrect for 62.7% and 39.2% respectively. Timing for adrenaline administration was correct in the majority of responses.

Table 3 shows the responses to methods of administration of an adrenaline auto-injector. Most responders thought that adrenaline in such indications could be erroneously administered intravenously in the deltoid or buttocks and most were not aware that the injector must be kept intramuscularly for 10 seconds post-administration.

Table 2 *Questions answered for prescription details of adrenaline auto-injector (n=102).*

Prescription details	Correct	Incorrect	No answer
The dose of adrenaline in adults over 20kg is 0.5mg, n(%)	32 (31.4)	64 (62.7)	6 (5.9)
In children 10 to 20kg, the adrenaline dose is 0.15mg, n(%)	55 (53.9)	40 (39.2)	7 (6.9)
Adrenaline should be administered immediately every time the patient notices he ingested an allergen, n(%)	102 (100)	0 (0)	0 (0)
Adrenaline should be administered immediately if patient exposed to allergen, is asymptomatic, but far away from hospital, n(%)	95 (93.1)	6 (5.9)	1 (0.1)

Table 3 *Questions answered for mode of administration of adrenaline auto-injector (n=102)*

Mode of Administration	Correct	Incorrect	No answer
Blue end of the EpiPen® is site which contains injection, n(%)	82 (80.4)	19 (18.6)	1 (0.98)
Orange end of the EpiPen® is site which contains injection, n(%)	70 (68.6)	25 (24.5)	7 (6.8)
Adrenaline can be injected standing up, n(%)	81 (79.4)	14 (13.7)	7 (6.8|)
Adrenaline can be given intravenously, n(%)	13 (12.7)	85 (83.3)	4 (3.9)
Adrenaline cannot be injected through clothes, n(%)	96 (94.1)	4 (3.9)	2 (1.9)
One of the injection sites is the buttock, n(%)	43 (42.2)	59 (57.8)	0 (0)
One of the injection sites is the thigh, n(%)	100 (98)	2 (1.9)	0 (0)
One of the injection sites is the deltoid muscle, n(%)	65 (63.7)	37 (36.2)	0 (0)
The injector must be kept inside the area for 10 seconds, n(%)	26 (25.5)	76 (74.5)	0 (0)

Table 4 shows the responses to management after administration of an adrenaline auto-injector.

When asked these questions, 68.6% of participants did not feel confident explaining to patients when to use an adrenaline auto-injector while 72.5% of participants did not feel confident explaining to patients how to use it.

DISCUSSION

Few studies have assessed medical professionals' knowledge and ability to use adrenaline auto-injectors. This has never been done locally. In recent years, self-administered adrenaline auto-injector pens have become commonly prescribed for patients at risk of anaphylaxis or severe allergic reactions.[18] EpiPen® was the only epinephrine auto-injector at the time of data collection in Malta. We included pharmacists in our survey since these professionals too play an important role when dispensing an auto-injector to ensure that a patient is provided with sufficient knowledge.

In a survey among members of the American College of Allergy, Asthma and Immunology to assess their self-reported practices and procedures in the management of anaphylaxis, adherence to practice parameter recommendations was not surprisingly high.[11] On the other hand, a small study in

Table 4 *Questions answered for post-administration management of adrenaline auto-injector (n=102)*

Post-Administration	Correct	Incorrect	No answer
A localised erythematous skin reaction is a common side-effect, n(%)	101 (99)	1 (0.9)	0 (0)
It is advised to massage the area after injection, n(%)	19 (18.6)	83 (81.4)	0 (0)
It is common to have pruritus in the area post-injection, n(%)	58 (56.9)	38 (37.3)	4 (3.9)
Injection can be repeated at least after 1 minute, n(%)	21 (20.6)	78 (76.5)	3 (2.9)
Injection can be repeated at least after 5 minutes, n(%)	97 (95.1)	4 (3.9)	1 (0.9)
Injection can be repeated at least after 8 minutes, n(%)	67 (65.7)	32 (31.4)	3 (2.9)
After injection it's not always necessary for patient to go to A&E, n(%)	49 (48)	50 (49.1)	3 (2.9)

Netherlands using an online questionnaire sent to pharmacists, a country were pharmacists supply adrenaline auto-injectors to patients and instruct patients how and when to use it, only 8% respondents gave correct answers concerning the proper adrenaline auto-injector demonstration to food-allergic patients.[16]

Risk factors for an anaphylactic reaction were defined as follows: a previously severe anaphylactic reaction to a food requiring emergency treatment or hospitalization, asthma or asthmatic reactions to food, adolescent or young adult age, systemic reaction to traces of food allergen, and having a peanut or nut allergy.[19] There are six absolute clinical indications for an adrenaline auto-injector prescription as follows : previous anaphylaxis with food, latex, aeroallergens such as animals or other unavoidable triggers, exercise-induced anaphylaxis, previous idiopathic anaphylaxis, co-existent unstable or moderate-to-severe persistent asthma with food allergy, venom allergy in adults with previous systemic reactions underlying mast cell disorders.[2] Not all respondents were aware that adrenaline must be given always even with a first anaphylactic reaction. Less than half of respondents were aware of the necessity to prescribe adrenaline in patients with food allergy and co-existent asthma. Co-existing asthma is a risk factor for anaphylaxis and fatal anaphylaxis, especially if it is severe and uncontrolled.[2] Foods are the most common anaphylaxis trigger in infants, children, teens, and young adults. A meta-analysis with data from 34 studies reported an incidence rate of food-induced anaphylaxis to be 0.14 per 100 person-years at all ages, and up to 7 per 100 person-years in children aged 0 to 4 years.[20]

The dose of adrenaline during an anaphylactic reaction in adults or children was poorly known. Intramuscular adrenaline(1mg/ml) should be given at a dose of 0.01ml/kg of body weight to a maximum total dose of 0.5mg. Patients weighing between 7.5 to 25 kg should receive 0.15 mg dose with patients being moved to 0.3 mg dose at 25 to 30 kg.[2,21] At the time of the survey, the adrenaline auto-injectors were available as 0.15 or 0.3mg only. There is no data as to which patients should receive a 0.5mg dose auto-injector when this is available. The same dose could be repeated every 5 to 15 minutes as necessary.[2]

In a survey conducted among 674 Japanese physicians regarding timing of adrenaline administration it was concluded that they did not necessarily understand the importance of timing of adrenaline administration.[22] Early injection of adrenaline for anaphylaxis, defined as initial injection before emergency department arrival, significantly reduced the hospital admissions, compared with injection post-arrival.[20] A large series of anaphylaxis-related fatalities were reported when delayed injection of adrenaline was reported when only 23% of 92 individuals received it prior to cardiac arrest.[20] Timing of administration was not questioned in our survey. The correct end of the colour-coded adrenaline injector was not known to all interviewed. This could be dangerous in view of possible injection of the administrator's digit instead of the patients' musculature. However, adrenaline auto-injectors tend to have very clear instructions on the cover of the injector, facilitating and providing readily available instructions for correct administration during an emergency.13.7% of our respondents replied that adrenaline can be administered standing up. This should not be allowed in view of the risk of developing 'empty ventricle syndrome' which can precipitate a profound loss of blood pressure and resultant death during the anaphylactic reaction.[21] 83.3% said that the adrenaline during the anaphylactic reaction could be given intravenously. Adrenaline during anaphylaxis should ideally be given intramuscularly. Not only is it important to promptly self-administer an autoinjector using the correct technique, but the exact location of adrenaline deposition is also very important. Significantly faster peak plasma concentrations due to more rapid absorption are achieved via the intramuscular route when compared to the subcutaneous route[21,24]or intramuscularly in the upper arm.[22] The site of administration was correctly recognised as the anterolateral thigh but other sites such as the deltoid were also erroneously considered. Many failed to recognise the importance of keeping the injection in for 10seconds. In a study in Toronto aimed at assessing community-based professionals' knowledge of epinephrine auto-injector use. The most common problem with the use of the auto-injector trainer device was forgetting to hold the auto-injector in site for 10 seconds(n=122).[14]

In a study by Lowe et al 18% of respondents would not routinely inform patients of the need to seek immediate medical attention in the event of having to use a pen.[18] Only 48% of our respondents were aware that patients still need to be referred to the emergency department post-adrenaline administration. Treatment of anaphylaxis is not complete following resolution of an acute episode.[20] Biphasic anaphylactic reactions have been reported to develop in up to 20% of reactions.[2] In order to decrease anaphylaxis morbidity and

mortality in the community, referral to an allergist is recommended so as to reduce the risk of future severe anaphylaxis requiring hospital admission.[20] Specialist advice from an allergist is essential during a follow-up visit is essential to investigate possible triggers and potential cofactors, to perform a risk assessment and to provide advice including avoidance measures so as to prevent future episodes.[2] It is recommended that to prevent future anaphylactic reaction, the mainstays of long-term management include developing a personalized risk reduction strategy using a formalised anaphylaxis action plan with an adrenaline auto-injector and a personalized emergency response plan is crucial.[2,4,22] Patients should be equipped to treat recurrences that occur despite attempts to avoid trigger exposure in the community.[3] Research has shown that specific interventions by allergists may improve patient adherence to recommendations for managing anaphylaxis.[11]

The lack of confidence reported by our participants when explaining how to use an adrenaline auto-injector indicated a limited knowledge on its therapeutic indication, also reflected in the questions related to clinical indications for its use. In an international survey, less than half of general practitioners felt confident in their use and only 359(65%) of those who had prescribed adrenaline pens would arrange demonstration of when and how to use them.[18] Recommendations state that doctors have a responsibility to ensure that patients know how and when to take any prescribed medication, and it is unacceptable to prescribe a dangerous drug with no demonstration on how to use it.[25]

Upon prescription of an adrenaline auto-injector, healthcare providers familiar with adrenaline autoinjectors must instruct the patient on how and when to use the device, together with regular review of technique is vital for patients who have been prescribed these devices.[22,26] Studies have shown that usage skills for an auto-injector tend to decrease with time. Sicherer et alreported a decline after one year after the initial training in food allergies[27]while a study by Topal et alwho compared skills between 3 and 6 months after initial training, skills were stable after 3 months but worse skills were reported after 6 months.[13] These studies emphasize the need for repeat training in patients at risk of anaphylaxis.

Limitations of this study include the small sample size particularly among the pharmacist group, which did not allow comparison between both health care professionals and between medical doctors across the various working grades. The fact that the investigator was present during completion of the questionnaire could have imposed a degree of psychological pressure on the respondent. However, the questionnaire was posted into a box, which was only opened on completion of data collection.

Our survey results indicate that education is urgently needed among health care professions on the indications for prescription, mode of administration as well as post-administration management of this potentially life-saving medication. With the development of an emergency action plan to be distributed among healthcare professionals for readily available distribution among patients, together with the delivery of lectures to healthcare professionals on adrenaline auto-injector use, we aim to increase the knowledge of adrenaline auto-injectors locally and hence provide a better service to our vulnerable allergic patients.

ACKNOWLEDGEMENTS

I would like to thank all healthcare professionals who agreed to complete the questionnaire thus making this possible.

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