

COMMENTARY

Intramuscular epinephrine as first-line treatment of anaphylaxis: still concerns about its safety in the elderly?

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Anaphylaxis is a severe condition that can affect patients of all ages. Elderly patients must be considered particularly vulnerable to severe anaphylaxis due to many risk factors such as concomitant diseases and medications. Intramuscular administration of epinephrine is recommended as first-line therapy for anaphylaxis and its use should be promoted in every setting. Intramuscular epinephrine is recognized as generally safe and there are no absolute contraindications to the prescription of self-injectable adrenaline in older patients at risk of anaphylaxis.

Key words: Anaphylaxis, Epinephrine, Adrenaline

Anaphylaxis is a severe and potentially fatal hypersensitivity reaction that can affect patients of all ages. Anaphylaxis occurring in the elderly is associated to increased mortality and occurrence of cardiovascular complications. In addition, elderly patients present many risk factors because of comorbid conditions such as cardiovascular, cerebrovascular and lung diseases, hypertension, cardiac arrhythmias and concomitant medication such as betablockers which may interfere with the pharmacologic effect of adrenaline administration¹⁻³.

Thus, elderly patients must be considered particularly vulnerable to severe anaphylaxis and concomitant medication such as betablockers may have a negative effect on the pharmacologic effect of adrenaline administration. Nonetheless, new selective betablockers are less likely to carry that risk. Moreover, the use of betablockers could improve the survival of patients suffering for heart disease and the benefit can be greater than the risk of aggravating anaphylaxis⁴. An evaluation on concomitant medication in elderly patients at risk of anaphylaxis should be made together with cardiologist on individual basis¹.

In patients with coronary artery disease mast cells are also present in the atherosclerotic plaques contributing to atherogenesis. Mast cell-released mediators potentially lead to vasospasm of large coronary arteries, to a reduction of myocardial blood flow by influencing the vasomotor tone of small intramural coronary arteries and may exert direct dysrhythmogenic effects⁵. Acute coronary syndrome may occur during anaphylaxis either through vasospasm or through acute plaque rupture and thrombus formation. This condition is known as Kounis syndrome³. Anaphylactic reaction may also induce takotsubo syndrome, a stress-induced cardiomyopathy characterized by reversible left ventricular systolic dysfunction without any significant coronary artery disease⁶.

During anaphylaxis, compensatory endogenous catecholamine is released and its increase may play a major role in pathophysiology of stress-induced cardiomyopathy. Excess doses of exogenous adrenaline would increase the plasma catecholamine levels and promote platelet activation inducing platelet aggregation and thrombosis. Exogenous adrenaline might then contribute to stent thrombosis, coronary spasm and

transient takotsubo syndrome. Since Kounis syndrome and takotsubo syndrome can also be induced by anaphylactic reactions, more research on their etiology and pathophysiology may help identify risk factors and better therapeutic approach aimed to avoid these acute conditions⁷.

Guidelines from European Academy of Allergy and Clinical Immunology and from World Allergy Organization recommend prompt intramuscular injection of epinephrine as the first-line therapy for anaphylaxis because a delayed administration has been shown to result in poor outcomes and fatality. Epinephrine can counteract some of the most severe symptoms of anaphylaxis. Adrenaline acts on the α_1 -adrenergic receptor inducing vasoconstriction, increase of blood pressure and decrease of mucosal edema. Activation of the β_1 -adrenergic receptor increases cardiac output, and activation of β_2 -adrenergic receptor increases broncodilation and reduces immune mediator release^{8,9}.

Intramuscular administration of adrenaline into the mid-antero-lateral aspect of the thigh is recommended because epinephrine has a vasodilator effect in skeletal muscle which facilitates rapid absorption into the central circulation and prompt pharmacologic effect. In contrast, the vasoconstrictor effect of epinephrine injected into subcutaneous tissue potentially delays epinephrine absorption. Therefore, subcutaneous route should be avoided³.

A recent literature review suggested that the majority of cardiovascular adverse events seem to occur when epinephrine is administered via endovenous route and epinephrine overdose seem to be responsible of many of the adverse events¹⁰.

Intramuscular administration of epinephrine is recognized as generally safe and is regarded as an effective therapy for anaphylaxis and its use should be promoted in every setting. The initial dose in the adult is 0.3-0.5 ml of a 1:1000 dilution that corresponds at concentration 1 mg/ml: if ineffective the administration can be repeated after at least a 5 minutes interval. Intravenous continuous infusion should only be given to patients not responding to intramuscular injection⁹.

There are no absolute contraindications to the prescription of self-injectable adrenaline in older patients at risk of anaphylaxis though the limited mobility of joint diseases, such as osteoarthritis of the hand could reduce the ability to use the device¹. There are no reports about significant adverse effects, such as ventricular arrhythmias, hypertensive crisis, and pulmonary edema using autoinjectors for the treatment of anaphylaxis¹¹. In conclusion allergic diseases and anaphylaxis are becoming more frequent during senescence and older population must be considered particularly vulnerable

to severe anaphylaxis also because elderly patients are less likely to be prescribed self-injectable adrenaline^{1,12}. There are no absolute contraindication to the administration of epinephrine through intramuscular route in a patient experiencing anaphylaxis since benefits outweigh the risks in the elderly and in patients with pre-existing cardiovascular disease. Epinephrine auto-injectors should be prescribed for all patients with a history of anaphylaxis. Patients and their caregivers should be taught why, when, and how to inject adrenaline and should be equipped with a personalized written anaphylaxis emergency action plan.

History of allergic reactions and anaphylaxis besides an emergency action plan should be noted in patient records in non-hospital care settings such as nursing homes and epinephrine should always be available. Further education of clinicians regarding the appropriate route of epinephrine administration in the management of anaphylaxis should be promoted to avoid adverse events.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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