

Nebulized Epinephrine Treatment in Pediatric Emergency Department

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Abstract

Epinephrine, first isolated around 1900, is the main sympathomimetic agent released by the adrenal gland. It plays an integral role in the treatment of several diseases in the emergency department. It effects on alpha and beta adrenergic receptors. In lower doses, it usually causes systemic and pulmonary vasodilatation, with some increase in heart rate and stroke volume. A high dose causes intense systemic vasoconstriction. Its metabolism is rapid and half-life is less than 5 minutes.

Keywords: Childhood; Nebulized epinephrine; Pediatric emergency medicine

Many formulations of epinephrine make it useful as a primary or adjunct treatment for a wide variety of illness and conditions. It can be used in different doses and different routes of administration such as intravenous injection/infusion, umbilical artery/vein injections, endotracheal, intramuscular, local injection or nebulization. Bolus doses of epinephrine are widely used during cardiopulmonary resuscitation or anaphylaxis. Continuous infusions of epinephrine are increasingly used to treat cardiac dysfunction and septic shock. Also, it is added to local anesthetic solutions to decrease systemic absorption and prolong the duration of action of the anesthetic.

Recently nebulized form of epinephrine has been used for angioedema, croup and bronchiolitis in pediatric emergency medicine [1]. In these conditions, it works by relaxing the muscles in the airways and tightening the blood vessels. Thus, bronchial and tracheal secretions and airway wall edema decrease. Nebulized racemic epinephrine is an accepted treatment for airway edema and obstruction. Nebulized L-epinephrine is commonly used for treatment of bronchiolitis in children having significant respiratory distress. A meta-analysis revealed that epinephrine may be favorable compared to placebo and albuterol for short-term benefits among outpatients [2]. Another study found that nebulized epinephrine significantly improved oxygenation and reduced hospitalizations as compared with albuterol [3]. Nebulized epinephrine has been a treatment of croup since the 1970s. Epinephrine is associated with clinically and statistically significant transient reduction of symptoms of croup 30 minutes post-treatment. There is no evidence to suggest that croup symptoms, on average, worsen after the treatment effect of nebulized epinephrine dissipates. A recent systematic review [4] recommends that nebulized epinephrine may be used to treat symptoms associated with moderate to severe viral croup. A few prospective studies have investigated the efficacy of epinephrine treatment for post-extubation stridor [5]. Breuer's study which was the first experience about using inhalative epinephrine suggested that moist inhalative epinephrine administration via a suitable inhaler device may provide therapeutic

efficacy in ambulatory emergency treatment of systemic hypersensitivity reactions [6].

The mechanism of action is believed to be constriction of the precapillary arterioles through the β -adrenergic receptors, causing fluid resorption from the interstitial space and a decrease in the laryngeal mucosal edema. Traditionally, racemic epinephrine, a 1:1 mixture of the d- and l-isomers of epinephrine, has been administered. Racemic epinephrine was initially chosen over the more active and more readily available L-epinephrine to minimize anticipated cardiovascular side effects such as tachycardia and hypertension. There is evidence that L-epinephrine is equally effective as racemic epinephrine and does not carry the risk of additional adverse effects. The use of L-epinephrine is efficacious, well tolerated, less expensive and more readily available in many countries. This information is both practical and important, because racemic epinephrine is not available outside the USA.

The recommended dose of nebulized epinephrine is 0.5 mg/kg (maximum 5 mg) of 1/1000 solution in patients with stridor at rest or severe respiratory distress. Some authors suggest the nebulized epinephrine dose should be 2.5 mg per dose diluted with 4-5 ml normal saline in patients less than 4 years. In four years and older patients 5mg dose is sufficient with no more dilution. The racemic epinephrine dose is 0.5 ml of a 2.25% solution with 2.5 ml normal saline. Nevertheless, there is wide variation in terms of the epinephrine doses described in the literature. Many physicians are reluctant to use of epinephrine due to side effects of the drug. Furthermore physicians who apply nebulized epinephrine beware of sufficient doses as they consider these doses as high. Thus, alternative medications are preferred. Excessive doses of epinephrine may cause chest pain, tachycardia, hypertension, ischemic heart disease and cardiac arrhythmia. Cardiorespiratory monitoring should be considered if administered more frequently than 2 hours [7].

Nebulized epinephrine can be used in outpatient treatment. It provides temporary amelioration. The duration of activity of nebulized epinephrine is less than 2 hours. Rebound symptoms may occur. Thus, if a response is noted and discharge to home is contemplated, the child should be observed for at least 2 hours to be certain that the respiratory symptoms do not recur [7].

Nebulized L-epinephrine has been described as a safe treatment method and patients treated with epinephrine show only mild side effects. There is no clinical trial reported significant adverse events associated with nebulized epinephrine. Only three case reports have been reported about the adverse effects of nebulized epinephrine. An infant patient had local facial cutaneous vasoconstriction after epinephrine nebulization [8]. Previously healthy two cases developed cardiogenic shock or myocardial infarction after receiving three doses of nebulized epinephrine. This raises concerns about potential cardiac toxicity [9,10]. Therefore the use of nebulized epinephrine is considered to be universally safe. There is no exact contraindication for nebulized epinephrine. However in some conditions such as hypovolemic shock, hypertension, pheochromocytoma, diabetes mellitus, cardiovascular disease (left ventricular outflow tract obstruction, coronary artery disease), thyroid disease, and cerebrovascular disease, it should be used with caution because it has alpha adrenergic effects.

In conclusion, nebulized epinephrine is an efficacious, well tolerated, less expensive and safe drug of choice in cases of croup, angioedema, bronchiolitis and post-extubation stridor.

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