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Oxymetazoline-induced postoperative hypertension

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Key points

Oxymetazoline, an α-adrenergic agonist, is a commonly used topical agent to prevent bleeding following ear, nose, and throat surgery. Although there is generally limited absorption, several factors including excessive dosing may result in adverse effects including perioperative hypertension.

Abstract

Oxymetazoline is a topical sympathomimetic agent that is commonly used in over-the-counter nasal decongestant sprays. It is an imidazoline derivative that causes vasoconstriction of blood vessels by its direct effect on α-adrenergic receptors. Its vasoconstrictive action is used during otorhinolaryngological procedures to improve visualization of the airway and to minimize postoperative bleeding. Although used as a topical vasoconstrictor, when administered in larger doses, systemic absorption of oxymetazoline may lead to serious complications. We report the development of postoperative hypertension in a 3-year-old child caused by the application of oxymetazoline nasal packing following inferior turbinate reduction. The potential adverse effects of oxymetazoline are presented, previous reports reviewed, and options for management discussed.

Keywords: oxymetazoline; hypertension; postoperative

Introduction

Oxymetazoline (Afrin®, Merck Schering-Plough Pharmaceuticals, North Wales, PA) is an α-adrenergic agonist that is commonly used as a topical sympathomimetic agent in over-the-counter nasal decongestant sprays. Its vasoconstrictive action on blood vessels defines its clinical utility as both a decongestant and a topical hemostatic agent. It is used during ear, nose, and throat surgery to improve visualization of the airway and to minimize postoperative bleeding. Although there is generally limited vascular absorption, when administered in larger doses, uptake of oxymetazoline can lead to significant systemic effects. We report the development of postoperative hypertension in a 3-year-old child caused by the application of oxymetazoline nasal pledgets following nasal turbinate reduction. The potential adverse effects of oxymetazoline are presented, previous reports concerning adverse effects reviewed, and options for management discussed. The need for consensus guidelines regarding maximum dosage is proposed.

Case report

The Institutional Review Board of Nationwide Children's Hospital (Columbus, Ohio) does not require approval for the presentation of isolated case reports. The patient was a 3-year-old, 14 kilogram boy who presented with chronic nasal obstruction secondary to inferior turbinate and adenoidal hypertrophy. He had a history of recurrent otitis media with snoring and mouth breathing. He had not received any immunizations other than hepatitis B vaccine at birth. He had no known allergies and his medications included fluticasone nasal spray (one spray into each nostril, once a day) and acetaminophen as needed. He had not undergone previous surgery. His upper airway was normal and he was in no acute distress. Breath sounds were equal and clear bilaterally, and no murmurs were heard. The remainder of his physical examination was unremarkable. Nasopharyngeal fiberoptic examination performed one month prior to admission revealed adenoidal hypertrophy as well as inflammation and hypertrophy of the nasal turbinates. The child was admitted on the morning of the surgery for bilateral resection of the inferior turbinates and adenoidectomy. He was held *nil per os* for 6 hours. Preoperative vital signs revealed an oxygen saturation of 100%, blood pressure of 107/60 mmHg, and a heart rate of 80 beats/minute. He was transported to the operating room and routine American Society of Anesthesiologists' monitors were placed. Anesthesia was induced with the inhalation of 8% sevoflurane in oxygen. His vitals remained stable after induction with an oxygen saturation of 100%, heart rate of 98 beats/minute and a blood pressure of 103/61 mmHg. Following inhalation induction, a 20 gauge peripheral intravenous cannula was inserted and propofol (40 mg) was administered to facilitate intubation of the trachea with a 4.0 mm cuffed endotracheal tube. Bilateral inferior turbinate reduction was performed by coblation® followed by out-fracturing of the turbinates. There was minimal bleeding following turbinate reduction and oxymetazoline (Afrin®) soaked pledgets were placed in both nostrils. Adenoidectomy was performed using electrocautery and hemostasis was augmented with topical application of oxymetazoline. As per our usual practice, the volume of oxymetazoline was not measured. After ensuring that there was no active bleeding, an oxymetazoline-soaked pledget was placed in both of the nares. Immediately following the placement of the pledgets, the blood pressure was 104/67 mmHg with a heart rate of 78 beats/minute. The child was then transferred to the post-anesthesia care unit (PACU) with continuous pulse oximetry monitoring and 100% oxygen delivered via bag and mask ventilation through the endotracheal tube. On arrival to the PACU, bradycardia was noted with a heart rate of 48 beats/minute. The blood pressure was 106/84 mmHg. Bilateral breath sounds were confirmed by auscultation. Atropine (0.1 mg) was administered intravenously, following which the heart rate increased to 135 beats/minute and the BP increased to 166/129 mmHg. The oxymetazoline-soaked nasal pledgets were removed immediately and 10 mg of propofol was administered. Hypertension persisted and propofol was given in incremental doses of 10 mg each. Since no direct acting vasodilators (hydralazine) were immediately available in the free-standing outpatient surgery center, labetalol was administered in 1 mg intravenous increments to a total of 2 mg. Blood pressure and heart rate remained elevated, but at a lower range of 124-98/69-88 mmHg and 111-128 beats/minute respectively. Over the ensuing hour, the heart rate and the blood pressure gradually normalized to 111 beats/minute and 106/70 mmHg respectively. The child's trachea was extubated and the remainder of his postoperative course was uncomplicated. No further hypertension was noted during his PACU stay or after discharge during follow-up with his pediatrician.

Discussion

Various factors may result in perioperative hypertension in the pediatric-aged patient including renal failure or insufficiency, volume overload, or activation of the sympathetic nervous system from pain and agitation.[1-3] In rare circumstances, pharmacologic agents either ingested prior to surgery or administered during the surgical procedure may result in hypertension. Although generally of no clinical consequence, postoperative blood pressure control may be of greater consequence following surgery in patients with various co-morbid conditions, or clinical scenarios where the hypertension may result in excessive bleeding, disruption of suture lines, or hematoma formation. During the perioperative period, various medications ingested preoperatively or administered intraoperatively may also result in hypertension.

Topical sympathomimetic agents are used in otorhinolaryngological procedures to improve visualization of the airway and minimize postoperative bleeding. Oxymetazoline, an imidazoline derivative, is a direct acting α-adrenergic agonist. The action of oxymetazoline on specific α-adrenergic receptors ($\alpha_{1A,}$ $\alpha_{2A,}$ α_{2B}) that are expressed on the nasal mucosa causes vasoconstriction and defines its use as a nasal decongestant and topical hemostatic agent.[4] Although used for its topical effects, systemic absorption of these agents can have systemic effects, most commonly hypertension related to its action on the α-adrenergic receptors of the smooth muscle of the vasculature. Furthermore, when used in even larger doses in young children, oxymetazoline can activate central adrenergic receptors and lead to serious adverse effects including cardiovascular instability, respiratory depression, and sedation, which may be potentially life-threatening.[5-8] These imidazole derivatives are rapidly absorbed across mucosal membranes in children. Hence, toxicity generally develops within minutes, while resolution may take up to 24 hours.[9,10]

The bradycardia caused by sympathomimetic agents is a reflex baroreceptor response, which primarily attempts to maintain mean arterial pressure within a narrow range to protect against sudden increases in blood pressure.[11] This involves activation of the baroreceptors that are present in the carotid sinus and the aortic arch and transmission of these impulses to the medullary center of the brainstem. In the operating room, this reflex bradycardia may not always occur because general anesthetics, particularly volatile anesthetic agents, attenuate the baroreceptor response. Bradycardia may also be a consequence of the direct action of oxymetazoline on central α adrenergic receptors in the *locus cereleus* and central vasomotor areas of the brainstem. This bradycardic response occurs in association with hypotension related to a central sympatholytic effect.[12]

In our patient, packing of the nasal cavity with oxymetazoline soaked nasal pledgets, in comparison with just intranasal spraying of the topical vasoconstrictor, may have accelerated and increased the absorption of the agent. Absorption may have been further increased by the out-fracturing of the turbinates with disruption of the nasal mucosa. Alternatively, this may have led to potentiation of the bradycardic effect through a trigeminocardiac reflex. The trigeminocardiac reflex, similar to the oculocardiac reflex, is a complication described during maxillofacial surgery that leads to bradycardia. Traction on the orbital muscles or compression of the globe during surgery activates the oculocardiac reflex.[13] Neuronal impulses are transmitted through the first branch of the trigeminal nerve to the motor nuclei of the vagus nerve. The efferent pathway involves the cardiac branches of the vagus nerve resulting in bradycardia. A similar reflex has been reported during midface surgery with the afferent impulse transmitted by the second branch of the trigeminal nerve. It has been observed that pre-existing cardiac disease, hypoxia and hypercarbia augment this reflex while ketamine anesthesia blunts it.[14,15]

Reigle et al. compared the use of oxymetazoline (0.05%), phenylephrine (0.25%) or cocaine (4%) during functional endoscopic sinus surgery in children.[16] Only phenylephrine was associated with an increase in blood pressure while subjective evaluation of bleeding and surgical visualization was significantly better with oxymetazoline. The authors concluded that oxymetazoline was the preferred vasoconstrictor in children. Higgins et al reviewed the use of topical vasoconstrictors during ear, nose and throat surgery.[17] They compared the efficacy against the risks associated with the topical use of phenylephrine, cocaine and oxymetazoline and proposed recommendations to reduce the incidence of systemic complications caused by these agents in the operating room. Halogenated volatile anesthetics, particularly halothane, have been shown to sensitize the myocardium to the arrhythmogenic action of adrenergic agents and its concurrent use with topical vasoconstrictors may worsen cardiac function.[18] However, sevoflurane, isoflurane and desflurane are not associated with an increase in the potential for arrhythmias. These authors recommended the use of oxymetazoline as first line agent for topical vasoconstriction because of its improved safety profile.

The key to the management of oxymetazoline-induced hypertension is diagnosis as its treatment is distinctly different from other causes of perioperative hypertension as treatment should be aimed at reducing the α-adrenergic receptor induced vasoconstriction. Non-specific β-adrenergic antagonists should be avoided because the resulting unopposed α-adrenergic effects will lead to vasoconstriction.[19] This results in profound vascular smooth muscle contraction leading to an increase in the peripheral vascular resistance and exacerbation of the hypertensive episode. The increase in the peripheral vascular resistance also shifts the blood from the systemic to the pulmonary circulation, which is less sensitive to the vasoconstricting properties of the α-adrenergic agonists, resulting in pulmonary edema and a decrease in the cardiac output.[20,21] The treatment of oxymetazoline-induced hypertension, should include directly acting vasodilators (hydralazine or sodium nitroprusside) or selective α-adrenergic antagonists such as phentolamine. Phentolamine can block both central and peripheral α-adrenergic receptors, and its action is easily titratable.[21] In cases of refractory bradycardia, anticholinergic agents like atropine or glycopyrrolate may be used, but with caution, owing to concerns of uncontrolled hypertension.[22] In our case, we initially asked for hydralazine, but this agent was not available in our outpatient surgery center. As such, incremental doses of propofol were used initially to rapidly control the hypertension followed by labetolol to provide a more lasting effect. Since this event, hydralazine has been added to the formulary at the outpatient surgery center.

Although used as topical vasoconstrictors, systemic absorption of agents such as oxymetazoline may lead to serious complications. Groudine et al proposed the New York State Guidelines for the safe use of phenylephrine as a topical hemostatic agent in 2000.[19] Their recommendations included the use of phenylephrine at minimal doses that would be sufficient to achieve topical vasoconstriction with an initial dose not to exceed 20 μg/kg/day in children weighing less than 25 kg or a maximum dose of 0.5 mg in patients weighing more than 25 kg and adults. However, there remain no specific recommendations on the 'maximum dosage' of topical oxymetazoline. More recently, Latham and Jardine reported oxymetazoline-induced hypertension in a 4-year-old child.[23] They also sought to investigate alterations in the amount of medication delivered based on the delivery method as well as the absorption of oxymetazoline onto pledgets. There was up to a 75-fold increase in the volume of medication administered when the bottle was held inverted. Squeezing the bottle in the upright position resulted in a mist with the delivery of 28.9 ± 6.8 μl of fluid. The amount delivered was effort-independent. When the bottle was inverted and squeezed, the volume administered was effort-dependent. The average volume delivered was 1037 ±

527 μl (range: 473-2196 μl). The volume of oxymetazoline absorbed by each surgical pledget was 1511 ± 184 μl.

As an over-the-counter medication, oxymetazoline's potential for morbidity may be under appreciated. Additionally, as it is delivered via a spray mechanism or via soaked cotton pledgets, attention to exact dosing or limitation of the dose is frequently absent. Given the occasional reports of adverse effects related to its use, it appears that it is essential to establish a consensus for the appropriate dosing of oxymetazoline. Until then, following the manufacturer's recommendations, restriction to 2-4 sprays per nostril seems appropriate. The bottle should not held inverted and squeezed into the nares as overdosing is likely to occur. When pledgets are used, attention should be directed toward the total volume administered.

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