Antihistamines for children with otitis media

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Abstract

Question Otitis media is a very common condition in pediatrics and can be quite distressing for children and their parents. Is there a role for antihistamines and decongestants in the management of acute otitis media or otitis media with effusion in children?

Answer Traditionally, antihistamines and decongestants have been used in the treatment of otitis media; however, recent guidelines, which are based on study findings with negative results, recommend against routine use. No antihistamine-decongestant combination has been shown to be of clinically significant benefit, and there are potential adverse events that need to be taken into account.

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Otitis media (OM) is one of the most common reasons for visits to family physicians and emergency departments by children, costing more than 3 billion dollars annually in the United States.[1,2] Most children (50% to 85%) will have an episode of acute otitis media (AOM) by the age of 3.3 Between 2008 and 2009 alone, it was estimated that 50% of Canadian children 2 to 3 years of age had at least 1 ear infection.4

Acute otitis media and otitis media with effusion (OME) are 2 distinct entities.[3] Despite being a common condition, one study found that among 165 clinicians, 147 different clinical definitions of AOM were described.[5] Acute otitis media can be defined by 3 components: acute onset (less than 48 hours); presence of middle-ear fluid; and clinical features such as otalgia, fever, and tympanic membrane redness.[5] Pneumatic otoscopy is the best procedure for diagnosis.[6] Otitis media with effusion is the presence of fluid in the middle ear in the absence of acute inflammation[5] and can precipitate or follow AOM; however, it is important to distinguish between the 2, as treatment varies considerably.[7]

Antihistamines and decongestants in OM

The pathogenesis of OM, although not well understood, is multifactorial, involving the host's immune system (adaptive and innate), as well as eustachian tube (ET) dysfunction, environmental factors, and microbial load (bacterial and viral).[3]

Both viruses and bacteria can produce histamines, as demonstrated in a study that examined 677 samples of middle-ear fluid from 248 children between the ages of 2 months and 7 years.[8] Thus, antihistamines might have a role in reducing inflammation and hence the potential to decrease duration of OM. The histamine–type 1 receptor in particular has been associated with allergic inflammation.[9] Decongestants are also believed to reduce mucous membrane swelling via vasoconstriction secondary to their action on adrenergic receptors.[6]

Three interventions have been investigated to assess the role of antihistamines and decongestants in OM: decongestant alone, antihistamine alone, and a decongestant-antihistamine combination.

Decongestant alone. Various preparations and doses have been studied to identify the effects of decongestants. In one American study of 196 children, approximately three-quarters of patients who received pseudoephedrine (34 of 45) and three-quarters of patients who received placebo (36 of 40) had resolution of tympanic membrane inflammation.[10] In a more recent Cochrane review of OME, including 16 randomized controlled trials (RCTs), the groups receiving decongestant alone had a relative risk (RR) of 1.06 (95% CI 0.92 to 1.22) compared with placebo for resolution of OME signs and symptoms within 1 month,[6] demonstrating no benefit.

Antihistamine alone. Most studies to date have used first-generation antihistamines.[2,11,12] In one RCT, in which 179 children with AOM between the ages of 3 months and 6 years were treated with ceftriaxone, treatment failure (requiring another treatment with antibiotics during the first 2 weeks) was documented in 18% of those receiving antihistamines and in 19% of those receiving only corticosteroids or placebo (P=.93).[11] Moreover, despite having a smaller sample size, the Cochrane review's antihistamine-only groups had an RR of 1.05

(95% CI 0.8 to 1.38) for delayed persistence of OME,[6] which suggests antihistamines alone might have a negative effect on children with OME.

Antihistamine-decongestant combination. In a recent Cochrane review of 15 RCTs that evaluated decongestant or antihistamine treatment for children with AOM, the antihistamine-decongestant group was found to have an RR of 0.76 (95% CI 0.60 to 0.96; number needed to treat = 10) for persistent AOM at 2 weeks.[13] This result, while statistically significant, had little clinical significance and might have been influenced by studies with poor allocation concealment and validity scores. In treatment of children with OME, the antihistamine-decongestant combination group had no benefit, with an RR of 0.97 (95% CI 0.89 to 1.04) for complete resolution of symptoms within 1 month.[6]

Possible explanations for the findings include the prominent role of other inflammatory mediators and cytokines, inflammatory cells, immunoglobulin, and complement, as well as bacterial antigens in OM.[11,14] Alternatively, the dose required to see an effect might be higher than the doses used in clinical trials.[11] It has also been postulated that antihistamines fail to substantially reduce histamine concentrations, as they target histamine–type 1 receptors as opposed to inhibiting mast cell mediator release.[12]

Safety of antihistamines and decongestants

Statistically significant higher rates (11%) of side effects (SEs) were documented for treatment of OME compared with placebo (RR of 2.70; 95% CI 1.87 to 3.88; number needed to harm = 9).[6] Side effects included sedation, irritability, and gastrointestinal upset. Moreover, the most commonly reported moderate SEs of antihistamines were drowsiness (22% to 34%), nervousness (7% to 20%), dry mouth (16% to 27%), diaper rash (7% to 32%), and an increased urine output (14% to 27%).[11] The commonly used antihistamines chlorpheniramine, cetirizine, and loratadine all had at least 2 SEs with a frequency of greater than 10%.[6] For the common decongestants phenylephrine and pseudoephedrine, the overall SE rates were 24% and 6%, respectively.[6] A study from the United Kingdom of children who were 3 to 10 years old had 12 SE-associated withdrawals; 9 of 12 children who used pseudoephedrine experienced "bad temper," irritability, dizziness, general malaise, and poor sleeping.[15]

Certain SEs caused by antihistamines, including visual alterations, are secondary to their action on antimuscarinic receptors.[9] Second-generation antihistamines might be better in treating OM because they do not cross the blood-brain barrier and are less sedating.[2,9] They also lack anticholinergic activity.[2]

Antihistamines have been associated with prolonging the duration of middle-ear effusion. The Cochrane review on decongestants and antihistamines in children with AOM found that patients treated with antihistamines alone were more likely to have AOM at 4 weeks (RR 1.91; CI 1.01 to 3.64; number needed to harm = 5.9).[13] It is possible that inhibition of ET function through reduced mucociliary function and anticholinergic properties might be the cause.[11] It is also possible that antihistamines increase the viscosity of middle-ear fluid by altering middle-ear secretory cell function and thus influence drainage and absorption.[11]

Guidelines and recommendations

In the American Academy of Pediatrics 2004 clinical practice guidelines, use of antihistamines and decongestants was not recommended owing to their lack of effectiveness.[16] This is similar to guidelines by the Canadian Paediatric

Society[17] and consistent with the most recent Cochrane reviews on OME and AOM,[6,13] as well as international guidelines.[18] The American Academy of Pediatrics' most recent guidelines on AOM do not even mention antihistamines and decongestants.[7]

Areas for research

It has been postulated in the past that allergy has a role in OME.[16] A 2008 randomized study of 15 allergic rats reported a statistically significant difference, in favour of treatment, in effusion volume at 2 to 6 hours between the control group and those given olopatadine ($P=.011$) and azelastine ($P\leq.001$).[19] This finding is consistent with a Greek study in rabbits[20] and does seem to suggest a role for antihistamines in allergy-induced ET dysfunction. Although patient safety considerations are yet to be resolved, future research should look into higher doses of drugs. Furthermore, research with second-generation antihistamines might allow higher doses of medication, as they have lower SE profiles.[2]

Conclusion

Current evidence does not support routine use of antihistamines and decongestants in children with OM, but they might be used for treatment of specific patients, such as those with OME due to allergies.

Competing interests
None declared

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