

Therapeutics for Upper Respiratory Infections

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Upper respiratory infections (URI) are very common in childhood, causing of 1/3 of pediatric consultations among children under five. In this age range, children may have between 4-14 URI per year depending on a number of variables. Younger age, day-care, exposure to pollutants (including cigarette smoke) and increasing number of cohabitants sharing living space are some of the risk factors for increased rate of infection. Most URI are caused by viruses and have a self-limited evolution, generally resolving within 7-14 days. Even though these infections generally have a self-contained course, it is estimated that 25% of all medications taken by children are for the symptomatic relief from URI. In this chapter we present the results of randomized and controlled studies describing the efficacies of the most commonly used medications for relief from these symptoms ¹⁻³.

Methods

MEDLINE and LILACS databases were mined using the following keywords: acute respiratory infections, common cold, therapeutics, saline solution, decongestants, antihistamines, mucolytics, expectorants, antitussive drugs, anti-pyretic, non-hormonal anti-inflammatory drugs, vitamin C and antibiotics. Randomized articles were selected with a double blind, controlled meta-analysis.

Results

Many of these medications lack strong evidence from the literature demonstrating their efficacy in children, therefore these medications should be used with caution in order to avoid any possible side effects.

Antihistamines and Antihistamine/Decongestant Associations

Nasal congestion is the most common symptom of URI and even though many medications claim to provide symptomatic relief, few comprehensive studies have evaluated their efficacy, particularly in children. Topical nasal decongestants, despite fast symptom relief, may have a rebound effect when the medication is stopped and their use in children is not recommended due to a high rate of side effects. In adults, some studies suggest ¹⁻³ that the use of pseudoephedrine alone or combined with antihistamines can bring some relief for nasal symptoms ⁴.

In a meta-analysis conducted by Tavener et al (2004) ⁵, 32 studies (n=8930 patients) were analyzed evaluating the value of antihistamines in alleviating URI symptoms (nasal congestion, rhinorrhea and sneezing) in both adults and children. The results of the study demonstrated:

- Single therapy with an antihistamine did reduce sneezing among both the adults and children, but had no effect on congestion or rhinorrhea.
- In 5 randomized controlled studies, dual therapy with antihistamines and decongestants demonstrated no benefit to children and little improvement (13%) in nasal symptoms among 286 adults.
- First generation antihistamines caused some adverse effects such as, sleepiness, numbness, bradycardia and hypertension.

Since dual therapy with antihistamines and decongestants only yielded about 10% improvement, this regimen appears to have little clinical value in treating adults with URI.

Currently there are no extensive studies for the use of these medications in children under 5 and as they are more prone to side effects, these medications are generally not recommended for this age group ⁴.

A recent study ⁵ of 238 adults complaining of nasal congestion, showed that oral intake/use of pseudoephedrine led to decreased nasal congestion in young adults on the first and second days of treatment, with slight elevation in the heart rate (2-4 bpm).

Saline Solution (SS - 0,9%) and Hypertonic Saline Solution (HSS - 3%)

Nasal hygiene with isotonic solutions (SS) is the most useful adjuvant treatment for URI in adults and children and its aim is helping mechanical washout of secretion and bacteria thereby increasing airway permeability ¹⁻².

In the last decade, many studies ⁷⁻¹³ have evaluated the use of hypertonic saline solution (HSS) in treating symptoms of URI among adults and children. In a study including 60 children and teenagers with symptoms of sinusitis for 4 weeks, the use of HSS 3,5% in conjunction with other medications was shown to be safe and effective in reducing the symptoms after three weeks. HSS was able to alleviate symptoms of 76 adults with chronic rhinosinusitis, improving quality of life and reducing the use of antihistamines and antibiotics. In this study ⁸, 87% adhered to treatment regimen and obtained a 10% benefit after two weeks of HSS use. However, in another study ⁹ comparing the effectiveness and safety of HSS vs SS in 140 adults, complaints of a burning discomfort were three times higher in the HSS group and 44% of individuals would not use HSS again due to discomfort.

In two studies with children ¹⁰⁻¹¹, HSS was also effective and had no adverse effect in a period up to six weeks of follow-up. However, the sample size was 44, 22 HSS and 22 controls.

HSS is thought to decrease tissue edema, as well as enhance ciliary movement thereby acting to decrease the nasal congestion. Although apparently safe, this kind of treatment can be associated with an increased incidence of local pain, burning and bleeding. There is evidence of increased airflow immediately after HSS use, but this effect is usually limited to 60 minutes. At higher concentrations (>3.5%) treatments may cause bronchoconstriction and nasal mucosal alterations, therefore they are contraindicated in children, especially asthmatics ^{7,12,13}. Even though these treatments are described as cost-effective in the literature, it is also important notice that they are not found in Brazil ¹⁴⁻¹⁵.

Two recent studies showed that the use of HSS in addition to epinephrine

inhalation was able to reduce hospital stays one full day in children hospitalized for bronchiolitis¹⁴⁻¹⁵. As HSS can cause bronchoconstriction in asthmatic children, we believe that further studies are necessary with higher number of cases to evaluate risks and benefits of this treatment.

Antitussives

Although some antitussive medications have proven in vitro activity, studies performed in children could not confirm any efficacy^{1-3, 16-18}. Many of these medications claim to improve the sleep quality of children as well as relatives, but in a randomized control study where dextromarfan, difenidramin and placebo were used in 100 children, it was noticed that all three groups were significantly better after second day of treatment. Therefore, it is unlikely that the antitussives have any effect on the natural course of the cough symptoms related to URI¹⁸.

Mucolytics and Expectorants

There are many medications for the treatment of cold symptoms¹⁻². Among the mucolytics and expectorants, it is important to mention that the iodine containing medications are no longer indicated for use due to the risk of allergic reactions and interference with thyroid function. The effectiveness and side effects of other substances such as ambroxol, has been poorly studied. Due to the absence of studies showing the effectiveness of these medications, they are not recommended for use in children. Many of the mucolytics and expectorants have artificial coloring, conservatives and may be prepared in combination with other medications, which can lead to adverse effects^{1-3,17,19-20}.

Antibiotics for Rhinosinusitis Secondary to Viral Infection

One meta-analysis of the use of antibiotics for the treatment of adults and children presenting with purulent nasal discharge for a period less than ten days, showed that it does not prevent complications and it is not without risk. The adverse effects of antibiotic use (allergic reactions, gastric reflux, difficulty isolating the etiology) do not only affect the individual, but can also be harmful to the community. Improper use of antibiotics is the main cause of increasing antibiotic resistant bacteria. In order to prevent antibiotic resistance it is important to avoid unnecessarily prescribing antibiotics for children and adults when the symptoms suggest a viral etiology^{12, 21}.

Vitamin C

In six randomized studies, including more than five thousand URI symptoms, evidence has demonstrated that vitamin C over 200 mg/day did not reduce the incidence of the disease when compared to placebo (RR = 0,99 / IC 95% : 0,93 - 1,04). The benefits of vitamin C were only observed in specific groups, such as marathon athletes and Artic-based soldiers. Administration of vitamin C after the onset of common cold symptoms was analyzed in fifteen studies including 2753 people and also did not demonstrate benefit for children or adults²².

Other Medications and Recommended Measures for the Treatment of URI

Non steroidal antinflammatory drugs (NSAID) are not recommended for children with URI symptoms because of higher toxicity among these medications when compared to regular analgesics, such as dipirone and paracetamol²³⁻²⁴. Some

authors propose zinc (tablets and topical use) for the relief of symptoms of URI; however, recent studies showed no they have no efficacy and may cause anosmia as well as have a bad taste ²⁵.

Herbal and household remedies

Herbal and household remedies are used in some communities, but these medications should be used with caution as there is no safety profile on them, as well as few controlled studies, which actually prove the efficacy of these remedies ²⁶⁻²⁷. Variations on concentrations and preparations make it hard to compare results. Use of local heat is also controversial; inhaling water vapor at 40 degrees centigrade may provide some relief of nasal congestion ²⁸⁻²⁹. Upon searching we did not find any studies detailing this treatment in children and due to risk of burn accidents, we do not recommend it.

Conclusions

The majority of medications used for the treatment of URI and other respiratory infections have no proven efficacy and can cause adverse side effects. Therefore, caution should be used when prescribing/recommending these medications. Finally, it is important to mention that many over the counter medications used to treat URI contain antipyretics and the combination of different medications may cause overmedication. The most important measures in decreasing the incidence of the URI are: frequent hand washing, avoiding crowded environments, decreasing exposure to pollutants such as cigarette smoke and maintaining good nasal hygiene by spraying saline solution (0,9%) ^{1,2,30-31}.

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