An Evidence-Based Approach to Management of the Common Cold

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Introduction

The common cold is one of the most frequent illnesses worldwide. Each year, the average adult develops two to four colds and the average child develops four to eight colds, resulting in a substantial amount of time lost from work and school [1]. Most colds are caused by rhinovirus, but several other agents can be involved [2,3]. Patients usually exhaust several home remedies and over-the-counter medications before seeking help from their physicians. The challenge of how to treat these patients should be addressed with the best evidence-based information available. Although no cure for the common cold is known, the medical literature describes a number of treatments. This article reviews the literature on treatments and presents a practical approach to caring for patients suffering with a common cold.

Methods

A MEDLINE search for articles published between 1966 and 1998 regarding management of common colds was done. Well-designed studies, reviews, and other references selected from articles cited were reviewed.

Review of Treatment Modalities

Treatments for the common cold can be grouped into four modalities: measures to relieve symptoms, pharmacologic blockers, antiviral medications, and other agents whose mechanism of activity has not yet been determined [4]. The two models used most often to study cold treatments are the virus-challenge model (ie, experimentally induced colds) and the naturally occurring cold model. Both models have advantages and disadvantages [5].

Symptomatic Measures

Antihistamines. The first-generation antihistamines doxylamine succinate, clemastine fumarate, and chlorpheniramine have been shown to alleviate rhinorrhea and sneezing but not other symptoms of the common cold [6–8]. However, attempts to confirm this subjective improvement by objective measures, such as rhinomanometry and tympanometry, were not consistently successful [9]. A disadvantage of first-generation antihistamines is that they must be administered frequently because of their relatively short half-life. Because these medications cause drowsiness, they are especially beneficial to patients whose sleep is disturbed by cold symptoms. Second-generation, long-acting antihistamines are less effective in relieving rhinorrhea and sneezing, most likely because of their selective action on histamine 1 receptors and lack of anticholinergic activity.

Anticholinergics (parasympatholytics). Intranasal application of ipratropium bromide [10] or atropine methonitrate [11] spray remarkably reduced sneezing and nasal drainage in both naturally occurring and experimentally induced common colds. Like first-generation antihistamines, anticholinergics are short-acting and require repeated application to maintain their therapeutic effect. Nasal dryness, headache, and occasional epistaxis are the most common side effects.

α-Adrenergic agonists (sympathomimetics). Oral and intranasal phenylephrine [12] and oxymetazoline [13] are potent decongestants that effectively relieve rhinorrhea associated with the common cold. It is important to note that some generic formulations of these medications were not found to be bioequivalent to the brand name products [14]. Prolonged or excessive use of α-adrenergic agonists results in a rebound phenomenon—rhinitis medicamentosa—after stopping the medication. In addition, patients receiving antihypertensive medications must be warned of the potential drug interactions and possible worsening of hypertension.

Nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs have long been used to alleviate fever, malaise, and headache in a variety of illnesses. Their therapeutic effects are attributed to the inhibition of prostaglandins involved in the pathogenesis of inflammation and fever. Earlier studies involving aspirin [15] and ibuprofen [16] warned about
possible prolongation of viral shedding and decreased serum-neutralizing antibody response with their use. More recently, naproxen, a cyclooxygenase inhibitor, was found not to cause these problems [17]. Aspirin and aspirin-containing products should be used with caution in children because of the risk of Reye syndrome. Gastric irritation is the most common side effect of NSAID use.

**Steam inhalation.** Breathing in steam from a bowl decreases the local nasopharyngeal irritation that accompanies colds. Studies to assess this maneuver under controlled circumstances have yielded conflicting results, thought to be due to differences in the devices used, treatment schedules, and placement of the heating nozzle [18,19]. However, it is clear that viral shedding and antibody response are not altered by raising the temperature inside the nasopharynx to 43°C [20]. The only possible adverse effect of steam inhalation is local irritation. Given the degree of precision needed to achieve a beneficial effect, this therapy may not be practical for the pediatric age-group.

**Expectorants/antitussive agents.** Cough suppressive agents are rarely needed during the initial stages of common colds. Expectorants, such as guaifenesin, may decrease sputum thickness, particularly when the patient is well hydrated. However, in controlled studies their effect was marginal compared to placebo [21].

**Summary:** Antihistamines, anticholinergics, and α-adrenergic agonists are effective in decreasing rhinorrhea. NSAIDs relieve headache and malaise accompanying colds. Steam inhalation may have a local soothing effect.

**Pharmacologic Blockers**

**Mast cell stabilizers.** Widely used in the prevention of asthma attacks, mast cell stabilizers inhibit the release of histamine and other chemical mediators from mast cells in response to infection and other triggers of inflammation. They also down-regulate intracellular adhesion molecules type 1 (ICAM-1), the receptors for rhinovirus attachment in the respiratory epithelium. In preliminary studies, both nedocromil sodium and sodium cromoglycate seemed to reduce the severity of rhinovirus colds [22,23]. Neither, however, affected the frequency of viral shedding or the serologic response to infection. Mast cell stabilizers cause minimal side effects, but larger studies to assess their effectiveness in treating the common cold are needed.

**NSAIDs.** As noted previously, these drugs are effective inhibitors of the inflammatory mediators involved in colds.

**Summary:** Mast cell stabilizers are promising agents for treating the common cold, but more studies are needed to assess their effectiveness.

**Antiviral Medications**

**Interferons.** These nonspecific antiviral agents have been studied widely in both natural cold and experimental cold models. Interferon alfa-2b was prophylactic in both models when given before symptoms developed, but its effect varied with the dosage, form, and frequency of administration [24,25]. On the other hand, interferon-β was ineffective in preventing the development of natural colds [26]. The main adverse effects of interferon-β and interferon alfa-2b were nasal irritation, dryness, and bleeding, which can be confused with the actual illness. Combining interferon with other antiviral agents may help achieve synergy, prevent emergence of resistance, and decrease some of these adverse effects [27].

Specific antiviral agents. Specific antiviral agents inhibit rhinovirus attachment or uncoating by binding to specific hydrophobic pockets in the virion capsid [28]. In vitro studies with ribavirin were promising [29], but the clinical application and usefulness of this agent in the management of colds are probably limited because of its side effects. Other oral agents, such as dichloroflavan [30], and intranasal agents, such as pirodavir [31], were not effective in preventing or treating colds in clinical trials, despite reducing viral shedding. The main factors impeding the development of effective antiviral agents for the common cold are the wide array of causative viruses that need to be targeted, the development of mutant or resistant viral strains, and the accompanying toxicities in treating such a self-limiting illness.

**Summary:** At this time, interferon alfa-2b and specific antiviral agents are not practical therapy for the management of the common cold.

**Other Agents**

**Zinc salts.** Four studies designed to assess zinc salts as treatment for the common cold showed them to have a therapeutic effect, whereas four similar studies showed them to have no effect. A recent meta-analysis of the eight studies did not find evidence to support the use of zinc lozenges in treating the common cold [32]; however, the results of this meta-analysis have been questioned [33]. Different causative viruses and variations in the dosages given may explain the discrepant results of these studies. The efficacy of zinc lozenges in treating common colds is thought to depend on the bioavailability of zinc ions [34].

The exact mechanism of action of zinc in the common cold is not known, but it has been hypothesized that zinc
blocks the binding of rhinovirus to the ICAM-1 receptors in the respiratory epithelium, inhibits viral capsid protein synthesis, has a membrane stabilizing effect, inhibits prostaglandin metabolites, or increases production of interferon. The main side effects of zinc lozenges are gastrointestinal upset, metallic taste, and potential copper deficiency.

**Vitamin C.** The controversy of whether to use vitamin C in the treatment or prevention of common colds continues. In 1975, a meta-analysis by Chalmers [35] found no evidence to support its use, given its minor questionable benefits and the lack of data on long-term toxicity at that time. More recently, Hemila [36] reanalyzed Chalmers’s review, pointed out several errors, and concluded that vitamin C significantly and safely reduces the severity and duration of common colds. The most appropriate dose has not been determined, but doses greater than 1 g per day are thought to provide the maximal benefit. The beneficial effects of vitamin C on common cold symptoms are thought to be due to the vitamin’s antioxidant properties.

**Glucocorticoids.** Two studies found that neither systemic nor intranasal steroids prevented or relieved colds caused by rhinovirus [37,38]. Nasal inflammation and kinin levels in nasal washes were reduced, but the mean viral titers were actually increased with prednisone. The side effects of steroids are myriad, further justifying the avoidance of glucocorticoids in the treatment of the common cold.

**Aqueous iodine (2%).** One small study [39] found that applying aqueous iodine to the hands of volunteers prevented transmission of rhinovirus. The use of iodine is probably cosmetically impractical, but other less visible substances may help prevent transmission among family members.

**Echinacea.** Echinacea is a native American plant that has been used in traditional medicine for several decades. It promotes wound healing and enhances the immune response by stimulating the phagocytic activity of polymorphonuclear neutrophilic granulocytes [40]. In addition, it was found to be effective for prophylaxis and treatment of cold and influenza symptoms [41,42]. Echinacea produces no known side effects, but it becomes immunosuppressive with continuous use for more than 6 weeks. However, the U.S. Food and Drug Administration does not regulate the dose and purity of such natural preparations, and standardization of the compound remains a concern [43].

**Ginsana G.** Ginsana G, a ginseng extract, was found to decrease the frequency of influenza and the common cold by potentiating the antibody response to influenza vaccine [44]. Its principal side effect is insomnia.

**Antibiotics.** Despite the lack of utility of antibiotics in the treatment of common colds, physicians continue to prescribe them to 51% of adults and 45% of children with colds, accounting for 10% and 12% of all antibiotic prescriptions, respectively [45,46]. The abuse of antibiotics is additionally attributable to patients’ misconceptions. One survey found that 32% of parents believed that antibiotics are indicated for treatment of their children’s colds and 18% actually had given their children antibiotics before consulting a physician [47]. Widespread antimicrobial resistance and the potential adverse effects of all antibiotics are good reasons to change such practices.

**Summary:** Controversy surrounding the use of zinc salts and vitamin C in the treatment of colds persists. The use of glucocorticoids or antibiotics for treating the common cold should be discouraged.

**A Practical Approach to Care**

The majority of common colds are benign and self-limited, but occasionally cases are associated with serious illness [48,49]. Differentiating common cold from other upper respiratory tract illnesses remains difficult. Allergic rhinitis is usually accompanied by nasal and eye itching with excessive lacrimation, usually occurring in children who have a family history of atopy. The rhinitis may be seasonal, perennial, hormonal, vasomotor, or gustatory [50,51]. Patients with streptococcal pharyngitis usually have fever, exudate on the posterior pharyngeal wall, and tender anterior cervical nodes [52]. Sinusitis is accompanied by headache and purulent nasal discharge. Patients with influenza are likely to have the systemic symptoms of myalgia, arthralgia, and malaise.

A major obstacle to effective management of colds is the inadequate education patients receive from their health care providers about appropriate treatment [53]. Physicians should be aware that patients’ satisfaction does not hinge on receiving prescription or nonprescription medicines [54]. Patients with colds should be advised to rest, to stay home during the initial period of the illness to prevent the spread of infection, and to drink plenty of fluids to avoid dehydration. Agents aimed specifically at alleviating rhinorrhea (eg, antihistamines, anticholinergics, α-adrenergic agonists) are usually helpful during the initial phase of the illness. NSAIDs can be given to alleviate malaise, headache, and fever. Vitamin C in doses exceeding 1 g per day and zinc lozenges when given during the first 24 hours of the illness may be effective in decreasing the symptoms of colds. Only a small subset of patients who harbor pathogenic bacteria in their nasopharyngeal secretions may benefit from antibiotics [55]. Prescribing antibiotics for the management of uncomplicated colds is clearly not indicated. Physicians should advise patients to call or return in a
few days for reassessment if their symptoms do not improve.

Finally, physicians should help patients avoid unnecessary and potentially harmful medications. Patients should be cautioned about the large number of over-the-counter combinations advertised as effective treatments for colds [56]. It is alarming that two-thirds of families keep several over-the-counter medications in their homes that are potentially toxic to children [57]. In 1996, 6.2% of all toxic pediatric exposures were from cough and cold preparations [58].

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References
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