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Complementary and Integrative Treatments Upper Respiratory Infection

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KEYWORDS

- Upper respiratory tract infection • Common cold • Alternative therapy
- Complementary therapy

KEY POINTS

- The current theory regarding upper respiratory tract infections (URIs) holds the inflammatory response to viral infection, rather than the virus itself, responsible for the symptoms.
- Treatment of URI remains focused on symptom management and the tincture of time.
- Antibiotics and surgery have no role in the treatment of an uncomplicated URI.
- Nasal decongestants offer modest but significant relief of nasal congestion, with a low incidence of adverse effects.
- Insufficient evidence supports the use of vitamin and herbal remedies in the prevention and/or treatment of URIs, although some studies have shown significant benefits in symptom reduction.
- Evidence supporting the use of acupuncture for URIs is too limited to offer a recommendation regarding this treatment.

OVERVIEW

The combination of nasal congestion, rhinorrhea, sore throat, cough, and malaise is the symptomatic profile that constitutes an uncomplicated upper respiratory tract infection (URI), also known as the common cold. It is a pervasive illness; approximately 25 million people in the United States visit their doctor every year seeking treatment for a URI.¹ Nationally, the economic burden of URI is estimated to be approximately \$40 billion per year, including \$22 billion from nearly 200 million lost work days every year.² Because no known cure exists for the common URI, numerous products are available for treatment, each marketed with the promise of alleviating the associated symptoms and/or shortening the duration of illness. The evidence supporting these

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Otolaryngol Clin N Am 46 (2013) 335–344

<http://dx.doi.org/10.1016/j.otc.2012.12.007>

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claims is variable and is the focus of this article, with an emphasis on complementary and integrative therapies because these are being used with increasing frequency in the United States.³

PATHOPHYSIOLOGY AND ANATOMY

URIs are caused by a plethora of viruses, with rhinovirus being the most common causative agent.^{4,5} Other responsible viruses include coronavirus, parainfluenza, respiratory syncytial virus, adenovirus, and enterovirus.^{4,5} It is even likely that a portion of URIs are caused by viruses that have not yet been identified.⁴

The pathophysiology of a URI begins with transmission of the offending agent, which may occur via 3 routes: touching one's nose or eyes after contacting either an infected person or a contaminated object, inhalation of small particle aerosols that were produced by the cough of an infected person, or the sneeze of an infected person resulting in large particle aerosols landing on the nasal mucosa or conjunctiva.^{4,5} The viral agent travels from the eye to the nasal mucosa via the nasolacrimal duct. Once the virus infects the nasal mucosa, it is propelled to the nasopharynx through mucociliary action of the respiratory epithelium lining the nasal cavities. The virus then binds to epithelial cell receptors, which allow it to gain entrance into these cells. Within the epithelial cells rapid viral replication occurs.

The current theory regarding URIs holds the inflammatory response to viral infection, rather than the virus itself, responsible for the symptoms. In response to viral infection of the nasal epithelial cells, an upregulation of inflammatory mediators occurs, including cytokines such as interleukins 6 and 8,^{4,5} which drive the host's inflammatory response. As a result, there is an influx of neutrophils, vasodilation, and an increase in vascular permeability that results in the leakage of plasma proteins into the nasal cavity. Additionally, parasympathetic stimulation occurs, which causes production of excess mucous.⁴ This process translates into nasal congestion, rhinorrhea, and sneezing.^{4,5}

One reason people are susceptible to recurrent URIs year after year is challenges to immunity. Some virus types, including respiratory syncytial virus, parainfluenza, and coronavirus, do not produce lasting immunity. Other viruses, including rhinovirus, adenovirus, and enterovirus, do produce lasting immunity but so many serotypes exist that one is still susceptible to recurrent infection. These challenges are also the reason that no antiviral medications are available that are effective in treating URIs. Thus, treatment of URIs remains focused on symptom management and the tincture of time.

SYMPTOMS

The symptoms of the common URI include nasal congestion, sneezing, rhinorrhea, sore throat, headache, myalgia, and malaise. Fever may be present but is more common in children than adults.⁴ Symptom duration is usually 7 to 10 days but can be as long as 3 weeks.⁴ Drainage from rhinorrhea often begins clear but then may become thicker and discolored. Yellow or green nasal discharge is not an indication of a bacterial infection but rather of neutrophil infiltration, which is the hallmark of the immune system response.⁵

MEDICAL TREATMENT APPROACHES AND OUTCOMES

Antibiotics

Antibiotics have no role in the treatment of an uncomplicated URI with or without purulent rhinorrhea.⁶ Specifically, antibiotics do not decrease severity or duration of

symptoms and commonly are associated with adverse effects, most commonly gastrointestinal issues, such as diarrhea.⁶ In the United States, unnecessary prescription of antibiotics results in an economic burden of nearly \$800 million per year and puts the patient and society at risk for developing antibiotic-resistant strains of bacteria.¹

Oral and Intranasal Decongestants

Nasal congestion is one of the most common and bothersome symptoms of a URI, and therefore many over-the-counter cold remedies are geared toward relieving this symptom. Common oral decongestants include pseudoephedrine and phenylephrine. Phenylpropanolamine was previously used in over-the-counter preparations but has been removed from the market because of an associated risk of intracranial hemorrhage.⁵ Pseudoephedrine, a popular over-the-counter remedy for nasal congestion, has come under scrutiny recently because of its use in the illicit manufacturing of methamphetamines. Although still available over-the-counter, it is now only accessible behind pharmacy counters and its purchase is monitored.⁵

A review of the current literature was completed in 2009 by Taverner and Latte⁷ to assess the efficacy of topical and oral decongestants in relieving nasal congestion. Only randomized, placebo-controlled trials were included in their review. Their analysis indicated that nasal decongestants offer modest but significant relief of nasal congestion with a low incidence of adverse effects. Symptomatic relief was supported by a physiologic response of a significant reduction in nasal airway resistance. The evidence supports recommending a single dose trial of decongestants for patients with a URI. Those who experience improvement in symptoms of nasal congestion should be encouraged to continue treatment for 3 to 5 days. It is important to inform patients to discontinue use of topical decongestants after this period because of the risk of a rebound increase in congestion, as is seen with rhinitis medicamentosa. Patients with hypertension and/or benign prostatic hypertrophy should be closely monitored if using oral decongestants because the α -adrenergic properties may exacerbate these conditions.

Intranasal Steroids

Topical steroid sprays used intranasally have been shown to have significant benefit in treatment of nasal inflammation that is characterized by a dominantly eosinophilic infiltration, such as allergic rhinitis and nasal polyposis. They have not, however, proven beneficial in the treatment of infectious nasal inflammation, such as the common cold/URI.^{8,9}

Intranasal Ipratropium Bromide

Ipratropium bromide is an anticholinergic agent that when used intranasally can decrease rhinorrhea associated with the common cold.¹⁰ It has not been shown to have an effect on nasal congestion.¹⁰ It is generally well tolerated, with nasal dryness, blood tinged mucous, and epistaxis being the most commonly reported adverse effects.¹⁰ For patients with a URI whose chief complaint is rhinorrhea, use of intranasal ipratropium bromide could be of benefit.

Antihistamines

Although antihistamines have a proven role in the treatment of allergy-associated nasal symptoms, they do not offer benefit in relief of sneezing, rhinorrhea, or nasal

congestion associated with a URI.¹¹ The main adverse effect is sedation, which is seen more commonly with first-generation antihistamines. The use of antihistamines is not recommended for the treatment of nasal symptoms associated with URI.¹¹

Nonsteroidal Anti-Inflammatory Agents

Nonsteroidal anti-inflammatory agents are known for their analgesic, antipyretic, and anti-inflammatory properties and have widespread use for a variety of ailments. For the common cold they have proven effective for reducing pain-related symptoms, including myalgias, headache, and otalgia.¹² Despite their anti-inflammatory properties, a literature review completed by Kim and colleagues¹² did not support the theory that they might be helpful in reducing respiratory symptoms associated with URI, such as cough, sneezing, or rhinorrhea.

Guaifenesin

Limited evidence is available on the utility of the expectorant guaifenesin in treating URI symptoms. In a review of 2 studies, Smith and colleagues¹³ identified conflicting data. In one study, patients reported no difference in cough but did report a decrease in the thickness of mucous; in the second study patients did experience a decrease in cough frequency. Because side effects are minimal, it is reasonable for patients to trial guaifenesin to determine if they experience benefit. Further study is needed to determine the overall effectiveness of guaifenesin in the treatment of URIs.

SURGICAL TREATMENT APPROACHES AND OUTCOMES

Surgical intervention has no role in the management of an uncomplicated URI.

PATIENT SELF-TREATMENTS

Nasal Saline Irrigation

Nasal saline irrigation is often used as an adjunctive treatment for URIs. It can be used in the form of an atomized spray or lavage irrigation. The utility of nasal saline lies in its ability to clear excess mucous from the nasal cavities, improve mucociliary clearance, and reduce cough associated with postnasal drip.¹⁴ In general, studies on the use of nasal saline are limited because of the difficulty using an adequate control and thus inability to perform a blinded study. Additionally, numerous formulations and delivery methods are available for nasal saline, making comparisons between studies more difficult. Finally, outcomes are often based on patients subjectively reporting symptoms, allowing the introduction of bias.

In 2010, Kassel and colleagues¹⁴ performed an exhaustive literature review to assess the efficacy of nasal saline irrigation in the treatment of symptoms associated with URIs, the duration and severity of these symptoms, and the incidence of adverse effects associated with nasal saline use. Although evidence was limited, they found no statistically significant improvement in symptom severity or duration associated with the use of nasal saline. However, a reduction in time off of work and a trend toward decreased antibiotic use were seen. Adverse effects were minor, with approximately one-third of subjects reporting a dry or irritated nose. In the adult population, none of these effects was significant enough to cease treatment with nasal saline. Overall, the authors concluded that nasal saline may offer some benefit to adults with a URI. However, the current evidence is not sufficiently convincing to make it a routine intervention.

Heated Humidified Air

Inhalation of heated, humidified air has long been used as home remedy for the common cold. It is thought to provide symptomatic relief of nasal congestion through improving mucous drainage, and the rise in temperature may impede viral replication.¹⁵ The current literature shows conflicting data evaluating its efficacy, with some studies finding improvement of nasal symptoms after inhalation of warm humidified air, and other studies not.¹⁵ A review by Singh and Singh¹⁵ in 2011 pooled the results of randomized controlled trials on the topic and did not find that steam inhalation offered any consistent benefit to sufferers of the common cold. A large-scale, double-blinded study producing evidence of benefit is needed before heated, humidified air can be recommended as standard intervention.

INTEGRATIVE TREATMENT APPROACHES AND OUTCOMES

Zinc

Zinc supplementation has long been regarded as a potentially beneficial adjunct in the treatment and prevention of URIs. In the ionized form, zinc has demonstrated direct antiviral activity.¹⁶ Available forms include syrup, tablet, or lozenge. It was previously marketed as an intranasal spray, but this product is no longer available because it was linked to irreversible anosmia.¹⁷ If zinc supplementation is initiated within 24 hours of symptom onset, it has been shown to be beneficial in reducing the duration and severity of cold symptoms.¹⁸ If it is taken in a prophylactic manner for a 5-month period, it has been shown to reduce the incidence of the common cold.¹⁸ Adverse effects are more likely associated with the lozenge and include nausea and bad taste. Further research is needed to determine to optimal dosing regimen.¹⁸

Vitamin C

The use of vitamin C, also known as ascorbic acid, has been widely popular for the treatment and prevention of URIs since the 1970s when it was endorsed by Nobel laureate Linus Pauling.¹⁹ A literature review and meta-analysis performed by Hemila and colleagues¹⁹ in 2010 evaluated the strength of the evidence supporting the benefit of vitamin C. Their research concluded that when taken prophylactically, it was not effective in reducing the incidence of common cold in the general population. It did, however, have a beneficial effect on the severity and duration of symptoms. In a population consisting of people who performed strenuous physical activity and/or were subjected to significant cold stress, it can reduce the incidence of URIs when taken prophylactically.¹⁹ When vitamin C was taken after the onset of cold symptoms, it did not exhibit a benefit on the severity or duration of symptoms, but this is an area that requires further study.¹⁹

Vitamin D

Vitamin D is known to play a role in immune system regulation. Studies have shown that vitamin D deficiency may result in more missed work days because of URIs.²⁰ Therefore, questions regarding its potential role in preventing or treating infection have been raised. A randomized controlled trial comparing vitamin D₃ supplementation versus placebo completed over 12 weeks during winter revealed no benefit in reducing the incidence of URIs or the severity of symptoms with vitamin

supplementation.²¹ However, the authors postulated that they could have failed to detect a benefit because of small sample size and late initiation of vitamin D supplementation during winter. They suggest that initiating supplementation during the fall could be more effective because it coincides with the time year when sunlight exposure decreases and would allow more time for vitamin D levels to stabilize.²¹ Therefore, further study seems warranted.

Probiotics

Probiotics are live microorganisms that may be found and consumed in dietary supplements and fermented foods, such as yogurt. Although the mechanism is unclear, probiotics are theorized to provide potential health benefits through modulation of the immune system. One area of potential health benefit is in prevention and treatment of URIs. In 2011, Hao and colleagues²² performed a literature review and meta-analysis to assess the effectiveness and safety of probiotics in preventing URIs. Their findings suggested that probiotics may decrease the rate of URIs, the number of subjects who experience URIs, and the use of antibiotics for URIs when compared with placebo. Hatakka and colleagues²³ showed similar results in a double-blind, randomized, controlled trial evaluating the use of probiotics in nearly 600 children who attended day care regularly in Finland. Adverse effects of probiotics are usually minor and consist of gastrointestinal discomfort.²² Although more study is needed, the current, albeit limited, evidence supports the use of probiotics for preventing URIs, but the specific regimen has yet to be determined.

Garlic

Garlic (*Allium sativum*) has been theorized to have antimicrobial, antiviral, and antifungal properties. Therefore, it has been alleged that garlic supplementation may have use in preventing and treating the common cold, but the literature lacks solid evidence supporting this claim.²⁴ One randomized controlled trial conducted by Josling²⁵ in 2001 indicated a decreased incidence of the common cold in the study group taking garlic supplement over a 3-month period. However, further studies with larger sample sizes and clear outcome measures are needed before one can confidently conclude that garlic supplementation is effective in preventing and/or treating the common cold.^{24,25}

Pelargonium sidoides

Pelargonium sidoides is a root from which an herbal supplement is prepared. This root has been shown to have immune system modulatory capabilities in vitro.²⁶ In one randomized controlled trial, this supplement proved to have benefit in treating the common cold, with decreased symptom severity, shorter symptom duration, fewer lost work days, and minimal associated adverse effects.²⁶ Because evidence is limited, this supplement cannot yet be recommended as a standard intervention but does show promise as an effective treatment.

Ginseng

Panax quinquefolius (North American ginseng) is a popular-selling root extract, partly because of claims of its efficacy in improving fatigue, depression, stress, sexual energy, and digestion; the promotion of general well-being; and the treatment and prevention of URIs.¹⁶ Data validating these claims regarding URIs are limited. A systematic review performed by Seida and colleagues²⁷ in 2008 revealed that *P quinquefolius* does seem to be effective in decreasing the duration of cold

symptoms when taken prophylactically for 2 to 4 months, but insufficient evidence showed a decrease in the incidence of URIs or severity of symptoms. However, no significant published studies have evaluated the short-term use of ginseng extract for treating URIs. Furthermore, the potential adverse effects of long-term ginseng therapy have not been investigated thoroughly. Therefore, long-term prophylactic use or short-term therapeutic use of North American ginseng for URIs cannot be recommended until further studies are completed.

Kan Jang

Kan Jang is a standardized extract that contains both *Andrographis paniculata* and *Acanthopanax senticosus*, which are theorized to provide benefit in the treatment of URIs because of their anti-inflammatory and immune-stimulatory properties.²⁸ Although, evidence supporting this is limited, it has been shown to improve symptoms of cough, throat irritation, and muscle soreness when taken 3 times daily for 3 days within 36 hours of symptom onset.²⁸ Thus, Kan Jang extract shows promise in providing symptomatic relief for URIs, but additional studies with larger sample size and assessment of associated adverse effects are needed before it may be recommended as standard treatment.

Echinacea

A plethora of Echinacea preparations made from a variety of species and methods is available. This heterogeneity makes comparative evaluation of the effects of Echinacea difficult. A recent review of the literature by Linde and colleagues²⁹ revealed that Echinacea has not proven effective in preventing URIs. However, the pressed juice of the aerial parts of the species *Echinacea purpurea* may be effective in decreasing the severity and duration of cold symptoms if initiated early in the disease course.²⁹ This is an area that warrants further study.

Quercetin

Quercetin (3,3',4',5,7-pentahydroxyflavone) is an antioxidant whose in vitro antiviral properties have made it a subject of study for possible efficacy in treating and preventing viral URIs.³⁰ It may be consumed as a supplement or within foods, such as broccoli, apples, berries, onions, and tea.³¹ In mice it has been shown to counteract the increased URI susceptibility that is associated with exercise stress³² and to decrease viral replication, expression of cytokines, and airway hyperresponsiveness.³¹ Its efficacy in humans was evaluated in a prospective, randomized, double-blind, placebo-controlled trial in which a supplement containing quercetin, vitamin C, and niacin was taken prophylactically for a 12-week period.³⁰ Within a subgroup of subjects aged 40 years and older with above-average fitness, a reduction in total sick days and symptom severity was seen.³⁰ However, the study did not include a control group consuming quercetin alone, without niacin or vitamin C, making it difficult to tie possible efficacy to quercetin alone. Additionally, when considering all subjects, an affect on URI rates, symptom severity, or symptom duration was not appreciated.³⁰

Multimodal Approaches

Acupuncture

Sinus and nasal symptoms are ailments frequently treated by licensed acupuncturists who report good efficacy.³³ However, evidence supporting the use of acupuncture for URIs is limited, and therefore, a well-designed randomized control trial is needed.

Summary box: treatment recommendations	
Treatment	Recommendation
Antibiotics	Not recommended for treatment of upper respiratory tract infection (URI)
Decongestants	Both oral and topical preparations may provide modest improvement in nasal congestion
Intranasal steroids	Not recommended for treatment of URI
Intranasal ipratropium bromide	Beneficial in treatment of rhinorrhea associated with URI
Antihistamines	Not recommended for treatment of URI
Nonsteroidal anti-inflammatory drugs	Beneficial in treatment of pain symptoms associated with URI
Guaifenesin	No clear benefit, but individual patients may trial to see if they experience benefit
Nasal saline irrigation	No clear benefit, but individual patients may trial to see if they experience benefit
Heated humidified air	No clear benefit, but individual patients may trial to see if they experience benefit
Zinc	When taken therapeutically, may reduce duration and severity of symptoms
Vitamin C	When taken prophylactically, may reduce incidence of URI
	When taken therapeutically, has not been shown to reduce duration or severity of symptoms
Vitamin D	When taken prophylactically, may reduce incidence of URI in those exposed to significant physical and/or cold stress
	No clear benefit, further study is needed
Probiotics	When taken prophylactically, may reduce incidence of URI
Garlic	No clear benefit, further study is needed
<i>Pelargonium sidoides</i>	When taken therapeutically, may reduce duration and severity of symptoms, but evidence is limited and further study is needed
Ginseng	When taken prophylactically, has not been shown to reduce incidence of URI but may decrease duration of symptoms; evidence is limited and further study is needed
Quercetin	Limited evidence showing benefit when taken in conjunction with Vit C and Niacin in a subset of subjects but further study is needed
Kan Jang	When taken therapeutically, may reduce severity of symptoms but evidence is limited and further study is needed
Acupuncture	Very limited evidence, further study is needed

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