Complementary and alternative medicine for prevention and treatment of the common cold

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Abstract

Objective To review the evidence supporting complementary and alternative medicine approaches to treatment and prevention of the common cold in adults.

Quality of Evidence MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews were searched from January 1966 to September 2009 combining the key words common cold or influenza with echinacea, garlic, ginseng, probiotics, vitamin C, and zinc. Clinical trials and prospective studies were included.

Main Message For prevention, vitamin C demonstrated benefit in a large meta-analysis, with possibly increased benefit in patients subjected to cold stress. There is inconsistent evidence for Asian ginseng (Panax ginseng) and North American ginseng (Panax quinquefolius). Allicin was highly effective in 1 small trial. For treatment, Echinacea purpurea is the most consistently useful variety; it was effective in 5 of 6 trials. Zinc lozenges were effective in 5 of 9 trials, likely owing to dose and formulation issues. Overall, the evidence suggests no benefit from probiotics for prevention or treatment of the common cold.

Conclusion Vitamin C can be recommended to Canadian patients for prevention of the common cold. There is moderate evidence supporting the use of Echinacea purpurea and zinc lozenges for treatment. Ginseng and allicin warrant further research.

Résumé

Objectif Examiner les données en faveur du recours aux médecines complémentaires et alternatives pour traiter et prévenir le rhume banal chez l’adulte.

Qualité des preuves On a consulté MEDLINE, EMBASE et la Cochrane Database of Systematic Reviews entre janvier 1966 et septembre 2009, en combinant les rubriques common cold ou influensa avec les rubriques Echinacea, garlic, ginseng, probiotics, vitamin C et zinc. Des essais cliniques et des études prospectives ont été inclus.

Principal message Pour ce qui est de la prévention, la vitamine C s’est avérée bénéfique dans une grande méta-analyse, avec une protection possiblement meilleure chez les sujets exposés au froid. Pour le ginseng asiatique (Panax ginseng) et le ginseng nord-américain (Panax quinquefolius), les données sont contradictoires. L’allicine était très efficace dans un petit essai. Pour le traitement, c’est l’Echinacea purpurea qui est le plus régulièrement utile, s’étant montré efficace dans 5 essais sur 6. Les losanges de zinc étaient efficaces dans 5 essais sur 9, possiblement à cause de différences de doses et de préparation. Dans l’ensemble, les données suggèrent que les probiotiques ne sont pas utiles pour prévenir ou traiter le rhume banal.

Conclusion On peut recommander la vitamine C aux patients canadiens pour prévenir le rhume banal. Il existe certaines données en faveur de l’utilisation de l’Echinacea purpurea et des losanges de zinc pour le traitement. Le ginseng et l’allicine devront être étudiées davantage.

KEY POINTS

- For prevention, the most consistent evidence supports use of at least 1 g of vitamin C daily, which decreased symptom duration by 8% in adults and 18% in children in several trials and which might be even more effective during Canadian winters. Use of ginseng and allicin could be considered; both show promise but larger trials are needed.
- Evidence from patients subjected to cold stress reinforces the importance of dressing warmly. For treatment, Echinacea purpurea taken at the first signs of a cold might reduce duration and severity of symptoms. Zinc lozenges might also be effective. Published studies are difficult to interpret in both cases because of differences in dose and formulation.

POINTS DE REPÈRE

- Pour ce qui est de la prévention, les probiotiques ont été moins solides obtenus dans plusieurs essais indiquent que la prise quotidienne d’au moins 1 g de vitamine C diminue la durée des symptômes de 8% chez l’adulte et de 18% chez l’enfant, et suggèrent que son efficacité pourrait être encore meilleure durant les hivers canadiens. Des résultats prometteurs permettent d’envisager l’usage du ginseng et de l’allicine, mais d’autres études seront nécessaires. Les données confirment l’importance d’être chaudement vêtu en cas d’exposition au froid. Pour ce qui est du traitement, l’allicine d’Echinacea purpurea aux premiers signes de rhume pourrait réduire la durée et la sévérité des symptômes. Les losanges de zinc pourraient aussi être efficaces. Dans ces deux derniers cas, les études publiées sont difficiles à interpréter en raison des différences de doses et de préparation.
The common cold is seen frequently by family physicians. It is almost always a viral illness; while rhinoviruses cause 30% to 50% of colds throughout the year and 80% of colds during peak season, up to 200 other viruses have been implicated. On average, it affects adults 2 to 4 times per year. Symptoms include nasal congestion and discharge, sneezing, cough, sore throat, and fever. While benign, they last for several days and cause 40% of all missed work days. Complications include sinusitis, otitis media and pneumonia, exacerbations of asthma and chronic obstructive pulmonary disease, and serious illness in immunocompromised patients. Influenza viruses cause 5% to 15% of acute respiratory infections, resulting in fever, headache, myalgia, and fatigue, and considerable overlap between influenza and the common cold can make accurate diagnosis difficult.

Few effective treatments exist. Nonsteroidal anti-inflammatory drugs reduce pain symptoms but not the overall duration or severity of a cold, and the antiviral drug oseltamivir only reduces symptom duration by 0.55 days in otherwise healthy adults. There is no role for antibiotics in the treatment of the common cold. While vaccination of healthy adults prevents influenza, it only reduces incidence of acute respiratory infections by 16%, and work absenteeism by 0.13 days.

Many patients use complementary and alternative medicine (CAM) therapies to treat the common cold. Canadians spend more than $1 billion per year on CAM therapies, but few physicians are familiar with their efficacy or safety. Here we review the evidence for frequently used CAM therapies to help physicians advise patients about the use of such therapies in treating and preventing the common cold.

Quality of evidence
MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews were searched from January 1966 to August 2009. Key words used were common cold or influenza with echinacea, garlic, ginseng, probiotics, vitamin C, and zinc. The interventions were selected based on literature reviews and clinical experience. We identified clinical trials and other prospective studies, systematic reviews, and meta-analyses. Only trials evaluating single agents, mostly in healthy adults, were selected. Review articles and references were screened for additional trials. Each article was reviewed separately by both authors.

The main limitation of the methodology used is the exclusion of other potentially useful interventions. This paper is not meant to be comprehensive, but rather to review the evidence for interventions that are commonly seen in clinical practice.

Main findings
Relevant findings for each search term are briefly summarized in Table 1 and are detailed as follows:

**Echinacea.** Echinacea roots and flowers were used medicinally by First Nations peoples and became popular in Europe for infectious problems. In laboratory studies, they activate macrophages, increase phagocytosis, enhance cytokine production and natural killer cell activity, and improve lymphocyte and monocyte cell counts because they have used different species and plant parts. Given this, this review is limited to echinacea, 8-15,42-44 6 trials evaluated *E purpurea* in 764 healthy adults with cold symptoms, and more for aerial parts than roots. Given this, this review is limited to studies of *E purpurea*.

**Treatment:** Of the 11 trials identified that studied echinacea, 8-15,42-44 6 trials evaluated *E purpurea* in 764 healthy adults with cold symptoms. Symptom severity was reduced in 4 of 6 trials, measured using total daily symptom scores and Jackson scores. Of the

<table>
<thead>
<tr>
<th>INTERVENTION</th>
<th>EVIDENCE FOR PREVENTION (LEVEL*)</th>
<th>EVIDENCE FOR TREATMENT (LEVEL*)</th>
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<tr>
<td><em>Echinacea purpurea</em></td>
<td>No evidence found in 2 RCTs (level IIa)6-9</td>
<td>Evidence found in 5 of 6 RCTs (level IIa)10-15</td>
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<tr>
<td>Zinc lozenges</td>
<td>No trials evaluate prevention</td>
<td>Evidence found in 5 of 9 RCTs (level IIa)16-24</td>
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<tr>
<td>Vitamin C</td>
<td>Evidence found in meta-analysis of 30 RCTs; more benefit in children and in adults under stress (level I)25</td>
<td>No evidence found in meta-analysis of 11 RCTs (level I)25</td>
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<tr>
<td>Ginseng</td>
<td>Inconsistent; evidence found in 2 of 4 RCTs (level IIb)26-29</td>
<td>No trials evaluate treatment</td>
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<td>Garlic (allicin)</td>
<td>Evidence found in 1 RCT (level IIb)30</td>
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<td>Probiotics</td>
<td>No evidence found in 4 of 6 RCTs (level IIa)31-36</td>
<td>No trials evaluate treatment</td>
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RCT—randomized controlled trial.
*Levels of evidence indicated are taken from the Oxford Centre for Evidence-Based Medicine.37*
Three trials studied healthy adults, 11,14,15 while the other 4 trials that measured duration of symptoms, 12-15 found significant reductions of 1.5, 2, and 4 days (P<.05 for all). Only 1 study found no reduction in symptom severity or duration.15

The 6 trials used 5 distinct preparations: 3 tinctures11,13-15 and 2 tablets derived from various extracts.10,12 Three trials studied healthy adults,11,14,15 while the other 3 studied adults with 2 or more colds in the previous year.10,12,13 Different clinical scoring systems were also used. There is moderate evidence that E purpurea might be effective for treatment of the common cold, but issues surrounding dose and formulation require clarification before it can be recommended for routine use.

Prevention: Two trials evaluating E purpurea in cold prevention found no reduction in symptom duration or severity.8,9

Safety and use: A typical dose of echinacea is 2000 to 3000 mg of crude extract, 6 to 9 mL of pressed juice, or 0.75 to 1.5 mL of tincture per day. The most important concern is allergy; echinacea is a member of the Asteraceae family and can cause serious reactions in susceptible patients.55 Reported side effects include gastrointestinal upset, headache, and rash.39,46,47 No herb-drug interactions have been identified. Its safety in pregnancy or for long-term use is unknown. The theoretical risk of worsening autoimmune disease has not been reported but should be considered.99

Ginseng. Panax means “heal-all” in Greek. Panax ginseng (Asian ginseng) has been used in Chinese medicine for millennia, and is believed to be an “adaptogen,” which enhances an individual’s ability to resist mental and physical stress.48 In animal and human studies, it has activated macrophages, natural killer cells, and lymphocytes, and increased cytokine and antibody production.49,50 Panax quinquefolius (North American ginseng) contains a similar chemical profile and is used to make COLD-fX, an extract standardized to polysaccharides and oligosaccharides.

Treatment: There are no trials evaluating ginseng for treatment of the common cold.

Prevention: Our search identified 3 trials comprising 564 patients that evaluated P quinquefolius for prevention of the common cold26-28; all were funded by the manufacturer. These trials were also identified in a recent systematic review.51 Unfortunately, none involved healthy adults. One summarized 2 separate studies of 89 and 109 nursing home patients26; another involved 44 elderly patients (older than 65 years of age)27; and a third examined 323 unvaccinated adults with more than 2 colds in the previous year.31 All patients received 200 mg per day of COLD-fX or placebo for 2 to 4 months.

Poor and misleading reporting of data makes it difficult to draw conclusions from these studies. The nursing home studies reported fewer laboratory-confirmed infections, but found no reduction in the number of colds or in the duration or severity of symptoms.26 The study of 44 elderly patients reported fewer days of cold symptoms but only in the last 2 months of the 4-month trial; the number of colds was not reduced.27 The final study reported that healthy adults at risk who took COLD-fX experienced milder symptoms (Jackson score 77.5 vs 112.3, P=.002) for fewer days (10.8 vs 16.5 days, P<.001).28

Only 1 trial has studied P ginseng; 227 vaccinated healthy adults took 100 mg of an extract or placebo for 12 weeks. Those in the group taking ginseng suffered far fewer colds (15 vs 42, relative risk 0.35, P<.001).29

Safety and use: Reported side effects include headache, gastrointestinal upset, anxiety, and insomnia. Ginseng should be avoided during pregnancy and lactation because of potential teratogenicity and estrogenic effects.52 Case reports have described potential herb-drug interactions with phenelzine (induction of mania from depression), warfarin (increased international normalized ratio), and alcohol (increased blood clearance).53

There is conflicting and unclear evidence that P quinquefolius prevents colds. Although it is chemically similar to P ginseng, 1 clinical trial of P ginseng yielded better results, and its long history of traditional use is reassuring. Larger ginseng trials are warranted.

Vitamin C. Albert Szent-Györgyi won the Nobel Prize for his discovery of vitamin C. Another Nobel laureate, Linus Pauling, popularized its use for disease prevention and longevity.54 Vitamin C has antioxidant properties, regenerates glutathione, and might stimulate neutrophil and monocyte activity.55

Treatment: A Cochrane systematic review identified 7 treatment trials evaluating 3294 cold episodes.25 One trial found that patients who took 8 g of vitamin C at the onset of symptoms had more “short colds” of less than a day than those who took 4 g (46% vs 39%, P=.046). All other trials found no benefit, even at similar doses.25

Prevention: The same review identified 30 prevention trials involving 11350 subjects. Overall, there was a very slight decrease in the number of colds (odds ratio [OR] 0.96, 95% confidence interval [CI] 0.92 to 1.0) but not in cold severity. Symptom duration decreased by 8.0% in trials that used more than 1 g daily in adults, and decreased by 18% (95% CI 7% to 30%) when this dose was used in children. Assuming that the average cold lasts for 7 to 10 days, this represents 1.5 to 2.0 days shorter duration, which is clinically relevant.

More important, the reviewers identified a subgroup of 6 trials of 642 subjects exposed to severe stress in the form of subarctic cold or intense physical activity. In these trials, those taking vitamin C at doses of 200 to 2000 mg daily had half as many colds as those taking...
placebo (OR 0.50, 95% CI 0.38 to 0.66). This seems very relevant to patients in many Canadian communities.

**Safety and use:** Vitamin C is considered safe in doses up to several grams per day. The only occasional side effect is gastrointestinal upset, and doses in excess of 10 g can cause diarrhea. No drug interactions are known.

Taking at least 1 g of vitamin C per day can be recommended for the prevention of colds based on good evidence of moderate reduction in symptom duration in adults and children. While it only reduces symptoms by 1 to 2 days, it is cheap, safe, and simple to use. It can also be recommended for use by athletes in intense training. Further research should explore the potential benefit in Canadians, who are subjected to cold winters.

**Allicin.** Allicin is an organosulfur compound found in garlic (*Allium sativum*), a food with known cardiovascular and anticancer benefits. Allicin is released when garlic is chopped or chewed, but is inactivated by cooking. It has demonstrated antiviral properties in vitro against rhinovirus and several other strains.

**Treatment:** There are no trials evaluating allicin for treatment of the common cold.

**Prevention:** One study of 146 healthy adults compared a high-dose allicin extract (180 mg daily) with placebo for 12 weeks during the winter months. The results were dramatic; the treatment group had 64% fewer colds (24 vs 65, P < .001), and symptom duration was reduced by 70% (1.52 vs 5.01 days, P < .001). Those in the treatment group were much less likely to develop more than 1 cold (2 vs 16 participants developed more than 1 cold).

**Safety and use:** It should be emphasized that the allicin preparation used in this trial is unlike typical garlic preparations. It contained 180 mg of allicin; fresh garlic contains 5 to 9 mg per clove, and most extracts contain less than this. The only side-effect reported in the trial was malodorous belching. Little is known about the safety of high-dose allicin, but its use could be considered.

**Probiotics.** The health benefits of fermented milk were first proposed in the early 20th century. These benefits are due to the presence of probiotic bacteria, which appear to be useful in several gastrointestinal and immune-mediated disorders. They interfere with toxin and cell binding sites, and improve mucosal barrier function, intestinal microflora, and gut-associated lymphoid tissue.

**Treatment:** There are no trials evaluating probiotics for treatment of the common cold.

**Prevention:** Probiotics were evaluated in 6 randomized controlled trials involving 1766 healthy adults. The number of colds was significantly reduced in only one of 6 trials, symptom severity in 1 of 6, and duration in 1 of 5 (P = .045). Two of the negative trials involved atypical populations (military cadets and marathon runners), but even when these are excluded, the results are unimpressive. There was no clear relationship between response and dose (measured in colony-forming units) or strain in studies that were large enough to be adequately powered. In a recent systematic review, there appeared to be more benefit in children, but this is beyond the scope of this review.

Despite their lack of efficacy and potential for harm, antibiotics are still prescribed to patients with the common cold. These drugs alter intestinal flora, which can lead to potentially harmful side effects and complications. We recommend that patients use probiotics whenever antibiotics are prescribed.

**Zinc lozenges.** Zinc is an essential mineral used in hundreds of biochemical pathways, and deficiency has long been associated with infection risk. Postulated mechanisms in the common cold include interfering with rhinovirus protein cleavage or capsid binding to intracellular adhesion molecule–1 in nasal epithelium, and protecting plasma membranes from microbial toxins and complement.

**Treatment:** Zinc was evaluated in 13 trials for treatment of the common cold in adults. A nasal spray was compared with placebo in 4 trials, and it reduced symptom duration and severity in only 2 of these. Irritation by the nasal sprays limits their use; they also appear to yield lower concentrations in the nasopharynx. Therefore, they are considered separately.

Zinc lozenges reduced symptom duration and severity in 5 of 9 trials. The results are difficult to interpret for 2 reasons. The first is dose; 4 of 5 studies that used higher doses of elemental zinc (13 to 23 mg per lozenge every 2 hours) found a 1.3- to 6.9-day reduction in symptom duration and reduced symptom severity. Negative trials using lower doses have been criticized.

The second issue is bioavailability. Negative trials have been criticized for using formulations that included citric or tartaric acids, sorbitol, or mannitol, all of which bind to and inactivate elemental zinc. More positive trials used acetate or gluconate, which do not bind to zinc as tightly as orotate or citrate. The importance of these differences is unclear. These factors might explain the variable results seen in a meta-analysis of 8 randomized controlled trials (OR 0.52, 95% CI 0.25 to 1.2) for symptoms after 7 days.

It appears that zinc might be effective for treatment of colds, but issues surrounding dose and bioavailability require clarification. Future studies should use higher doses and ensure that formulations do not contain agents that could bind to or otherwise interfere with elemental zinc.

**Prevention:** There are no trials evaluating zinc for prevention of the common cold.
Safety and use: Lozenges containing at least 13 mg of elemental zinc can be used every 2 hours at the first sign of a cold. Reported side effects include bitter taste, nausea, and decreased smell and taste. Prolonged use of zinc (6 to 8 weeks) is not recommended, as it can lead to copper deficiency.

Conclusion
For prevention, the most consistent evidence supports the use of at least 1 g of vitamin C per day, which decreased symptom duration by 8% in adults and 18% in children in several trials and which might be even more effective during Canadian winters. Use of ginseng and allicin can be considered; both show promise but larger studies are difficult to interpret in both cases because of differences in dose and formulation. Once again, more trials are needed.

These simple, safe recommendations might improve outcomes for patients with the common cold. Of equal importance, they offer an alternative when advising patients whose viral infections do not require antibiotics.

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Competing interests None declared.

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