

Complementary medicines and the common cold Information for health professionals

As the winter months approach, there will undoubtedly be an increase in the demand for drug treatments of the common cold. Three of the more popular complementary medicines that have been used in the treatment or prevention of the common cold are vitamin C, echinacea and zinc. Efficacy, precautions and safety issues with their use are discussed below. Although other agents such as garlic and horseradish are promoted for use in the common cold, there are limited clinical studies investigating their role.

Summary:

- *Studies suggest that vitamin C given for the treatment of common colds may reduce the duration of symptoms. Controlled studies of zinc and echinacea have provided only marginal evidence of efficacy.*
- *Data on use in prevention of common cold for vitamin C, echinacea and zinc where available, is at best equivocal.*
- *It should be emphasised that these substances are medicines and the potential to cause adverse effects must be weighed against their marginal benefit for the treatment of common cold symptoms.*

Vitamin C

Vitamin C does not prevent the common cold, however, it may reduce the duration of symptoms during treatment.

Many studies have been conducted to determine the role of vitamin C in the prevention and treatment of the common cold.¹ The largest studies of vitamin C supplementation, as prophylaxis, suggest that vitamin C does not have a preventative effect.^{1,2,3} Some studies however suggest that it may reduce common cold incidence in those groups with a low dietary vitamin C

intake (less than 60 mg per day).^{2,3} A recent Cochrane review of thirty trials concluded that, whilst not affecting incidence of the common cold, vitamin C may reduce the duration of symptoms by a little less than half a symptom day per cold episode.¹ There is no evidence that large amounts of vitamin C (greater than ~ 1 g/day) confer extra benefits.⁴ One trial found that vitamin C doses in excess of 1 g daily produced results that were no different to doses less than the minimum recommended daily intake.⁴ The recommended dietary allowance of vitamin C is 60 mg per day. Recent epidemiological studies report no association between dietary vitamin C intake and incidence of colds.^{5,6} Doses greater than 1 g per day can lead to oxaluria, uricosuria, renal stones, diarrhoea and rebound scurvy.⁷

Echinacea

A number of different echinacea species have been used in clinical trials. Until the active constituents of echinacea are established, efficacy in the treatment or prevention of the common cold cannot be successfully determined. Results of trial data are equivocal. In addition, the potential of echinacea to cause immune suppression with long-term use suggests caution in this setting.

The most common echinacea species for medicinal purposes are *Echinacea (E.) angustifolia*, *E. purpurea*, and *E. pallida*.⁸ They contain alkylamides of at least 20 different types, available as leaves, tinctures, capsules or tablets.⁹ A recommended dosage has not been established with doses from 0.3 to 1 g as a dried root or tea to 0.25 to 1 ml of fluid extract as a 1:1 preparation reported, usually taken three times daily. Echinacea has become very popular as a cold remedy

due to its purported action as an immunostimulant. *In-vitro* data support an increased activity in phagocytic cell lines.⁹ Controlled clinical studies have failed to confirm an immunostimulant activity.

A 1998 Cochrane Review of sixteen published clinical trials evaluated the efficacy of echinacea in prevention (n=8) and treatment (n=8) of the common cold.⁸ This concluded that most studies examining treatment reported positive results and those examining prophylaxis did not demonstrate significant efficacy over placebo. Variation in the preparations used, different extraction procedures and methodological quality of the studies, prevented recommendation of echinacea for both indications. The lack of a defined active constituent across the species is likely to account for the variation in response seen in these studies.

Two recent double-blind placebo randomised controlled trials (RCTs)^{10,11} have failed to clarify the evidence for echinacea in the treatment of common cold. In the first, echinacea treatment was commenced at the onset of cold symptoms.¹⁰ Whilst lower symptom severity ratings on days 2-7 for the echinacea group compared with placebo (p<0.01) were reported, symptoms also improved in the placebo group. As group baseline (day 1) symptom ratings for each group were not reported, it cannot be clarified that a difference between groups did not already exist at baseline. The second RCT reported no statistically significant differences between echinacea and placebo groups in either duration of cold or in symptom severity.¹¹

The use of echinacea in children has been the focus of recent discussion including two double-blind placebo RCTs. Children aged 2 to 11 years (n=252) were randomised to receive either alcohol free, unstandardised *E. purpurea* in syrup administered twice daily or placebo.¹² Study medicine (dose unspecified) was commenced at the start of an upper respiratory tract infection, and continued until symptoms resolved (10 day maximum). There were no significant differences between the groups on measures such as duration or severity of

symptoms or use of antibiotics. Results were similar regardless of age group or use of day care. The incidence of rash was significantly higher in the echinacea group (7.1% vs 2.7%, p=0.008). In a second RCT, 430 children, aged 1-5 years, were randomised to a mixture of *E. purpurea*, *E. angustifolia*, bee propolis and vitamin C or a placebo preparation, twice daily, for 12 weeks.¹³ If an acute episode of respiratory illness occurred, the dose was doubled until symptoms subsided. 328 children completed the study. The treatment group had fewer cold episodes (0.9 vs 1.8 episodes), fewer illness days (2.6 vs 6.2), shorter episode duration (1.6 vs 2.9 days) and less use of antipyretics and antibiotics (all p<0.01). It is unclear whether these positive outcomes demonstrate a potential prophylactic effect due a different echinacea extract, additive effects of the propolis or vitamin C, or a combination of these factors. Adverse reactions, primarily gastrointestinal, were reported in 9 children on the active preparation and 7 receiving placebo.

The safety of echinacea has only been evaluated over short-term studies. It appears to be safe in people without autoimmune disorders or sensitivities to echinacea or its excipients.¹⁴ It should be avoided in pregnant or breast-feeding women due to the lack of evidence regarding its safety in these settings.¹⁵ An *in-vitro* study has shown the potential for immune suppression to occur with long term use of echinacea.⁹ Some texts have recommended that echinacea be contraindicated in patients with severe illness, especially autoimmune diseases such as systemic lupus and ulcerative colitis,¹⁶ and used with caution in people with human immunodeficiency virus (HIV), multiple sclerosis and tuberculosis.¹⁴ Patients and health care providers should be aware of the differences in the chemical composition of available echinacea preparations and the potential impact on both efficacy and safety.

Zinc

Controlled studies on the role of zinc in the treatment of the common cold have produced conflicting results. Limited studies have, to date, not supported a prophylactic role for zinc. Adverse effects associated with zinc, including anosmia (loss of sense of smell), mouth irritation and nausea warrant monitoring.

A 1997 Cochrane Review of seven trials (754 cases) revealed inconclusive evidence regarding the effects of zinc lozenges for treating the common cold. Results from two trials suggest that zinc lozenges reduce the severity and duration of cold symptoms, however there was significant potential for bias, warranting further research. Overall, the results suggested that treatment with zinc lozenges does not reduce the duration of the common cold.¹⁷ More recent studies have revealed conflicting results. The first involved 273 patients with experimental rhinovirus colds and the second, 281 patients with natural colds. In each, patients were randomised to receive oral lozenges containing 13.3 mg zinc gluconate, 5 mg or 11.5 mg zinc acetate or placebo. The median duration of illness in the zinc gluconate recipients with experimentally induced colds was 2.5 days, compared to 3.5 days in the placebo group ($p=0.035$).¹⁸ In this group, zinc gluconate had no effect on symptom severity while zinc acetate had no effect on either duration or severity of symptoms. Neither formulation had an effect on the duration or severity of natural cold symptoms.¹⁸ In contrast, a RCT of 55 ambulatory volunteers taking either 1 lozenge of 12 mg zinc acetate or placebo every 2 to 3 hours found that zinc was associated with a reduced duration (4.5 vs 8.1 days) and severity of cold symptoms, especially cough.¹⁹

An open label study examined the prophylactic effect of zinc gluconate glycine (13.3 mg) lozenges in 178 children aged 12-18 years. Data from a retrospective study of young people not receiving zinc treatment

were used as a comparator. Children receiving one lozenge daily (increased to 4 daily when two or more symptoms of cold emerged) had average cold duration of 6.9 days compared to 9.0 days in the comparator group ($p<0.001$). The mean number of colds was 1.28 compared to 1.7 in the retrospective study ($p<0.05$), and no individuals received antibiotic treatment, compared with 39% in retrospective study.²⁰ Formulation also appears to be important, for example the addition of citric acid or tartaric acid to the lozenges may reduce efficacy, due to chelation of zinc ions.²¹ Common adverse effects include unpleasant taste, anosmia, or mouth irritation and nausea.²¹

An alternative approach is intranasal zinc. The efficacy of zinc nasal gel administered via metered dose inhaler 4 times daily (total daily dose 2.1 mg) was evaluated in 80 adults with common cold. Participants randomly allocated to the gel exhibited reduced duration of cold symptoms (4.3 days vs 6 days, $p=0.002$), and reduced symptom severity.²² Case reports and animal studies however suggest that intranasal zinc may produce anosmia which may be irreversible.²³

Low dose zinc supplementation is unlikely to be associated with clinical benefits for the common cold. Epidemiological studies suggest no relationship between dietary zinc intake and incidence of the common cold.⁶ Improvement of clinical symptoms with zinc treatment is believed to be related to a decrease in pro-inflammatory cytokine levels.²⁴ Zinc may also exert local effects, inhibiting viral replication and adhesion to the respiratory tract.²⁴ Any benefit appears to be maximal if zinc is started at the onset of symptoms.²⁴

The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decision based on this information should be made in the context of the individual clinical circumstances of each patient.

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NPS publication data April 2002, updated by TAIS June 2004.