COLD-fX

Anne Nguyen, PharmD Victoria Slavik, PharmD

Predy GN, Goel V, Lovlin R, Donner A, Stitt L, Basu TK. Efficacy of an extract of North American ginseng containing poly-furanosyl-pyranosyl-saccharides for preventing upper respiratory tract infections: a randomized controlled trial. *CMAJ* 2005;173(9):1043-8.

Research question

Do *Panax quinquefolius* saccharides (COLD-fX) prevent colds?

Relevance to family physicians

Because COLD-fX is available in many retail outlets, it is important for family physicians to be aware of this product, as many Canadians might be using it. The compound is being marketed for both the common cold and flu, and contains a proprietary extract (CVT-E002) derived from North American ginseng. The common *cold* can be caused by numerous viruses (eg, rhinovirus, coronavirus, adenovirus, respiratory syncytial virus, parainfluenza virus), whereas the *flu* is caused by the influenza viruses (influenza A, B, C).

The manufacturer has dosing recommendations for the *treatment* of colds and flu, but published trials with clinical end points cannot be found to support these recommendations.[1] For the *prophylactic* use of COLD-fX, 2 studies with clinical end points have been published.[2] This Critical Appraisal will assess the trial that was conducted in Canada.

Type of article and design

This randomized, double-blind, placebo-controlled trial was conducted in Edmonton, Alta, during the influenza season (September 2003 to April 2004). Volunteers were healthy adults recruited through media advertisements and included if they had contracted *at least* 2 colds in the past year. They were excluded if they were immunized against influenza in the previous 6 months. This study was funded by the manufacturer.

The extract CVT-E002 was given as 400 mg orally (two 200-mg capsules), once daily, for 4 months; matching placebo was provided to the control group. Subjects were asked to complete a daily log of their cold-related symptoms (sore throat, runny nose, sneeze, nasal congestion, malaise, fever, headache, hoarseness, earache, cough), and to rate each of these symptoms on a 4-point scale. These scores were used in 2 ways. First, a 2-day total symptom score of more than 14 was used to indicate a cold (modified Jackson-verified cold). Second, a daily total symptom score higher than 4 was used to quantify the following: total symptom score (symptom severity), number of days cold symptoms were reported, and duration of colds. Patients were also asked to record adverse effects. Cultures and antibody titres were not collected. Blinding was assessed at the end of the study by asking subjects what they thought they received.

Results

There were 323 patients randomized, but those who did not start the intervention (21 in the placebo arm and 23 in the CVT-E002 arm) were excluded from analysis. Thus 149 patients were analyzed in the placebo arm, and 130 patients were analyzed in the CVT-E002 arm. Patients included in the analysis were, on average, 42 years old and female (>60%).

Patients in the CVT-E002 arm had *fewer colds per person* (modified Jackson criteria) over 4 months (0.93 colds/person taking placebo, vs 0.68 colds/person taking CVT-E002, difference = 0.25, 95% confidence interval 0.04-0.45). In addition, during the 4-month period, patients in the CVT-E002 arm also had a better total symptom score of all colds with a daily total symptom score >4 and fewer total days with cold symptoms (16.5 days for those taking placebo vs 10.8 days for those taking CVT-E002, $P<.05$), but no significant difference was found in the duration of each cold. There was no difference in adverse effects. The authors stated that blinding was effective because the percentage of people who thought they were taking the active drug was 77.3% in the placebo arm and 69.8% in the CVT-E002 arm (*P* value not provided).

Analysis of methodology

The editorial for the Canadian study acknowledged that the authors addressed problems associated with studies on natural remedies: assessment of blinding and standardization of product to ensure batch-to-batch consistency of the proprietary extract.[3]

However, there were also flaws in this study: reliance on self-reporting of symptoms, the Jackson cold definition was modified and used in a non-validated manner, and no laboratory data were collected. Without diagnostic confirmation from the laboratory, it was unknown whether patients had the common cold or influenza because patients were at risk for both; this further invalidates the chosen scoring system, because the Jackson score was developed using a rhinovirus

← FOR PRESCRIBING INFORMATION SEE PAGE 571

challenge (ie, for colds, not flu). In addition, even if the scoring system were valid, the clinical relevance of this difference of 0.25 fewer colds per person over 4 months is unknown. The editorial also suggested that the case definition used by the authors limited the evaluation to only the most severe illnesses, thus the utility in milder illness was not assessed.[3]

Application to clinical practice

While we await more data to quantify the efficacy and toxicity of CVT-E002, the wholesale cost for 4 months at 400 mg/d is approximately $80.00 (cost to patients could be higher). However, there is one intervention that, if performed correctly and frequently, can help reduce the incidence of outpatient visits for acute respiratory infections.[4] It has a great safety profile, is inexpensive, and is freely available (at least in North America): advise people to *wash their hands frequently*.

Ms Nguyen *is the pharmacist coordinator of the British Columbia Community Drug Utilization Program at Lions Gate Hospital in North Vancouver, BC.* **Ms Slavik** *is currently the Pharmacotherapeutic Specialist in Emergency Medicine at Vancouver General Hospital.*

References

1. Cold fX (monograph). In: *Natural Medicines Comprehensive Database*. Stockton, Calif: Therapeutic Research Faculty; 2006. Available at **www.naturaldatabase.com**. Accessed 2006 August 22.
2. McElhaney JE, Gravenstein S, Cole SK, Davidson E, O'neill D, Petitjean S, Rumble B, Shan JJ, et al. A placebo-controlled trial of a proprietary extract of North American ginseng (CVT-E002) to prevent acute respiratory illness in institutionalized older adults. *J Am Geriatr Soc* 2004;52(1):13-9. Erratum in: *J Am Geriatr Soc* 2004;52(2):following 856.
3. Turner RB. Studies of "natural" remedies for the common cold: pitfalls and pratfalls. *CMAJ* 2005;173(9):1051-2.
4. Ryan MA, Christian RS, Wohlrabe J. Handwashing and respiratory illness among young adults in military training. *Am J Prevent Med* 2001;21(2):79-83. Comment in: *Am J Prevent Med* 2001;21(2):151-1.

BOTTOM LINE

- There are no published data with clinical end points using COLD-fX for the treatment of cold and flu.
- When taken for 4 months to prevent colds and flu, COLD-fX might decrease the number of colds by 0.25 colds/person among adults who had had more than 2 colds in the previous year. However, the clinical relevance of this decrease is unknown.
- At this time, data are insufficient to recommend the routine use of COLD-fX.
- If patients insist on using COLD-fX to prevent colds and flu, then it should be used for no longer than 4 months (maximum duration of published clinical trials).
- To help reduce the incidence of outpatient visits for acute respiratory infections, advise people to wash their hands frequently.

POINTS SAILLANTS

- Il n'existe pas de données publiées sur les résultats cliniques après l'abandon du traitement avec le COLD-fX pour le rhume et la grippe.
- Lorsqu'il est pris pendant 4 mois pour prévenir les rhumes et la grippe, le COLD-fX peut réduire le nombre de rhumes dans une proportion de 0,25 rhume/personne chez les adultes qui avaient eu plus de deux rhumes durant l'année précédente. Par ailleurs, la pertinence clinique de cette réduction est inconnue.
- En ce moment, les données sont insuffisantes pour recommander l'utilisation systématique du COLD-fX.
- Si les patients insistent pour prendre du COLD-fX pour prévenir les rhumes et la grippe, ils ne devraient pas l'utiliser pendant plus longtemps que 4 mois (la durée maximale des études cliniques publiées).
- Pour aider à réduire l'incidence des visites en clinique externe des patients pour des infections respiratoires aiguës, conseillez aux gens de se laver les mains fréquemment.

FOR PRESCRIBING INFORMATION SEE PAGE 554 ➔