# Zinc nasal gel for the treatment of common cold symptoms: A double-blind, placebo-controlled trial

Michael Hirt, MD
Sion Nobel, MD
Ernesto Barron, BS

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## Introduction

The common cold is caused by a viral infection in the nose.[1] Its symptoms, which vary in severity, include sneezing, rhinorrhea, nasal congestion, sore and/or scratchy throat, cough, hoarseness, and mild general symptoms such as headache, fever, and body aches.[1,2] Of the more than 100 different cold viruses, the most important are rhinoviruses.[3] The lack of effective treatments for the common cold is of concern because adults contract an average of approximately three colds each year, and children experience twice as many.[2] The number of work days lost to cold-related illness is substantial.[4]

The use of zinc formulations for the treatment of common cold symptoms has been receiving increasing attention in the medical literature as well as in the lay press. Some studies in humans have shown that zinc lozenges were effective in shortening the duration of common cold symptoms in adults.[5-7] There have also been some negative reports concerning the use of zinc lozenges, but these findings appear to be related to the use of formulations that did not allow the release of ionized zinc into the oral cavity.[8,9] It has been shown that ionized zinc has direct antirhinoviral activity,[10,11] protects cells from damage by viral toxins,[12] and might inhibit the rhinovirus' ability to attach to, enter, and infect human nasal cells.[13]

Recently, a new approach to zinc therapy -- an over-the-counter nasal gel formulation (Zicam™) -- was the subject of a preliminary study (C.B. Hensley, PhD, and R. Davidson, PhD, unpublished data, 1999). That study demonstrated that the direct application of the nasal gel containing 33mmol/L of ionic zinc within 24 hours of the onset of common cold symptoms significantly shortened the duration of those symptoms. The researchers hypothesized that the delivery of ionic zinc directly to the site of infection should be more effective than oral delivery.

The goal of our study was to attempt to reproduce those results and independently assess the effect of zinc nasal gel on the duration of common cold symptoms.

## Materials and methods

Our methodology was similar to that used by Mossad et al in their clinical evaluation of zinc lozenges in 1996.[7] Subjects were recruited at four sites in the Los Angeles area. The study population consisted of 213 subjects; they were randomly assigned to receive either zinc nasal gel (n=108) or placebo (n=105).. Only subjects whose cold symptoms had been manifest for 24 hours or less were enrolled in the study. Subjects were required to have had at least three of the following symptoms: cough, headache, hoarseness, muscle

ache, nasal drainage, nasal congestion, scratchy throat, sore throat, or sneezing. All participants provided informed consent upon enrollment. Exclusion criteria were pregnancy, an immunocompromised state, a duration of common cold symptoms beyond 24 hours, and the use of certain medications.

The zinc nasal gel consisted of zinc gluconate in an emulsion of benzalkonium chloride, glycerin, hydroxyethylcellulose, sodium chloride, and sodium hydroxide; its pH level was 7.2. The composition of the placebo gel was identical except that it did not contain zinc.

Both gels were dispensed in a double-blind fashion in metered doses of 120ml in applicators supplied by Botanical Laboratories (Ferndale, Wash.). Subjects were instructed to spray one dose into each nostril every 4 hours (9 a.m., 1 p.m., 5 p.m., and 9 p.m.) for as long as they experienced symptoms. Participants were instructed not to take any other cold remedies or any drugs that might affect symptom scores.

Patients were provided with a diary to document the severity of their symptoms. Twice each day (at 9 a.m. and 9 p.m.), patients graded each of nine symptoms on a scale of 0 (absent) to 3 (severe). The total daily symptom scores were added together, and the mean and standard deviations were calculated for each patient.

The primary endpoint was the complete resolution of symptoms, which was determined when the total symptom score fell to zero. Subjects were asked to return to their study site within 24 hours of symptom resolution for verification and follow-up.

**Results**

The duration of each patient's cold was defined as the number of days from study entry to the complete resolution of symptoms. The zinc nasal gel had a significant effect in shortening their duration (figure 1). The mean resolution time was 2.3 days (±0.9) for the zinc patients and 9.0 days (±2.5) for the controls (figure 2).. The difference was statistically significant ($p<0.05$).

Subjects had also been provided a list of five potential side effects (nausea, bad taste reactions, odor, dizziness, and drowsiness) and asked during the study and again at the end of the study whether they had experienced these or any others. While none of the subjects reported any of these five side effects, 45 zinc patients (42%) and 39 controls (37%) did report that they had experienced a slight tingling or burning sensation.

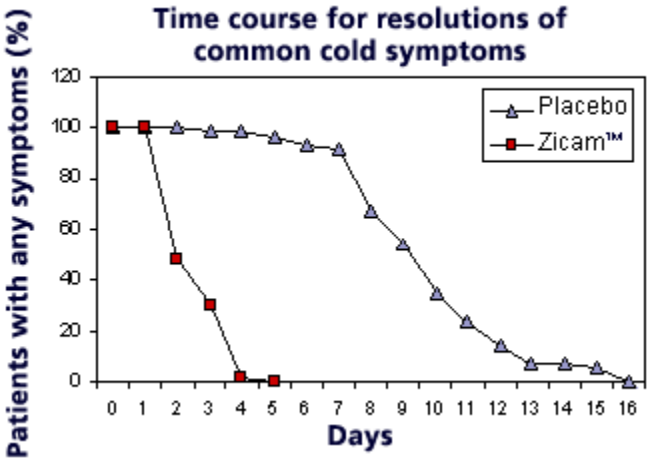


Figure 1

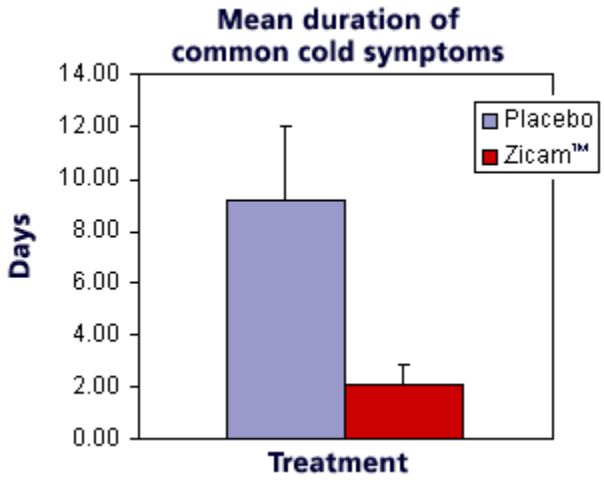


Figure 2

## Discussion

The 75% difference in the duration of symptoms in our study is consistent with the 85% reduction reported by C.B. Hensley, PhD, and R. Davidson, PhD (unpublished data, 1999).. Although zinc nasal gel's precise mechanism of action has yet to be elucidated, data suggest that ionic zinc has a direct effect on the ability of rhinovirus to infect and/or reinfect the nasal epithelium.[10,11]. Zinc ions form complexes with rhinovirus coat proteins. This interaction causes an irreversible alteration in the coat proteins and interferes with the assembly mechanism of the virus particles.[11] In addition, Novick et al reported that ionized zinc can directly inhibit the rhinovirus' ability to attach to, enter, and infect human nasal cells.[13] The crystalographically modeled surface features of human rhinovirus-14 provide binding sites for approximately 360 zinc ions. The binding. of ionic zinc is stabilized by histidine, methionine, tyrosine, and carboxyl/carboxylate groups that line the rhinovirus-14 surface canyons.. It has been proposed that this interaction blocks the rhinovirus' ability to dock with intercellular adhesion molecule binding sites.

In conclusion, our results support the findings of the previous study on the effectiveness of zinc nasal gel. Further research is needed to understand the interaction of

ionic zinc and rhinoviruses, as well as the extent of susceptibility of other viruses to this treatment.

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From the Center of Integrative Medicine, Tarzana, Calif.