

# Zinc fights common cold and antimicrobial resistance



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**F**luids, rest, and symptomatic treatment. Physicians know these three are still the cornerstones of management of non-specific viral upper respiratory infections (URIs), otherwise known as the common cold. Except for infrequent cases of bacterial coinfection, patients with viral URIs generally do not need antibiotics. Yet there is often an unspoken pressure from patients for their doctors to give them a prescription that contains more than advice their own grandmothers could have given them. Against their better judgment, therefore, many physicians resort to prescribing antibiotics for viral URIs.

During the recent 2015 Annual Convention of the Philippine Society for Microbiology and

Infectious Diseases, Dr Joseph Adrian Buensalido, an infectious disease specialist who was a 2014 Balik Scientist Awardee of the Department of Science and Technology and is currently a clinical associate professor at UP-PGH, proposed a more prudent alternative: zinc.

## The common cold

Viral URIs are generally mild and self-limited, but they are clinically significant because of their frequency in the general population. Children have 6 to 10 colds per year, with as many as 12 in children of school age. Adults, on the other hand, have 2 to 4 URI episodes annually, which account for 40 percent of time lost from work. The losses in productivity coupled with patients' expenditures for treatment add up to a significant economic burden. However, "Even an only

partially effective medication could markedly reduce morbidity and economic losses,” said Buensalido.

Approximately half of all common colds are caused by rhinoviruses, 25-30 percent by influenza viruses, 10-15 percent by coronaviruses, and the rest by adenoviruses, parainfluenza viruses, respiratory syncytial virus, metapneumovirus, enteroviruses and the human bocavirus. Due to this diversity of etiology, there is no specific therapy yet for viral URIs except for influenza, which can be treated with neuraminidase inhibitors such as oseltamivir and zanamivir.

Present management of viral URIs consists of fluids, rest and symptomatic therapy such as adrenergic agents for nasal obstruction and antihistamines for rhinorrhea. Antibacterial therapy generally has no place in the therapeutic regimen for viral URIs – and yet, according to Buensalido, more than one-third of patients who saw a doctor received an antibiotic prescription.

### **Unnecessary antibiotic use leading to resistance**

A majority of antibiotic prescriptions are for patients with respiratory illnesses, despite the fact that many of these conditions are viral, including nearly 30 percent of pneumonias. Why, then, is there such widespread use of antibiotics in viral URIs?

In 2010, Faber et al [*Euro Surveill* 2010;15(35)] surveyed 1,076 persons aged 15-78 and found that:

- 10.5 percent expected to be prescribed antibiotics for the common cold

- 92.7 percent expected an antibiotic prescription for pneumonia

- 37.6 percent believed that common cold or flu can be effectively treated with antibiotics

Moreover, a 2015 meta-analysis of 46 studies by Gualano et al [*Pharmacoepidemiol Drug Saf* 2015;24:2-10] revealed that:

- 53.9 percent of respondents did not know that antibiotics were not useful against viruses

- 59.4 percent were aware of antibiotic resistance; however:

- 26.9 percent did not know that misuse of antibiotics can lead to resistance

- 47.1 percent stopped taking antibiotics when they started feeling better

It is because of patients' expectations, said Buensalido, that physicians often find themselves prescribing antibiotics for viral URIs.

Unsurprisingly, antibiotic misuse is leading to drug resistance. The 2014 Annual Report of the Antimicrobial Resistance Surveillance Program showed:

- A nearly 20 percent resistance rate of *Streptococcus pneumoniae* for cotrimoxazole

- A sharp increase from the previous year in the resistance of *Salmonella typhi* to cotrimoxazole

- An over 90 percent resistance of *Staphylococcus aureus* to penicillin and an increasing trend of resistance of the same organism to oxacillin

Many interventions have been proposed to curb unnecessary antibiotic prescriptions for viral URIs: patient education, public information campaigns, delayed antibiotic prescribing, antibiotic stewardship measures, etc. Among these

strategies is the use of zinc as both a treatment and stewardship tool.

### Zinc reduces duration of viral URIs

Zinc is perhaps more known as a supplemental treatment for diarrhea in children. However, numerous clinical trials have also explored the use of zinc for the common cold. For the latter indication, zinc is believed to have the following mechanisms of action:

- Inhibits rhinovirus binding to intracellular adhesion molecule-1 (ICAM-1) in the nasal mucosa
- Inhibits viral replication by preventing formation of viral capsid proteins
- Inhibits proteolysis during the rhinovirus cell cycle and blocks facial nerve and trigeminal nerve conduction, thus reducing nasal congestion and sneezing
- Stabilizes cell membranes, preventing histamine release and inhibiting prostaglandin metabolism
- Increases levels of IFN- $\gamma$  levels by 10-fold

Buensalido cited three major systematic reviews that support the use of zinc in viral URIs. In a 2011 review by Hemila [*Open Respir Med J* 2011;5:51-8], 8 of 13 trials showed significant reduction in the average duration of colds in patients taking zinc vs. placebo. Pooled data from the trials that used high-dose ( $\geq 75$  mg/day) zinc acetate found a 42 percent reduction in the duration of colds, while trials that used high doses of other zinc salts found a 20 percent reduction in cold duration.

A 2012 review by Science et al [*CMAJ* 2012;184:E551-61] compared reductions in



symptom duration between different patient groups:

- 2.63 days in adult patients vs. only 0.26 days in children
- 2.75 days in those taking high-dose zinc vs. only 0.84 in those taking low-dose zinc
- 2.67 days in patients taking zinc acetate vs. 1.72 days in those taking zinc gluconate and only 0.31 days in those taking zinc sulfate
- 1.65 days overall reduction in symptom duration

Finally, a 2013 Cochrane review by Singh and Das [*Cochrane Database Syst Rev* 2013;6:CD001364] showed a reduction of 1.03 days in the duration of cold symptoms in patients taking zinc – a mean difference of 1.97 days in trials using high-dose zinc and an insignificant difference of 0.13 days in trials using low-dose zinc. The incidence rate ratio of developing a cold was also significantly lower in the zinc group.

More adverse events were likely to be reported in patients taking zinc; however, the most common adverse events were minor, such as bad taste and nausea.

Buensalido therefore recommends that instead of prescribing antibiotics to patients with

viral URIs, physicians should prescribe zinc instead.

### Prescribing zinc for URIs

In Buensalido's experience, 75 percent of URIs are viral in etiology, 22 percent are bacterial, and only 3 percent are viral-bacterial coinfections. For bacterial infections, he prescribes amoxicillin-clavulanic acid (>80 percent of the time), clarithromycin or clindamycin, in addition to paracetamol, salbutamol/guaifenesin and chlorpheniramine or diphenhydramine as appropriate for symptom relief.

For viral URIs, aside from paracetamol, chlorpheniramine and salbutamol-guaifenesin, Buensalido prescribes zinc. He recommends prescribing solo preparations of zinc – and not zinc combined with other minerals/vitamins – so that the dose can be titrated to the desired therapeutic level of zinc without the physician

having to worry about the effect of increased doses of other minerals/vitamins.

Zinc acetate appears to be the most beneficial formulation of zinc for URIs based on the medical literature, but it is not readily available in the Philippines. Zinc gluconate is available as a 70 mg tablet or a 70 mg/5 ml syrup. Buensalido prescribes two 70 mg zinc gluconate tablets four times a day for 7 days – zinc gluconate contains 14.3 percent elemental zinc, so one 70 mg tablet contains 10.01 mg elemental zinc, for a total daily dose of 80.08 mg (ie, high dose) zinc. At current prices, a 7-day course of zinc would cost less than P300.

By encouraging physicians to prescribe zinc for viral URIs, Buensalido hopes not only to promote its therapeutic benefits but also to reduce unnecessary antibiotic prescriptions and thereby help prevent antimicrobial resistance.

