

Evidenced Based Critically Appraised Topic  
Oseltamivir and Influenza Prevention

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Date: February 24<sup>th</sup>, 2013

Clinical Scenario

A 52 year old female presents to the clinic for general malaise, runny nose, congestion. Patient inquires about risk of exposure to influenza A. Patient's mother is in nursing home and is exposed to influenza A recently. Patient's mother was put on Oseltamivir. Patient's last contact with mother was three days ago. Lab reports a WBC 10.52 and culture for influenza is negative, patient was afebrile. Patient's only medication is multivitamin and Zolof 50mg hs. Immunizations are up to date, however did not get the influenza vaccine this year. Patient is concerned about contracting the virus and "wants something for it" to help reduce the symptoms.

Clinical Question

When healthy adults are exposed to influenza, are neuraminidase inhibitors (oseltamivir and zanamivir) effective in reducing the symptoms after exposure versus placebo?

Articles

Erlick, I., Abraham, S., and Kondamudi, V.K. (2010). Management of Influenza. *American Family Physician*, 82(9), 1087-1095.

Jefferson, T., Jones, M., Doshi, P., Del Mar, C., Heneghan, C.J., Hama, R., and Thompson, M.J. (2012).

Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children. *Cochrane*

*Database of Systematic Reviews*, Issue 1, Art. No.: CD008965. DOI: 10.1002/14651858.CD008965.pub3.

Summary and Appraisal of Key Evidence

**Study 1** Erlick et al. (2010) reviewed several studies related to the effectiveness of oseltamivir and zanamivir in outpatient populations. The level of evidence is grade A level I. They looked at studies that used the medications on healthy adults and children older than 1 years of age. They assessed and extracted the data on methods, participants, interventions and outcomes on participants that exhibited influenza-like illnesses. Influenza-like illness was defined as fever, myalgia, headache, rhinitis, sore throat and cough. They based their data extraction on the guidelines from the World Health Organization and the Centers for Disease Control and Prevention.

They evaluated a 2009 systematic review that included randomized, double blinded, placebo control studies involving healthy adults and persons at risk of influenza-related complications. Oseltamivir reduced the duration of symptoms by 0.55 days among healthy adults and by 0.74 days in persons at risk of complications. Erlick et al. (2010) also compared a 2009 systematic review and meta-analysis of oseltamivir and zanamivir use in healthy adults. This was also a randomized, double blinded, placebo control study. It was concluded that the use in children produced a faster resolution of symptoms by 0.5 to 1.5 days.

**Study 2** Jefferson et al. (2012) objective was to update a 2005 Cochrane review that assessed the effects of neuraminidase inhibitors in preventing or ameliorating the symptoms of influenza, the transmission of influenza, and complications from influenza in healthy adults, and to estimate the frequency of side effects. This article's level of evidence is grade A level IIa. They searched for randomized placebo controlled studies of neuraminidase inhibitors in otherwise healthy adults to naturally occurring influenza. Studies had to include 75% or more of patients aged 14-60. Twenty trials were included; four on prophylaxis, twelve on treatment, and four on post

exposure prophylaxis. Overall, 20 trials in 19 publications were used. Only five trials were judged adequate by the Cochrane Collaboration methods

Jefferson et al (2012) found that two trials compared a total of 697 adults treated with zanamivir 10mg daily and 602 with placebo and two trials compared 675 adults treated with oseltamivir 75mg daily and 413 with placebo. Evidence was insufficient to support or refute the effect of these medications on prophylaxis of influenza-like illness: risk ratio 1.28 for oseltamivir and 1.51 for zanamivir. Zanamivir was found to reduce the chance of symptomatic laboratory confirmed influenza, along with oseltamivir. Neither was found to be protected against asymptomatic influenza. Postexposure against influenza was found on two trials for the drugs, with a risk ratio of 0.9130 and 0.219. Jefferson et al (2012) also found some evidence of benefit in shortening the duration of the illness if taken within 48 hours on the onset of symptoms for both drugs.

### Results

Both studies suggest that neuraminidase inhibitors are effective at reducing symptoms of influenza; however, the evidence is of modest benefit. The reduction of symptoms was reduced by about one day. For this effect to take place, it was found that the medications need to be taken within 48 hours of exposure and/or the symptoms of the illness. However, both reviews found that the trials were of small sample size and that many trials were performed by the manufacturer. Also, follow up with participants was inconsistent or not found to be done at all.

### Clinical Bottom Line

According to the two studies, the uses of neuraminidase inhibitors have modest effectiveness in reducing influenza-related symptoms in healthy adults at low risk of complications. Patients at high risk of complications should be treated with these medications within 48 hours of symptoms onset. For healthy adults exposed, the medications improve the symptoms and reduce the illness time by a half a day versus placebo. It was also suggested that the same effects could be possible with over-the-counter antipyretics and anti-inflammatory agents.

### Implications for Practice

I would not recommend the use of neuraminidase inhibitors to this patient. Since the symptoms of influenza are only decreased by 0.5 to 1.0 day, I would suggest using an antipyretic or anti-inflammatory medication instead. However, there are certain circumstances where I think the medication would be beneficial. I think that immunocompromised or patients with at risk complications (lung and heart co-morbidities) would benefit from the medication. I think that it is very hard to determine when the onset of symptoms truly occurs. Unless a patient comes in right after exposure, it would be difficult to obtain the information. It is also under scrutiny from the studies, that the influenza culture may have false-negative results when receiving the medications, since there is an abundance of antibodies. Advocating for the influenza vaccine would be more beneficial. More research needs to be performed on mortality and morbidity factors associated with non-treated patients to determine the true efficacy of the drug.

### Reference

Erlikh, I., Abraham, S., and Kondamudi, V.K. (2010). Management of Influenza. *American Family Physician*, 82(9), 1087-1095.

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