Neuraminidase Inhibitors Are Effective for Treatment and Prevention of Influenza


Study Overview

Objective. To summarize available evidence regarding efficacy of neuraminidase inhibitors for the treatment and prevention of influenza.

Design. Systematic review and meta-analysis.

Methods. Authors collected data from every randomized, double-blind, placebo-controlled trial of zanamivir or oseltamivir that was published in English prior to 31 December 2001 and that reported at least one endpoint of interest for the treatment or prevention of influenza. 3 population groups were defined: children aged 12 years and under, healthy individuals aged 12 to 65 years, and high-risk adult populations (ie, 65 years and older or those with certain chronic diseases).

Main outcome measures. Median time to symptom alleviation (treatment trials) or number of influenza cases avoided (prevention trials).

Main results. 17 treatment trials and 7 prevention trials were identified. Children, healthy individuals aged 12 through 65 years, and high-risk adults treated with zanamivir experienced reduced median days of symptoms with a difference of 1.0 (95% confidence interval [CI], 0.5–1.5), 0.8 (0.3–1.3), and 0.9 (–0.1–1.9), respectively. Oseltamivir also reduced days of symptoms for these 3 populations with a difference of 0.9 (95% CI, 0.3–1.5), 0.9 (0.3–1.4), and 0.4 (–0.7–1.4). The relative risk of developing influenza was reduced by 70% to 90% by both drugs across a variety of treatment strategies and populations studied.

Conclusion. Available randomized controlled trials support the use of neuraminidase inhibitors for treatment and prevention of influenza; however, evidence is limited for some populations and prevention strategies.

Commentary

Each year, influenza virus infections cause thousands of deaths and hospitalizations despite the availability of an effective vaccine [1]. Because of gaps in vaccination coverage and poor compliance with vaccination, treatment options for acute influenza are still sorely needed. Oseltamivir and zanamivir were introduced in the late 1990s to join the existing influenza antivirals (amantidine and rimantadine). The new drugs offer improved side effect profiles and expand coverage of influenza A and B; however, neither drug is widely prescribed for treatment of influenza, perhaps reflecting the perception that their modest benefits for a typically self-limited illness may not outweigh the substantial cost or minor risk of adverse effects. In this well-executed systematic review and meta-analysis of neuraminidase treatment trials, there is little to change this perception, but the consistency of the treatment effect supports the efficacy of both oseltamivir and zanamivir.

The authors found these agents reduced the median duration of symptoms by 0.4 to 1.0 days and resulted in a 29% to 43% relative reduction in the odds of developing bacterial complications. Although these numbers may not be impressive enough for wide use of the inhibitors, they raise the question of whether some subgroups benefit more than others. Surprisingly, the “high risk” groups in this review (ie, the chronically ill, elderly, and children) did not have substantially greater benefit from treatment than healthy adults. Also, this analysis did not address outcomes pertinent to these groups, such as hospitalization, death, and adverse drug events, presumably because of insufficient sample size or data collection. Other subgroups not examined in this review have shown a greater magnitude of symptom benefit, such as when patients present within 24 hours of symptom onset [2] or following exposure to household contact with influenza [3].

Using a seasonal prophylaxis strategy with either oseltamivir or zanamivir can result in a 70% to 90% relative reduction in the odds of developing influenza, but little data are available to describe whether these benefits persist in vaccinated populations. Vaccination is the mainstay of influenza prevention, with proven cost-effectiveness and safety. Only 1 of the 7 prevention trials had a high proportion of vaccinated subjects (80%), and it showed that 75 mg of
oseltamivir daily prevented 11 cases of influenza in a population of 276 elderly residential home residents. These limited data suggest that neuraminidase prophylaxis may be beneficial in vaccinated high-risk populations, but further studies are needed on the cost-effectiveness and safety of this approach.

Applications for Clinical Practice

The early use of neuroaminidase inhibitors for influenza treatment is effective at reducing symptom duration, but further evidence is needed before prophylaxis programs in vaccinated high-risk populations are instituted.

--Review by Josh F. Peterson, MD

References

