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Q/ Does oseltamivir shorten flu symptom duration?

EVIDENCE-BASED ANSWER

A/ YES. Treatment of influenza virus infection with oral oseltamivir reduces time to alleviation of symptoms in adults and children by approximately one day compared with placebo. It reduces symptom duration even when initiated more than 2 days after symptom onset (strength of recommendation: **A**, systematic review of randomized controlled trials [RCTs], meta-analysis of observation trials, RCT).

Evidence summary

A 2014 systematic review included 8 RCTs in adults (3954 patients) and one RCT in children (669 patients) with influenza and compared time to alleviation of symptoms with oseltamivir and placebo.¹ Symptoms were defined as local (nasal discharge, dry cough, sore throat) and systemic (fever, myalgia, headache, fatigue). Methodology for diagnosis varied by trial.

Oral oseltamivir (75, 150, or 300 mg for 5 to 10 days) reduced time to first alleviation of symptoms by 17 hours (95% confidence interval [CI], 8.4-25 hours) compared with placebo for adults and 29 hours (95% CI, 12-47 hours) for the otherwise healthy children.

The systematic review also included 2 RCTs involving 660 children with chronic asthma who received treatment with oseltamivir. Researchers found no reduction in time to symptom alleviation with the oseltamivir.

Treatment with oseltamivir increased the risk of nausea (number needed to harm [NNH]=28) and vomiting (NNH=22) in adults and the risk of vomiting (NNH=19) in children. Sources of bias included industry sponsorship of all trials, differing placebo components, inadequate recruitment, and use of other medication.

Shorter fever duration?

A 2012 meta-analysis of 6 observational studies (5842 patients) compared the effect of oral oseltamivir with no treatment on duration of signs and symptoms (definition not given) in patients with influenza (method of diagnosis not stated).² Oseltamivir reduced fever duration by 33 hours (95% CI, 21-45 hours) compared with no treatment.

The authors describe the evidence as being of very low quality because of study heterogeneity, lack of control for confounding variables, selection bias, and study sources (many unpublished industry studies).

There's benefit even with late Tx

A 2014 double-blind RCT, not included in the previously described reviews, of 130 adults and 1070 children with a positive rapid influenza test examined the effect of oseltamivir and placebo on symptom duration.³ Research assistants visited participants at home each day until patients were asymptomatic for 7 consecutive days.

Treatment with oseltamivir reduced symptom duration by a median of one day compared with no treatment (hazard ratio=0.87; 95% CI, 0.79-0.95). This benefit was observed regardless of whether treatment was initiated fewer or more than 48 hours after symptom onset. One notable limitation was failure to control for paracetamol (acetaminophen) usage, a possible confounder for duration of symptoms, such as fever.

JFP

References

1. Jefferson T, Jones MA, Doshi P, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children. *Cochrane Database Syst Rev.* 2014;(4):CD008965.
2. Hsu J, Santesso N, Mustafa R, et al. Antivirals for treatment of influenza: a systematic review and meta-analysis of observational studies. *Ann Intern Med.* 2012;156:512-524.
3. Fry AM, Goswami D, Nahar K, et al. Efficacy of oseltamivir treatment started within 5 days of symptom onset to reduce influenza illness duration and virus shedding in an urban setting in Bangladesh: a randomised placebo-controlled trial. *Lancet Infect Dis.* 2014;14:109-118.