# Tips from Other Journals



Tips from Other Journals are written by the medical editors of *American Family Physician.*

The trade names of drugs listed in Tips from Other Journals are based on what is currently available and not necessarily the brand of drug that was used in the study being discussed.

## Oseltamivir Effective for Reducing Influenza Duration in Children

**Background:** Influenza is a common illness in children that often leads to outpatient visits, hospitalizations, secondary bacterial complications, and sometimes death. Oseltamivir (Tamiflu), a neuraminidase inhibitor, is currently the only recommended therapy for the treatment of influenza in children younger than five years. A meta-analysis of the evidence, published in 2009, showed that when oseltamivir was started within 48 hours of the onset of symptoms, it modestly shortened the duration of influenza in children by 0.5 to 1.5 days. Heinonen and colleagues conducted a randomized, double-blind, placebo-controlled trial to evaluate the effectiveness of oseltamivir in reducing the duration of influenza when treatment is started within 24 hours of the onset of symptoms.

**The Study:** Children one to three years of age were recruited from two influenza seasons (2007 to 2008, and 2008 to 2009) in Turku, Finland. During these seasons, parents were asked to bring their children to the clinic if they had fever or signs of respiratory infection. Eligible participants had a fever for less than 24 hours, and at least one sign or symptom of a respiratory infection or a positive rapid influenza test. Children with a confirmed viral disease other than influenza, a potential bacterial infection, a poorly controlled underlying medical condition, immunosuppression, allergy to oseltamivir, treatment with the study medication in the previous four weeks, or participation in another clinical trial with an investigational drug were excluded.

Participants were randomized to receive placebo or oseltamivir twice daily for five days. Parents were responsible for filling out symptom diaries on days 1 through 21 by recording the child's temperature; the presence and severity of symptoms; the return to normal activities; absences from day care or work; and administration of the study drug, relief medications, or antibiotics. Influenza illness was confirmed with viral culture, and further testing with reverse transcriptase polymerase chain reaction assays was conducted when necessary.

The primary outcome was the development of acute otitis media in children with confirmed influenza. Secondary outcomes were the time to resolution of illness, time to resolution of all symptoms, resolution of fever, absence from day care and work, use of relief medications or antibiotics, incidence of complications other than acute otitis media, and hospitalization. Subgroup analysis was performed depending on whether the patient was found to have influenza A or influenza B.

**Results:** Of the 408 participants who received an intervention, 203 received oseltamivir and 205 received placebo. Laboratory testing confirmed the presence of influenza in 37 patients in the oseltamivir group and 61 patients in the placebo group.

No significant reductions in otitis media occurrence were observed in any group or subgroup when oseltamivir was started within 24 hours of the onset of symptoms. However, an 85 percent reduction in the development of acute otitis media was found in patients with any type of influenza who were taking oseltamivir and began the medication within 12 hours of the onset of symptoms.

Oseltamivir shortened the duration of illness by 1.4 days in all children and by 3.5 days in those with confirmed influenza A. Oseltamivir also significantly reduced parents' absence from work, children's absence from day care, and the use of antipyretics and analgesics. No child with influenza developed pneumonia or was hospitalized during the study period. Vomiting was the main complication associated with oseltamivir use. Oseltamivir had no notable effect on influenza B infections, possibly because of the small number of patients who had influenza B or because of resistance to the drug.

**Conclusion:** The authors conclude that initiation of oseltamivir within 24 hours of the onset of influenza symptoms significantly reduces the duration of symptoms, absence from work, absence from day care, and use of antipyretics and analgesics, particularly in children with a confirmed influenza A viral infection. The authors acknowledge that it is challenging to clinically diagnose influenza early enough to initiate treatment within 24 hours, especially because only 25 percent of the study population actually had laboratory-confirmed influenza.

DANIEL GIBBS, MS III

**Source:** Heinonen S, et al. Early oseltamivir treatment of influenza in children 1–3 years of age: a randomized controlled trial. *Clin Infect Dis.* October 15, 2010;51(8):887-894.

## Preventing Psychotic Disorders in High-Risk Patients

**Background:** Dysfunctional fatty acid metabolism may contribute to the development of psychosis. Omega-3 polyunsaturated fatty acids (PUFAs) are known to interact with the dopaminergic and serotoninergic systems, and reduced levels of these acids have been reported in patients with schizophrenia. Therefore, omega-3 PUFA supplementation might be useful in preventing the transition to a psychotic state. Amminger and colleagues conducted a randomized, double-blind, placebo-controlled trial to determine if use of omega-3 PUFAs could prevent a first episode of psychosis.

**The Study:** The authors randomized 81 participants at high risk of developing a psychotic disorder to receive 1.2 g per day of omega-3 PUFAs (i.e., marine fish oil, including 700 mg of eicosapentaenoic acid [EPA] and 480 mg of docosahexaenoic acid [DHA]) or a placebo. Participants were 13 to 25 years of age and were classified as high-risk based on the presence of one or more of several criteria: attenuated positive psychotic symptoms (i.e., moderate to high levels of delusions, hallucinations, suspiciousness, or conceptual disorganization), spontaneously resolving transient psychosis (lasting less than one week), or having schizotypal personality disorder or a first-degree relative with a psychotic disorder. Patients were excluded if they had a history of psychosis or mania, neurologic disorders (e.g., epilepsy), substance dependence, previous use of an antipsychotic or mood stabilizer, or an IQ of less than 70. Participants received the treatment drug or placebo for 12 weeks and were followed for one year, with a primary end point of conversion to psychotic disorder. ▶

**Results:** The risk of developing psychosis was significantly reduced for patients taking omega-3 PUFAs (4.9 versus 27.5 percent for placebo, respectively). The PUFA group also had significantly greater reductions in positive and negative psychotic symptoms, and a greater improvement in overall functioning (final mean Global Assessment of Functioning scores of 78.7 versus 67.2 for placebo, from respective baselines of 61.0 and 60.0). The groups also had similar adherence rates, antidepressant and benzodiazepine use, and need for interval psychological and psychosocial interventions.

**Conclusion:** The authors conclude that use of omega-3 PUFA supplementation for 12 weeks significantly reduces the likelihood that a high-risk patient will transition to a psychotic disorder, and improves symptoms and functioning for 12 months after treatment is initiated. The authors caution that their results were based on a small number of patients, and the effectiveness of omega-3 PUFAs beyond 12 months is unknown. However, they state that even delaying the onset of psychosis is a worthwhile achievement.

KENNETH T. MOON, MD

**Source**: Amminger GP, et al. Long-chain omega-3 fatty acids for indicated prevention of psychotic disorders: a randomized, placebo-controlled trial. *Arch Gen Psychiatry.* February 2010;67(2):146-154.

EDITOR'S NOTE: Although omega-3 fatty acids are most touted for cardiovascular health, their contribution to neuronal synaptic transmission has generated interest in their potential role in psychiatric disorders. For instance, close adherence to a Mediterranean-type diet (which is high in omega-3 PUFAs and monounsaturated fatty acids) has been associated with a greater than 30 percent reduction in unipolar depression.[1]

A 2006 review and meta-analysis by the Omega-3 Fatty Acids Subcommittee of the American Psychiatric Association concluded that omega-3 fatty acids (especially EPA and DHA) have a protective effect in patients with unipolar and bipolar depression, and that they may be useful as adjunctive therapy for schizophrenia and attention-deficit/hyperactivity disorder. They recommended that patients with mood, impulse control, or psychotic disorders consume 1 g total of EPA plus DHA daily. Those with mood disorders may also benefit from omega-3 supplementation (approximately 1 to 9 g per day). Although generally well-tolerated, high doses of omega-3 fatty acids can increase bleeding risk (especially if anticoagulants are also being used), and consuming more than 3 g per day of EPA plus DHA should be monitored by a physician for potential complications.[2]—K.T.M.

**REFERENCES**

1. Sánchez-Villegas A, Delgado-Rodríguez M, Alonso A, et al. Association of the Mediterranean dietary pattern with the incidence of depression: the Seguimiento Universidad de Navarra/University of Navarra follow-up (SUN) cohort. *Arch Gen Psychiatry.* 2009; 66(10):1090-1098.
2. Freeman MP, Hibbeln JR, Wisner KL, et al. Omega-3 fatty acids: evidence basis for treatment and future research in psychiatry [published correction appears in *J Clin Psychiatry.* 2007;68(2):338]. *J Clin Psychiatry.* 2006; 67(12):1954-1967.

## Internal vs. External Monitoring of Uterine Contractions

**Background:** Monitoring uterine contractions by internal tocodynamometry is advised by the American Congress of Obstetricians and Gynecologists in certain situations (e.g., maternal obesity, when one-on-one nursing care is not available, when response to oxytocin [Pitocin] is limited). However, this recommendation is based on expert opinion, and several small trials have not shown reductions in adverse neonatal outcomes or in operative delivery rates with internal versus external monitoring. Bakker and colleagues conducted a randomized, multicenter clinical trial to determine if using an intrauterine pressure catheter during labor would lead to better outcomes than those associated with external monitoring.

**The Study:** The authors randomized 1,456 women to receive internal or external monitoring of uterine activity during labor. All participants had a singleton pregnancy in cephalic position with a gestational age of more than 36 weeks and an indication for induction or augmentation of labor. Patients were excluded if they had a uterine scar, were positive for hepatitis B or human immunodeficiency virus infection, or had signs of an intrauterine infection or fetal distress. The use of intrauterine pressure catheters was allowed in the external monitoring group if there were insufficient uterine contractions, if cervical progression had been absent for two hours, or if cesarean delivery was being considered.

**Results:** No significant difference was noted in operative delivery rates between the groups (31.3 and 29.6 percent in the internal and external monitoring groups, respectively). The groups also were similar in the time to delivery and in antibiotic and analgesic use. Adverse neonatal outcomes (e.g., Apgar scores of less than 7 at five minutes, umbilical artery pH scores of less than 7.05, neonatal admission to the hospital for more than 48 hours) were equivalent between the groups. Post hoc analyses showed no notable interactions between monitoring type and the type of labor (induced versus augmented), body mass index (30 kg per $m^2$ or less versus more than 30 kg per $m^2$), or parity (primiparous versus multiparous) with regard to adverse neonatal outcomes or the need for operative delivery.

**Conclusion:** The authors conclude that compared with external monitoring of uterine activity in women with induced or augmented labor, internal tocodynamometry does not improve the rates of operative delivery or adverse neonatal outcomes.

KENNETH T. MOON, MD

**Source:** Bakker JJ, et al. Outcomes after internal versus external tocodynamometry for monitoring labor [published correction appears in *N Engl J Med.* May 13, 2010; 362(19):1849]. *N Engl J Med.* January 28, 2010;362(4): 306-313.

## Can HSV-2 Suppression Reduce HIV-1 Transmission?

**Background:** Having symptomatic herpes simplex virus type 2 (HSV-2) infection is thought to increase a patient's risk of contracting human immunodeficiency virus type 1 (HIV-1) infection. Several trials have shown that daily HSV-2 therapy can reduce plasma HIV-1 levels by 0.25 to 0.50 $\log_{10}$ copies per mL. Celum and colleagues conducted a randomized, double-blind, placebo-controlled trial to evaluate if suppression of HSV-2 infection might prevent transmission of HIV-1 infection.

**The Study:** The authors recruited 3,408 heterosexual couples with discordant HIV/HSV status (i.e., one partner was seropositive for HIV-1 and HSV-2, and the other partner was HIV-negative but could be positive or negative for HSV-2). Partners with HIV-1 infection were randomized to receive acyclovir (Zovirax), 400 mg twice daily, or a placebo, and both partners were monitored for two years for changes in health status and HIV transmission. The primary end point was a new diagnosis of HIV-1 in the previously negative partner. Exclusion criteria for partners with HIV-1 infection included pregnancy or persistent genital ulcers. These patients were also excluded if they were taking antiretroviral therapy, had a CD4 count of less than 250 cells per $mm^3$ ($250 \times 10^9$ per L), or had evidence of AIDS.

**Results:** Mean HIV-1 plasma concentration was significantly reduced by 0.25 $\log_{10}$ copies per mL in the acyclovir group compared with the placebo group, as was the risk of symptomatic genital ulcer disease (risk ratio = 0.39). However, HIV-1 transmission rates were equivalent between the groups. No differences in transmission rates were noted with respect to sex, partner's HIV-1 viral load or symptomatic genital ulcer disease, or to the level of adherence with the assigned treatment.

**Conclusion:** The authors conclude that daily acyclovir therapy is ineffective in preventing transmission of HIV-1 infecton from a partner who is HIV-1– and HSV-2–positive to the partner who is HIV-negative, even with reductions in HIV viral load.

KENNETH T. MOON, MD

**Source:** Celum C, et al. Acyclovir and transmission of HIV-1 from persons infected with HIV-1 and HSV-2. *N Engl J Med.* February 4, 2010;362(5):427-439. ■