

to evaluate the efficacy and safety of topiramate for migraine prevention in pediatric subjects 12 to 17 years of age. *Pediatrics* 2009;123:924-34.

Question Among adolescents with a history of migraines, is topiramate (compared with placebo) effective and safe for prophylaxis of migraines?

Design Randomized, controlled trial.

Setting Multi-center study, both in the US and outside the US.

Participants 106 adolescents (12–17 years of age) with a ≥ 6 -month history of migraine.

Intervention 16 weeks of daily treatment with topiramate (50 or 100 mg/day) or placebo.

Outcomes Percent reduction in monthly migraine attacks, with the use of the 48-hour rule, from the prospective baseline period to the last 12 weeks of the double-blind phase. The 48-hour rule defined a single migraine episode as all recurrences of migraine symptoms within 48 hours after onset. Secondary efficacy measures included the reduction from baseline in the monthly migraine day rate and the 50% responder rate, safety, and tolerability.

Main Results A total of 29 (83%) of 35 subjects treated with topiramate at 50 mg/day, 30 (86%) of 35 subjects treated with topiramate at 100 mg/day, and 26 (79.0%) of 33 placebo-treated subjects completed double-blind treatment. Topiramate at 100 mg/day, but not 50 mg/day, resulted in a statistically significant reduction in the monthly migraine attack rate from baseline versus placebo (median: 72% vs 44%) during the last 12 weeks of double-blind treatment. Topiramate at 100 mg/day, but not 50 mg/day, also resulted in a statistically significant reduction in the monthly migraine day rate from baseline versus placebo. The responder rate favored topiramate at 100 mg/day (83% vs 45% for placebo). Upper respiratory tract infection, paresthesia, and dizziness occurred more commonly in the topiramate groups than in the placebo group.

Conclusions The 100 mg/day topiramate group demonstrated efficacy in the prevention of migraine in pediatric subjects. Overall, topiramate treatment was safe and well tolerated.

Commentary Most childhood migraine patients will have only one or two migraine headaches a month. When the frequency is more than weekly, the use of a migraine preventative is considered. Headache doctors feel that the preventatives are successful if they can reduce the frequency of headaches by 50%. Sometimes the severity of the headaches is reduced as well. This study demonstrates that topiramate is an effective migraine preventative in teenagers, and secondly, that low dosages of topiramate are no more effective than placebo, and one needs to find an appropriate dose (100 mg a day) for efficacy. Based on my personal referral-based experience, I think the latter finding is the critical point for our practice. Many patients rarely get to 100 mg a day before coming to see me as a headache specialist. As pediatricians, I do wonder if we have a tendency to inadequately

dose pain medications for our patients. There are, however, concerns that the paper did not address. A commonly associated side effect of topiramate is problems with word finding and difficulty concentrating. In the references quoted in the Lewis et al paper, these adverse effects were noted in over 10% of adult patients. Unfortunately this current study adds no insight as to the frequency in which these side effects occur in teens. An additional challenge for the field of headache medicine is to determine which of the preventative medications is best for the teenage or preteen patient. Is topiramate more efficacious than amitriptyline, propranolol, or cyproheptadine? Which medication is the most cost effective? The price of a one month supply of amitriptyline is \$5, whereas the brand name version of topiramate (Topamax) is over \$200 per month. Fortunately, a generic version of topiramate is recently available, which is much lower in cost.

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Primary care hearing screening is of limited utility

Halloran DR, Hardin JM, Wall TC. Validity of pure-tone hearing screening at well-child visits. *Arch Pediatr Adolesc Med* 2009;163:158-63.

Question Among children, how sensitive and specific is pure-tone audiometry hearing screening in the primary care setting?

Design Prospective cohort study.

Setting Eight academic and private pediatric practices in Alabama.

Participants A subset of children from a convenience sample of 1061 children between 3 and 19 years of age were screened for hearing loss using pure-tone audiometry.

Intervention Formal audiologic evaluations (gold standard) for those children referred by their primary care physician (28 children) and for a random sample of children not referred (102 children).

Outcomes Audiologic evaluations.

Main Results A total of 28 children were referred to an audiologist for formal hearing testing after pure-tone audiometry screening during a well-child visit, at which 25 children did not pass the initial screening and 3 could not complete the screening. Of the 25 children, only 7 were evaluated by an audiologist, for a follow-up rate of 25%. One child was diagnosed as having hearing loss. Formal audiologic assessment was also performed on a random sample of 102 children who were not referred to the audiologist. For the random sample, hearing loss was identified in 2 of 76 (3%) children who passed and 1 of 16 (6%) children who did not pass pure tone audiometry screening. The sensitivity and specificity of pure-tone audiometry were 50% and 78%, respectively (positive likelihood ratio (LR) = 1.8, negative LR = 0.64).

Conclusions In light of the increasing burden on physicians to provide preventive care, this study calls into question the value of hearing screening using pure-tone audiometry during well-child visits given the poor test characteristics and lack of follow-up after referral.

Commentary Pure-tone audiometry screening is one of the many components of usual well-child care for which there is little underlying scientific evidence. This study finds that many children do not follow-up with an audiologist after an abnormal hearing screen and that the accuracy of audiometry compared with a formal audiologic evaluation is poor. The story may be even worse if the actual diagnoses, which were not presented in this report, were considered. For example, some of these children may have had serous otitis media, which would likely simply resolve over time. This study raises important healthcare delivery questions. For example, many states require repeated hearing screens as part of well-child care for Medicaid-enrolled children. This report suggests that such policies may be a significant waste of limited healthcare resources. It should be noted that in contrast to pure-tone audiometry, newborn hearing screening has led to dramatic improvements in the diagnosis of significant hearing loss. Unfortunately, there have also been barriers to the timely follow-up after an abnormal newborn hearing screen.

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Traumatic brain injury results in prolonged increase in risk of epilepsy in children

Christensen J, Pedersen MG, Pedersen CB, Sidenius P, Olsen J, Vestergaard M. Long-term risk of epilepsy after traumatic brain injury in children and young adults: a population-based cohort study. *Lancet* 2009;373:1105-10.

Question Among children with traumatic brain injury, how does the risk of epilepsy change over time?

Design Cohort study.

Setting Denmark.

Participants 1,605,216 people born between 1977 and 2002.

Outcomes Relative risks (RR) of epilepsy over time.

Main Results Risk of epilepsy was increased after a mild brain injury (RR 2.22, 95% CI 2.07–2.38), severe brain injury (7.40, 6.16–8.89), and skull fracture (2.17, 1.73–2.71). The risk was increased more than 10 years after mild brain injury (1.51, 1.24–1.85), severe brain injury (4.29, 2.04–9.00), and skull fracture (2.06, 1.37–3.11). RR increased with age at mild and severe injury and was especially high among people older than 15 years of age with mild (3.51, 2.90–4.26) and severe (12.24, 8.52–17.57) injury. The risk was slightly higher in women (2.49, 2.25–2.76) than in men (2.01, 1.83–2.22). Patients with a family history of epilepsy had a notably high risk of epilepsy after mild (5.75, 4.56–7.27) and severe brain injury (10.09, 4.20–24.26).

Conclusions The longlasting high risk of epilepsy after brain injury might provide a window for prevention of post-traumatic epilepsy.

Commentary Head trauma is an important cause of epilepsy and this study is an important contribution to our understanding of the problem. Using data from the Danish National Hospital Register, the investigators identified 78,572 persons who experienced at least one head injury and 17,470 persons with a diagnosis of epilepsy, of whom 1,017 persons had had a prior head injury, in a population of 1,605,216 persons born in Denmark. The relative risks of developing epilepsy in those with mild and severe head injury, with or without a family history of epilepsy, were compared with the risks of epilepsy in those without head injury at yearly time points after the injury and standardized for age, sex, and calendar year. Overall, the relative risks of epilepsy were found to be raised approximately two-fold (RR 2.2) after a mild and seven-fold after a severe head injury (RR 7.4). The risk of epilepsy increased with age and was highest for people older than 15 years at the time of injury for both mild (RR 3.5) and severe (12.2) head injuries. In children, the risk of posttraumatic epilepsy was highest in those aged 0-5 years after severe head injury (RR 7.2), and the risk following mild injury were similar for all aged 0-15. The rate of development of epilepsy was greatest in the few years immediately after head injury, with an over five-fold increase remaining for 2-3 years after a severe head injury, but the excess risk extended for 10 years after mild brain injury, longer than previously reported.¹ This study is of commendable size and completeness, with an excellent and sophisticated statistical design, and in our opinion should be considered the reference study in the field.

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Reference

1. Annegers JF, Hauser WA, Coan SP, Rocca WA. A population-based study of seizures after traumatic brain injuries. *N Engl J Med* 1998;338:20-4.

Evidence is not yet clear on impact of pacifiers on breastfeeding

O'Connor NR, Tanabe KO, Siadaty MS, Hauck FR. Pacifiers and breastfeeding: a systematic review. *Arch Pediatr Adolesc Med* 2009;163:378-82.

Question Among infants who are breastfeeding, does the use of a pacifier increase the risk of decreased breastfeeding duration or exclusivity?

Design Systematic review.

Data Sources MEDLINE, CINAHL, the Cochrane Library, EMBASE, POPLINE, and bibliographies of identified articles.