

## Translating Best Evidence Into Best care

**EDITOR'S NOTE:** Studies for this issue were identified using alerts from *Archives of Disease in Childhood-Education and Practice*, *Archives of Disease in Childhood-Fetal and Neonatal*, *Archives of Disease in Childhood*, *British Medical Journal*, *Journal of the American Medical Association*, *New England Journal of Medicine*, *Pediatric Infectious Disease Journal*, *Pediatrics*, *The Journal of Pediatrics*, and *The Lancet*. Search terms were “paediatrics” [All Fields] OR “pediatrics” [All Fields] OR “pediatrics” [MeSH Terms]. Cleo Pappas, MLIS, Library of the Health Sciences, University of Illinois at Chicago, contributed to the review and selection of this month's abstracts.

—Jordan Hupert, MD

**EVIDENCE-BASED MEDICINE PEARL: ODDS RATIO (OR):** The OR often is used in studies measuring risk of an outcome given a specific exposure. The odds of an outcome occurring is the the ratio of the probability of the outcome occurring divided by the probability of the outcome not occurring. Mathematically, this is  $p/(1-p)$ , where  $p$  is the probability. The OR is the odds of an outcome occurring in the exposed population divided by the odds of the same outcome occurring in the unexposed population—a measure of association. The OR may be used in many types of studies, but perhaps is most used in case-control studies. For example, in a case-control study evaluating the association of childhood migraines with a history of infantile colic, 72.6% of children with migraines and 26.5% of children without migraines had a history of infantile colic. The OR is  $(72.6\%/26.5\%)/(27.4\%/73.5\%) = 7.35$ . This is known as the crude OR. The aOR (adjusted by a computer for possible confounders such as gestational age, colic in first-degree relatives, etc) listed in the case-control study by Romanello et al, is 6.61 (95% CI 4.38-10.00). Thus, patients with childhood migraines were 6.61 times more likely to have a history of infantile colic than patients without childhood migraines. This association is statistically significant, as the 95% CI does not cross 1 (see the Romanello et al; JAMA 2013;309:1607-12).

—Jordan Hupert, MD

**EVIDENCE-BASED MEDICINE LIBRARIAN PEARL: “PEARL CULTURING”:** Five valuable techniques may increase the number of relevant articles retrieved on a desired topic using those articles already retrieved: (1) In PubMed, after finding applicable articles either by a search or by Single Citation Matcher, select related citations; (2) In PubMed, change the view of applicable articles from summary or abstract to Medline. Then look for medical subject headings (MeSH terms) that have been assigned to the applicable article. Perform a search with those terms; (3) Look for other articles written by the authors of applicable articles; (4) Plug applicable articles into Web of Science to determine references cited and citing articles of applicable articles; and (5) Plug applicable articles into Google Scholar to determine citing articles. These techniques are particularly useful for topics that have not been extensively studied.

—Cleo Pappas, MLIS

### Childhood migraine is associated with a history of infantile colic

Romanello S, Spiri D, Marcuzzi E, Zanin A, Boizeau P, Riviere S, et al. Association between childhood migraine and history of infantile colic. *JAMA* 2013;309:1607-12.

**Question** Among otherwise healthy infants, what is the association of infantile colic with later development of childhood migraine headaches?

**Design** Case-control study.

**Setting** 3 European tertiary care hospitals (Robert Debré, Paris, France; Sacco, Milan, Italy; and Santa Mariadella Misericordia, Udine, Italy).

**Participants** Consecutive children presenting to the emergency department, 6-18 years old, who were diagnosed with primary headaches by a pediatric neurologist. Control participants were children in the same age range who visited the emergency department of each participating center for minor trauma.

**Intervention** Childhood migraine headache.

**Outcomes** The primary outcome was the difference in the prevalence of infantile colic between children with and without a diagnosis of migraine.

**Main Results** Children with migraine were more likely to have experienced infantile colic than those without migraine, (72.6% vs 26.5%; OR, 6.61, 95% CI 4.38-10.00,  $P < .001$ ) either migraine without aura ( $n = 142$ ; 73.9% vs 26.5%; OR, 7.01, 95% CI 4.43-11.09,  $P < .001$ ), or migraine with aura ( $n = 66$ ; 69.7% vs 26.5%; OR, 5.73; 95% CI 3.07-10.73,  $P < .001$ ). This association was not found for children with tension-type headache (35% vs 26.5%; OR, 1.46, 95% CI 0.92-2.32;  $P = .10$ ).

**Conclusions** The presence of migraine in children and adolescents aged 6 to 18 years was associated with a history of infantile colic.

**Commentary** Infantile colic is a common and distressing disorder of early infancy characterized by excessive and often inconsolable crying in an otherwise healthy infant. The infants often are assumed to be experiencing abdominal pain, despite no direct evidence for this localization. Moreover,

therapies aimed at reducing intestinal gas or altering the infants' diet have been largely unsuccessful.<sup>1</sup> The study by Romanello et al is a case-control study that demonstrates that children with migraine headaches are more likely to have had colic as infants.<sup>2,3</sup> Further bolstering the evidence for an association, mothers with migraine are >2.3 times as likely to have an infant with colic.<sup>4</sup> Infants with migraines are more sensitive to stimuli, both during and often between attacks. It is possible that infant colic is an early life manifestation of those genes that later in life are expressed as migraine headache. Infants with colic may be more sensitive to the stimuli they encounter in the first weeks of life as their sensory processing abilities rapidly develop, and may express this sensitivity through excessive crying. Prospective longitudinal infant cohort studies are needed to rigorously examine this association. If infant colic is a migraine-related disorder, there are major treatment implications. Behavioral therapies, such as limiting certain types of stimulation, or pharmacologic migraine therapies known to be safe in early infancy, such as acetaminophen, could be studied.

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## Thin catheter surfactant administration during spontaneous breathing in very low birth weight infants is associated with reduced need for mechanical ventilation

Kanmaz HG, Erdevé O, Canpolat FE, Mutlu B, Dilmen U. Surfactant administration via thin catheter during spontaneous breathing: randomized controlled trial. *Pediatrics* 2013;131:e502-9.

**Question** Among very low birth weight infants, what is the therapeutic efficacy of thin catheter administration of surfactant during spontaneous breathing, compared with surfactant administration via endotracheal intubation (and then extubation), on the rates of early mechanical ventilation and the development of bronchopulmonary dysplasia (BPD)?

**Design** Randomized, controlled trial.

**Setting** Neonatal intensive care unit of Zekai Tahir Burak Maternity Teaching Hospital, Ankara, Turkey.

**Participants** Inborn preterm infants with gestational age < 32 weeks with respiratory distress syndrome (RDS).

**Intervention** Thin catheter surfactant administration during spontaneous breathing versus the endotracheal tube intubation/ventilation/extubation technique for administration of surfactant.

**Outcomes** Primary outcome: mechanical ventilation within the first 72 hours after birth. Secondary outcomes: duration of nasal continuous positive airway pressure (CPAP), duration of mechanical ventilation, and development of BPD.

**Main Results** Mechanical ventilation in the first 72 hours of life was significantly lower in the thin catheter group compared with the endotracheal tube group (30% vs 45%, number needed to treat = 7, 95% CI 4-58). Mean duration of both nasal CPAP and mechanical ventilation were significantly reduced in the thin catheter group (78 hours vs 116 hours  $P < .006$  and 35.6 hours vs 64.1 hours  $P < .002$ , respectively). The BPD rate was marginally statistically lower among infants treated with the thin catheter technique (absolute risk reduction 9.9%, 95% CI 0.03-19.8%; number needed to treat = 11, 95% CI 6-3339).

**Conclusions** The thin catheter technique significantly reduces the need for and duration of mechanical ventilation, as well as the BPD rate in very low birth weight infants.

**Commentary** Recent trials (COIN, SUPPORT) have demonstrated that aggressive continuous positive airway pressure can prevent BPD in the highest risk neonates.<sup>1,2</sup> Unfortunately, 50%-80% of infants in these trials eventually required intubation. These findings have led to renewed interest in less invasive ways to administer surfactant in order to prevent prolonged intubation and mechanical ventilation. Kanmaz et al have developed a technique to deliver surfactant quickly and safely without the use of forceps, utilizing a small-bore catheter in spontaneously breathing infants <32 weeks gestational age with signs and symptoms of RDS. This technique resulted in a lower rate of mechanical ventilation and less BPD when compared with infants treated with endotracheal intubation administration of surfactant. Kanmaz et al should be applauded for their ingenuity in attempting to administer surfactant in the most physiologic, least invasive way possible. Whether this protocol will provide benefit over the endotracheal method when applied at other centers by different operators remains to be demonstrated. Another interesting question is whether this technique would provide additional benefits beyond endotracheal surfactant administration if performed prophylactically, prior to the development of RDS.<sup>3</sup>

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