

Possible Connection Found Between Infantile Colic and Pediatric Migraine

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ARTICLE IN BRIEF

Investigators reported that nearly 73 percent of 208 children and teens who were diagnosed with migraine at emergency departments had a history of colic in infancy, compared with 26.5 percent of a control group of children. The findings raise the possibility that there is a common mechanism behind colic and migraine.

Babies with colic may be at heightened risk for developing migraines later in childhood, according to a new study that helps provide some clues about the inconsolable crying — usually more than three hours a day in infants up to six weeks old — that can leave new parents frustrated and sleepless.

The European study of 208 children and teens who were diagnosed with migraine at emergency departments found that nearly 73 percent of them had a history of colic in infancy, compared with 26.5 percent of a control group of children.

The findings, published April 17 in the *Journal of the American Medical Association (JAMA)*, raise the possibility that colic might be an early form of migraine — which probably will come as a surprise to many new moms and dads who often blame their newborn's periods of excessive crying on painful gastrointestinal gas, perhaps due to a breastfeeding mother's diet or an allergy to cow's milk.

"This study raises questions about basic assumptions regarding infantile colic," noted an editorial that accompanied the study. "If colic is an early

manifestation of migraine, this may explain the consistent lack of efficacy of treatments directed at a gastrointestinal etiology."

The editorial, written by Leon G. Epstein, MD, and Phyllis C. Zee, MD, PhD, of Northwestern University, noted that other periodic disorders of early childhood have been thought to be variants of migraine, including benign paroxysmal vertigo, benign paroxysmal torticollis, and cyclic vomiting syndrome. Many children with cyclic vomiting syndrome go on to develop migraine.

"Migraine disorders may represent a continuum from colic in infancy to cyclic vomiting syndrome in young children to childhood and adult migraine," they wrote.

STUDY METHODOLOGY

The *JAMA* study — which builds on previous research suggesting a colic-migraine link — was conducted at three European hospitals, one in Paris and two in Italy. Investigators enrolled 208 consecutive children between ages six to 18 who came to the emergency department (ED) and were diagnosed with primary headache by a pediatric neurologist. The control group consisted of 471 children in the same age range who presented to the ED with minor trauma and who did not have a history of headache.

Parents were given a structured questionnaire to determine the child's history of colic as well as demographic and other medical information. Physicians also examined each child's personal national health booklet — which is given to new parents and travels with the child from birth to adulthood as medical encounters occur — to see whether a colic diagnosis had been



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recorded on any medical visit. Parents did not know the study was specifically about a possible connection between colic and migraine.

STUDY RESULTS

Parent recall, as it turned out, was very good. All children for whom a history of colic was reported by their parents also had colic recorded in their health booklets. None of the children who weren't described as colicky had a colic diagnosis in their booklet.

The researchers' findings were striking. Among children with migraine, 72.6 percent (151 of 208) reported infantile colic. In the migraine with aura group, 69.7 percent (44 of 66) had colic, and in the migraine without aura group, 73.9 percent (105 of 142) had had colic. The prevalence of colic was much lower in the control group: just 26.5 percent (125/471).

The researchers also did a second study involving 120 children who had tension-type headaches. In that group, 35 percent (42 of 120) had been colicky babies — a rate similar to the control group.

"In our study, the association with infantile colic was significant for migraine without aura as well as migraine with aura," the researchers wrote, "suggesting a common pathophysiology of migraine and infantile colic." They noted that pulsating pain was more common in young migraine patients with a history of colic than in migraine patients who did not have colic as babies.

Luigi Titomanlio, MD, PhD, a study investigator who is chief of the Pediatric Migraine & Neurovascular Disease Clinic and consulting physician in the ED at Robert Debré Hospital in Paris, told *Neurology Today*, "There possibly is a common mechanism at the origin of colic and migraine. The mechanism could be the sensitization of perivascular nerve terminals. The inflammation around brain vessels occurs during migraine attacks. It could be imagined that infants with colic could suffer from a similar sensitization of the perivascular nerve terminals in the gut, which leads to abdominal pain, in the first month of life."

Dr. Titomanlio said in an e-mail that drug therapies used for migraine might be useful for colic, though he said ethical issues would have to be addressed in designing a trial that involved infants.

"Although it is currently difficult to imagine that clinical trials will be conducted with off-label drugs for the treatment of a benign condition such as infantile colic, it is also true that infantile colic causes pain in babies and high levels of stress in parents," he wrote.

According to the *JAMA* editorial, colic occurs in more than 20 percent of infants. Having a colicky baby can make parents feel helpless because nothing

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REM Sleep Behavior Disorder

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a clinical researcher the one thing that is the hardest thing to control is who walks through your door." Patients with relatively severe RBD are perhaps more likely to go to a sleep disorders center, and the Mayo Clinic is a major center for dementia diagnosis and treatment, "so there's a chance that there's a bit of dementia enrichment here." And finally, he said, autopsied patients are probably

more likely to have been those with serious neurodegenerative disease.

"That being said, I think the results are very robust," he said. That 98 percent chance of a synucleinopathy in a patient with dementia "is without having any further information about the patient at all. Combine that with all the skills you have in clinical diagnosis and you can do better than that. And so, clearly, combined with a full evaluation, REM sleep behavior disorder is a major, powerful diagnostic tool." •

LINK UP FOR MORE INFORMATION:

- AAN annual meeting abstract (2013): Clinicopathologic correlations in 172 Cases of REM sleep behavior disorder ± a coexisting neurologic disorder: <http://bit.ly/18pJrSg>.
- Postuma RB, Bertrand JA, Gagnon JF, et al. Rapid eye movement sleep behavior disorder and risk of dementia in Parkinson's disease: a prospective study. *Mov Disord* 2012;27(6):720-726. E-pub 2012 Feb 9.
- Postuma RB, Gagnon JF, Montplaisir JY, et al. Olfaction and color vision identify impending neurodegeneration in rapid eye movement sleep behavior disorder. *Ann Neurol* 2011; 69(5):811-818. E-pub 2011 Jan 18.
- *Neurology Today* archive on REM sleep behavior disorder: <http://bit.ly/ZBqPbo>.
- *Neurology* archive on REM sleep behavior disorder: <http://bit.ly/11c4IEi>.

Colic, Migraine

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they do will calm their baby. Well-intended family and friends often offer all kinds of advice — swaddle the baby, don't swaddle the baby, don't eat certain foods if you're breastfeeding. Treatments for colic range from medication, nutritional changes, behavioral strategies, and alternative medicine, according to the *JAMA* report.

Pediatric migraine occurs in 1 to 3 percent of children ages three to seven; 4 to 11 percent of children seven to 11 years old, and 8 to 23 percent of children ages 11 to 15 years old, according to the editorial. Migraine can be debilitating for children and teens, causing missed days from school and sidelining them from sports and other activities. Research indicates that children with migraine are at risk for poor school performance.

Oversensitivity to stimuli might be a common characteristic of colic and migraine.

MOMS WITH MIGRAINE

Amy Gelfand, MD, a child neurologist at University of California, San Francisco who does migraine research, said this latest study adds to evidence that there is a common genetic link between colic and migraine. She was part of team that published a study in *Neurology* in September 2012 that found that babies whose mothers had migraine were 2.6 times more likely to have colic than infants without a maternal history of migraine.

Dr. Gelfand said oversensitivity to stimuli might be a common characteristic of colic and migraine. "Colicky babies may be more sensitive to the stimuli they are encountering out in the world that they weren't experiencing in the womb. They maybe are overwhelmed and express it by excessive crying, often later in the afternoon or evening."

Stephen Ashwal, MD, distinguished professor and chief of the Division of Child Neurology at Loma Linda University in California, told *Neurology Today* that "we've known for many years that there is a strong relationship between the brain and the gastrointestinal system, which forms the basis of many of the autonomic nervous system pathways. There are many neurological

disorders that have both brain symptoms and gastrointestinal symptoms."

He said genetics studies will likely lead to the identification of genes common to colic and migraine. "Looking at specific genes and the enzymes they control could lead to new targeted treatments," he said.

Dr. Ashwal, who coauthored the AAN guideline on treating pediatric migraine, said that given that a number of medications have good track records

in treating migraine in both adults and children, it is not inconceivable that one day a drug therapy will be tested in colicky babies. •

LINK UP FOR MORE INFORMATION:

- Romanello S, Spiri D, Titomanlio L, et al. Association between childhood migraine and history of infantile colic. *JAMA* 2013;309(15):1607-1612.
- Epstein LG, Zee PC. Editorial: Infantile colic and migraine. *JAMA* 2013;309(15):1636-1637.
- *Neurology Today* archive on migraine: <http://bit.ly/ZCjVpK>.
- AAN annual meeting abstract (2012): Infant colic is associated with maternal migraine: <http://bit.ly/13YBr7j>.