Cochrane for Clinicians

Putting Evidence into Practice

These are summaries of reviews from the Cochrane Library.

This series is coordinated by Corey D. Fogleman, MD, Assistant Medical Editor.

A collection of Cochrane for Clinicians published in *AFP* is available at http://www.aafp.org/afp/cochrane.

CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz Questions on page 208.

Author disclosure: No relevant financial affiliations.

Acetaminophen for the Treatment of Pain in Newborns

DONNA COHEN, MD, MSc, *Lancaster General Hospital Family Medicine Residency Program, Lancaster, Pennsylvania*

Clinical Question

Is acetaminophen an effective treatment for neonates with pain caused by medical procedures?

Evidence-Based Answer

Acetaminophen does not significantly reduce pain associated with heel lance, eye examinations, or assisted vaginal births in newborns. Acetaminophen may reduce the total amount of morphine a newborn needs in the first 48 hours following major abdominal or thoracic surgery. (Strength of Recommendation: B, based on inconsistent or limited quality patient-oriented evidence.)

Practice Pointers

Neonates are often exposed to painful interventions during routine newborn care or complicated neonatal intensive care unit hospitalizations. Pharmacologic therapies for pain relief include opiates, benzodiazepines, anesthetics, nonsteroidal anti-inflammatory drugs, and acetaminophen, and nonpharmacologic therapies include oral sweet solutions, sucking, swaddling, and kangaroo care.[1-3] Despite increased awareness of the importance of pain prevention, the effectiveness and safety of these modalities remain controversial, and they may be underused for the treatment of pain in neonates.[3]

The authors of this Cochrane review identified eight studies evaluating the effectiveness of acetaminophen for the treatment of pain in 614 neonates (30 days or younger). Pain was measured by validated tools examining newborn facial actions, body movements, cry, heart rate, and/or oxygen saturation. The painful procedures included heel lance, assisted vaginal birth, eye examination for retinopathy of prematurity, and postoperative care following abdominal or thoracic surgery.

In infants undergoing heel lance, oral acetaminophen (20 mg per kg) did not significantly reduce pain compared with sterile water, lidocaine/prilocaine (EMLA) cream, or cherry elixir. At higher doses of 40 mg per kg, oral acetaminophen was no more effective than sterile water at reducing pain. Oral glucose solution appeared to be more effective than oral acetaminophen (20 mg per kg) at reducing pain scores following heel lance (Premature Infant Pain Profile [PIPP] score, range = 0 to 21 points; mean difference [MD] = 2.21; 95% confidence interval [CI], 0.72 to 3.70). For eye examinations performed to evaluate retinopathy of prematurity, oral acetaminophen (15 mg per kg) did not reduce pain compared with sterile water; and PIPP scores were significantly higher in infants who received oral acetaminophen (15 mg per kg) compared with infants who received sucrose (approximately 25% solution; MD = 3.90; 95% CI, 2.92 to 4.88).

Acetaminophen suppositories (doses ranging from 50 to 70 mg based on infant weight) did not decrease pain in infants born via assisted vaginal delivery (vacuum extraction or forceps). When infants exposed to assisted vaginal births underwent a heel lance at two to three days of life, pain scores and time spent crying were increased in the acetaminophen suppository group (doses ranging from 60 to 100 mg based on weight) vs. the placebo group (MD = 19 seconds; 95% CI, 14 to 24). In a separate study examining infants undergoing major thoracic or abdominal surgery, the total morphine rescue dose in the 48-hour postoperative period did not differ significantly between infants randomized to intravenous acetaminophen and those randomized to continuous morphine.

No two trials used the same assessment tool for the outcome of pain; therefore, a meta-analysis could not be conducted and

tests for heterogeneity were not applicable. Despite the small sample sizes of the individual trials, the risk of bias was considered low and the quality of evidence considered good. The authors did not identify any studies on the use of acetaminophen for the prevention of pain. No adverse effects were noted, but no studies assessed the long-term effects of acetaminophen use, so there was insufficient evidence to comment on its safety.

The American Academy of Pediatrics recommends that caregivers routinely implement effective strategies for the prevention and treatment of pain associated with medical procedures in newborns. It also suggests that acetaminophen not be used alone but as an adjunct for severe pain, after minor procedures, or in the later postoperative period.[3] This Cochrane review supports these guarded recommendations. Further study is warranted to determine the benefit of acetaminophen in reducing postoperative pain and pain associated with other procedures in neonates.

SOURCE: Ohlsson A, Shah PS. Paracetamol (acetaminophen) for prevention or treatment of pain in newborns. *Cochrane Database Syst Rev.* 2015;(6):CD011219.

The practice recommendations in this activity are available at http://summaries.cochrane.org/CD011219.

REFERENCES

1. Hall RW. Anesthesia and analgesia in the NICU. *Clin Perinatol.* 2012;39(1):239-254.
2. McPherson C, Grunau RE. Neonatal pain control and neurologic effects of anesthetics and sedatives in preterm infants. *Clin Perinatol.* 2014;41(1):209-227.
3. American Academy of Pediatrics Committee on Fetus and Newborn, American Academy of Pediatrics Section on Surgery, Canadian Paediatric Society Fetus and Newborn Committee, Batton DG, Barrington KJ, Wallman C. Prevention and management of pain in the neonate: an update [published correction appears in *Pediatrics.* 2007;119(2):425]. *Pediatrics.* 2006;118(5):2231-2241.

Capsaicin for Nonallergic Rhinitis

ANNE L. MOUNSEY, MD, and CATHY M. FELLER, MD
University of North Carolina School of Medicine, Chapel Hill, North Carolina

Clinical Question

Is intranasal capsaicin effective for nonallergic rhinitis?

Evidence-Based Answer

Intranasal capsaicin is safe and effective for reducing symptoms of nonallergic rhinitis (number needed to treat = 4; 95% confidence interval [CI], 1 to 22). There is insufficient evidence to compare the effectiveness of capsaicin to other topical or systemic medications. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Nonallergic rhinitis is a broad term used to describe a heterogeneous group of sinus diseases that are not triggered by aeroallergens.[1] The prevalence of nonallergic rhinitis is 5% to 10% worldwide,[2] and symptoms include nasal congestion, blockage or obstruction, sneezing, clear rhinorrhea, and nasal itching. Nonallergic rhinitis is diagnosed by exclusion of symptoms related to aeroallergen exposure or infection and anatomic abnormalities through the history and physical examination.[3] The authors of this Cochrane review evaluated the effectiveness of intranasal capsaicin in the management of nonallergic rhinitis.

This Cochrane review included two randomized controlled trials (RCTs) and two quasi-RCTs with a total of 302 participants 16 to 65 years of age with nonallergic rhinitis. They all had symptoms lasting at least one hour per day for at least five days during the two weeks preceding the study. Patients with allergic rhinitis, acute or chronic rhinosinusitis, autoimmune rhinitis, or rhinitis related to anatomic abnormalities were excluded. Nasal capsaicin was used in total daily dosages of 42 to 107 mcg given during various treatment periods of three days to four weeks. The primary outcomes were overall symptom scores (global symptom scores, daily record chart score), individual symptom scores (nasal congestion, rhinorrhea, sneezing, nasal itching), and adverse effects. The risk of bias in these studies was low to unclear.

Overall, the results support the use of intranasal capsaicin as an effective way to manage nonallergic rhinitis. In one RCT (n = 24), patients received capsaicin (30 mcg) or placebo every two to three days for a total of seven treatments in two weeks. Capsaicin use improved overall nasal symptoms on a 10-point visual analogue scale during week 2 (mean difference [MD] vs. placebo = –3.34; 95% CI, –5.24 to –1.44); week 12 (MD = –3.73; 95% CI, –5.45 to –2.01); and week 36 (MD = –3.52; 95% CI, –5.55 to –1.48) posttreatment. Another study compared different dosages of capsaicin (1 mcg, 2 mcg, and 4 mcg three times per day for three consecutive days) and showed that at four weeks posttreatment, only the 4-mcg dosage was more effective than placebo for resolution of nasal symptoms (relative risk = 3.17; 95% CI, 1.38 to 7.29).

A third study comparing two treatment regimens of capsaicin (in each regimen the participants used a total of 82.5 mcg) reported that five treatments in one day was more effective in improving rhinorrhea than five treatments every two to three days over two weeks; numerical data were not provided. An RCT of 40 patients showed that although there was no improvement in individual symptom score with capsaicin in a dosage of 10.5 mcg

once weekly for four weeks vs. intranasal budesonide (Rhinocort), capsaicin use did improve aggregate symptom relief scores at four weeks on a 10-point visual analogue scale (MD = 2.50; 95% CI, 1.06 to 3.94). Study heterogeneity precluded meta-analysis.

Only one study measured adverse effects. These included nasal blockage, itching, sneezing, and coughing, which are also symptoms of nonallergic rhinitis. Because the study did not clarify when these symptoms were measured, no definitive conclusions could be drawn. Intranasal capsaicin has been reported to cause burning, lacrimation, rhinorrhea, and cough.[4]

Capsaicin is available over the counter as an inexpensive nasal spray. Clinical guidelines from the National Asthma Council Australia and The British Society for Allergy and Clinical Immunology support the use of capsaicin for nonallergic rhinitis as a complementary treatment.[5,6]

SOURCE: Gevorgyan A, Segboer C, Gorissen R, van Drunen CM, Fokkens W. Capsaicin for non-allergic rhinitis. *Cochrane Database Syst Rev.* 2015;(7):CD010591.

The practice recommendations in this activity are available at http://summaries.cochrane.org/CD010591.

REFERENCES

1. Lieberman P, Pattanaik D. Nonallergic rhinitis. *Curr Allergy Asthma Rep.* 2014;14(6):439.
2. Van Gerven L, Alpizar YA, Wouters MM, et al. Capsaicin treatment reduces nasal hyperreactivity and transient receptor potential cation channel subfamily V, receptor 1 (TRPV1) overexpression in patients with idiopathic rhinitis. *J Allergy Clin Immunol.* 2014;133(5):1332-1339.
3. van Rijswijk JB, Gerth van Wijk R. Capsaicin treatment of idiopathic rhinitis: the new panacea? *Curr Allergy Asthma Rep.* 2006;6(2):132-137.
4. Kushnir NM. The role of decongestants, cromolyn, guafenesin, saline washes, capsaicin, leukotriene antagonists, and other treatments on rhinitis. *Immunol Allergy Clin North Am.* 2011;31(3):601-617.
5. National Asthma Counsel Australia. Managing allergic rhinitis in people with asthma. 2012. http://www.nationalasthma.org.au/uploads/publication/allergic-rhinitis-asthma-hp.pdf. Accessed November 22, 2015.
6. Scadding GK, Durham SR, Mirakian R, et al.; British Society for Allergy and Clinical Immunology. BSACI guidelines for the management of allergic and non-allergic rhinitis. *Clin Exp Allergy.* 2008;38(1):19-42. ■