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.

Early Exercise Helps Rehabilitate Ankle Sprains

Background: Ankle sprains are a common musculoskeletal injury, causing acute pain and loss of function. They result in 302,000 visits to emergency departments in the United Kingdom annually. Of patients presenting with ankle sprains, 25 percent miss school or work for more than seven days, and long-term risks include a propensity for reinjury and residual deficits. Classic treatment of sprains includes protection, rest, ice, compression, elevation, and sometimes non–weight-bearing with crutches or immobilization with a cast. Meta-analyses have shown that functional treatment, such as early active use of the injured soft tissue, may be more effective for improving recovery from an ankle sprain. Bleakley and colleagues conducted a randomized controlled trial to compare early functional rehabilitation with current treatments for acute ankle sprains.

The Study: Patients 16 to 65 years of age who presented to an emergency department or a sports medicine clinic in Northern Ireland with a grade 1 or 2 ankle sprain that had occurred within the previous six days were eligible for the study. Patients with a grade 3 sprain (complete ligament rupture), a bony ankle injury, multiple injuries, or a contraindication to ice therapy; who did not speak English; who were under the influence of drugs or alcohol; or who had an unclear address for follow-up were excluded. Patients were randomized to an early exercise group or a standard treatment group. At the study onset, both groups were given written instructions for applying ice and compression (two 10-minute ice and compression sessions with 10 minutes of rest in between, done three times a day for the first week after injury). Also in the first week, the exercise group engaged in therapeutic exercises. This group received written and verbal instructions and a DVD that showed how to perform the exercises. Participants turned in a treatment diary at the first of four weekly follow-up visits that included treatment and analgesic use, and was used to assess compliance. External ankle support (i.e., bracing, taping, and bandaging) and analgesics were not routinely provided to either group.

During weeks 1 through 4 after injury, both groups had standardized ankle rehabilitation, which included muscle strengthening, proprioception training, and sports-specific exercises. This rehabilitation was supervised once per week by the research physiotherapist and done four times per week at home without supervision. Outcomes were assessed weekly for the first four weeks after injury and again at 16 weeks. The primary outcome was subjective ankle function (using the Lower Extremity Functional Scale, a self-completed questionnaire). Secondary outcomes included pain at rest and with activity, swelling, physical activity, and reinjury rates.

Results: Between July 2007 and August 2008, the authors randomized 50 participants to each group. From baseline to week 2 of follow-up, patients in the exercise group reported significantly better ankle function. Patients in the exercise group were more active, with increases in time spent walking, step count, and time spent in light physical activities compared with those in standard treatment. There was no difference between groups in the amount of swelling or pain at rest or with activities, and the study was not ▶

adequately powered to detect differences in the secondary outcomes. More participants dropped out of the exercise group (11 in the exercise group, four in the standard group). The reinjury rate was low (two injuries in each group). There were no statistically significant differences between groups at the end of 16 weeks for any measure.

Conclusion: The authors conclude that performing active ankle exercises in the first week after a mild to moderate ankle sprain results in improved short-term function.

AMY CRAWFORD-FAUCHER, MD

Source: Bleakley CM, et al. Effect of accelerated rehabilitation on function after ankle sprain: randomised controlled trial. *BMJ.* May 10, 2010;340:c1964.

Probiotics Help to Reduce Crying in Colicky Infants

Background: Infantile colic affects 3 to 28 percent of healthy newborns. It is characterized by fussy crying lasting three or more hours a day, for three or more days a week, for at least three weeks, causing distress to infants and their parents. The etiology of colic is poorly understood, but increased counts of gas-producing anaerobic gram-negative intestinal bacteria have been implicated, and lower counts of lactobacilli have been recovered in the stool of colicky infants. Previous studies suggested a benefit of lactobacilli supplementation compared with simethicone therapy. Savino and colleagues conducted a randomized controlled, double-blind study to test the safety and effectiveness of a particular lactobacillus strain, *Lactobacillus reuteri* (DSM 17938), in colicky infants.

The Study: Fifty full-term, colicky infants with birth weights of 2,500 to 4,000 g (5 lb, 8 oz to 8 lb, 13 oz) who were exclusively breastfed were recruited between two and 16 weeks of gestation. Infants with evidence of chronic illness, gastrointestinal disease, any antibiotic or probiotic use in the previous week, or any formula feeding were excluded. Mothers were instructed to avoid cow's milk in their diet during the study. Infants were randomized to receive 8 $\log_{10}$ colony-forming units of *L. reuteri* (provided as a freeze-dried suspension in a mixture of sunflower oil and medium-chain triglyceride oil) or identical placebo. Five drops of the supplement and placebo were given 30 minutes before the first feeding of the day for 21 days. The primary outcome was a reduction in crying time to less than three hours per day by day 21. Secondary outcomes included the number of children who had a 50 percent reduction in crying time at days 7, 14, and 21. Intestinal microflora also were analyzed to determine the effect the probiotic had on select intestinal bacteria.

At enrollment, parents were interviewed to determine daily crying time, and the infant's growth parameters were measured. Parents kept a detailed daily diary to record crying times, stooling patterns, and any adverse effects. Fecal samples were collected at enrollment and on day 21.

Results: All but four infants in the placebo group completed the study, and no infants were withdrawn because of adverse effects. Median crying times were similar between the groups at baseline (370 minutes per day in the lactobacilli group and 300 minutes per day in the placebo group). Infants in the probiotic group had significantly reduced daily crying times (35 versus 90 minutes per day) by day 21 compared with infants in the placebo group, although there was still a marked decrease in the placebo group. Moreover, infants in the probiotic group had significantly less crying at days 7, 14, and 21. By day 21, only four of the 25 infants in the probiotic group cried for more than 180 minutes per day compared with 12 of the 21 infants in the placebo group. Stool samples confirmed the presence of *L. reuteri* in the treatment group, whereas no infants in the placebo group had the probiotic in their stool. There was a greater decrease in *Escherichia coli* counts in the treatment group compared with the placebo group.

Conclusion: The authors conclude that although all colicky infants improved during the course of this study, the probiotic *L. reuteri* is well tolerated and more effective than placebo in reducing colic-related crying.

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Source: Savino F, et al. *Lactobacillus reuteri* DSM 17938 in infantile colic: a randomized, double-blind, placebo-controlled trial. *Pediatrics.* September 2010;126(3):e526-e533.

DHA Supplementation Does Not Benefit Mothers or Infants

Background: Studies have suggested that pregnant women who increase their intake of n-3 long-chain polyunsaturated fatty acids, specifically docosahexaenoic acid (DHA) from fish and seafood, have a lower risk of maternal depression and improved neonatal development. Human studies have been inconclusive, mostly because of methodologic flaws; however, the nutritional supplement industry markets prenatal supplements with DHA, and some organizations recommend supplementation to improve brain function in the mother and infant. Makrides and colleagues designed the DHA to Optimize Mother Infant Outcome (DOMInO) trial to better quantify any benefits and identify any risks to mothers and infants receiving DHA supplementation.

The Study: This double-blind, multicenter, randomized controlled trial was conducted in five Australian medical centers. Women with singleton pregnancies earlier than 21 weeks of gestation were invited to participate. Women already taking DHA supplements, with a bleeding disorder in which tuna oil was contraindicated, taking anticoagulants, with a pregnancy complicated by a known fetal abnormality, or with documented drug or alcohol abuse were excluded. Groups were stratified by center and by parity (first versus subsequent birth) and randomized to take three capsules daily of 500 mg of fish oil concentrate or a similarly appearing vegetable oil capsule. The fish oil capsules provided 800 mg of DHA and 100 mg of eicosapentaenoic acid per day; these doses were estimated to be above the threshold associated with lower rates of maternal depression and improved infant development outcomes. The vegetable oil capsule was designed to match the fatty-acid profile of the average Australian diet. Women were instructed to take the supplements until delivery. Participants were contacted two weeks after enrollment and at 28 and 36 weeks of gestation to assess adverse effects and to encourage compliance. Adherence was measured by DHA concentrations in cord blood.

The primary outcome for mothers was a high level of postpartum depression, as suggested by a score of more than 12 on the Edinburgh Postnatal Depression Scale, which the women completed six weeks and six months after delivery. The primary childhood outcome was neurodevelopment at 18 months of age. Study psychologists administered the Cognitive and Language Composite Scales of the Bayley Scales of Infant and Toddler Development, Third Edition.

Results: The authors enrolled 1,197 women in the DHA group and 1,202 in the control group, and the study was powered to detect a 4.2 percent absolute reduction in depressive symptoms. Similarly, the offspring sample size, which required at least 572 children, was designed to detect a clinically meaningful difference of 4 points in developmental scores. All 96 preterm children were assessed and 630 full-term children were randomly chosen during the first year of life to be tested. The baseline characteristics of both groups were similar and the drop-out rate was less than 4 percent in all groups. Adverse effects were similar in each group except for an increased incidence of eructation in the DHA group.

There was no difference in maternal depression outcomes between the DHA and control groups, and there was no difference in mean cognitive scores between children in each group. Secondary analyses suggested decreased incidence of very early preterm births in the DHA group, but also increased postterm pregnancies requiring induction with or without cesarean delivery. Boys had no language development differences between groups, whereas girls exposed to DHA had lower mean language scores, an increased risk of language delay, and lower mean adaptive scores than girls in the control group.

Conclusion: The authors conclude that the results of the DOMInO trial do not support the routine use of DHA supplementation in pregnant women to reduce levels of postpartum depression or improve cognitive and language development in early childhood.

AMY CRAWFORD-FAUCHER, MD

Source: Makrides M, et al. Effect of DHA supplementation during pregnancy on maternal depression and neurodevelopment of young children: a randomized controlled trial. *JAMA.* October 20, 2010;304(15):1675-1683. ■