Translating Best Evidence Into Best Care

EDITOR'S NOTE: Journals reviewed for this issue: *Archives of Disease in Childhood, Archives of Pediatrics and Adolescent Medicine, British Medical Journal, Journal of the American Medical Association, The Journal of Pediatrics, The Lancet, New England Journal of Medicine, Pediatric Infectious Diseases Journal,* and *Pediatrics.* Heidi Marleau, MLS, Ebling Library for the Health Sciences, University of Wisconsin, contributed to the review and selection of this month's abstracts.

—John G. Frohna, MD, MPH

Adding prednisolone to standard immunoglobulin therapy is beneficial for patients with severe Kawasaki disease

Kobayashi T, Saji T, Otani T, Takeuchi K, Nakamura T, Arakawa H, et al. for the RAISE Study Group. Efficacy of immunoglobulin plus prednisolone for prevention of coronary artery abnormalities in severe Kawasaki disease (RAISE study): a randomised, open-label, blinded-endpoints trial. *Lancet* 2012;379:1613-20.

Question Among patients with severe Kawasaki disease (KD), does the addition of prednisolone to intravenous immunoglobulin (IVIG) with aspirin reduce the incidence of coronary artery abnormalities?

Design Multicenter, prospective, randomized, open-label, blinded-endpoints trial.

Setting 74 hospitals in Japan between September 2008 and December 2010.

Participants 248 patients with severe KD.

Intervention Control: IVIG (2 g/kg for 24 hours and aspirin 30 mg/kg per day). Intervention: IVIG plus prednisolone (the same IVIG regimen as the control group plus prednisolone 2 mg/kg per day given over 15 days after concentrations of C-reactive protein normalized).

Outcome Incidence of coronary artery abnormalities during the study period.

Main Results The incidence of coronary artery abnormalities was significantly lower in the IVIG plus prednisolone group than in the IVIG group during the study period (four patients [3%] vs 28 patients [23%]; risk difference 0.20, 95% CI 0.12–0.28, $P < .0001$, Number Needed to Treat = 5). Serious adverse events were similar between both groups.

Conclusions The addition of prednisolone to the standard regimen of IVIG improves coronary artery outcomes in patients with severe KD in Japan. Further study of intensified primary treatment for this disease in a mixed ethnic population is warranted.

Commentary High-dose IVIG therapy, together with aspirin, is the standard of care in treatment of acute KD. Despite timely IVIG treatment, approximately 4% of affected children develop coronary abnormalities, and 1% develop giant aneurysms. Among the strongest risk factors for coronary aneurysms is persistent or recrudescent fever after IVIG infusion, termed IVIG resistance. The study used a validated risk score to select Japanese children with KD at highest risk for IVIG resistance, and hence for coronary aneurysms, in whom to test the efficacy of adjunctive primary corticosteroid therapy. In this population, the addition of an extended course of corticosteroids to conventional therapy with IVIG and aspirin lowered the rate of coronary aneurysms, fever duration, and inflammatory markers. These results highlight the importance of aggressively targeting the patients with highest-risk KD for adjunctive therapies early after disease onset and of providing sustained anti-inflammatory treatment over the ensuing weeks. Japanese scoring systems for IVIG resistance and aneurysms have low sensitivity in North American populations. Future studies should refine methods for early identification of non-Japanese children at highest risk, as well as evaluate the utility of the RAISE regimen for rescue therapy of patients who fail initial IVIG.

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A computerized self-help intervention is as effective as face-to-face counseling for adolescents seeking help for depression

Merry SN, Stasiak K, Shepherd M, Frampton C, Fleming T, Lucassen MF. The effectiveness of SPARX, a computerised self help intervention for adolescents seeking help for depression: randomised controlled non-inferiority trial. *BMJ* 2012;344:e2598-606.

Question Among adolescents with depression, does a computerized cognitive behavioral therapy intervention reduce depressive symptoms as much as or more than usual treatment?

Design Multicenter, randomized controlled, noninferiority trial.

Setting 24 primary care health centers in New Zealand.

Participants Of the 213 adolescents assessed for eligibility, 187 were randomized, 170 were assessed after intervention, and 168 were assessed at the three-month follow-up.

Intervention 7 computerized modules of cognitive behavioral therapy (SPARX) were completed between 4 and 7 weeks. Usual treatment utilized face-to-face counseling.

Outcomes The primary outcome was score change in children's depression rating scale-revised. Secondary outcomes

were the Reynolds adolescent depression scale-second edition, the mood and feelings questionnaire, the pediatric quality of life enjoyment and satisfaction questionnaire, the Spence children's anxiety scale, the Kazdin hopelessness scale for children, change in clinical global impression scale, and participant satisfaction with intervention.

Main Results Participants who underwent the SPARX treatment had a nonsignificantly greater reduction in children's depression rating scale-revised compared with the treatment as usual group for both per protocol (2.73, CI -0.31 to 5.77) and intention to treat analyses (1.60, CI -1.21 to 4.41). All secondary measures demonstrated either noninferiority or an advantage of SPARX. Remission rates were higher in the SPARX compared with treatment as usual group (17.3% difference, CI 1.6% to 31.8%), but rates of response were not different between the groups (difference 7.9%, CI -7.9% to 24%). Of the 22 total adverse events that were possibly or probably related to the intervention, 11 were in the SPARX group and 11 were in the treatment as usual group. Benefits were maintained at three months after completion of the program and results were not related to sex, age, ethnicity, or setting.

Conclusions A computerized cognitive behavioral therapy program was as effective as treatment as usual for help seeking adolescents with depression, significantly reducing symptoms of depression, anxiety, and hopelessness while increasing quality of life.

Commentary Depression is a significant and common problem in adolescents, with a cumulative incidence of 15-20%.[1] Although cognitive behavioral therapy is an effective treatment with mild to moderate major depressive disorder, only 20% of adolescents are very willing to utilize mental health services.[2] The study by Merry et al represents an important effort towards increasing access to mental health services in this population because it demonstrates that a computerized cognitive behavioral therapy program can be as effective as face-to-face therapy in the primary care setting. The results of this study should be fairly generalizable because there were minimal exclusion criteria, the participants were accessing services, and the sites were primary care and community environments. In addition, there were good retention rates and low refusal rates. One limitation of the study was that there was no placebo group, although a previous study from the same group demonstrated superiority of computer-based therapy over waitlist.[3] Other limitations include the reliance on self-report for adherence data and the fact that the study was underpowered to detect superiority of intervention or subgroup differences. It is interesting that more people receiving treatment as usual would recommend that to their friends compared with those who used SPARX. Likely this was due to the fact that the face-to-face experience with treatment as usual counseling provided a therapeutic relationship that could not be reproduced in a computerized environment; this is reflected by the fact that those who underwent treatment as usual cited the fact that someone was there to support them and someone listened to them as favorable features of the program. Likely, a multimodal solution with both in-person as well as computerized components would be the most amenable to the greatest number of patients; one model could be starting the therapeutic relationship in person and then having follow-up online. Advantages of the online services include increased access and cost savings. Overall, SPARX represents an important effort to provide relief to adolescents with depression who have difficulty accessing appropriate mental health services.

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2. Chandra A, Minkovitz CS. Stigma starts early: gender differences in teen willingness to use mental health services. J Adolesc Health 2006;38:754.e1-e8.
3. Fleming T, Dixon R, Frampton C, Merry S. A Pragmatic Randomized Controlled Trial of Computerized CBT (SPARX) for Symptoms of depression among adolescents excluded from mainstream education. Behav Cogn Psychother 2011 Dec 5;1-13.

Whole-body hypothermia for neonatal hypoxic–ischemic encephalopathy reduces mortality into childhood

Shankaran S, Pappas A, McDonald SA, Vohr BR, Hintz SR, Yolton K, et al. Childhood outcomes after hypothermia for neonatal encephalopathy. *N Engl J Med* 2012;366:2085-92.

Question Among infants with neonatal hypoxic–ischemic encephalopathy (HIE), does whole-body hypothermia reduce the rates of death, cognitive impairment, or neurologic disability at 6 to 7 years of age?

Design Randomized, multicenter trial.

Setting Participating sites of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Neonatal Research Network.

Participants 208 trial participants, of whom primary outcome data were available for 190.

Intervention In the original trial, infants with moderate or severe encephalopathy were assigned to usual care (the control group, n = 93) or whole-body cooling to an esophageal temperature of 33.5°C for 72 hours, followed by slow rewarming (the hypothermia group, n = 97).

Outcomes Primary outcome was death or an IQ score below 70 at 6 to 7 years of age. The authors also evaluated cognitive,