Collaboration Key to Treating With Propranolol

BY DIANA MAHONEY

BOSTON — Establishing a treatment protocol and seeking the collaboration of cardiologists who treat children may limit the potential for serious complications associated with the off-label use of propranolol for the treatment of severe infantile hemangiomas, according to Dr. Elaine C. Siegfried.

In her own practice, Dr. Siegfried, professor of pediatrics and dermatology at St. Louis University, has developed such a protocol. However, she said she continues to use first-line prednisolone for infants with severe hemangiomas.

Prednisolone “really is the path of least resistance, and it’s the treatment we know the most about,” said Dr. Siegfried.

“For children who don’t respond to the prednisolone or who cannot tolerate it, I consider propranolol,” she said.

Interest in the treatment rose after a report of serendipitous improvement of severe hemangiomas in two infants treated with propranolol for cardiac arrhythmias and hypertension as well as good responses in nine infants who were subsequently treated with propranolol alone.

“The report was the most exciting news in pediatric dermatology in the past year,” she said.

Interest in propranolol’s potential risks as well as best practices for initiating and monitoring the therapy for this unapproved indication, Dr. Siegfried said at the American Academy of Dermatology’s Academy 2009 meeting.

Before using propranolol for severe infantile hemangiomas, pediatricians and sub specialties who know the most about the drug and come up with a consensus approach to using it, she recommended.

The treatment protocol developed by Dr. Siegfried and her colleagues includes obtaining a baseline pulse, respiration rates, blood pressure measurement, and echocardiography and 48-hour monitoring (inpatient or outpatient with home nursing visits) of vital signs and blood glucose levels. An initial propranolol dose of 0.16 mg/kg of body weight is given every 8 hours and doubled incrementally to a maximum of 0.67 mg/kg (a maximum daily dose of 2 mg/kg), as long as vital signs and glucose levels remain normal, she said, noting that the drug is gradually tapered over a 2-week period.

Because of its potential for hypotensive, hypothermic, and bradycardic side effects, the protocol includes hydrotherapy and bradycardia— known side effects of propranolol—and subclinical hypoglycemia, according to Dr. Siegfried.

She and her associates noted their concerns about complications and protocols in a letter written in response to the original publication (N. Engl. J. Med. 200.3:2846-7).

Parents need to be carefully trained regarding administration of the drug. The formulation is highly concentrated, and children need to be fed frequently to prevent hypoglycemia, Dr. Siegfried said.

“Sustained hypoglycemia has been associated with long-term neurodevelopmental outcomes.” Further, the clinical features of complications such as tachycardia, jitteriness, and hypotension can be blunted by the skin and coat.

Complication risks could be high in infants with large hemangiomas and in those with miliary hemangiomas, which put them at risk for high-outcome cardiac compromise. Infants with PHACES syndrome have arterial abnormalities that put them at risk for hypoperfusion and ischemic skin. There have been no reports of propranolol complications in infants with PHACES, “but it’s something you have to watch,” she said.

Close monitoring is critical in high-risk subsets of patients with hemangiomas, for example, “you want to look very closely at the hepatic artery and portal vein (via abdominal ultrasound) because dilatation can be an early sign of cardiac compromise.” In infants with large facial or extensive skin exposure to trinitin may enhance the risk of hypoglycemia. While LBBB and LAH tight are a definite stimulator, this effect has been more pronounced in infants with severe liver disease, low birth weight, or infants with complex congenital heart disease. Increased blood levels of propranolol and digitalization were not significantly different in patients with severe liver disease in the prospective study compared to those with greater than 1 mm Hg systolic blood pressure (SBP) and 95% or greater than 10 mm Hg diastolic blood pressure (DBP) in the retrospective review. The mean (± standard deviation [SD]) age of 25 patients with severe liver disease who died within the study was 3.6 months (±3.3) versus 6.8 months (±4.6) in the 23 patients who survived.

The mean (±SD) SBP and DBP in patients with severe liver disease at the age of 25 who died within the study was 73 (±10) mm Hg and 46 (±11) mm Hg versus 75 (±11) mm Hg and 53 (±11) mm Hg in the 23 patients who survived.

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