Is cardiovascular evaluation necessary prior to and during beta-blocker therapy for infantile hemangiomas?

A cohort study

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Background: Although consensus guidelines for pretreatment evaluation and monitoring of propranolol therapy in patients with infantile hemangiomas (IH) have been formulated, little is known about the cardiovascular side effects.

Objectives: We sought to analyze cardiovascular evaluations in patients with IH at baseline and during treatment with an oral beta-blocker.

Methods: Data from 109 patients with IH were retrospectively analyzed. Patient and family history, pretreatment electrocardiogram (ECG), heart rate, and blood pressure were evaluated before initiation of beta-blocker therapy. Blood pressure and standardized questionnaires addressing side effects were evaluated during treatment.

Results: Questionnaire analyses (n = 83) identified 3 cases with a family history of cardiovascular disease in first-degree relatives. ECG findings were normal in each case and no serious complication of therapy occurred. ECG abnormalities were found in 6.5% of patients but there were no contraindications to beta-blocker therapy and no major complications. Hypotension in 9 patients did not require therapy adjustment. In all, 88 parents (81%) reported side effects during beta-blocker treatment.

Limitations: The relatively small patient cohort is a limitation.

Conclusion: Pretreatment ECG is of limited value for patients with an unremarkable cardiovascular history and a normal heart rate and blood pressure. Hypotension may occur during treatment. (J Am Acad Dermatol 2015;72:465-72.)

Key words: beta-blocker therapy; cardiovascular side effects; infantile hemangioma; treatment evaluation.

Infantile hemangiomas (IH) are common with a 9.9% prevalence in the Dutch population.[1] In 2008, Léauté-Labrèze et al[2] reported a remarkable response to treatment with the nonselective beta-blocker propranolol. As we encountered adverse effects such as hypoglycemia and bronchial hyperreactivity in several patients with IH treated with propranolol,[3] atenolol (a hydrophilic selective beta-1-receptor blocker) has become our primary treatment choice.[4,5]

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Consensus guidelines for pretreatment evaluation and monitoring of propranolol therapy in infants with IH were formulated recently.[6] These include a pretreatment electrocardiogram (ECG) if the heart rate (HR) is below normal, if arrhythmia is detected on cardiac examination, or if there is a family history of arrhythmias or maternal connective tissue disease. Repeated cardiovascular monitoring is not advocated, unless the dose of propranolol is altered, in patients without comorbidity showing normal vital signs during the first hours after therapy initiation; this corresponds with the peak effect of oral propranolol on HR and blood pressure (BP) 1 to 3 hours after administration.

Despite these recommendations, the value and necessity of pretreatment screening examinations and monitoring remain unclear. This prompted us to acquire cardiovascular data from all our patients with IH treated with beta-blockers (Fig 1) with the aim of providing evidence-based data for future treatment recommendations.

CAPSULE SUMMARY

- Although consensus guidelines for propranolol treatment of infantile hemangioma were recently formulated, data on cardiovascular monitoring are lacking.
- Our study found pretreatment electrocardiogram screening to be of no additional value in the vast majority of patients with infantile hemangioma. Late dose-response effects of beta-blocker therapy on blood pressure were observed, although this hypotension was asymptomatic.
- A medical history and physical examination are the cornerstone for safe initiation and monitoring of beta-blocker treatment in infantile hemangioma. Electrocardiogram (and ongoing blood pressure monitoring) can be reserved for a small group of patients potentially at risk.

METHODS

Patients

All consecutive patients treated with propranolol or atenolol for IH at the Center for Congenital Vascular Anomalies of the Children's Hospital Utrecht, between July 2008 and August 2012, were included in the study. Parents received written information about the possible effects and side effects of oral beta-blockers and gave their consent before starting treatment. All data were retrospectively and anonymously analyzed from questionnaires and medical records. Approval by the institutional ethics committee was obtained (protocol nr 12-501).

Patients were treated as outpatients and only hospitalized when indicated (eg, age <1 month, increased risk of side effects, or pain caused by ulceration; see protocol) (Fig 1). The indication for initiation of therapy was noted. The starting dose of propranolol was 1 mg/kg/d (in 2 divided doses) and was increased to 2 mg/kg/d after at least 5 doses. During treatment, the dose was adjusted for weight gain. If the clinical response was inadequate, the dose of propranolol was increased stepwise to a maximum of 4 mg/kg/d. The starting dose of atenolol was 0.5 mg/kg/d (once daily). After 1 week of treatment, the dose was increased to 1 mg/kg/d and adjusted for weight during treatment. If clinical response was inadequate, the dose of atenolol was gradually increased to a maximum of 3 mg/kg/d.

Patient history

Patients were screened for contraindications to treatment during their first outpatient visit. Parents were asked about their child's development, existence of comorbidities, and family history of cardiovascular disease. We conducted an extensive parental survey for each patient emphasizing potential risks for beta-blocker use (available as online supplement). The questionnaire inquired whether the patient had a heart condition or if the child had ever experienced loss of consciousness. A history of relatives with congenital heart disease, cardiac arrhythmias, heart disease before the age of 60 years, or death from unknown cause before the age of 40 years was also documented.

Electrocardiogram

A pretreatment ECG was performed and examined by a pediatric cardiologist to detect bradycardia and/or any pre-existing cardiac conduction disturbance. Bradycardia was defined as HR below normal for gender and age.[7] If abnormalities were detected, the infant was clinically evaluated by a pediatric cardiologist, including cardiac ultrasound if indicated, to ensure that beta-blocker therapy could be safely initiated.

Blood pressure

BP measurements were carried out by experienced hospital staff members using a Dinamap (GE Healthcare, Waukesha, WI) with an age-sized cuff. BP was monitored at baseline and at 2