Scoring the therapeutic effects of oral propranolol for infantile hemangioma: A prospective study comparing the Hemangioma Activity Score (HAS) with the Hemangioma Severity Scale (HSS)

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Background: Validated and reliable instruments to measure disease severity are needed to substantiate the benefit of therapies for infantile hemangioma. Two purpose-made systems have been described: the Hemangioma Activity Score (HAS) and the Hemangioma Severity Scale (HSS).

Objective: We sought to compare the HAS with the HSS in terms of ease of use, accuracy, and outcome in infants treated with oral propranolol.

Methods: A prospective study of 54 infants with infantile hemangioma was conducted from October 2009 to December 2012. Propranolol was initiated at 0.5 mg/kg/d and increased to 2 mg/kg/d on day 3. The HAS and the HSS were applied independently by 2 observers.

Results: Intraclass correlation coefficients of the HAS and HSS between the observers was comparable but HSS scores often remained the same upon improvement of the infantile hemangioma and therefore did not reflect disease severity. HAS decreased over time, with a dramatic drop in the first week reflecting an immediate therapeutic response.

Limitations: This is a single-institution study and there may have been some selection bias in the patients who were referred for treatment.

Conclusions: This study suggests that the HAS is preferable to the HSS in evaluating infantile hemangioma response to treatment. (J Am Acad Dermatol 2015;73:258-63.)

Key words: disease severity scale; Hemangioma Activity Score; Hemangioma Severity Scale; infantile hemangioma; scoring system.

Validated and reliable instruments are needed to measure disease severity given the increasing number of studies of propranolol treatment for infantile hemangioma. Two systems have been described. The Hemangioma Activity Score (HAS), developed by our group, is based mainly on the color of the infantile hemangioma,[1] which changes from bright red in the proliferative phase to red/purple/blue and a grayish discoloration in the involution phase. Swelling and

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ulceration are also assessed (Fig 1). The HAS is used prospectively (on patients) and retrospectively (on photographs). It is objective with only 1 subjective measurement: estimation of whether the swelling of a deep infantile hemangioma has shrunk by more or less than half. Haggstrom and colleagues[2] developed another scoring system, the Hemangioma Severity Scale (HSS), which measures the overall severity of an infantile hemangioma, using both objective (size, location, risk for associated structural anomalies, and complications) and subjective (pain and risk of disfigurement) items. This system is less valuable when used retrospectively on photographs.

We compared ease of use, accuracy, and outcomes of the HAS and the HSS in patients treated with propranolol and evaluated the treatment outcomes.

CAPSULE SUMMARY

- Two systems are available to measure infantile hemangioma severity: the Hemangioma Activity Score and the Hemangioma Severity Scale.
- The Hemangioma Activity Score is faster to apply, detects minor changes with treatment, and can be used on photographs and patients.
- We recommend the Hemangioma Activity Score for evaluating therapies for infantile hemangioma.

METHODS

This was a prospective study in our first cohort of patients with infantile hemangioma treated with oral propranolol from October 2009 to December 2012. All patients were evaluated until April 2013. This study is part of the "Aardbeesie" (strawberry) project addressing the pathogenesis and therapy of infantile hemangioma, and was approved by the medical ethics review board of the Erasmus Medical Center and conducted according to the Declaration of Helsinki principles. Parents gave informed consent for off-label use of oral propranolol in the treatment of infantile hemangioma.

All cases of infantile hemangioma requiring treatment with oral propranolol were reviewed. Indications for therapy were mainly functional impairment or ulceration. Exclusion criteria were: previous systemic or intralesional therapy, internal hemangioma only, and propranolol therapy initiated elsewhere. Patients for whom propranolol was contraindicated and cases of PHACE syndrome (posterior fossa malformation, hemangioma, arterial cerebral anomalies, coarctation of the aorta and other cardiac defects, eye abnormalities[3]) were also excluded.

Because propranolol therapy for infantile hemangioma was novel at the time, we followed a cautious protocol. Therapy was started after physical examination by a pediatrician, blood pressure measurements, blood glucose, electrocardiogram and, if necessary, consultation with a pediatric cardiologist. All patients were hospitalized to start therapy. At day 1, propranolol 0.5 mg/kg/d was given in 3 divided doses; at day 2, the dose was increased to 1 mg/kg/d, and at day 3 to 2 mg/kg/d. At day 4, patients were discharged if dailyelectrocardiogram, blood pressure, and blood glucose measurements were satisfactory. Patients were followed up at 2 weeks, 6 to 8 weeks, 12 weeks, 0.5 year, 1 year, 1.5 years, 2 years, and 2.5 to 3 years after baseline. Propranolol was tapered and discontinued after approximately 1 year.

Photographs were taken at all visits and were independently assessed using the HAS and HSS by 2 observers (S. R. J. and A. P. O.). Scoring of the HAS[1] and the HSS[2] is described elsewhere. Global scores of both physician and parents were recorded (1 = very good result, 2 = good result, 3 = stable, 4 = deterioration).

Baseline characteristics are reported by descriptive statistics. To show the effectiveness of propranolol we used scatterplots of mean HAS and mean HSS over time and fitted these with local regression lines. A sophisticated longitudinal statistical model is not necessary for this relatively simple question. No patients were lost to follow-up. We used intraclass correlation coefficients per visit interval to determine interobserver agreement for the HAS and the HSS. Finally, to assess differences in different types of infantile hemangiomas (superficial, deep, or mixed), we made separate scatterplots.

RESULTS

Patient characteristics are summarized in Table I.

Fig 2 shows the evolution of the mean HAS and mean HSS scores of the 2 observers, respectively, with regard to time from baseline. The HAS clearly show a decreasing trend with a dramatic decrease after initiation of treatment. This pattern is less pronounced for the HSS scores. Fig 3 shows the global scores of physician and parents, respectively. After initiation of treatment a good result is shown, which gradually changes to "stable" over time.

Mean intraclass correlation coefficients of the HAS and the HSS per time interval were comparable