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ORIGINAL ARTICLE

Treatment With Propranolol for Infantile Hemangioma in 13 Taiwanese Newborns and Young Infants

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Key Words
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Background: Hemangioma in infants has a benign self-limited course, but the 10% of cases with complications need further treatment. Successful treatment with propranolol in western countries has been reported over the past few years. We evaluated the efficacy of propranolol for treating infantile hemangioma in Taiwanese newborns and young infants.
Methods: Patients below 1 year of age treated with propanolol between November 2009 and March 2011 were enrolled. Demographic data, clinical features, imaging findings, treatment regimens of propranolol, and outcome were investigated.
Results: Thirteen patients were treated with propranolol at a dose of 2—3 mg/kg/day. Seven (53.8%) patients had solitary hemangioma and six had multiple ones. The indications for treatment were risk of local event in nine patients, functional risk in four, local complication in one, and life-threatening complication in one. The median age for starting propranolol was 4 months (range: 1—11 months). Responses to propranolol, such as decolorization, regression in tumor size, or improvement of hemangioma-associated complications were observed in all patients within 1—2 weeks after treatment. Propranolol-associated adverse effects occurred in two patients. One infant had occasional tachypnea, and the other had occasional pale-looking appearance. The symptoms resolved after dosage tapering.

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Conclusion: Propranolol may be a promising therapeutic modality for infantile hemangioma. Therapeutic strategies are needed to evaluate the optimal treatment protocol and long-term adverse effects.

1. Introduction

Infantile hemangioma (IH) is the most common benign vascular tumor of infancy, and its onset usually begins during the neonatal period. The incidence is estimated at 4–5%[1] and is higher in girls and premature infants.[2] IH classically manifests as a rapid proliferation phase in the first year after birth, followed by a spontaneous involution phase that lasts for several years.[3] It usually has a self-limited course with minimal sequelae, and the mainstay of therapy is conservative observation. However, even transient cosmetic disfigurement during the long involution phase frequently induces psychological stress in the affected children and their parents.[4] Moreover, approximately 10% of IH cases need further intervention due to local or life-threatening complications.[5,6] Some IH can cause local complications such as ulceration, pain, bleeding, scarring, secondary infection, and permanent disfigurement. Others may cause significant functional impairment, vital organ compromise, or life-threatening complications. For these complicated IH cases, systemic corticosteroids are generally considered to be the first-line of pharmacological therapy. Although there is a 78–89% response rate,[7] a high recurrence rate of up to 36% and adverse effects limit its use.[8] Alternative therapeutic options, such as vincristine,[9] interferon α,[6] and cyclophosphamide,[10] are used for steroid-refractory and critical patients, but their potential toxicities are a major concern.

The dramatic response to propranolol in the treatment of IH was first described by Léauté-Labrèze et al[11] in 2008, and a number of successful cases have been reported worldwide.[12] To the best of our knowledge, the efficacy of propranolol in Taiwanese hemangioma patients has not been evaluated. We investigated the therapeutic effect of propranolol in 13 Taiwanese newborns and young infants with IH at a tertiary pediatric medical center.

2. Patients and Methods

In this retrospective observational study, we reviewed data from Taiwanese patients, aged <1 year, diagnosed with IH and treated with propranolol between November 2009 and March 2011. Demographic data, clinical features, results of imaging for IH, propranolol dosage, treatment outcome, and complications were collected from medical charts.

Before initiation of propranolol treatment, comprehensive history taking, vital signs, and physical examinations were performed in all patients to confirm that there was no associated medical history or contraindications for propranolol, such as past cardiopulmonary disease, hyperactive airway disease, asthma, sinus bradycardia, secondary or third-degree heart block, cardiogenic shock, and allergy to propranolol. Treatment regimens and potential adverse effects of propranolol were explained to the families of the patients. Informed consent for propranolol treatment and use of the patients' photographs was obtained from their parents.

The patients were first treated with 0.5–1 mg/kg/day propranolol divided into two or three doses, and weekly follow-up at the outpatient clinic was arranged. At each clinic visit, baseline heart rate was recorded and the dosage of propranolol was doubled to a maximum of 2–3 mg/kg/day as tolerated. Parental education included: (1) observation for tachypnea, wheezing, symptoms and signs of hypoglycemia, and signs of poor perfusion; (2) advice on taking the drugs with or after a meal to avoid hypoglycemia; (3) monitoring of heart rate and withholding drugs in the event of bradycardia, defined as a heart rate <100 beats/minute,[13] and signs of poor perfusion; (4) withholding drugs temporarily with acute illness; and (5) making a note of any possible propranolol-associated discomfort. During the stable course of treatment, monthly outpatient clinic follow-up was arranged. When IH had regressed and flattened sufficiently, propranolol was gradually tapered over 1 month by halving the dosage each week.

3. Results

Thirteen patients treated with 2–3 mg/kg/day propranolol were identified between November 2009 and March 2011. The demographic data, clinical features, imaging findings, and treatment outcomes of these patients are summarized in Table 1. There was a predominance of female (10/13, 76.9%) and premature (7/13, 53.8%) infants among the patients. Seven patients (53.8%) had solitary hemangioma, whereas the other six had multiple ones. The onset of IH in 12 patients (92.3%) occurred in the neonatal period. These hemangiomas were located on the trunk (6/13, 46.2%), extremity (4/13, 30.8%), face (3/13, 23.1%), scalp (3/13, 23.1%), liver (2/13, 15.4%), retro-orbital, intracranial area and ethmoid sinus (1/13, 7.7%), neck (1/13, 7.7%), hard palate (1/13, 7.7%), and external auditory meatus (1/13, 7.7%). No patients had thrombocytopenia, consumptive coagulopathy or Kasabach–Merritt syndrome.

The indications for treatment in our patients were divided into four categories: (1) risk of local complication, defined as high risk of local complication due to frequent friction or scratching, in nine patients (69.2%, Figure 1A, 1B and 1E); (2) functional risk, defined as impairment of vision, hearing, feeding, or motility caused by IH, in four patients (30.8%, Figure 1C–1E); (3) local complication in one patient (7.7%, painful ulceration and secondary infection with *Pseudomonas aeruginosa* of hemangioma over the left