

Research Article

Propranolol for infantile hemangiomas: Our preliminary experience

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Abstract

Objective: Propranolol has recently been introduced as a novel pharmacologic treatment for infantile hemangiomas. This study explores the impact of propranolol on infantile hemangiomas.

Study Design: Prospective study

Materials and Methods: Propranolol was given to 38 children (21 girls and 17 boys) propranolol was administered with a dose of 2mg/kg per day, given in 2 or 3 divided doses. Children between ages 3 weeks to 12 weeks included in study. Oral propranolol given between February 2013 to January 2014. Serial photographs taken at 6-8 weeks interval during the course of their therapy to record clinical response.

Results: thirty eight children with complete photo documentation were treated with oral propranolol for infantile hemangiomas between February 2013 to January 2014. Out of 38 patient 36 patients showed improvement in their hemangiomas by effects on color and rapid/progressive reduction in size during propranolol therapy. Lesions were determined as complete resolution (n -3, 7.5%), ongoing resolution (n -33, 86.8%), or no sign of resolution ie no response (n - 2, 5%). No serious side effects of propranolol were observed in any patients.

Conclusion: Propranolol may revolutionize the treatment of hemangiomas. At therapeutic doses (2mg/kg/day), propranolol is safe and effective in the treatment of infantile haemangiomas.

Keywords: Propranolol, hemangioma, beta-blocker.

1. Introduction

Hemangiomas of infancy (HOI) are common, benign, self-limited tumors, but a significant percent of these lesions are associated with substantial morbidity in infancy and childhood^{1,2} Tumors that often require treatment include those involving the periorbital area, central face, airway, skin folds, and anogenital area, these sites are high risk for ulceration, dysfunction, or disfigurement.³ Current treatment options for problematic hemangiomas include systemic or intralesional corticosteroids, chemotherapeutic agents (vincristine, alpha-interferon), laser, surgery or a combination of these therapies^{4,5,6} Unfortunately, each treatment option has limited therapeutic benefit with its own side-effect profile and risks.

Propranolol is a known nonselective beta-blocker used in treating infants with cardiac and pulmonary conditions^{7,8,9,10}. Few cases have been reported the finding that hemangiomas regress rapidly when infantile haemangioma treated with propranolol¹¹.

In this study, we have explored the impact of propranolol on infantile hemangiomas at our centers.

2. Materials and Methods

This is a prospective study. An approval from local ethical committee was obtained before starting of study. In all cases, informed consent was obtained from both parents. Total 38 patients from 3 weeks to 12 months with 21 girls and 17 boys were included in this study. The study period was between February 2013 to January 2014. Detail clinical examination included site and size of lesion. Histories of previous treatment with beta blocker with any contraindication for propranolol (e.g. bronchial asthma, hypoglycemia, reflux etc) were recorded, and such children were excluded from the study. An oral dose of 2mg/kg/day divided 2 to 3 times was given to each child as determined safe and potentially effective by Leaute-Labreze and colleagues¹². To record the response of propranolol serial clinical photos were taken at the starting of treatment with propranolol then every 6-8 weeks interval. Doses were adjusted as the child grows by taking regular body weight of the child. Propranolol was weaned at the end of treatment, by reducing the dose by one half for 1 to 2 weeks, then stopping¹³. Hemangioma lesions were rated as complete resolution, ongoing resolution, or no sign of resolution depending on the response of lesion to haemangioma treatment.

3. Results

Over a 12 months period, 38 cases (21 females and 17 male) with infantile hemangiomas were started on oral propranolol. Patients in the both the proliferative (n - 19) and involuting (n - 19) stages of hemangioma growth were treated at a mean age of 5.4 and 37.2 months, respectively

Two babies had received oral prednisolone in the first and second month of life, followed by intralesional steroid injections, but without any obvious clinical improvement were also included in the study and started on propranolol treatment.

36 patient (94.73%), treated with propranolol displayed some improvement of their lesions in the form of shrinkage in size, softening in consistency, and decrease in redness.

3. Discussion

Currently, systemic or intralesional steroids are the mainstay of treatment for complicated IHs, which has been well documented in literature^{14,15,16}. Whilst steroids were effective, but the children were liable to complications, including: gastric upset, Cushing's syndrome, and growth retardation¹⁷. For periorbital lesions, intralesional steroid (triamcinolone acetonide, 10-40 mg/mL) injection was given, but could cause central retinal artery occlusion and even eyelid necrosis^{18,19}. Since the introduction of propranolol as a treatment it becomes a good option for problematic hemangiomas, our center offered this therapy to help manage over 38 children with these lesions in various stages of growth.

Within hours of starting therapy, propranolol produces vasoconstriction, resulting in a reduction in the color of the hemangioma. Its primary effect, however, appears to be alteration in the progression of angiogenesis in the hemangioma. Regulation of hemangioma growth involves basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF). Léauté-Labrèze and colleagues theorized that propranolol may decrease expression of bFGF and VEGF. Based on examination of hemangioma tissue, Truong and coworkers have also speculated that beta-adrenergic antagonists may ablate catecholamine receptor signaling, decreasing cyclic AMP and reducing levels of VEGF. In addition, propranolol may promote involution of hemangiomas by triggering apoptosis in endothelial cells.^{20,21}

Treatment with oral propranolol has been well tolerated in most of the cases of infantile hemangioma published to date. The primary adverse effects reported with propranolol use in infants have been somnolence, hypotension, bradycardia, bronchospasm, and hypoglycemia.²² These reactions typically respond to dose reduction and may not require discontinuation of therapy.

Side effects, in our study occur in three patients gastroesophageal reflux (n = 1), allergic rash (n = 1), asymptomatic hypotension (n=1) was managed with propranolol dose adjustments.

In a follow-up letter to the initial publication by Léauté-Labrèze and colleagues, Siegfried, Keenan, and Al-Juraidini first described a treatment protocol for oral propranolol in infants with hemangiomas²³. Therapy is typically initiated with a propranolol dose of 0.5-1 mg/kg/day (divided and given orally three times daily). If tolerated, the dose may be increased to 2-3 mg/kg/day. Treatment is typically continued for 6-12 months, with doses adjusted for weight gain on a monthly basis. At the conclusion of treatment, propranolol should be tapered off, with a 50% reduction in dose for 1-2 weeks prior to discontinuation. At this time, there are no recommendations to guide parenteral propranolol dosing for infants with hemangiomas.

4. Conclusion

Based on the successful results of our study and numerous case series, Propranolol appears to be a valuable and effective treatment option for infantile hemangiomas. It has a tolerable side-effect profile, and there have been no serious side effects reported in appropriately screened patients. Although more comparative, randomized studies with a greater number of patients are needed to confirm the safety and efficacy of the drug.

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