Oral Propranolol for Treatment of Pediatric Capillary Hemangiomas

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Purpose: To report the long-term results of treatment of pediatric capillary hemangiomas with oral propranolol.

Methods: Three infants, 3 to 4 months of age, with periocular capillary hemangiomas were treated with oral propranolol solution (Inderal, 20mg/5ml) 2-3 mg/kg per day divided in 2 doses. Propranolol was continued up to the end of the first year of life and tapered over 2-3 weeks. All infants were followed for 20 months. Lesion size and evolution were assessed during the follow-up period.

Results: Significant improvement was noted in all patients in the first 2 months of therapy with slow and continuous effect throughout the follow-up period. No serious complications were observed.

Conclusion: Oral propranolol can be used as a first line agent in children with capillary hemangiomas.

Keywords: Oral Propranolol; Capillary Hemangioma

INTRODUCTION

Capillary hemangiomas account for 8-10% of benign pediatric tumors. Treatment is necessary when ulceration, facial disfigurement and risk of amblyopia is present. Corticosteroids, in various forms are the mainstay of treatment. Local injection of corticosteroids is the most common route of administration; however it is associated with serious adverse effects such as occlusion of the ophthalmic artery or central retinal vein, retinal embolization, adrenal suppression and hypopigmentation at the site of injection. Topical application of corticosteroids has been used for superficial lesions only. Unfortunately, well-designed studies that demonstrate the efficacy of corticosteroids are scarce and the response to this therapy, which can be accompanied by grave side-effects, is unpredictable. Other systemic drugs such as vincristine, alpha-interferon and cyclophosphamide may also entail significant adverse effects.

There are limited studies on the duration, long-term effects and complications of propranolol therapy for capillary hemangiomas and to the best of our knowledge, propranolol is a relatively safe drug for use in young patients. Herein, we report the long-term results of oral propranolol on congenital capillary hemangiomas in three patients.

METHODS

We describe three infants with congenital capillary hemangiomas who received treatment from the age of 3-4 months up to the end of the first year of life. The study was approved by the Ethics Committee of the Ophthalmic...
Research Center at Shahid Beheshti University of Medical Sciences. Informed consent was obtained from the patients’ guardians prior to the study. All patients were admitted and monitored for 3 days, and underwent a complete baseline ophthalmic examination. Laboratory studies including complete blood count, blood urea nitrogen (BUN), serum creatinine, blood sugar, sodium and potassium levels were performed at the beginning of the study. All cases underwent examination and baseline echocardiography by a pediatric cardiologist.

Treatment was initiated at a dose of 1mg/kg/day propranolol solution (Inderal 20mg/5ml) on the first day; if vital signs and blood sugar were stable the dose was doubled on the following day. The maintenance dose was 1-2mg/kg/day divided in two doses. Patients were fed 2 to 3 hours after administration of propranolol. They were followed twice a week for 2 months and then monthly for 20 months. If no further benefit was observed during follow-up, propranolol was tapered over 2-3 weeks. Cases 1 and 2 are described together due to similarity and case 3 is described separately.

RESULTS
Cases 1 and 2

Cases 1 and 2 were three and four-month-old female infants with upper lid hemangiomas causing complete ptosis and eyelid fissure closure (Fig. 1). Perinatal history was unremarkable

![Figure 1. Photographs of 3 patients with eyelid capillary hemangiomas before and after treatment with propranolol.](image-url)
and no systemic disorders were present. The hemangiomas were red lobulated lesions which faded slightly on diascopy. Examination of the orbits revealed no abnormality. Two weeks after treatment the lesions regressed by 30% and the patients were able to open their eyes. By the end of the second month, the lesions had been reduced to one-third of their original size.

Propranolol was continued in both children until one year of age after which it was discontinued gradually. In case #2, propranolol was discontinued by the parents for two weeks resulting in regrowth of the tumor. Propranolol was reinitiated and the lesion responded to treatment without any problem.

Case 3
This patient was a three-month-old female infant with a massive lesion on the left side of her face which included the eye and ear. Ulceration of the lesion had led to upper lid margin necrosis and ptosis with the risk of deprivation amblyopia. She was treated with oral propranolol and the lesion regressed to nearly half of its visible size over one month. After one year, propranolol was tapered over a period of 2-3 weeks (Fig. 1).

DISCUSSION
Capillary hemangiomas are common childhood tumors reaching their maximum growth in the first year of life. Complete spontaneous regression of the tumor occurs in 32-60% of patients by the age of four and in 72-76% by the age of seven years. Due to this long period for spontaneous resolution, there is a possibility of amblyopia due to axial myopia secondary to ptosis or astigmatism in which the positive axis lies parallel to the mass. Amblyopia occurs in 44-64% of cases due to anisometropia or visual deprivation. Additionally, massive hemangiomas alter skin structure by stretching or injury to the surface texture, and may cause disfigurement. Our patients were treated for one of these indications.

There are some reports on the dramatic effect of oral propranolol on the size and volume of vascular masses which was replicated in our patients as well. It is interesting that the first visible and measurable response to treatment was observed within 48 hours of initiating treatment in superficial cases. Lesion size decreased to half of its original size after 2 months. This rapid response, as compared to corticosteroid-based treatments, is especially valuable in terms of preventing amblyopia.

Beneficial effects of propranolol are probably due to reduction of the expression of genes for vascular endothelial growth factor, basic fibroblast growth factor and matrix metalloproteinase 9 in addition to induction of apoptosis in capillary endothelial cells. Bradycardia and hypotension are the most common side effects of propranolol. Propranolol induced hypoglycemia or the masking of its symptoms are particularly important in children; these may be easily diagnosed and treated by employing the precautions mentioned in our study and other reports. History of prematurity, age less than 3 months, comorbidities, and asthma are factors associated with a higher risk of side effects. Wheezing and hyperkalemia have also been reported.

During the follow-up period and after discontinuation of treatment we observed no complications, tumor regrowth, or general growth impairment in our cases. None of our patients developed anisometropia or obstruction of the visual axis. Compared to other published reports on treatment of capillary hemangiomas with propranolol, our cases had longer duration of follow-up.

Based on the good results and a low risk profile, we recommend propranolol as a safe and effective first line therapy for capillary hemangiomas in children. A randomized clinical trial could enrich the existing knowledge and improve the management of periocular and orbital hemangiomas. Further research should focus on management of older subjects with aesthetic issues.

Conflicts of Interest
None.
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