Combined Low-Dose Oral Propranolol and Oral Prednisolone as First-Line Treatment in Periocular Infantile Hemangiomas

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Abstract

Purpose: The purpose of this report was to describe 2 cases of periocular infantile hemangiomas (IHs) that were successfully treated with low-dose oral propranolol alone and in combination with oral prednisolone.

Methods: Two infants aged 3 months and 6 weeks, respectively, were referred for management of vision-threatening periocular IHs causing ocular displacement and obscuration of the visual axis. The first infant had a superficial left upper eyelid capillary hemangioma with extraconal extension and the second infant had a deep preseptal capillary hemangioma in the right lower eyelid with intraconal extension. Both cases were started on oral propranolol 0.5 mg/kg/day in divided doses and titrated up to 1.5 mg/kg/day as first-line therapy. The first infant was also given oral prednisolone 2 mg/kg/day during the initial first month of treatment.

Results: Rapid regression in sizes of the hemangiomas was seen within the first 3 days of treatment. By 2 months of therapy, both infants had achieved normal ocular alignment. The second infant experienced a transient period of hypotension after the first dose of propranolol was started but recovered spontaneously. Both infants did not experience any adverse effects of propranolol throughout the treatment period.

Conclusions: Low-dose oral propranolol is an effective first-line therapy for the management of vision-threatening IH. Dose escalation in combination with oral prednisolone after pediatric assessment might be useful in avoiding adverse effects of propranolol in young infants.

Introduction

Oral propranolol has recently emerged as the treatment of choice for periocular infantile hemangioma (IH). Our report describes 2 infants who were given oral propranolol as first-line therapy for vision-threatening periocular IH—one in combination with oral prednisolone and the other on oral propranolol only.

Case Reports

Case 1

A healthy 3-month-old boy who was born prematurely at 30 weeks presented with a rapidly enlarging left upper eyelid superficial IH obscuring the visual axis. He also had a left upper eyelid coloboma. The IH measured 2.5 × 3 cm and the left eye was proptosed and hypotropic (Fig. 1A). MRI of the orbits and brain revealed orbital extension of the IH into the extraconal space, causing proptosis of the left eye (Fig. 1B). However, there was no intracranial involvement.

After systemic evaluation by the pediatrician and pediatric cardiologist, the infant was started on oral prednisolone 2 mg/kg/day and oral propranolol 0.5 mg/kg/day BID. Close cardiac monitoring with serial blood pressure and finger-prick blood glucose was measured as an inpatient. From the second day onward, the dose of propranolol was titrated up by 0.5 mg/kg/day until a dose of 1.5 mg/kg/day was achieved. He was discharged on the third day with the dose of oral prednisolone reduced to 1 mg/kg/day. His blood pressure and glucose measurements were stable throughout admission.

The infant was seen again in the outpatient clinic at 2 weeks later and oral prednisolone was titrated down over a month while the oral propranolol was maintained at the same dosage since discharge despite the increase in body weight (Fig. 1C). Significant reduction in size and softening of the IH was noted at 3 days after initiation of therapy. Propranolol was maintained for 4 months without any adverse reactions and then tapered off over 1 month. At 1 year of age, the IH had almost completely regressed, leaving behind only superficial telangiectatic vessels.

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Case 2

A healthy 6-week-old girl presented with a progressively enlarging deep IH at the inferotemporal aspect of the right lower eyelid, causing proptosis and hypertropia of the right eye. The swelling measured 2·3 cm and threatened to cause strabismic amblyopia (Fig. 1D). MRI showed that the IH was mainly preseptal with an inferotemporal intraconal orbital extension causing upward displacement of the globe (Fig. 1E).

Following pediatric consult, she was commenced on oral propranolol 0.5 mg/kg/day TID as an inpatient, with close observation of blood pressure every half-hourly for 2 h and hourly monitoring of blood sugar. Within the first 2 h of treatment, her blood pressure had dropped by 20 mmHg systolic and 10 mmHg diastolic despite feeding. However, she remained alert and did not show signs of pallor or cold clammy skin. She recovered spontaneously with observation. On the second day, the dose was increased to 1 and 1.5 mg/kg/day on the third day. By the third day, the swelling was less tense, although the size remained unchanged. She was discharged home on oral propranolol 1.5 mg/kg/day TID.

At 3 weeks of treatment, the eyes had become orthophoric, and after 3 months on oral propranolol without any change in dosage since discharge, the palpebral apertures and lower lid creases were symmetrical bilaterally (Fig. 1F). The swelling had almost completely subsided with only redundant skin overlying it. The infant is still on propranolol at the time of writing of this article.

Discussion

The fortuitous discovery of oral propranolol as an effective treatment for infantile capillary hemangiomas by Léauté-Labréze et al. in 2008 has led to the widespread usage of propranolol in the treatment of these hemangiomas of infancy in all regions of the body. A few case series (Table 1) have reported this off-label usage of propranolol and its adverse reactions, but a treatment protocol has to be yet recommended for the treatment of periocular IH.

Initial case reports described the usage of propranolol as second-line therapy in the management of complicated IH, whereas latter series showed a trend toward using propranolol as first-line treatment. Some authors started oral

Table 1. Studies Using Oral Propranolol in the Treatment of Periocular Infantile Hemangiomas

<table>
<thead>
<tr>
<th>Reference no.</th>
<th>Authors</th>
<th>Subjects with periocular infantile hemangiomas</th>
<th>Subjects previously treated with corticosteroids</th>
<th>Final dose of propranolol (mg/kg/day)</th>
<th>Mean age at which treatment was started (months)</th>
<th>Mean duration of treatment (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Léauté-Labréze et al.</td>
<td>7</td>
<td>3</td>
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<td>3.4</td>
<td>6.4</td>
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<td>14</td>
<td>7</td>
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<td>3</td>
<td>Haider et al.</td>
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<tr>
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<td>Manunza et al.</td>
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<td>Mishra et al.</td>
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<tr>
<td>7</td>
<td>Li et al.</td>
<td>4</td>
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<td>2</td>
<td>10</td>
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propranolol at dosages of 2 mg/kg/day,\textsuperscript{3,4,7} whereas others have been more conservative by opting for an escalating dose of up to 2 mg/kg/day.\textsuperscript{3,4,7} One even titrated up to 3 mg/kg/day.\textsuperscript{9} Propranolol is a nonselective beta-blocker that has been in use for around 4 decades by cardiologists, endocrinologists, pediatricians, and psychiatrists. Its safety profile is well established when given to appropriate patients. The use of propranolol in pediatric patients covers both cardiac and noncardiac pathologies. The most common adverse events are bradycardia and hypotension.\textsuperscript{9} Bronchospasm can happen in patients with reactive airway diseases, whereas hypoglycemia\textsuperscript{10} is a known association in young children. The recent increase in interest in using propranolol as first-line treatment of IH needs to be accompanied with caution. Even though there has not been any reported mortality due to propranolol, occasional adverse events can happen and cause extreme anxiety to both the parents and the caregivers.

Initiation of propranolol therapy is a multidisciplinary approach and patients, especially neonates, would require close monitoring during the initiation period. Both our patients demonstrated excellent results for low-dose oral propranolol as first-line therapy in the treatment of periocular IH with and without skin surface involvement. This was achieved on an escalating dose of propranolol until a maximum of 1.5 mg/kg/day. Titration of the drug avoids the adverse events that had been reported in young children on propranolol.\textsuperscript{10} Even though our second patient was only given a single 0.17 mg/kg dose of propranolol, she developed a sudden drop in blood pressure. In contrast, our first patient remained stable throughout the therapy despite being given a first dose of 0.25 mg/kg.

The older age of the first infant and the concurrent usage of prednisolone could have played a protective role in the prevention of hypotension. Systemic corticosteroids have known side effects such as water retention, hypertension, and hyperglycemia, which could counter the adverse effects of propranolol. This was used as the basis of incorporating prednisolone into the treatment of the first patient after consultation with the pediatric cardiologist who was concerned of the hypotensive effect of propranolol. However, prolonged usage of corticosteroids could lead to hypoglycemia on cessation because of adrenal suppression. To avoid complications, corticosteroid usage in our first patient was kept to a short period and tapered off.

Conclusions

Oral propranolol 1.5 mg/kg/day is effective in inducing involution of IH. Concurrent systemic corticosteroid administration during the initiation period could be useful in preventing the adverse effects of propranolol. However, further studies are required to compare the adverse effects using propranolol alone and in conjunction with corticosteroids. The minimum effective dosage of oral propranolol in the treatment of periocular IH also needs to be studied.

Author Disclosure Statement

The authors have no financial interests to declare.

References


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AU2: Please define NA.