

Complicated Infantile Hemangioma Successfully Treated with Topical Timolol 0.5% Solution: A Case Report

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Abstract

Infantile hemangiomas (IHs) are common benign lesions involving most part of the body. It can regress spontaneously but these hemangiomas should be treated early on course of evolution to prevent further complications. Different treatment options are available for its management. Topical timolol 0.5% solution available as eye drops or gel can be used as first-line therapy even in complicated IH. We have successfully treated a large complicated facial IH by using topical timolol 0.5% solution.

Keywords: Complicated, infantile hemangioma, topical timolol

INTRODUCTION

Infantile hemangioma (IH) is one of the most prevalent benign vascular tumors of infancy and childhood. It affects about 4–6% of infants in the first year of life and more common in Whites than in Blacks. Hemangioma is often present at birth, although it may not be noticed until a few weeks later, when the lesion begins its proliferative phase. During initial 6 months, it grows rapidly and then stabilizes by 4 years of age.^[1-3] The majority of lesions are benign, regress spontaneously over a period of time, only a few lesions require active intervention, and it is closely associated with the disorder of angiogenesis and vasculogenesis. Cosmetic disfigurement, involvement of eye, and parental distress are major factors to initiate treatment. Topical corticosteroids have been used for so long but for these, propranolol, a non-selective beta-blocker, has emerged as an alternative systemic treatment to corticosteroids. Recently, the use of topical timolol maleate for IH was identified.^[4] Timolol maleate is a non-selective β -blocker readily available as an ophthalmic preparation as both a solution and gel-form. But there is scarcity of information for off-label use, safety, and pharmacokinetic data for management of hemangioma-affected skin.^[5] Many large studies also show that topical application of 0.5% timolol maleate eyedrops and hydrogel is safe and effective for superficial IH.^[1] We have successfully treated a child with aggressive complicated IH with application of only timolol 0.5% eye drop.

CASE HISTORY

A 3-month-old female child was referred to us with a large red facial lesion. According to mother, they noticed it soon after birth but was smaller in size and typically present over the right upper eyelid, right cheek, and right side of the forehead. Gradually, it progressed and involved entire right side of face and caused obstruction to the right eye [Figure 1]. On examination child was hemodynamically stable, thriving well on exclusive breast feeding and achieved age-appropriate milestones. There was no family history of similar lesions or history of seizures in child. On local examination, reddish erythematous-raised lesion was present over the right side of the face involving forehead, cheek, preauricular areas, periorbital region including upper and lower eyelids, and tip of nose. There was no bleeding or ulceration. The child was not able to open her right eye due to mass effect. Detailed systemic examination and ophthalmic evaluation do not reveal any other finding. The child was evaluated for other internal lesions and syndromic association. USG of orbit and internal organs including liver was performed, which did not show any abnormalities. We also performed MRI brain to see any vascular malformations but it was normal.

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PHACES syndrome was ruled out as there was no vascular lesion seen in MRI brain; cardiac evaluation was also done using 2D echocardiography which shows no abnormalities. A clinical diagnosis of complicated IH was made, and timolol 0.5% eye drop was prescribed to apply locally all over the lesions twice a day. Mother was advised to spread it all over the lesions with clean hands and to wash hands after application. She was also advised to be cautious while applying eye drops over the lesion as it may go into the eye. Parents visited OPD with baby after 3 days of therapy and she was hemodynamically stable without any side effects. They were advised to attend OPD fortnightly; after 3 months of therapy at 6 months of age, a significant reduction in lesion was observed without any evident adverse events [Figure 2]. There was almost complete disappearance of lesion observed at 10 months of age [Figure 3]. Child is on regular follow-up with us and there is no recurrence till date.

DISCUSSION

IHs are benign tumors and can regress spontaneously at around second year of life; intervention or treatment is not necessary in most of the cases. Complicated or large hemangiomas may require early initiation of treatment. Small hemangiomas causing obstruction, situated near eyes, nostril, or lip, large and bulky hemangiomas leading to disfigurement of face, and hemangiomas present near various openings with high chances of complication and causing high output cardiac failure should be treated. Various treatment options are available including surgical interventions and systemic and topical medications. For many years, surgical management was considered as standard of care, laser and cryosurgery were also used, but nowadays it is considered as therapeutic modality for hemangioma refractory to medical

therapy. Management of IH was dramatically changed after use of oral propranolol. Propranolol is a non-selective beta-blocker that suppresses growth of IH by inhibition of angiogenesis and vasoconstriction and inducing apoptosis.^[6] Various studies including meta-analysis show 95–98% efficacy of oral propranolol when used 2–3 mg/kg/day for a mean duration of 6 months.^[7] Very few side effects



Figure 2: At 6 months of age after initiation of topical timolol eye drops locally



Figure 1: At time of presentation, i.e. 3 months of age showing hemangioma completely covering the right eye with disfigurement of face



Figure 3: At 10 months of age showing almost complete resolution of hemangioma

such as sleep disturbance, irritability, and somnolence are observed but these are rare and reversible. Hypoglycemia and hypoglycemic seizures are two serious side effects when used in smaller infants. Oral corticosteroids (prednisolone) could be considered for complicated hemangiomas not responding to propranolol or those who have primary contraindications and who developed side effects during treatment. Sirolimus, an mTOR inhibitor, have potent anti-angiogenic activity in Kaposiform hemangioendothelioma but will require further studies and pharmacokinetic study to use in IHs. Considering its high efficacy and high safety profile, oral propranolol became first-line drug for the management of IH. Topical timolol available in market as 0.5% eye drops and gel is recently used as an alternative for oral propranolol. Considering less systemic side effects, topical timolol is a better alternative. Many large studies reveal that topical timolol has therapeutic efficacy as good as oral propranolol with lesser side effects.^[8-10] We have used 0.5% eye drop timolol as topical agent due to non-availability of timolol gel in market and cost-effectiveness. Danarti *et al.*^[11] observed in total 278 cases; surface area reduction of superficial IHs by timolol maleate 0.5% solution and gel was better than those that received topical ultrapotent corticosteroids without difference in side effect profile. Bradycardia, bronchospasm, hypoglycemia, sleep disturbance, and peripheral vasoconstriction are major systemic side effects of timolol. Systemic absorption is very rare but regular monitoring was advised during therapy when used over large area.^[11] In index case, we advised them to follow-up regularly and there were no side effects observed during course of treatment. Starting treatment early, i.e. during proliferative phase with topical medication, has good result compared with those who received later. Ovadia *et al.*^[9] in a systemic review and meta-analysis conclude that topically administered β -blockers (including timolol eye drops and gel) are effective for superficial IHs with fewer adverse effects. It should be considered as primary treatment option for IH.^[9] In a large meta-analysis conducted by Zheng and Li,^[12] results showed that topical timolol alone as a primary treatment agent is better than laser, placebo, and only observation in terms of response rate and adverse events. The same study also concluded that it has better safety profile than propranolol with equal efficacy. Most of the studies show that topical timolol can be used in small and uncomplicated hemangiomas but we treated such large complicated hemangiomas by timolol eye drops without any side effect with complete resolution as evident in serial images. So, we conclude that topical timolol 0.5% eye drops can be used even in complicated IHs considering its excellent safety profile, cost-effectiveness, and good efficacy similar to other agents.

CONCLUSION

We have successfully treated an infant with complicated IH by using topical timolol. Timolol 0.5% eye drops used

topically can be considered as a first-line drug for IH with lesser side effect profile, availability, cost-effectiveness, and good therapeutic outcome. It can be used in even complicated IH.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

Ethical approval and informed consent

Ethical approval not applicable. Informed consent taken from father to publish images after editing with blackout bars over patient's eye.

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