Infantile hemangiomas (IH) are benign tumors that arise from endothelial cells. They are the most common tumors of infancy and usually originate from the skin or subcutaneous tissue of the head and neck (60%), trunk (25%), and extremities (15%). Of all the facial hemangiomas, 24.3% are located in the periorocular region. The incidence of IH is around 4.5% in neonates and infants during the first 9 months of life. Incidence increases in Caucasians, premature populations, and low-birthweight infants. Females are also more susceptible, with a 4:1 female-to-male ratio.

The clinical course of these benign tumors begins in the first few weeks of life, followed by a proliferative, rapid growth phase for 3–9 months, usually achieving 80% of their size by a mean age of 3 months. A slower involution phase then follows spontaneously over the years. Recent studies revealed that complete involution of IH was found in 50% by the age of 5 years, 70% by the age of 7 years, and 90% by the age of 9 years.

Most lesions are self-limiting and require no intervention. They are kept to run their clinical course, enlarge, and then spontaneously involute. However, for cosmetic reasons, many parents prefer active treatment over the “watch and wait” method. In the past, the threshold for surgical intervention was very low especially for problematic IH in periorbital area. This was attributed to the fact that many surgeons were concerned about the possible complications that might arise, such as amblyopia, displacement of the globe, proptosis, and/or optic nerve compression. Further complications that might happen with such lesions are the destruction of the nasal cartilage and permanent deformity if it is extending to the nasal area.

Currently, surgical management is only indicated in certain cases especially in the head and neck region. These indications include suspicion of adjacent structural or functional damage, risk of airway blockage, excess skin, fibro-fat residual that results in a significant impact on the patients, and residual telangiectasias. Conservative and less-invasive modalities are superior alternatives to surgical intervention. These include oral/systemic steroids, oral/topical beta-blockers, or Pulsed Dye Laser (PDL).

**THE CASE**

This is a case of a girl aged 3 years, 7 months, who was born at full term by normal vaginal delivery with no medical problems. She presented to the plastic surgery clinic with right periorbital infantile hemangioma at the
age of 1 month, causing disfigurement. The lesion was bright red in color, soft in consistency, with a smooth compressible surface, and blanching. There was significant swelling over the right medial canthal area, nasium, and encroaching the right lateral nasal sidewall, extending to the nasolabial fold (Fig. 1). There was a displacement of the right eyebrow and eyelid but not reaching central vision area, displacement of the medial canthus, and right lateral nasal sidewalls, with progressive swelling causing pseudo-hypertelorbitism. An MRI scan of the head was done, which showed a mass lesion in the superior-medial aspect of the right orbit, extending inferior to the lateral aspect of the nose, measuring 5.8 × 4.1 × 4.8 cm, representing facial hemangioma with the superior orbital artery as the feeding vessel. There was no intracranial extension. The lesion was causing a pressure effect on the right orbit, displacing it laterally with intra-orbital extension to the medial wall of the right orbit.

At the age of 4 months, the patient was started on Inderal (propranolol) with a dose of 5 mg/day divided into 2 doses. It was gradually increased until it reached 25 mg/day and was continued for a total period of 13 months. During the period of treatment with Inderal, the mother reported 1–2 episodes of nightmares with no other adverse events. Due to the unavailability of the liquid form of Inderal, the mother resorted to crushing the tablets and mixing them with milk or water. The mother was educated and instructed about the nature of the disease, complications, and side-effects of the medication. She closely monitored the infant at home with proper documentation of the pulse rate and blood sugar during the treatment phase. While on treatment, the patient suffered from trauma at the site of hemangioma, resulting in bleeding, which was managed and controlled only with pressure. Her mother was advised to continue her treatment (Fig. 2).

During the follow-up period the patient showed significant improvement of the hemangioma, with a reduction in the size and color (Fig. 3).

While the patient was on treatment, she was following up with a multidisciplinary team that included the plastic surgeons, ophthalmologists, and dermatologists. Ophthalmology report showed that the patient did not suffer from amblyopia.

The dose of the Inderal was gradually tapered according to a scheduled timetable that was handed to the mother of the patient, thus completing a treatment course that lasted 13 months, with no significant side effects reported. During follow up, the patient showed marked improvement in the hemangioma, with no rebound growth after 2 years since the completion of treatment (Fig. 3).

**DISCUSSION**

Propranolol is a nonselective beta-adrenergic receptor blocker that was first observed to have an effect on IH by Léauté-Labrèze et al incidentally while treating a patient with hypertrophic cardiomyopathy. Although the patient's

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*Fig. 1.* Photograph of the patient at 4 months of age before starting Inderal.

*Fig. 2.* The patient at the age of 6 months during treatment.
oral beta-blockers. Another systematic review published was a 98% improvement rate in the lesions treated with more than 1200 patients with cutaneous hemangiomas, there is no ideal age for when to start patients on treatment. However, some reports had demonstrated that propranolol can also be effective when given during the involution phase and can be used in older children. In the studies, the age of starting treatment ranged from 1 month, 3–5 years, and up to 10 years.

Currently, there are no guidelines and protocols for pretreatment evaluation, dosage, and duration of medication, but different protocols have been described; we recommend all the patients to be evaluated and screened for possible pre-existing risk factors. High-risk patients include those with a family history of congenital heart disease, maternal history of connective tissue diseases, and personal history of arrhythmias. These patients were required to undergo an extensive cardio-pulmonary work-up, including an electrocardiogram diagnosis. Low-risk patients with no risk factors did not require the work up panel; and they were commenced on treatment after cardiology and pulmonary consultations only. One of the most common side effects of using propranolol was the occurrence of hypoglycemic attacks. However, because screening for serum glucose before starting treatment was not routinely done (Fig. 4). Propranolol can be administered orally at a starting dose of 1 mg/kg/day. It can be increased to reach a maximum target dose of 3 mg/kg/day, divided into 3 equal doses. Most physicians prefer a regular 2 mg/kg/day steady dose throughout the treatment, and twice-daily dosing, which was proved to be effective (Fig. 4). Parents were guided to administer the medication during or after feeding to prevent hypoglycemic episodes.

All medications come with their own panel of side effects. However, risks and benefits are weighed when choosing a treatment modality. Due to its fewer side effects, propranolol has been favored over other therapies such as steroids, vincristine, and interferon. Those with large or complicated facial hemangiomas that might lead to significant morbidity are candidates for the use of propranolol. Lesion’s size, location, risks for impairment of function, and potential for permanent deformity are all indications for treatment.

Most common adverse events of the use of propranolol are bronchospasm in patients with a history of bronchial asthma, bradycardia, hypotension, hyperkalemia, and hypoglycemia. The development of these side effects usually results in the termination of treatment. Therefore, patients with pulmonary diseases such as asthma, or with a
history of cardiac diseases (including heart failure, second or third-degree heart block, hypotension, and bradycardia) are contraindicated to the use of propranolol. A relative contraindication is hypersensitivity to propranolol. Other less severe side effects include acrocyanosis, sleep disturbances such as insomnia and nightmares, diarrhea, and restlessness. One meta-analysis that included 85 articles about IH reported 56% of patients who used propranolol had no complications, whereas the rest suffered from major and minor side effects. Consequently, it is essential to closely monitor patients for systemic adverse events while on treatment.2,3

Discontinuing therapy with propranolol before the age of 11 months reported a higher incidence of relapse rates.2 Around 20%–40% of patients treated with propranolol were reported to have rebound growth of the hemangioma upon sudden cessation of treatment. Thus, it is of utmost importance to gradually taper down the medication. Rebound cases were mostly mild and responded well to re-treatment.2,3 The optimal timing for discontinuing propranolol is still controversial, and many reports indicate to stop medication by hemangioma regression and some authors described use of color Doppler ultrasound to check lesion regression.2

There is no consensus on an ideal tapering regime. Most physicians follow the half rule: halving the dose for the first 2 weeks and then halving it further for the next 2 weeks, before stopping the medication completely. This way, they can closely observe for any regrowth patterns and avoid complications. Patients were followed up regularly thereafter for 6 months, and then yearly up to the age of 10 years to monitor the hemangioma progress.3

IH can be categorized into superficial, deep, or mixed according to their location on the skin. Superficial

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**Flowchart for administration of beta-blockers.**
lesions are those that do not extend beyond the dermis. Deep lesions are considered when adipose tissue is involved, and mixed lesions are those that involve both layers (apply to our case). Unlike oral propranolol, topical beta-blockers can be effective only for superficial lesions if used at an earlier age. Timolol maleate is a topical beta-blocker that has been proved effective against superficial IH. This can be contributed to the fact that the barrier of the skin is still underdeveloped before the age of 1 year. The latest data support the use of more selective beta-blockers in their topical form to minimize the adverse events that are commonly seen in the oral formulation.

Although known for use in IH either alone or as combined with another modality, PDL is mainly used for vascular anomalies, especially port-wine stains. However, some physicians use it to manage residual telangiectasia and erythema. In one study, Reddy et al reported that concomitant treatment of IH with propranolol and PDL resulted in faster and more complete clearance of the lesion compared with the use of propranolol alone or with beta-blockers and then PDL consecutively. PDL use alone on IH showed no difference when compared with “watchful waiting,” as reported by Betta et al. Strength of the evidence was not strong for the results of laser in comparison with those of beta-blockers.

When comparing with propranolol, atenolol is a more selective beta-blocker with more favorable side effects; sometimes it is used in patients who could not tolerate propranolol due to its side effects. Another form of beta-blocker (acebutolol) has been reported in literature, with a patient taking 10mg/kg/day over a period of 2 months for a hemifacial hemangioma causing visual complications. This treatment resulted in significant resolution, with no complications. Nevertheless, more studies and data are needed to confirm the outcomes of its use for IH.

CONCLUSIONS
The use of oral beta-blockers should become the mainstay treatment for problematic IH as they are safe with no significant side effects with careful monitoring. However, there is still no consensus on the administration and total duration of treatment.

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PATIENT CONSENT
Parents or guardians provided written consent for the use of the patient’s image.

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