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Infantile haemangiomas and use of propranolol

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Abstract

Cutaneous IH can be cosmetically disfiguring and may cause parental apprehension. About 5-13% of cutaneous IH ulcerates, may lead to pain, bleeding, and scarring. Glottic IH can extend to the supraglottic and subglottic regions and can partially occlude the airway. Periorbital IH may lead to vision deprivation, astigmatism and strabismus. Extensive IH may occur in PHACE syndrome (posterior fossa malformations, hemangiomas, arterial lesions, coarctation of the aorta and other cardiac defects, and eye abnormalities) Propranolol can be tried as first-line therapy in IH irrespective of age, location, extent, and phase of growth. Treatment might also help downgrade the size and local complications of IH, making the lesion more amenable to surgical excision. Due to the lack of long-term long-terms and its high response rate, propranolol therapy may prove to be superior to existing therapies.

Keywords: Infantile, Hemoangioma, Involution phase, PHACE syndrome

Introduction

Infantile haemangiomas are the most common benign tumors of infancy. They affect approximately one in ten infants. The male to female ratio is variable with some reports suggesting the condition is up to four times more common in females. A higher incidence is observed in premature babies and those who were subject to chorionic villous sampling in utero. The majority of haemangiomas are located in the head and neck region with lesions on the trunk and extremities being less common. The cutaneous lesions present soon after birth and are characterized by rapid proliferation during the first year of life, followed by a gradual involution over the next five to ten years. Whilst most haemangioma are non-problematic, requiring no treatment, approximately 10% cause significant morbidity predominantly through airway obstruction, ocular compression, functional impairment, or ulceration. Until recently treatment options for problematic haemangioma have included intralesional and systemic steroids, chemotherapeutic agents including vincristine and interferon-alpha, laser therapy, or surgical intervention.

High-risk infantile haemangiomas (IHs)

I am considered high risk if they can cause life-threatening complications or functional impairment, have a risk of ulceration/disfigurement, or are associated with clinically significant structural anomalies.

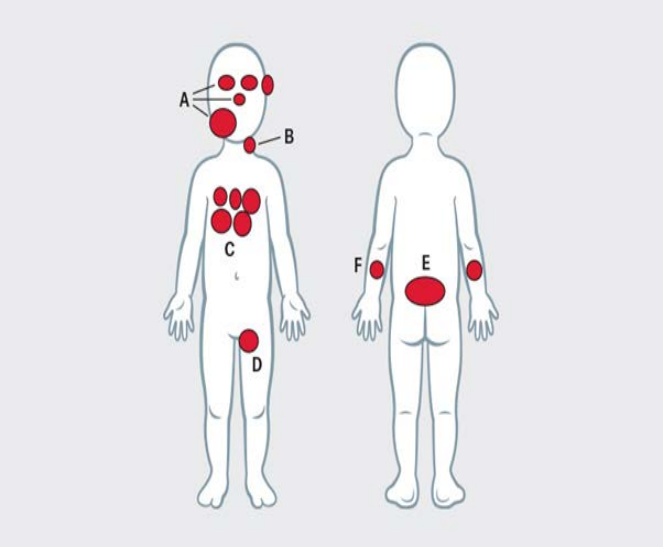

Figure 1

A. IHs involving the lower face increase risk of airway obstruction and may indicate underlying PHACE syndrome; IHs involving the nose, lips, and ears are at increased risk of ulceration and disfigurement; IHs involving the eyes increase risk of vision impairment and disfigurement;

B. Neck haemangiomas have an increased risk of ulceration and may indicate underlying PHACE syndrome;

C. Five or more haemangiomas indicate an increased risk of liver haemangiomas, cardiac failure, and hypothyroidism;

D. IHs involving intertriginous areas are at higher risk of ulceration;

E. Lumbosacral IHs may indicate underlying spinal dysraphism;

F. Segmental IHs on extremities are at high risk of ulceration

Complications for babies with hemangiomas of the skin

Although rare, infants with large infantile hemangiomas in these locations can have multiple other birth defects. This condition is called PHACE syndrome. PHACE is that stands for-

- Posterior fossa (refer to possible abnormal structures in the brain, especially the cerebellum)
- Hemangioma
- Arterial (refers to possible abnormal arteries in the brain, neck, eye or heart)
- Cardiac (refers to possible heart abnormalities)
- Eyes (refers to possible eye abnormalities).

If a baby has a large hemangioma on the lower back, it could be a sign of associated spinal cord abnormalities. Even if the condition looks like it is not causing the baby any problems, babies who may have conditions should be evaluated promptly by a doctor.

Infantile Hemangioma: Natural History & Treatment

- Involution phase: 50% of infantile hemangiomas show complete involution by age 5 years & 70% by age 7 years.
- Medical care of clinically significant hemangiomas has been limited to a few medications: corticosteroids, interferon alfa, vincristine, & imiquimod.
- Beta-blockers, most specifically Propranolol, have recently been serendipitously been shown to induce involution of infantile hemangiomas.

Mechanism of Action Propranolol

- Several mechanisms of action for propranolol have been suggested. Results from combined grayscale and color Doppler ultrasound imaging suggest that propranolol reduces vessel density.
- Propranolol has a dose-dependent cytotoxic effect on cultured hemangioma endothelial cells via the hypoxia-inducible factor 1á pathway, leading to decreased secretion of VEGF.
- In vitro propranolol decreases plasmalemmal expression of GLUT-1 though no study has evaluated

this hypothesis to date concerning IH. Other possible mechanisms of action include inhibition of matrix metalloproteinases, down-regulation of interleukin-6, and modulation of stem-cell differentiation.

Management approach to infantile Hemangioma

1. Indications for Propranolol Therapy in Infantile Hemangioma

- Non-resolution of IH
- Failure of other treatments
- IH location inaccessible to surgery and/or parents unwilling for surgery
- Obstruction of the airway, visual axis, or other vital structures
- Severe cosmetic disfigurement
- Severe ulceration, the existence of deep component, or otherwise locally complicated
- Intolerance to other therapies, i.e., deranged liver function test

2. Therapeutic Approaches

- As first-line therapy in cutaneous variants
- As a part of a multimodal approach (surgery and/or steroids)

3. Baseline Investigations

- Initial review by a pediatric surgeon
- Cardiovascular examination (blood pressure, heart rate, echocardiogram, electrocardiogram)
- Blood count; Prothrombin time, and partial thromboplastin time
- Blood urea nitrogen, creatinine; Liver function tests; Electrolytes If segmental/craniofacial: MRI to rule out intracranial anomalies.

4. Dosing Protocol

Oral suspension produced by dissolving 10 mg tablet in 5 mL of water

- Inpatient monitoring for first six hours
- Incremental dosage increase: Dosing strategy: 1 mg/kg/day for one week, then increase to 2-3 mg/kg/day
- Target daily dose administered as three divided doses.

5. Parent Education

- Common side effects: Bradycardia, hypoglycemia, hypotension

6. Follow up

- Repeat measurement and/or serial photography of hemangioma to assess response
- Assessment of change in size and color, decrease in ulceration and inflammation
- Maximal follow up interval 2 weeks in initial period of treatment for dose adjustment, monitoring, and education
- Intervals can be extended up to 1 month towards the end of therapy
- Repeat imaging
- Discontinue when IH has been static for 2 weeks or when regressed/resolved for 2 weeks.
- Taper by serial halving to discontinue
- Pediatric surgical consultation for counseling, reassurance, and surgical intervention.

Clinical pictures of before and after use of propranolol

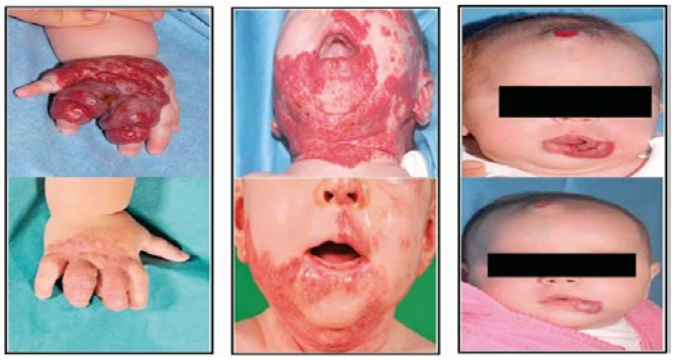

Figure 2

Summary and Conclusion

Cutaneous infantile haemangiomas affect approximately 1 in 10 children. They tend to follow a natural course of rapid proliferation during the first year of life and subsequently regress over 5-10 years. Most haemangiomas are non-problematic, but a few become problematic, through ocular, airway or functional impairment, or ulceration. Oral propranolol therapy has been observed to inhibit the proliferation and incite regression of these lesions during their proliferative phase. At present, there are no nationally agreed guidelines on propranolol use in pediatric patients with infantile haemangioma.

Treatment should be decided based on individual circumstances, such as the size and location of the tumor, complications, the phase at the time of evaluation, the involvement of other organs, and psychological factors. Propranolol is proving very effective in this setting and its use is therefore growing. As a result, surgical intervention is usually needed only when involution has been incomplete and removal of residual tissue or other corrective measures are required.

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