Management of Infantile Hemangioma

KEY ISSUE

Access to early treatment may be critical for a subset of children facing significant impact from infantile hemangioma (IH). This is a summary of a systematic review[1] evaluating the evidence regarding the efficacy, comparative effectiveness, and adverse effects of pharmacological and surgical therapies for IH. The systematic review included 148 unique studies published from 1982 to June 2015. The full report, listing all studies, is available at *www.effectivehealthcare.ahrq.gov/infantile-hemangioma.*

BACKGROUND

Infantile hemangioma (IH) is generally a benign vascular neoplasm. The International Society for the Study of Vascular Anomalies (ISSVA) classifies IH lesions as vascular tumors, which are differentiated from vascular malformations.[2] IH affects 4 to 5 percent of children in the United States, with a higher prevalence among babies who are white or born prematurely.

IH commonly develops in neonates within their first month of life. Most IH lesions undergo rapid initial proliferation, plateau in infants aged about 9 to 12 months, and then enter an involution phase.

With a course of expectant observation, many patients experience a complete involution without significant sequelae. However, in a fraction of patients, early referral for treatment is important. These patients include:

» children who have IH in functionally sensitive areas (e.g., eyes, liver, or airways);

» children whose IH causes pain, ulceration, and bleeding; and

» children whose IH causes significant disfigurement (e.g., large lesions on the face).

Management of IH is highly individualized and may include pharmacotherapy or surgery.

Propranolol (Hemangeol™) is an oral medication that was approved by the U.S. Food and Drug Administration as treatment for IH. Steroids used to treat IH mainly include oral steroids and intralesional steroids (e.g., triamcinolone). Surgical interventions such as resection, laser ablation, and radiofrequency ablation may be used as primary management of high-risk lesions prone to complications. The most common type of lasers used to treat IH are pulse dye lasers.

Uncertainty exists about which interventions might be most beneficial as first-line therapies for IH and about when alternative therapies are appropriate after first-line treatment is unsuccessful.

Summary of Evidence From the Systematic Review[1]

- ✓ Propranolol and steroids are effective in reducing the size of IH lesions (i.e., lesion clearance). *(See Table 1.)*
- ✓ Propranolol is more effective than steroids in reducing the size of IH lesions. *(See Table 1.)*
- ✓ Limited evidence suggested that pulse dye laser treatments may be more effective in clearing IH lesions when compared with observation. *(See Table 1.)*
- ✓ Clinically important, short-term harms of propranolol included hypotension, hypoglycemia, bradycardia, bronchospasm, and seizures.
- ✓ Clinically important harms of steroids—some of which may be short lived—included Cushingoid facies, irritability/mood changes, abdominal pain, growth retardation, hypertension, and infection.
- ✓ Harms associated with pulse dye lasers included hypopigmentation, bleeding, pain, and scarring.

*Considerations for Programs and Policies**

- ✓ Early identification of the subset of children in whom lesion proliferation can lead to functional impairment and disfigurement is key to improving treatment effectiveness and preventing complications such as ulceration, psychosocial sequelae, or both.
- ✓ Policymakers may have an important role to play in decisionmaking that leads to timely diagnosis and treatment to optimize health outcomes.

* These considerations were not evaluated in the systematic review but are offered to assist policymakers in applying this evidence.

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Table 1: Summary of Findings and Strength of Evidence for the Effectiveness of Treatment Interventions for Infantile Hemangioma

Intervention	Outcome	Studies	N	Finding	SOE
BETA-BLOCKERS					
Propranolol vs. observation or placebo	Improvement in IH	Network meta-analysis 4 additional studies	555	Propranolol more effective	●●●
	Rebound growth/need for further treatment	2 studies	501	Low level of rebound growth/need for further treatment in propranolol arm (fewer than 15% of children)	●●○
Propranolol vs. steroids	Improvement in IH	Network meta-analysis 5 additional studies	237	Propranolol more effective	●●○
Propranolol vs. other beta-blockers (atenolol or nadolol)	Improvement in IH	3 studies	100	Equivalent response	●○○
Topical timolol vs. placebo or observation	Improvement in IH	Network meta-analysis 3 additional studies	188	Timolol more effective	●○○
STEROIDS					
Oral steroids vs. observation or placebo	Improvement in IH	Network meta-analysis	N/A	Oral steroids more effective	●●○
Intralesional steroids (triamcinolone) vs. observation or placebo	Improvement in IH	Network meta-analysis	N/A	Intralesional steroids more effective	●○○
LASER TREATMENTS					
Pulse dye laser vs. observation	Improvement in IH	2 studies	143	Pulse dye laser more effective	●○○
	Quality of life	2 studies	143	No significant difference	●○○
Long-pulse dye laser vs. other laser types and protocols	Improvement in IH	3 studies	264	No significant difference	●○○

IH = infantile hemangioma; N = number of subjects enrolled; N/A = not applicable; SOE = strength of evidence

STRENGTH OF EVIDENCE SCALE

●●● **HIGH**–High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.

●●○ **MODERATE**–Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.

●○○ **LOW**–Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.

○○○ **INSUFFICIENT**–Evidence either is unavailable or does not permit a conclusion.

RESOURCES FOR CLINICIANS AND CONSUMERS

The clinician research summary, *Management of Infantile Hemangioma,* and the consumer research summary, *Treating Infantile Hemangiomas in Children: A Review of the Research for Parents and Caregivers,* are free companions to this policymaker research summary. They are meant to assist clinicians and children's parents or caregivers in informed decisionmaking.

ORDERING INFORMATION

For electronic copies of this policymaker research summary, the clinician research summary, the consumer research summary, and the full systematic review, visit *www.effectivehealthcare.ahrq.gov/infantile-hemangioma.*

REFERENCES

1. Chinnadurai S, Snyder K, Sathe N, et al. Diagnosis and Management of Infantile Hemangioma. Comparative Effectiveness Review No. 168. (Prepared by the Vanderbilt University Evidence-based Practice Center under Contract No. 290-2010-0009-I.) AHRQ Publication No.16-EHC002-EF. Rockville, MD: Agency for Healthcare Research and Quality; January 2016. *http://www.effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=2170.*

2. Wassef M, Blei F, Adams D, et al; ISSVA Board and Scientific Committee. Vascular Anomalies Classification: Recommendations From the International Society for the Study of Vascular Anomalies. Pediatrics. 2015 Jul;136(1):e203-14. PMID: 26055853.

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