International heterogeneity in admission criteria and monitoring for the initiation of propranolol in infantile hemangioma

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Infantile hemangioma is the most common vascular tumor of infancy, and although the majority of such hemangiomas are innocuous, 10% to 15% are regarded as complex and require treatment.[1] Propranolol has emerged as the systemic therapy of choice, and in recent years, several groups have issued guidelines on its use in the treatment of infantile hemangioma.[1-4] The guidelines are largely congruent; however, there are some areas of difference, including indications for initiation, evaluation, admission criteria, starting dose, and monitoring (Table I). As expected, these domains correlate with those least defined in the literature, instead being centered on expert consensus, potentially accounting for divergence among the guidelines.

Local health policy is often shaped by published guidelines; however, in this setting the published recommendations diverge in some finer points. When health policy is generated, it is prudent to perform rigorous assessment of these differences to establish protocols relevant to the local health district, taking into consideration cost, accessibility, and resource provision. For instance, one important area of divergence noted was the indications for admission with the initiation of propranolol. Hospital admission for propranolol initiation is associated with considerable use of health care resources. Chaturvedi and colleagues[5] completed a modeled costing study that estimated that the price of commencing propranolol on an outpatient basis was on average $138 compared with $2,603 for inpatient initiation. There is also variability in recommendations regarding monitoring during admission both in terms of which observations are required (heart rate, blood pressure, and blood sugar) and frequency of monitoring. There are obvious challenges with striking the correct balance between optimizing patient safety and identifying adverse effects while minimizing unnecessary investigation and undue use of health care resources.

Completing high-quality clinical studies in this setting is difficult because propranolol emerged serendipitously as a treatment for infantile hemangioma. Because it was a medicine that had been readily available for decades, the usual requirements for clinical trials to guide dosing and monitoring were not required. Completing prospective studies is challenging because of ethical issues relating to the established benefit of propranolol, the need for urgent treatment in many complex infantile hemangiomas, and the vulnerable patient cohort that all pediatric studies contain. A potential avenue forward may be audits of infants who have begun receiving propranolol as inpatients, including evaluation of different thresholds for admission (for example, what proportion of infants weighing <2 kg develop clinically significant complications?, or how often completing measurements of heart rate every 30 minutes would identify an adverse outcome compared with every 60 minutes). These thresholds may then be used as inclusion criteria in prospective trials, in turn shaping the next generation of health policy.

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Table I. International guidelines on the commencement of propranolol for infantile hemangioma

Region of origin	Krowchuk et al, United States	Solman et al, United Kingdom	Smithson et al, Australia	Hoeger et al, Europe
Indication for propranolol				
Periorificial (periorbital, nasal, perioral)	X	X	X	X
Auditory canal		X		X
Airway	X	X	X	X
Intertriginous	X			X
Perineum	X		X	X
Breast (female)	X			X (large)
Risk of disfigurement	X	X	X	X
Ulceration	X	X	X (with significant pain)	X
Functional impairment	X	X	X	X
Spinal cord myelopathy	X	X	X	
Cardiac impairment	X		X	X
Hypothyroidism	X		X	
Systemic hemangiomatosis	X	X	X	
Parental concern			X	
PHACES/LUMBAR	X	X		X
Evaluation				
Heart rate	X	X	X	X
Blood pressure	X	X		X
Indications for baseline BSL				
Prematurity		X		X
Small for date		X		X
Failure to thrive		X		X
History of hypoglycemia		X		X
Indications for ECG				
Arrhythmia, tachycardia, bradycardia		X		X
Family history of sudden cardiac death or arrhythmia		X		
Loss of consciousness		X		
Maternal connective tissue disease		X		
Indications for echocardiogram				
PHACES	X	X	X	X
Heart rate outside of normal range		X		
Heart murmur		X		
Initiation				
Dose, mg/kg/d	2−3	1 in 3 divided doses; lower in high risk	1−2 in 2 divided doses; lower in high risk	1
Criteria for admission				
Age, mo		<1	<1	≤2
Weight, kg			<2.5	<3.5
Low birth weight		X	X	
Poor feeding or FTT		X		
Life-threatening IH				X
Clinical concern			X	
Significant comorbidity		X		X
Poor social support				X
Duration of admission, h		2−4	3	2
Monitoring during admission				
Heart rate		Every 30 min	Every hour	Every hour
Blood pressure		Every 30 min		Every hour

Continued

Table I. Cont'd

Region of origin	Krowchuk et al, United States	Solman et al, United Kingdom	Smithson et al, Australia	Hoeger et al, Europe
BSL monitoring	No	Only with higher risk of hypoglycemia*	At 3 h for those at higher risk of hypoglycemia*	No
Target dose, mg/kg	2—3	2; 3 if recalcitrant	2; 3 if recalcitrant	2—3/d in 2 divided doses
Follow-up		2—3 monthly intervals	Monthly until involution; then 3/mo	Monthly to titrate dose
Length of treatment, mo	6—12	12	Up to 24	6

BSL, Blood sugar level; *ECG*, electrocardiogram; *FTT*, failure to thrive; *IH*, infantile hemangioma; *LUMBAR*, lower-body infantile hemangioma, urogenital anomalies, ulceration, myelopathy, bony deformities, anorectal malformations, arterial anomalies, and renal anomalies; *PHACES*, posterior fossa brain malformations, hemangiomas, arterial anomalies, cardiac anomalies, eye abnormalities, and sternal clefts.
*Preterm, low weight, failure to thrive, poor feeding, history of hypoglycemia.

Given the frequency of infantile hemangioma, further clarification regarding which patients may safely begin receiving propranolol as outpatients warrants elucidation, as does the monitoring required for those infants admitted.

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