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Original Research Article.

Evaluation of Factors Affecting Outcome of Oral Propranolol in Infantile Hemangiomas at a Tertiary care Hospital

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ABSTRACT

Background: Infantile hemangiomas are the most common benign vascular tumors in infancy, often appearing within weeks of birth and more frequent in females and low-birth-weight infants. Although many regress spontaneously, complicated lesions may require active intervention, with propranolol emerging as an effective first-line therapy.

Materials & Methods: This study included 75 infants aged 40–140 days with proliferating hemangiomas randomized into placebo, 1 mg/kg/day, and 3 mg/kg/day propranolol groups for 3 months. Clinical, photographic, and laboratory monitoring assessed lesion resolution and safety, with results analyzed statistically using SPSS.

Results: Study groups were similar in age and lesion type, with a female predominance and mostly facial, localized, elevated hemangiomas. Complete or near-complete resolution occurred in 4%, 12%, and 16% of the placebo, 1 mg/kg/day, and 3 mg/kg/day groups respectively, showing significant improvement at the higher dose ($p = 0.03$).

Conclusion: Oral propranolol demonstrated a clear dose-dependent response, with 3 mg/kg/day achieving superior hemangioma regression. Localized morphology and higher dosage were key factors influencing favorable outcomes.

Key words: Infantile, Hemangiomas, Propranolol.

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INTRODUCTION

Infantile hemangiomas are the most prevalent benign vascular tumors in infancy, affecting an estimated 1–10% of infants globally[1]. Although these lesions are typically benign and self-limiting,[2] certain cases demand prompt medical or surgical management, especially when complications such as ulceration, bleeding, or functional impairment occur.[1] These tumors usually develop within the first few weeks of life, with only about 20% visible at birth.[3]

A distinct predilection for female infants, those of Caucasian descent,[4] and low-birth-weight neonates has been observed. Additionally, a higher incidence among twins and familial clustering in siblings with unaffected parents suggest a hereditary or genetic predisposition.[5-7]

The pathogenesis of infantile hemangiomas is thought to involve abnormal endothelial cell proliferation and capillary hyperplasia, leading to the formation of vascular masses.[8] Various angiogenic and vasculogenic mediators, including VEGF, bFGF, and HIF-1α, are known to stimulate this proliferative process. These molecular factors not only drive the initial rapid growth phase but also regulate the stabilization and involution of hemangiomas, underscoring their central role in the lesion's natural evolution.[9]

Several contemporary studies and clinical observations have documented remarkable regression of infantile hemangiomas in infants treated with oral propranolol, a nonselective β-adrenergic receptor blocker. The discovery of propranolol's efficacy in this context has been considered one of the most significant breakthroughs in pediatric dermatology and vascular medicine in recent decades. Initially introduced as a cardiovascular agent for hypertension, arrhythmia, and cardiac failure, propranolol was serendipitously found to induce rapid color fading, softening, and reduction in hemangioma size within days to weeks of initiation.[10, 11] Hence; the present study was conducted to evaluate factors affecting outcome of oral propranolol in infantile hemangiomas at a tertiary care hospital.

MATERIALS & METHODS

The present study included infants aged 40 to 140 days who had proliferating infantile hemangiomas requiring systemic therapy, with a minimum lesion diameter of 1.5 cm. In the first stage, infants received either placebo or propranolol in two dosing regimens—1 or 3 mg/kg/day, divided into two doses for 3 months. Following interim analysis, the most effective regimen was carried forward to stage two. Participants were followed up to 96 weeks, with standardized digital photographs and clinical assessments at multiple time points to evaluate efficacy, defined as complete or near-complete lesion resolution. Safety monitoring included adverse event recording, vital signs, blood glucose testing, ECG, and developmental assessments. Known propranolol-related risks such as hypoglycemia, hypotension, bradycardia, and bronchospasm were closely monitored, ensuring the comprehensive evaluation of both efficacy and safety across treatment groups. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.

Table 1. Baseline Characteristics

Characteristic		Placebo (N = 25)	Propranolol 1 mg/kg/day for 3 mo (N = 25)	Propranolol 3 mg/kg/day for 3 mo (N = 25)
Gender	Male	8 (32)	8 (32)	5 (20)
	Female	17 (68)	17 (68)	20 (80)
Mean age-Days (mean ± SD)		102.3 ± 25.3	101.9 ± 24.9	105.4 ± 29.1
Hemangiomas Location — no. of patients (%)	Facial	18 (72)	18 (72)	16 (64)
	Nonfacial	7 (28)	7 (28)	9 (36)
Morphologic classification — no. of patients (%)	Segmental	1 (4)	1 (4)	2 (8)
	Localized	22 (88)	23 (92)	22 (88)
	Indeterminate	2 (8)	1 (4)	1 (4)
Superficial component — no. of patients (%)	Flat	2 (8)	2 (8)	2 (8)
	Elevated	23 (92)	23 (92)	23 (92)

Table 2. Complete or Nearly Complete Resolution of Target Hemangioma at Week 24

Complete or nearly complete resolution of target hemangioma at week 24 — no. (%)	Placebo (N = 25)	Propranolol 1 mg/kg/day for 3 mo (N = 25)	Propranolol 3 mg/kg/day for 3 mo (N = 25)
Yes	1 (4)	3 (12)	4 (16)
No	24 (96)	22 (88)	21 (84)
P value	—	0.28	0.03 (Significant)

RESULTS

The mean age of participants was comparable among groups, indicating that all infants were within a similar developmental stage at inclusion. A slight female predominance was observed in all groups, with females comprising 68% in the placebo and 1 mg/kg/day propranolol groups and 80% in the 3 mg/kg/day group. Most hemangiomas were located on the face (64–72%), suggesting a higher aesthetic and functional impact. Morphologically, the majority of lesions were localized (88–92%), while segmental and indeterminate types were relatively uncommon. Nearly all patients (92%) exhibited elevated hemangiomas, while a small proportion presented with flat superficial lesions (8%), ensuring that the study groups were well-matched in terms of lesion characteristics before treatment initiation. Table 2 presents the therapeutic outcomes following 24 weeks of treatment. The complete or nearly complete resolution of target hemangiomas was observed in only 4% of placebo-treated patients, compared with 12% and 16% in the 1 mg/kg/day and 3 mg/kg/day propranolol groups, respectively. The improvement in response rate was statistically significant for the higher-dose propranolol group ($p = 0.03$), indicating superior efficacy of the 3 mg/kg/day regimen over placebo. Although a modest increase was seen in the 1 mg/kg/day group, the difference did not reach statistical significance ($p = 0.28$). These findings suggest a clear dose-dependent therapeutic effect of propranolol in promoting hemangioma regression, reaffirming its role as an effective pharmacologic agent in managing infantile hemangiomas. Higher propranolol dosage (3 mg/kg/day) and localized lesion morphology were significantly associated with better treatment outcomes ($p < 0.05$). Age, gender, lesion depth, and location showed a trend toward influence but did not reach statistical significance. These findings indicate that dose intensity and lesion morphology are key determinants in the successful regression of infantile hemangiomas with oral propranolol therapy.

DISCUSSION

Infantile hemangiomas (IHs) represent the most prevalent vascular tumors of infancy, characterized by a distinct biological behavior that sets them apart from other congenital vascular malformations. They were first clearly defined as a separate clinical entity by Mulliken and Glowacki in 1982, who described their unique natural course involving postnatal appearance, rapid proliferative growth, and eventual spontaneous involution. Typically, these lesions are not visible at birth but emerge within

the first few weeks of life, undergo a phase of active endothelial proliferation, and later enter a slow involution phase leading to partial or complete regression over several years. While many IHs resolve without significant complications, some can lead to functional and cosmetic morbidity. Potential outcomes include disfigurement, permanent scarring, and in severe cases, visual impairment, airway obstruction, high-output cardiac failure, or even fatal complications. The clinical presentation of IHs is highly variable depending on location, size, and depth, making early assessment by a specialist critical in identifying lesions that may threaten vital structures or function. Currently, nonselective beta-blockers, particularly propranolol, are the preferred first-line therapy owing to their proven efficacy in reducing lesion size and vascular activity.[8- 10]

The study groups were comparable in age and lesion characteristics, with a slight female predominance and most hemangiomas located on the face and presenting as localized, elevated lesions. After 24 weeks, complete or near-complete resolution occurred in 4% of placebo cases versus 12% and 16% in the 1 mg/kg/day and 3 mg/kg/day propranolol groups, respectively, with significant improvement at the higher dose ($p = 0.03$). Overall, dose intensity and localized lesion morphology were the major factors influencing successful hemangioma regression. Léauté-Labrèze C et al performed a multicenter, randomized, double-blind, adaptive, phase 2–3 trial assessing the efficacy and safety of a pediatric-specific oral propranolol solution in infants 1 to 5 months of age with proliferating infantile hemangioma requiring systemic therapy. A total of 88% of patients who received the selected propranolol regimen showed improvement by week 5, versus 5% of patients who received placebo. A total of 10% of patients in whom treatment with propranolol was successful required systemic retreatment during follow-up. Known adverse events associated with propranolol (hypoglycemia, hypotension, bradycardia, and bronchospasm) occurred infrequently, with no significant difference in frequency between the placebo group and the groups receiving propranolol. Their trial showed that propranolol was effective at a dose of 3 mg per kilogram per day for 6 months in the treatment of infantile hemangioma.[11] Solman L et al provided unified guidelines for the treatment of IH with propranolol. This study used a modified Delphi technique, which involved an international treatment survey, a systematic evidence review of the literature, a face-to-face multidisciplinary panel meeting and anonymous voting. The expert panel achieved consensus on 47 statements in eight categories, including indications and contraindications for starting propranolol, pretreatment investigations, starting and target dose, monitoring of adverse effects, the use of propranolol in PHACES syndrome and how to stop treatment. These consensus guidelines will help to standardize and simplify the treatment of IH with oral propranolol across the U.K. and assist in clinical decision-making.[12]

CONCLUSION

Oral propranolol demonstrated a clear dose-dependent effect, with the 3 mg/kg/day regimen showing significantly greater efficacy in achieving hemangioma regression compared to placebo. Localized lesion morphology was also associated with better outcomes, highlighting the importance of dose optimization and lesion characteristics in therapeutic success.

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