

Propranolol in the Treatment of Infantile Hemangiomas: A Single-Center Experience

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Abstract

Objective. Infantile hemangiomas (IH) are common benign vascular tumors of infancy that typically undergo gradual spontaneous regression over several years, although a minority require treatment. Propranolol, a non-selective β -adrenergic antagonist, is the first-line therapy for complicated or high-risk IH, demonstrating both efficacy and a favorable safety profile. **Materials and Methods.** We retrospectively analyzed 37 infants treated with oral propranolol at a single center. Patients were monitored in-hospital during treatment initiation and at regular, outpatient visits. The response was assessed using clinical measurements, ultrasonography, and standardized photographs. **Results.** Most patients had solitary lesions predominantly located in the head region. Complete regression occurred in 26 patients (70.3%) and partial regression in 11 (29.7%). Treatment duration ranged from 2 to 24 months (mean 10.1 months). Adverse events were rare and mild, including one case of hypoglycemia and one of transient somnolence. **Conclusion.** Oral propranolol is a safe and effective first-line therapy for IH, particularly when initiated early during the proliferative phase.

Key Words: Infantile Hemangioma ■ Propranolol ■ Pediatric ■ Vascular Tumor.

Introduction

Infantile hemangiomas (IH) represent the most common benign tumors in infancy, with an estimated prevalence of 3–10% (1). They are rarely present at birth and typically become clinically apparent within the first weeks of life. The clinical course of IH generally follows a well-defined pattern, progressing through an initial growth phase (proliferative phase), followed by stabilization (plateau), and subsequent gradual spontaneous regression. While the majority of cases remain clinically benign, approximately 12% are associated with complications that require specialist evaluation and management (2).

Over the past decade, propranolol has emerged as the preferred therapeutic option for problematic IH, despite the relative scarcity of large randomized controlled studies (3). Although widely accepted as first-line therapy, reports describing institutional clinical experience remain valuable for documenting treatment outcomes and safety in clinical practice. Such data may contribute to optimizing treatment protocols and monitoring strategies in pediatric patients.

In the present study, we describe our institutional experience with oral propranolol therapy, and evaluate treatment response and safety in pediatric patients receiving an oral propranolol solution for up to 24 months.

Materials and Methods

A retrospective study included 37 children (13 males and 24 females) with IH who were consecutively treated with systemic propranolol over a three-year period (January 1, 2015 to December 31, 2017) at the Department of Pediatrics, Clinical Hospital Centre Rijeka, Croatia. Data were collected from the integrated hospital information system (IBIS) and patient medical charts.

Baseline pretreatment evaluations included laboratory tests—complete blood count, blood glucose, liver and renal function, and thyroid function—as well as electrocardiography. Propranolol was administered as a hydrochloride oral suspension, always with a feed, starting at a daily dose of 1 mg/kg—divided into two doses—for the first week to assess patient tolerance. All infants were hospitalized for the first two days of initial treatment for close monitoring. Post-initiation bedside monitoring of blood pressure and heart rate was performed using a noninvasive monitor, and fingerstick blood glucose levels were measured at baseline (before the first dose) and 2 hours after the first three administrations. After the first week, the dose of propranolol was increased to 2 mg/kg/day for the second week, followed by a final maintenance dose of 3 mg/kg/day.

The patients underwent regular outpatient follow-up every two weeks and were weighed monthly to allow dose adjustment of propranolol as required. Treatment efficacy was assessed using standard measurements (for superficial lesions), measurements obtained by serial ultrasonography (for deep and combined lesions), and evaluation of digital photographs by two independent readers for all visible lesions.

Ethics Statement

The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of the Faculty of Health Studies, University of Rijeka, Croatia (Class: 602-11/18-01; No.: 2133-61-04-18-01; approval date: March 26, 2018).

Statistical Analyses

Statistical analysis of quantitative data was conducted with descriptive statistics. Continuous variables are presented as mean \pm standard deviation and range, and categorical variables as counts and percentages. Minimum and maximum values were reported where relevant. All statistical analyses were performed using Microsoft Excel 2016.

Results

Of the 37 patients, 31 (83.8%) presented with a solitary IH, while 6 (16.2%) had multiple lesions (five with two and one with three hemangiomas). Lesions were most located in the head region (21, 47.8%), followed by the trunk—back (8, 18.2%), chest wall and abdominal wall (3 each, 6.8%), the extremities—upper (6, 13.6%) and lower (1, 2.3%), and the gluteal region (2, 4.5%). Most IH had a widest diameter of 1–3 cm (27, 61.4%). Nine lesions (20.4%) measured >3–6 cm, four (9.1%) were \leq 1 cm, and one (2.3%) was >6 cm; lesion size was not documented in three patients (6.8%). Regarding hemangioma type, 7 lesions were superficial (2 flat and 5 elevated), 9 were deep, and 28 were mixed.

The primary indication for propranolol therapy was rapid lesion growth in 33 patients (89.2%). Two patients (5.4%) had complicated (ulcerated) IH, and one patient each (2.7%) was treated due to the risk of functional impairment (periocular location) and for cosmetic reasons. Propranolol therapy was initiated before 3 months of age in 12 patients (32.4%), and between 3 and 6 months in 25 patients (67.6%). The mean age at treatment initiation was 3.7 ± 2.1 months (range 35 days – 6 months).

Treatment duration was \leq 6 months in seven patients (18.9%), >6–12 months in 24 patients (64.9%), >12–18 months in one patient (2.7%), and >18 months in five patients (13.5%). The mean duration of propranolol therapy was 10.1 ± 5.9 months (range 2 – 24 months). Complete regression of IH was observed in 26 patients (70.3%), while partial regression occurred in 11 patients (29.7%). No patient demonstrated a lack of response to propranolol (Figure 1).



Figure 1. A. Infantile hemangioma in a 4-month-old female infant. B. After 4 months of propranolol therapy. C. After 8 months of propranolol therapy, showing almost complete regression. [Case reproduced from our patient; reproduced with permission from Reference 4.]

Table 1. Patient Baseline Characteristics, Hemangioma Features, and Propranolol Therapy

Patients (N=37; %)		Type (N; %)	
Gender (N; %)		Superficial	7 (15.9)
Male	13 (35.1)	Deep	9 (20.5)
Female	24 (64.9)	Combined	28 (63.6)
Age at treatment initiation, months (N; %)		Treatment (N=37; %)	
0 – 3	12 (32.4)	Reason for initiation (N; %)	
3 – 6	25 (67.6)	Rapid growth	33 (89.2)
Number of lesions (N; %)		Complications (ulceration)	2 (5.4)
Solitary	31 (83.8)	Location	1 (2.7)
Multiple	6 (16.2)*	Cosmetic reasons	1 (2.7)
Hemangiomas (N=44; %)		Duration, months (N; %)	
Location (N; %)		≤6	7 (18.9)
Head	21 (47.8)	>6–12	24 (64.9)
Trunk	14 (31.8)	>12–18	1 (2.7)
Extremities	7 (15.9)	>18	5 (13.5)
Gluteus	2 (4.5)	Response (N; %)	
Size (widest diameter, cm) (N; %)		Complete regression	26 (70.3)
≤1	4 (9.1)	Partial regression	11 (29.7)
1–3	27 (61.4)	Adverse effects (N; %)	
>3–6	9 (20.4)	Yes	2 (5.4)
>6	1 (2.3)	No	35 (94.6)
Not documented	3 (6.8)		

*Six patients had more than one hemangioma; total number of hemangiomas = 44.

Mild hypoglycemia was recorded in one patient (2.7%), and transient somnolence in another (2.7%); no additional adverse events were observed (Table 1). No differences were observed between male and female patients in lesion location, size, indication for propranolol therapy, age at treatment initiation, treatment duration, therapeutic response, or adverse events.

Discussion

In this retrospective study, oral propranolol demonstrated high effectiveness and an excellent safety profile in the treatment of IH. Complete regression was observed in 70.3% of patients, with the remaining 29.7% showing partial regression, and no patient failed to respond. These findings are consistent with previous studies reporting

propranolol as the first-line therapy for complicated or high-risk IH (3, 4). Propranolol, a non-selective β -adrenergic antagonist, exerts its effects in IH via multiple mechanisms. It induces vasoconstriction, resulting in early color and volume changes; inhibits angiogenic pathways, including downregulation of vascular endothelial growth factor (VEGF) and other pro-angiogenic factors; and promotes endothelial cell apoptosis and reduced proliferation, contributing to involution of vascular tissue (5).

In addition to oral propranolol, several other treatment options for IH have been evaluated. Topical β -blockers, such as timolol maleate 0.5% solution, have been increasingly used for superficial IHs, demonstrating comparable efficacy to oral propranolol in selected cases with a lower incidence of systemic side effects, and may be considered particularly for small, uncomplicated superficial lesions (6). Oral selective β -blocker atenolol has been compared with oral propranolol in several randomized trials and systematic reviews, showing similar efficacy in terms of complete remission, reduction in Hemangioma Activity Score (HAS), relapse rates, and overall adverse events, although the certainty of evidence is low (7). Other systemic agents, including corticosteroids, were historically used but are associated with a broader range of adverse effects and lower overall efficacy compared with propranolol (8). In addition, combination approaches such as β -blockers with laser therapy have been explored in network meta-analyses, with some evidence suggesting enhanced outcomes compared with monotherapy (9). In our cohort, oral propranolol was preferred as first-line systemic therapy due to its well-established effectiveness, extensive clinical experience, and favorable overall safety profile, consistent with current practice guidelines.

Early initiation of therapy contributed to favorable outcomes. One third of patients began treatment before 3 months of age, and the remainder between 3 and 6 months. This timing corresponds to the proliferative phase of IH, when intervention is most likely to achieve rapid stabilization and regression. Treatment duration in our study ranged

from 2 to 24 months (mean 10.1 months), and prolonged administration was not associated with additional adverse effects, supporting individualized treatment duration based on clinical response.

Propranolol was well tolerated, with only mild hypoglycemia in one patient and transient somnolence in another. No serious adverse events occurred, corroborating the safety profile reported in the literature (3). However, close monitoring during treatment initiation remains essential to promptly detect and manage potential side effects, particularly in infants less than 2 months of age due to an increased risk of hypoglycemia.

Lesion characteristics in our cohort were similar to those reported in previous studies, with the majority being solitary and located in the head region (1, 2). Most lesions were small to medium in size (≤ 3 cm in 70.5%) and mixed-type hemangiomas predominated (63.6%). The primary indication for therapy was rapid lesion growth in 89.2% of patients, reflecting current clinical practice in selecting patients for systemic therapy.

Our study has several limitations. Its retrospective design and relatively small sample size may restrict the generalizability of the findings. Being a single-center study, patient selection could be influenced by referral patterns and institutional practices, introducing potential selection bias. Data collection relied on existing medical records, which may have led to incomplete or inconsistent documentation (information bias). The absence of a control group prevents direct comparison with alternative treatment strategies and limits the ability to draw causal inferences. Despite these limitations, our results contribute to the growing body of evidence supporting propranolol as a safe and effective therapy for IH, and provide practical guidelines on dosing schedules, monitoring strategies, and treatment duration in clinical practice.

Conclusion

Oral propranolol is highly effective for the treatment of IH, particularly when initiated early in the proliferative phase. The therapy is well tolerated, with minimal adverse effects, and can achieve

complete or substantial regression in the majority of patients. These findings support the continued use of propranolol in pediatric practice.

What Is Already Known on This Topic:

IH are common benign vascular tumors of infancy that usually regress spontaneously but may require treatment when complicated or high-risk. Oral propranolol is established as the first-line therapy for complicated IH, with proven efficacy in inducing regression and a favorable safety profile.

What This Study Adds:

This single-center retrospective study confirms high rates of complete or partial regression of IH with oral propranolol in a pediatric setting. The findings support early initiation of therapy and individualized treatment duration, with minimal adverse effects observed.

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