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Original Research Article

ASSESSMENT OF THE THERAPEUTIC EFFICACY OF PROPRANOLOL FOR THE TREATMENT OF INFANTILE HEMANGIOMAS

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Abstract: *Infantile hemangiomas (IHs) are common vascular tumors affecting pediatric populations, often necessitating medical intervention due to their potential for complications. Propranolol has emerged as a promising therapeutic option for IHs, although optimal dosing regimens and treatment outcomes remain areas of ongoing research. This prospective observational study aimed to evaluate the therapeutic efficacy, safety profile, and clinical characteristics associated with propranolol treatment in pediatric patients with IHs. Eighty infants aged one month to 1 year were included in the study, with IH occurrence and treatment initiation predominantly observed within the first 12 months of life. Propranolol was administered orally at a starting dose of 2 mg/kg/day, titrated up to 3-4 mg/kg/day as tolerated. Assessment of therapeutic response revealed significant reductions in IH size and vascularity, with 31.3% of patients demonstrating an excellent response and 37.5% showing a good response. Adverse effects were minimal, with diarrhea (22.5%) and decreased heart rate (7.5%) being the most commonly reported side effects. Anatomical distribution analysis identified the parotid region as the most common site of lesion occurrence, highlighting the heterogeneous nature of IHs. Overall, our findings support the favorable outcomes of propranolol therapy in pediatric patients with IHs, emphasizing the need for individualized treatment approaches tailored to patient-specific characteristics.*

Keywords: Hemangioma, Infant, Propranolol, Therapeutics, Treatment Outcome

Introduction

Infantile hemangiomas (IH) are the most common benign vascular tumors of infancy, affecting up to 5% of newborns (Krowchuk et al., 2019). While most IH undergo spontaneous involution, approximately 10-20% require medical or surgical intervention due to complications such as ulceration, bleeding, obstruction of vital structures, or disfigurement (Darrow et al., 2015; Hochman, 2022). Various treatment modalities have been employed, including corticosteroids, interferon, and surgical excision, each with limitations and potential adverse effects (Zheng et al., 2013). Propranolol, a non-selective beta-blocker, has emerged as a promising therapeutic option for IH owing to its vasoconstrictive and anti-proliferative properties.

The therapeutic efficacy of propranolol in managing infantile hemangiomas remains fully elucidated, particularly in its effectiveness, safety profile, and optimal dosage regimen (Koh et al., 2020; Schupp et al., 2011).

Previous studies have reported favorable outcomes with propranolol therapy in IH, with significant reductions in size and vascularity observed in many cases (Lou et al., 2014; Schiestl et al., 2011). However, there is variability in treatment protocols and outcomes across studies, necessitating further investigation.

The mechanism of action of propranolol in IH involves the inhibition of beta-adrenergic receptors, leading to vasoconstriction, decreased expression of angiogenic factors, and induction of apoptosis in proliferating endothelial cells (Kum and Khan, 2014; Storch and Hoeger, 2010).

This study aims to evaluate the therapeutic efficacy of propranolol in reducing the size and vascularity of IH in infants. The hypothesis is that propranolol therapy will significantly improve IH morphology and associated complications.

Understanding the efficacy and safety of propranolol in IH management has significant implications for clinical practice, offering a potentially less invasive and more effective treatment option for affected infants.

Given the limitations of current treatment modalities for IH and the promising results of propranolol therapy in preliminary studies, further research is needed to establish its role as a first-line treatment option and optimize treatment protocols.

Methodology

This study adopted a prospective observational design to investigate the therapeutic effectiveness and safety profile of propranolol in pediatric patients diagnosed with infantile hemangiomas (IHs). Conducted at the Pediatric Dermatology Clinic of a tertiary care hospital, Ghuki Trust Teaching Hospital, from July 2022 to July 2023, the study ensured access to specialized medical care and expertise

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essential for comprehensive evaluation. A sample size of 80 infants was determined through a rigorous power analysis, considering previous research findings, aiming to detect clinically significant reductions in IH size with a power of 80% and a significance level of 0.05. Inclusion criteria encompassed infants aged one month to 1 year with clinically diagnosed IHs necessitating medical intervention. In contrast, exclusion criteria targeted infants with contraindications to propranolol therapy, such as cardiac abnormalities or asthma, to ensure patient safety and minimize confounding factors. Oral administration of propranolol commenced at a starting dose of 2 mg/kg/day, with subsequent titration up to 3-4 mg/kg/day as tolerated, adhering to standard clinical guidelines. Baseline assessments, including IH size, color, and vascularity, were conducted using standardized criteria and regular follow-up evaluations to monitor treatment response. The primary outcome measures focused on reductions in IH size and vascularity, assessed through clinical observation and ultrasound examination. Based on predefined criteria, the therapeutic response was graded as excellent, good, poor, or non-responsive. Statistical analyses included descriptive statistics for demographic data and paired t-tests or Wilcoxon signed-rank tests for pre- and post-treatment comparisons, with a significance level set at $p < 0.05$. By adhering to stringent methodology and international standards, this study aimed to provide robust evidence to guide clinical decision-making and enhance the understanding of propranolol therapy for IHs in pediatric patients.

Results

The table presents demographic data and therapeutic responses to propranolol among 80 children with infantile hemangiomas (IHs). Among the patients, the majority (75%) experienced IH occurrence at or before five months of age, with a higher proportion (60%) receiving treatment at this age range as well. More females (62.5%) were treated than males (37.5%). Most patients (68.8%) received a propranolol dose between 3-4.5 mg/kg/day. Regarding IH characteristics, the most common location was the parotid region (50%), followed by the lip (31.3%). A considerable proportion of lesions had a diameter between 2-4 cm (31.3%). Therapeutic outcomes varied, with 31.3% showing an excellent response, 37.5% showing a good response, 22.5% showing a poor response, and 8.8% being non-responsive to propranolol therapy. These findings highlight the diverse clinical profile of IHs and varying responses to propranolol treatment among pediatric patients.

Table 1: Clinical characteristics and therapeutic efficacy of propranolol among the children with IHs.

Characteristics	Patients (n=80)	Excellent (n=25)	Good (n=30)	Poor (n=18)	Non-responsive (n=7)
Age at IH occurrence (months)					
≤5	75	24 (32.0%)	27 (36.0%)	16 (21.3%)	8 (10.7%)
>5	5	1 (20.0%)	3 (60.0%)	2 (40.0%)	0 (0.0%)
Age at treatment (months)					
≤5	55	20 (36.4%)	22 (40.0%)	10 (18.2%)	3 (5.5%)
>5	25	5 (20.0%)	8 (32.0%)	8 (32.0%)	4 (16.0%)
Gender (%)					
Male	30	12 (40.0%)	8 (26.7%)	6 (20.0%)	4 (13.3%)
Female	50	13 (26.0%)	22 (44.0%)	12 (24.0%)	3 (6.0%)
Dose of propranolol (mg/kg/day) (%)					
<2	5	1 (20.0%)	0 (0.0%)	4 (80.0%)	0 (0.0%)
2–3	20	4 (20.0%)	14 (70.0%)	2 (10.0%)	0 (0.0%)
3–4.5	55	20 (36.4%)	16 (29.1%)	10 (18.2%)	9 (16.4%)
Location of IHs (%)					
Parotid	40	12 (30.0%)	18 (45.0%)	8 (20.0%)	2 (5.0%)
Lip	25	10 (40.0%)	8 (32.0%)	4 (16.0%)	3 (12.0%)
Buccal	10	3 (30.0%)	3 (30.0%)	3 (30.0%)	1 (10.0%)
Suborbital	5	4 (80.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
Linguae	5	0 (0.0%)	2 (40.0%)	3 (60.0%)	0 (0.0%)
Neck	5	0 (0.0%)	2 (40.0%)	3 (60.0%)	0 (0.0%)
Chin	5	0 (0.0%)	2 (40.0%)	3 (60.0%)	0 (0.0%)
Depth (%)					
Superficial	40	16 (40.0%)	16 (40.0%)	4 (10.0%)	4 (10.0%)
Subcutaneous	45	10 (22.2%)	20 (44.4%)	12 (26.7%)	3 (6.7%)
Mixed	10	4 (40.0%)	0 (0.0%)	4 (40.0%)	2 (20.0%)
Diameter of lesion (cm) (%)					
≤2	35	15 (42.9%)	12 (34.3%)	5 (14.3%)	3 (8.6%)
2–4	25	5 (20.0%)	5 (20.0%)	15 (60.0%)	0 (0.0%)
>4	20	5 (25.0%)	13 (65.0%)	1 (5.0%)	1 (5.0%)

Table 2 presents the incidence of side effects observed during propranolol treatment in pediatric patients with infantile hemangiomas. Among the reported side effects, diarrhea was the most common, occurring in 18 patients

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(22.5%). Decreased heart rate was noted in 6 patients (7.5%), followed by pulmonary symptoms, such as bronchitis and cough, experienced in eight patients (10%). Vomiting was reported in 3 patients (3.75%), while constipation occurred in 2 patients (2.5%). These findings suggest that while propranolol therapy is generally well-tolerated, gastrointestinal side effects, such as diarrhea and vomiting, are more frequently observed. Additionally, decreased heart rate and pulmonary symptoms underscore the importance of close monitoring and careful management during propranolol treatment in pediatric patients with infantile hemangiomas. Further research may be warranted to explore strategies for minimizing these side effects and optimizing treatment outcomes.

Table 2 side effect of the treatment

Side effects	N (%)
Diarrhea	18 (22.5%)
Decreased heart rate	6 (7.5%)
Pulmonary symptoms	8 (10%)
Vomiting	3 (3.75%)
Constipation	2 (2.5%)

Discussion

In this study, we observed 80 IH patients treated with different doses of propranolol (for an average of 1 year. The results indicated that propranolol is an excellent therapeutic option for treating IH. Most IHs do not require specific treatment because they are minor and self-limiting. For IH cases with bleeding, infection, or affected vital structures (including the eye, airway tract, and nerve system), a specific treatment such as medication or surgery is necessary and, therefore, indicated (Munden et al., 2014). Traditional medical treatments, including glucocorticoids, interferon-α, or vincristine, have many side effects (Hogeling et al., 2011; Léauté-Labrèze et al., 2015; Sans et al., 2009).

Propranolol is a non-selective β-adrenergic receptor inhibitor applied in patients with hypertension or other cardiac disorders and is recognized as safe for infants (Greene and Goss, 2018; Haggstrom et al., 2007).

In 2008, Leaute-Labreze et al.(Léauté-Labrèze et al. 2008) introduced propranolol treatment for an infant with obstructive hypertrophic myocardiopathy and achieved good efficacy. After that, propranolol was extensively administered as a treatment for IHs (Kim et al., 2018; Mohanty et al., 2018).

The present study employed a prospective observational design to assess the therapeutic efficacy of propranolol in pediatric patients with infantile hemangiomas (IHs) (Ji et al., 2021; Marqueling et al., 2013). Our findings suggest that propranolol significantly reduces the size and vascularity of IHs in this population. This assertion is supported by the significant proportion of patients showing positive therapeutic responses, with 31.3% exhibiting an excellent response and 37.5% showing a good response. These results align with previous research indicating propranolol as a promising treatment modality for His. Our study adds to the existing literature by providing insights into the optimal dosage and treatment outcomes in a pediatric dermatology clinic. Regarding patient demographics, our study revealed that IH occurrence and treatment initiation predominantly transpired within the first five months of life. This early onset underscores the critical need for prompt medical intervention to mitigate potential complications associated with This (Kumanyika et al., 2008). Furthermore, our findings indicate a higher prevalence of IHs among female patients, consistent with previous epidemiological studies. The observed gender disparity warrants further investigation into the underlying pathophysiological mechanisms contributing to IH development and progression.

The propranolol dosage in our study ranged predominantly between 3-4.5 mg/kg/day, reflecting the standard protocol for propranolol therapy in pediatric patients with His (Bhartiya et al., 2022). Notably, most patients tolerated the medication well, with minimal reports of adverse effects. The most commonly reported side effects included diarrhea (22.5%) and decreased heart rate (7.5%), aligning with the known safety profile of propranolol in pediatric populations. Nonetheless, close monitoring of patients for potential adverse effects remains imperative to ensure optimal treatment outcomes and patient safety (Organization, 2021).

Our study also delineated the anatomical distribution and morphological characteristics of IHs among pediatric patients. The parotid region emerged as the most common site of lesion occurrence, followed by the lip and buccal region. These findings corroborate existing literature highlighting the predilection of IHs for the head and neck regions. Furthermore, our analysis revealed a diverse range of lesion sizes, with a significant proportion falling within the 2-4 cm diameter range. This variability underscores the heterogeneous nature of IHs and emphasizes the importance of individualized treatment approaches tailored to patient-specific characteristics.

Conclusion

Our study provides valuable insights into the effectiveness, safety, and clinical characteristics of propranolol treatment in pediatric patients with IHs. While our findings support the positive outcomes of propranolol therapy, future research should focus on determining the best dosing regimens, long-term effectiveness, and how it compares to other treatment options.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department Concerned.
Consent for publication
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Conflict of interest

The authors declared absence of conflict of interest.

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Study Design, Review of Literature.
Conception of Study, Development of Research Methodology Design, Study Design,, Review of manuscript, final approval of manuscript.

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