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Original Research Article

Oral Atenolol versus Propranolol in the Treatment of Infantile Hemangioma

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Abstract: *Infantile hemangiomas (IH) are the most common benign vascular tumors of infancy. Propranolol has been established as the first-line therapy; however, its adverse effects have prompted the search for safer alternatives. Atenolol, a selective β-1 blocker, has been suggested to offer similar efficacy with fewer side effects. This study compared the efficacy and safety of propranolol and atenolol in treating problematic IHs in Pakistani infants.* ***Objective:*** *To evaluate and compare the therapeutic efficacy and safety profiles of oral propranolol and atenolol in infants with IH.* ***Methods:*** *A randomized controlled trial was conducted at the Department of Pediatric Surgery, Sheikh Zayed Hospital, Rahim Yar Khan, from December 2024 to May 2025. A total of 120 infants with problematic IHs were randomly assigned to propranolol (n=60) or atenolol (n=60). Propranolol was initiated at 1 mg/kg/day in two divided doses and subsequently increased to 2 mg/kg/day. Atenolol was started at 0.5 mg/kg/day once daily and subsequently increased to 1 mg/kg/day. Treatment duration was six months. The primary outcome was complete/near-complete involution (PGA-5: ≥90% improvement). Secondary outcomes included time to PGA-5 and incidence of adverse events. Data were analyzed using SPSS v25, employing chi-square and t-tests, with $p < 0.05$ considered significant.* ***Results:*** *Of the 120 infants (mean age 5.2 ± 2.1 months; 56.7% females), 70% in the propranolol group and 63.3% in the atenolol group achieved PGA-5 (p=0.41). The mean time to PGA-5 was 14.2 ± 3.5 weeks for propranolol and 15.0 ± 3.7 weeks for atenolol (p=0.23). Adverse events were significantly higher in the propranolol group (18.3%) compared with the atenolol group (6.7%) (p = 0.048). Most adverse events were mild and manageable, with no life-threatening complications.* ***Conclusion:*** *Both propranolol and atenolol were effective for treating infantile hemangiomas. While propranolol showed slightly higher rates of complete involution and faster response, atenolol demonstrated a safer profile with fewer adverse effects. Atenolol may serve as a viable alternative for infants at risk of propranolol-related complications.*

Keywords: Infantile Hemangioma, Atenolol, Propranolol, β-Blockers, Treatment Outcome

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Introduction

Infantile hemangiomas (IH) are the most common benign tumors arising in infancy, with an approximate prevalence of 3-10% in infants, predominantly affecting female patients and those with low birth weights (1,2). Characterized by a phase of rapid proliferation followed by spontaneous involution, IHs often require medical intervention, particularly when they pose risks to vital structures or aesthetic concerns arise. Propranolol, a nonselective β-blocker, has been established as the first-line treatment due to its effectiveness in inducing rapid regression of these vascular anomalies (3,4). However, propranolol's potential adverse effects, including bradycardia, hypoglycemia, and bronchospasm, have sparked interest in alternative treatments that maintain efficacy while minimizing risk (5).

Emerging data have favorably positioned atenolol, a selective β-1 blocker, as a potential alternative. Recent investigations suggest that atenolol can achieve comparable therapeutic outcomes to propranolol in controlling hemangioma proliferation, with an improved safety profile (4,6). For instance, studies indicate similar efficacy rates, with atenolol successfully halting progression in approximately 92.5% of affected infants, while reports indicate fewer occurrences of serious adverse effects (7,8). This may be attributed to atenolol's hydrophilic nature, which limits its penetration into the central nervous system, theoretically reducing neuropsychiatric side effects (5).

Preliminary findings from comparative trials advocate for a reevaluation of treatment protocols for infantile hemangiomas. A systematic review specifically highlighted atenolol's noninferiority in therapeutic outcomes compared to propranolol, noting that both agents effectively reduce the hemangioma activity score while managing adverse events more favorably in the atenolol group (5). Additionally, systematic assessments have uncovered the potential of atenolol to serve as an alternative option for patients intolerant to propranolol or those necessitating a safer treatment modality (9,10).

The rationale for researching the efficacy and safety of oral atenolol versus propranolol in treating infantile hemangiomas within the context of the Pakistani population is particularly compelling. In Pakistan, healthcare access disparities and varying patient demographics profoundly influence treatment modalities. The lower incidence of adverse side effects with atenolol may foster adherence to treatment protocols in a population previously reluctant to initiate therapy due to concerns surrounding propranolol's side effects. Moreover, identifying effective alternatives could significantly improve health outcomes in children with vascular anomalies, addressing both clinical efficacy and augmenting patient safety (11). As such, the findings from this comparative study could lend support to reforming treatment guidelines tailored for pediatric vascular anomalies in Pakistan, potentially leading to improved health initiatives targeting infantile hemangiomas.

Methodology

The present study was designed as a randomized controlled trial conducted in the Department of Paediatric Surgery at Sheikh Zayed Hospital, Rahim Yar Khan, Pakistan, from December 7, 2024, to May 7, 2025. The study aimed to compare the effectiveness and safety of propranolol and atenolol in managing infantile hemangiomas in infants under one year of age. A total of 120 infants were recruited through non-probability consecutive sampling, with 60 infants allocated to each treatment group. The sample size was calculated using the known effectiveness of propranolol at 70% and atenolol at 45% from previous studies, with a power of 80% and a type I error of 0.05.

Participants in the study included infants with problematic hemangiomas, defined as potentially disfiguring lesions located on cosmetically or functionally sensitive areas, such as the face, glabella, nasal tip, eyelids, limbs, and genitalia, as well as those with ulcerated or segmental hemangiomas. Children with uncomplicated progressive hemangiomas with unpredictable growth patterns were also included. Exclusion criteria comprised infants with congenital heart disease, arrhythmias, bronchial obstructive disorders, premature birth with corrected gestational age below 40 weeks, type 1 diabetes mellitus, liver failure, visceral hemangiomas, PHACES syndrome, and abdominal tumors associated with hypertension, such as neuroblastoma.

Upon enrollment, each infant underwent a detailed baseline clinical examination, which included weight, height, heart rate, respiratory rate, oxygen saturation, and random blood sugar levels. Electrocardiography was performed to rule out underlying arrhythmias, and ophthalmological evaluation was carried out in cases involving periorbital lesions. Standardized clinical photographs of the hemangiomas were obtained at baseline and during each subsequent follow-up visit, using a digital camera positioned at a fixed distance from the subject. All patients were admitted for 48 hours at the initiation of treatment to monitor cardiovascular and metabolic parameters, including blood pressure, pulse, oxygen saturation, blood glucose, and respiratory status, during dose escalation.

Participants were randomly assigned to two groups using a computer-generated block randomization sequence. Group A received oral propranolol, starting at 1 mg/kg/day in two divided doses, which was increased to 2 mg/kg/day after 24 hours if well tolerated. Group B received oral atenolol, starting at 0.5 mg/kg/day once daily, and the dose was titrated to 1 mg/kg/day after 24 hours. Both treatments were continued for six months. The prescribing physicians and parents were aware of the treatment allocation; however, the assessment of outcomes was performed by an independent physician who was blinded to the group assignment.

Treatment response was measured using the Physician Global Assessment (PGA) grading scale, which evaluates the reduction in thickness, color, and surface area of hemangiomas. Scores ranged from 0 (no change or regrowth) to 5 (>90% improvement or complete clinical involution). PGA assessments were performed monthly for up to six months using clinical examination, ultrasound evaluation, and serial photographs. The primary efficacy outcome was the proportion of patients achieving PGA-5 by the end of treatment. Secondary outcomes included the mean time taken to reach PGA-5 and the degree of partial improvement recorded at intermediate PGA levels.

Safety assessments were conducted every month and included growth chart monitoring, cardiovascular and respiratory examinations, and screening for adverse events. Hypoglycemia was assessed through random blood sugar monitoring at each visit, with levels below 80 mg/dl considered significant. Hypotension was defined as systolic blood pressure below 70 mmHg, measured using a mercury sphygmomanometer. Sleep disturbances were evaluated through a structured sleep disturbance scale completed by caregivers. More serious adverse events, including arrhythmias and respiratory distress, were monitored using electrocardiography and clinical observation, and any participant experiencing severe adverse effects was withdrawn from the study and reported to the safety committee.

Data were entered and analyzed using SPSS version 25.0. Continuous variables, such as age, weight, and time to PGA-5, were expressed as mean and standard deviation or as median with interquartile range, depending on distribution. Categorical variables, such as gender, type of hemangioma, stage, and treatment response, were presented as frequencies and percentages. Group comparisons were performed using the Chi-square test or Fisher's exact test for categorical outcomes, and the independent t-test or Mann–Whitney U test for continuous outcomes, as appropriate. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 120 infants with infantile hemangiomas were included and randomly assigned equally to the Propranolol group (n = 60) and the Atenolol group (n = 60). The overall mean age at enrollment was 5.2 ± 2.1 months (range: 1–11 months). Males accounted for 52 (43.3%), while females accounted for 68 (56.7%), reflecting a slightly higher prevalence in female infants. The distribution of baseline demographic characteristics between the two groups was statistically comparable (p>0.05). (Table 1)

At the end of 6 months, the proportion of infants achieving PGA-5 (>90% improvement/complete clinical involution) was higher in the propranolol group (70%) compared with the atenolol group (63.3%). However, the difference was not statistically significant (p = 0.41). (Table 2).

Table 1. Demographic profile of study participants (n=120)

Variable	Propranolol Group (n=60)	Atenolol Group (n=60)	Total (n=120)	p-value
Mean Age (months ± SD)	5.1 ± 2.2	5.3 ± 2.0	5.2 ± 2.1	0.64
Gender – Male, n (%)	26 (43.3%)	26 (43.3%)	52 (43.3%)	1.00
Gender – Female, n (%)	34 (56.7%)	34 (56.7%)	68 (56.7%)	
Mean Weight (kg ± SD)	6.8 ± 1.5	6.7 ± 1.4	6.75 ± 1.4	0.78
Type of IH – Segmental	14 (23.3%)	12 (20.0%)	26 (21.7%)	0.65
Type of IH – Focal	46 (76.7%)	48 (80.0%)	94 (78.3%)	

The mean time to achieve PGA-5 was slightly shorter in the propranolol group (14.2 ± 3.5 weeks) compared to the atenolol group (15.0 ± 3.7 weeks), but the difference was statistically non-significant (p=0.23). (Table 3) Both groups showed good tolerability. Adverse effects were mild and manageable, with no life-threatening complications or treatment discontinuations. (Table 4)

Table 2. Treatment efficacy outcomes at 6 months

Outcome (PGA Score)	Propranolol Group (n=60)	Atenolol Group (n=60)	p-value
PGA 5 (≥90% improvement)	42 (70.0%)	38 (63.3%)	0.41
PGA 4 (75–90% improvement)	10 (16.7%)	12 (20.0%)	
PGA 3 (50–74% improvement)	6 (10.0%)	7 (11.7%)	
PGA 2 or less (<50% change)	2 (3.3%)	3 (5.0%)	

Table 3. Time to achieve PGA-5

Group	Mean Time (weeks ± SD)	p-value
Propranolol (n=42)	14.2 ± 3.5	
Atenolol (n=38)	15.0 ± 3.7	0.23

Table 4. Adverse events during treatment

Adverse Event	Propranolol Group (n=60)	Atenolol Group (n=60)	p-value
Hypoglycemia	3 (5.0%)	1 (1.7%)	0.31
Hypotension	2 (3.3%)	1 (1.7%)	0.56
Sleep disturbances	5 (8.3%)	2 (3.3%)	0.24
Respiratory distress	1 (1.7%)	0 (0%)	0.31
Any adverse event	11 (18.3%)	4 (6.7%)	0.048*

*Statistically significant difference in favor of atenolol.

Both propranolol and atenolol demonstrated high efficacy in the management of infantile hemangiomas in Pakistani infants. While propranolol showed a slightly higher rate of complete clinical involution and shorter mean time to achieve PGA-5, atenolol was associated with a lower incidence of adverse events, particularly hypoglycemia and sleep disturbances. Overall, both medications appear effective, but atenolol may offer a safer alternative in infants prone to β2-related side effects.

Discussion

In this discussion, we analyze the findings of our study, comparing the efficacy and safety of oral propranolol and atenolol in the treatment of infantile hemangiomas (IH) over six months, and correlate these findings with current literature in the field.

Firstly, the demographic profile of infants in our study indicates a mean age of 5.2 months, with a gender distribution favoring females (56.7%). This reflects existing literature that reports a higher prevalence of IH in females (Gatts et al., 12, 13). Consistent with our findings, a study by Ji et al. noted a similar demographic breakdown, corroborating that female infants typically present with these benign vascular tumors more frequently than males (14).

In assessing treatment outcomes, our results indicated that 70% of infants in the propranolol group achieved ≥90% improvement, compared to 63.3% in the atenolol group, although the difference was statistically insignificant ($p = 0.41$). This finding aligns with prior systematic reviews, which indicate that while propranolol remains the gold standard treatment, exhibiting superior efficacy, atenolol can be a viable alternative, demonstrating comparable effectiveness in causing clinical involution in some studies (15, 16). A systematic review highlighted that while slight variations in efficacy were noted, patients reported similar outcomes regarding hemangioma resolution (17). Hence, our findings suggest that while propranolol may still be favored for first-line therapy, atenolol's efficacy is noteworthy and merits consideration, particularly in cases where the side effects of propranolol are concerning.

Moreover, we recorded a mean time to achieve ≥90% improvement of 14.2 weeks for propranolol and 15.0 weeks for atenolol, indicating a trend favoring the former. However, this difference was not statistically significant ($p = 0.23$). This aligns with findings from Liu et al. that reported similar timelines for achieving adequate hemangioma resolution between the two β-blockers, reinforcing the idea that clinical outcomes may vary slightly but generally follow a common foundation in both treatment regimens (18).

Regarding adverse events, both treatment groups exhibited good tolerability; however, the propranolol group reported higher rates of adverse effects such as hypoglycemia and sleep disturbances. Our study revealed that 18.3% of the propranolol group experienced any adverse event, compared to 6.7% in the atenolol group—a statistically significant difference ($p = 0.048$). This finding is consistent with those of Gumina and Yan, who emphasized the reduced incidence of adverse effects, particularly sleep disturbances, associated with atenolol as a significant benefit over propranolol (19). Furthermore, studies have indicated that atenolol's selective β-1 blocking nature leads to a more favorable safety profile (20).

Thus, our study corroborates the existing literature suggesting that while propranolol remains effective as the standard treatment for infantile hemangiomas, atenolol presents as a safer alternative in specific patient populations, especially those at risk for adverse drug reactions. These findings are particularly pertinent in the Pakistani context, where healthcare accessibility and concerns about side effects could influence treatment adherence and family decisions regarding therapy. Future research within this demographic could further clarify the efficacy and safety profiles of atenolol compared to propranolol, potentially shaping clinical guidelines for the management of infantile hemangiomas in similar settings.

This study was conducted at a single center with a relatively small sample size, which may limit the generalizability of findings. The six-month study duration restricted the assessment of long-term recurrence or relapse. Additionally, the open-label design may have introduced observer bias despite blinded outcome assessment.

Conclusion

Both propranolol and atenolol proved effective in treating infantile hemangiomas, with propranolol showing a slightly higher rate of complete involution and a faster response. However, the difference was not statistically significant. Atenolol, however, demonstrated a significantly better safety profile, with fewer adverse events, making it a safer alternative in infants at risk of propranolol-related side effects. These findings suggest that while propranolol remains the standard first-line therapy, atenolol can be considered an effective and safer option in selected patient populations. Larger multicenter studies with longer follow-up are recommended to validate these results and guide future treatment protocols.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-24)

Consent for publication

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The authors declared the absence of a conflict of interest.

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