

Comparison between topical timolol and oral propranolol for the treatment of superficial infantile hemangioma

©Tasniya Tarannum^{*1}, ©Abdullah Al Faisal², ©Kabirul Islam³

¹Department of Pediatric Surgery, Dhaka Medical College & Hospital, Dhaka, Bangladesh

²Department of Pediatric Surgery, Shaheed Suhrawardy Medical College & Hospital, Dhaka, Bangladesh

³Department of Pediatric Surgery, Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh

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*Corresponding Author: Tasniya Tarannum, drtasniya@gmail.com

ABSTRACT

Aims: Infantile hemangiomas are the most common benign paediatric vascular tumors. In spite of good results in the management of infantile hemangioma with oral propranolol, it may cause systemic side effects in the long run. The use of topical timolol can minimize systemic side effects, and it is easy to apply in the paediatric age group. This study aimed to evaluate a safer, more effective, and more easily applicable drug for the treatment of infantile hemangioma.

Methods: It was a prospective comparative interventional study that was conducted in Dhaka Shishu (Children) Hospital from May 2018 to September 2020. A total of 89 patients with superficial infantile hemangioma were selected purposively for this study who completed 6 months of follow-up after the initial treatment. They were randomly assigned to the topical timolol group (group A=44) and oral propranolol group (group B=45). Regression of size, change of color, adverse effects, and parent satisfaction regarding the mode of administration of drugs were statistically compared between the two groups.

Results: The age range of the patients was 1 to 12 months, where the majority of the patients were female. Most of the lesions were in the head and neck region in both groups. In group A 72.7% patients showed excellent response in size regression, compared to group B 68.9% patients, which showed no statistically significant difference. In group A 75% had an excellent color regression, compared to group B 68.9% ($p=0.0784$). Regarding adverse effects in group A, only 3 children (6.8%) developed adverse effects compared to 12 (26.7%) in group B which was statistically significant ($p=0.021$). In group A (97.7%) parents were more satisfied than in group B (80.0%) regarding the mode of administration of two drugs, which was statistically significant ($p=0.015$).

Conclusion: Use of topical timolol turns out to be a good choice for the treatment of patients with superficial infantile hemangioma. It has the same efficacy, but the adverse effect is comparatively less than oral propranolol. Applying topical timolol is easier for the parents than oral propranolol.

Keywords: Hemangioma, capillary, propranolol, timolol

INTRODUCTION

Infantile hemangiomas (IHs) are the most common benign vascular tumors in infancy, with an incidence of about 4-5%, higher in females and premature infants, and lower in dark-skinned babies.^{1,2} According to the International Society for the Study of Vascular Anomalies (ISSVA), benign cutaneous vascular tumors include IH, congenital hemangioma, tufted angioma, pyogenic granuloma, and others.³ IHs usually appear shortly after birth and are characterized by rapid proliferation during the first year of life, followed by gradual involution.⁴ Most lesions are solitary (80%) and commonly involve the head and neck (60%), trunk (25%), and limbs (15%). About 20% of patients may present with multiple

lesions.¹ The life cycle includes proliferative, involuting, and involuted phases.⁵ Although many IHs regress spontaneously, some can cause complications such as hemorrhage, ulceration, disfigurement, or functional impairment requiring early intervention.^{6,7} Historically, treatment options included corticosteroids, vincristine, interferon- α , laser therapy, or surgery, but these were often associated with significant adverse effects.⁸ In 2008, propranolol—a non-selective lipophilic β -blocker—was serendipitously found to induce hemangioma regression.⁹ Subsequent studies confirmed its high efficacy,¹⁰⁻¹³ including research conducted locally.^{14,15} However, systemic propranolol may cross the blood-brain



barrier, raising concerns about potential adverse effects such as bradycardia, hypotension, hypoglycemia, bronchospasm, and possible neurocognitive effects.¹⁶⁻¹⁹ Topical timolol, another non-selective β -blocker long used for pediatric glaucoma,²⁰ was first reported effective against superficial IHs in 2010.²¹ A large series later demonstrated its efficacy and safety without cardiovascular adverse effects.²² To minimize systemic risks of propranolol, topical timolol has gained increasing acceptance for treating superficial IHs.^{6,23} This study aims to evaluate the efficacy, safety, and parental satisfaction of topical timolol in treating IHs compared with oral propranolol under continuous clinical monitoring.

METHODS

Ethics

The study protocol was reviewed and approved by the Ethical Review Committee of the Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital (Date: 05.03.2018, Decision No: BICH-ERC-11-01-2018). Written informed consent was obtained from the parents or legal guardians of all participating infants prior to enrollment, following a detailed explanation of the study objectives, interventions, and potential risks.

Study Design

This prospective comparative interventional study was conducted in the Division of Paediatric Surgery, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital, Dhaka, over two and a half years (May 2018-September 2020).

Study Population

Patients attending the surgical outpatient department with clinically diagnosed superficial IH during the study period were enrolled using a purposive sampling technique until the desired sample size was achieved.

Selection Criteria

Inclusion: All patients with superficial IH in the proliferative phase.

Exclusion: Patients with previously treated or infected hemangiomas, life-threatening conditions, and cardiovascular disorders contraindicate propranolol use.

Sample Size and Randomization

Sample size was calculated using the formula:

$$n = [(P_1(1-P_1) + P_2(1-P_2)) / (P_1 - P_2)^2] \times (Z\alpha + Z\beta)^2,$$

where $P_1=0.03$, $P_2=0.22$, $Z\alpha=1.96$, and $Z\beta=0.85$, yielding 44 per group. Considering a 10% dropout rate, 50 patients were taken per group (total 100). Simple randomization was utilized to allocate patients into group A (topical timolol) and group B (oral propranolol). Allocation concealment was maintained using sequentially numbered, opaque, sealed envelopes drawn by an independent coordinator.

Data Collection and Measurements

Information was obtained from parents via interview and physical examination. Lesion size was measured with a

soft tape, and color change was analyzed digitally (Adobe Photoshop) using serial photographs taken with a 13MP digital camera. To ensure objectivity, these clinical and photographic evaluations were independently confirmed by two physicians who were blinded to the group allocation. Vital parameters (heart rate, blood pressure, and random blood sugar) were monitored before and after drug administration at each follow-up. Adverse effects and parental satisfaction were recorded.

Intervention

Group A received 0.5% topical timolol maleate solution (2–4 drops twice daily) and group B received oral propranolol (1–3 mg/kg/day in two doses). Dosage was titrated based on clinical response and tolerance.

Follow-up and Outcome Measures

Patients were followed at 2 weeks, 1, 2, 3, 4, 5, and 6 months. Regression of size and color was calculated as a percentage of pretreatment values. Responses were graded as excellent (80–100%), good (50–80%), fair (25–50%), or poor (<25%).

Statistical Analysis

Data were analyzed using SPSS v25. Continuous variables were assessed by Student's t-test and categorical variables by Chi-square/Fisher's exact test, with $p<0.05$ considered significant.

RESULTS

A total of 100 infants aged between 1 to 12 months were included, and 89 completed the six-month follow-up (44 in group A: timolol, and 45 in group B: propranolol). The mean age was 5.39 ± 2.94 months in group A and 6.38 ± 3.17 months in group B, with no significant difference ($p=0.134$) (Table 1). The majority were term babies (95.5% vs 93.3%) and females (61.4% vs 68.9%), showing no statistical difference between groups (Table 2, 3). A positive family history of hemangioma was noted in 4.5% of group A and 8.9% of group B ($p>0.05$) (Table 4).

Table 1. Comparison of patients by age

Age (months)	Group A (n=44)	Group B (n=45)	p value
Mean $\pm$ SD	5.39 $\pm$ 2.94	6.38 $\pm$ 3.17	0.134
Range	2–12	1–12	

SD: Standard deviation

Table 2. Comparison by gestational age

Gestational age	Group A n (%)	Group B n (%)	p value
Preterm	2 (4.5)	3 (6.7)	1.000
Term	42 (95.5)	42 (93.3)	

Table 3. Comparison by gender

Gender	Group A n (%)	Group B n (%)	p value
Male	17 (38.6)	14 (31.1)	0.509
Female	27 (61.4)	31 (68.9)	

Table 4. Family history of hemangioma

Family history	Group A n (%)	Group B n (%)	p value
Absent	42 (95.5)	41 (91.1)	0.677
Present	2 (4.5)	4 (8.9)	

Lesion distribution was similar in both groups, predominantly affecting the head and neck region (65.9% in group A and 77.8% in group B), followed by lesions on the chest wall, abdominal wall, and extremities.

The mean pretreatment size of lesions was $4.43 \pm 1.78 \text{ cm}^2$ in group A and $5.09 \pm 1.52 \text{ cm}^2$ in group B ($p=0.062$). After six months, post-treatment size significantly reduced in both groups ($0.74 \pm 0.79 \text{ cm}^2$ and $0.91 \pm 0.87 \text{ cm}^2$ respectively; $p<0.001$ within each group). However, intergroup comparison showed no significant difference in mean size reduction ($p=0.333$) (Table 5).

Table 5. Size regression before and after treatment

Parameter	Group A	Group B	p value
Pre-treatment size (cm^2)	4.43 ± 1.78	5.09 ± 1.52	0.062
Post-treatment size (cm^2)	0.74 ± 0.79	0.91 ± 0.87	0.333

Regarding categorical response, 72.7% of group A and 68.9% of group B achieved excellent size regression, while 25.0% and 28.9% had good responses respectively ($p=0.905$) (Table 6). For color regression, excellent response was observed in 75.0% of group A and 68.9% of group B ($p=0.0784$), with no significant difference between groups (Table 7). Complete regression occurred in 29.6% of group A and 17.8% of group B ($p=0.220$) (Table 8). Most complete regressions occurred within 4–5 months of treatment (Figures 1-12).

Table 6. Regression of size between two groups

Response	Group A n (%)	Group B n (%)	p value
Excellent	32 (72.7)	31 (68.9)	0.905
Good	11 (25.0)	13 (28.9)	
Fair	1 (2.3)	1 (2.2)	

Table 7. Regression of color between two groups

Response	Group A n (%)	Group B n (%)	p value
Excellent	33 (75.0)	31 (68.9)	0.0784
Good	10 (22.7)	12 (26.7)	
Fair	1 (2.3)	2 (4.4)	

Table 8. Complete regression of lesions

Complete regression	Group A n (%)	Group B n (%)	p value
Occurred	13 (29.6)	8 (17.8)	0.220
Not occurred	31 (70.5)	37 (82.2)	

Adverse effects were significantly more frequent in the propranolol group (26.7%) than in the timolol group (6.8%) ($p=0.021$) (Table 9). In group A, 4.5% had local pruritus and 2.3% had sleep disturbance. In group B, bradycardia and

**Figure 1.** Pretreatment figure**Figure 2.** After 3 months of treatment with timolol**Figure 3.** After 6 months of treatment with timolol**Figure 4.** Pretreatment figure



Figure 5. After 2 months of treatment with timolol



Figure 9. After 6 months of treatment with propranolol



Figure 6. After 6 months of treatment with timolol



Figure 10. Pretreatment figure



Figure 7. Pretreatment figure



Figure 11. After 3 months of treatment with propranolol



Figure 8. After 3 months of treatment with propranolol



Figure 12. After 6 months of treatment with propranolol

hypoglycemia each occurred in 6.7%, hypotension in 4.4%, with minor cases of sleep disturbance and diarrhea (4.4% each).

Table 9. Comparison of adverse effects

Adverse effects	Group A n (%)	Group B n (%)	p value
Absent	41 (93.2)	33 (73.3)	0.021
Present	3 (6.8)	12 (26.7)	

Parental satisfaction regarding drug administration was notably higher in the timolol group (97.7%) than in the propranolol group (80.0%), which was statistically significant ($p=0.015$) (Table 10).

Table 10. Parents' satisfaction regarding drug administration

Satisfaction	Group A n (%)	Group B n (%)	p value
Satisfied	43 (97.7)	36 (80.0)	0.015
Not satisfied	1 (2.3)	9 (20.0)	

DISCUSSION

This prospective study compared the clinical outcomes of topical timolol and oral propranolol in 100 patients with superficial IHs, randomly divided into two groups. Six patients in group A and five in group B dropped out due to difficulty maintaining follow-up. Most lesions presented in the proliferative phase, which lasts until about 10–12 months of age. The mean age was 5.39 ± 2.94 months in group A and 6.38 ± 3.17 months in group B, showing no statistical difference, consistent with Wu et al.²⁴ Although previous studies suggest a higher incidence of IH in preterm infants,^{3,25} only 5.61% of our patients were preterm. This variance from the literature may be influenced by our specific clinical setting as a single-center study, regional variations in patient presentation, or potentially incomplete gestational records. Female predominance was observed in both groups—61.4% in group A and 68.9% in group B—similar to other reports.^{1,25} A positive family history was found in 6.7% of cases, comparable to Kabir.¹⁵ Hemangiomas were most common in the head and neck region—65.9% in group A and 77.8% in group B—likely due to the region's rich vascularity. Similar distributions were reported by Weibel et al.²⁶ and Yu et al.⁶ In group A, mean pre-treatment size was 4.43 ± 1.78 cm², reducing to 0.74 ± 0.79 cm² post-treatment. Topical timolol caused vasoconstriction and inhibited angiogenic growth factors, producing significant regression, as also reported by Weibel et al.²⁶ In group B, mean lesion size decreased from 5.09 ± 1.52 cm² to 0.91 ± 0.87 cm². Oral propranolol suppresses hemangioma proliferation by modulating endothelial cell activity and pericyte contractility.¹⁴ There was no significant difference in regression between groups, consistent with Wu et al.,²⁴ likely due to their similar β -blocking mechanisms. Excellent size regression ($\geq 80\%$) was observed in 72.7% of group A and 68.9% of group B. Variation in lesion size may explain the difference in individual responses. No significant difference between groups aligns with previous findings.²⁴ Color regression from dark red to lighter or normal skin tone occurred in 75% of group A and 68.9% of group B. Topical timolol caused vasoconstriction through nitric oxide inhibition, while propranolol reduced capillary perfusion via

β -adrenergic blockade. Our higher excellent regression rate compared with Wu et al.²⁷ may be due to different evaluation criteria. Complete regression of both size and color occurred in 29.6% of group A and 17.8% of group B, with no statistical significance. Most complete regressions were in small lesions after six months of therapy. The lower rate compared with Nagdeve and Saoji²⁸ may be due to our shorter follow-up duration. Adverse effects occurred in 6.8% of group A—mainly local pruritus and mild sleep disturbance—and 26.7% of group B, including bradycardia, hypotension, hypoglycemia, diarrhea, and sleep disturbance. Systemic absorption of propranolol explains its higher incidence of side effects.^{14,15} Adverse effects were significantly fewer in the topical group, matching Wu et al.²⁴ Parental satisfaction was significantly higher with topical timolol (97.7%) compared with oral propranolol (80.0%) because topical administration was easier and better tolerated. In our study, both topical timolol and oral propranolol are effective for superficial IH, showing comparable efficacy. However, topical timolol has a superior safety profile and higher parental satisfaction, making it a preferable first-line option for uncomplicated superficial lesions.

Recommendations

- Considering efficacy and safety, topical timolol could be the first line of treatment for superficial infantile hemangioma.
- A multi-center study with a large sample size and long follow-up is recommended.
- Future studies incorporating pharmacokinetic profiling and serum bioavailability assays are recommended to better elucidate the dose-response relationships and specific mechanistic differences between these topical and systemic therapies.

Limitations

- Long-term follow-up could not be possible.
- Depth of the hemangioma could not be measured.
- This analysis was done in a single center in Bangladesh, and the sample only represents a small fraction of patients with hemangioma.
- The absence of a comparative pharmacological analysis, including pharmacokinetics and serum bioavailability, limits our ability to explain the mechanistic differences between the evaluated drugs.

This study has certain limitations that should be acknowledged. First, conducting a direct pharmacological comparison between the two interventions is inherently challenging. While oral propranolol was administered using precise weight-based dosing (mg/kg/day), topical timolol was applied using a fixed drop count. Consequently, the exact volume applied and the degree of transdermal systemic absorption could not be quantified, limiting a strict dose-response analysis.



CONCLUSION

Topical timolol is as effective as oral propranolol for the treatment of superficial IH. It has fewer adverse effects and its mode of application is more satisfactory to parents compared to oral propranolol.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study protocol was reviewed and approved by the Ethical Review Committee of the Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital (Date: 05.03.2018, Decision No: BICH-ERC-11-01-2018).

Informed Consent

Informed consent was obtained from a parent or legal guardian. Where appropriate, age-adjusted assent was also obtained from the child. The inclusion of vulnerable populations in this study adhered to national and international ethical guidelines. Extra care was taken to ensure voluntary participation, understanding, and protection of participant dignity and autonomy.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

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Author Contributions

Concept: TT; Design: TT; Control: KI; Resources: TT, AAF; Materials: TT, AAF; Data Collection and/or Processing: TT, AAF; Analysis and/or Interpretation: TT, AAF; Literature Review: AAF; Writing the Article: TT, AAF; Critical Review: KI; Final Approval: TT, AAF, KI; Accountability: TT, AAF, KI.

REFERENCES

- Kulungowski AM, Fishman SJ. Vascular anomalies. In: Coran AG, Adzick NS, Krummel TM, Laberge J, Shamberger RC, Caldamone AA, eds. *Pediatric Surgery*. 7th ed. Elsevier; 2012.
- Chen TS, Eichenfield LF, Friedlander SF. Infantile hemangiomas: an update on pathogenesis and therapy. *Pediatrics*. 2013;131:99-108. doi:10.1542/peds.2012-1128
- Darrow DH, Greene AK, Mancini AJ, Nopper AJ. Diagnosis and management of infantile hemangioma. *Pediatrics*. 2015;136(4):e1060-e1104. doi:10.1542/peds.2015-2485
- Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. *Plast Reconstr Surg*. 1982;69:412-422. doi:10.1097/00006534-198203000-00002
- Frieden IJ, Haggstrom AN, Drolet BA, et al. Infantile hemangiomas: current knowledge, future directions. Proceedings of a research workshop on infantile hemangiomas, April 7-9, 2005, Bethesda, Maryland, USA. *Pediatr Dermatol*. 2005;22(5):383-406. doi:10.1111/j.1525-1470.2005.00102.x
- Yu L, Li S, Su B, et al. Treatment of superficial infantile hemangiomas with timolol: evaluation of short-term efficacy and safety in infants. *Exp Ther Med*. 2013;6(2):388-390. doi:10.3892/etm.2013.1176
- Drolet BA, Esterly NB, Frieden IJ. Hemangiomas in children. *N Engl J Med*. 1999;341(3):173-181. doi:10.1056/NEJM199907153410307
- Leonardi-Bee J, Batta K, O'Brien C, Bath-Hextall FJ. Interventions for infantile hemangiomas (strawberry birthmarks) of the skin. *Cochrane Database Syst Rev*. 2011;11(5): CD006545. doi:10.1002/14651858.CD006545.pub2
- Léauté-Labrèze C, Dumas de la Roque E, Hubiche T, Boralevi F, Thambo JB, Taieb A. Propranolol for severe hemangiomas of infancy. *N Engl J Med*. 2008;358(24):2649-2651. doi:10.1056/NEJMc0708819
- Lawley LP, Siegfried E, Todd JL. Propranolol treatment for hemangioma of infancy: risks and recommendations. *Pediatr Dermatol*. 2009;26(5):610-614. doi:10.1111/j.1525-1470.2009.00975.x
- Holmes WJ, Mishra A, Gorst C, Liew SH. Propranolol as first line treatment for infantile hemangiomas. *Plast Reconstr Surg*. 2010;125(1):420-421. doi:10.1097/PRS.0b013e3181c2a731
- Manunza F, Syed S, Laguda B, et al. Propranolol for complicated infantile hemangiomas: a case series of 30 infants. *Br J Dermatol*. 2010;162(2):466-468. doi:10.1111/j.1365-2133.2009.09597.x
- Hermans DJ, van Beynum IM, Schultze Kool LJ, van de Kerkhof PC, Wijnen MH, van der Vleuten CJ. Propranolol, a very promising treatment for ulceration in infantile hemangiomas: a study of 20 cases with matched historical controls. *J Am Acad Dermatol*. 2011;64(5):833-838. doi:10.1016/j.jaad.2011.01.025
- Haque MM, Ferdous KMN, Saha BK, Paul SK, Islam MK. Oral propranolol and prednisolone in the treatment of infantile hemangioma: a comparative study. *Chattagram Maa-O-Shishu Hosp Med Coll J*. 2014;13(1):26-31. doi:10.3329/cmshmcj.v13i1.19414
- Kabir KA. Treatment of infantile hemangioma with atenolol and propranolol [master's thesis]. University of Dhaka; 2016.
- Kroes MC, Strange BA, Dolan RJ. Beta-adrenergic blockade during memory retrieval in humans evokes a sustained reduction of declarative emotional memory enhancement. *J Neurosci*. 2010;30(11):3959-3963. doi:10.1523/JNEUROSCI.5469-09.2010
- Solman L, Murabit A, Gnarra M, Harper JI, Syed SB, Glover M. Propranolol for infantile hemangiomas: single centre experience of 250 cases and proposed therapeutic protocol. *Arch Dis Child*. 2014;99(12):1132-1136. doi:10.1136/archdischild-2014-306514
- Hoeger PH. Propranolol for infantile hemangiomas: certain chances, potential risks. *Br J Dermatol*. 2015;172(1):3-4. doi:10.1111/bjd.13535
- Langley A, Pope E. Propranolol and central nervous system function: potential implications for paediatric patients with infantile hemangiomas. *Br J Dermatol*. 2015;172(1):13-23. doi:10.1111/bjd.13379
- Plager DA, Whitson JT, Netland PA. Betaxolol hydrochloride ophthalmic suspension 0.25% and timolol gel-forming solution 0.25% and 0.5% in pediatric glaucoma: a randomized clinical trial. *J AAPOS*. 2009;13(4):384-390. doi:10.1016/j.jaapos.2009.04.017
- Guo S, Ni N. Topical treatment for capillary hemangioma of the eyelid using beta-blocker solution. *Arch Ophthalmol*. 2010;128(2):255-256. doi:10.1001/archophthalmol.2009.370
- Püttgen K, Lucky A, Adams D, et al. Topical timolol maleate treatment of infantile hemangiomas. *Pediatrics*. 2016;138(3):e20160355. doi:10.1542/peds.2016-0355
- Chan H, McKay C, Adams S, Wargon O. RCT of timolol maleate gel for superficial infantile hemangiomas in 5- to 24-week-olds. *Pediatrics*. 2013;131(6):e1739-e1747. doi:10.1542/peds.2012-3828
- Wu HW, Wang X, Zhang L, Zheng JW, Liu C, Wang YA. Topical timolol vs oral propranolol for the treatment of superficial infantile hemangiomas. *Front Oncol*. 2018;8:605. doi:10.3389/fonc.2018.00605
- Rialon KL, Fishman SJ. Vascular and lymphatic anomalies. In: Ashcraft's Pediatric Surgery. 6th ed. Elsevier; 2014.
- Weibel L, Barysch MJ, Scheer HS, et al. Topical timolol for infantile hemangiomas: evidence for efficacy and degree of systemic absorption. *Pediatr Dermatol*. 2016;33(2):184-190. doi:10.1111/pde.12767
- Wu HW, Liu C, Wang X, et al. Topical application of 0.5% timolol maleate hydrogel for the treatment of superficial infantile hemangioma. *Front Oncol*. 2017;7:137. doi:10.3389/fonc.2017.00137
- Nagdeve NG, Saoji RG. Study of effectiveness of topical timolol maleate in the management of superficial infantile haemangioma. *J Evid Based Med Healthc*. 2018;5(41):2886-2889.