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COMPARATIVE EFFICACY ANALYSIS OF ORAL PREDNISOLONE WITH OR WITHOUT PROPRANOLOL IN INFANTILE HEMANGIOMA: AN INSTITUTIONAL BASED STUDY

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ABSTRACT

Background: Infantile hemangioma is a common benign vascular tumour of infancy that may cause ulceration, functional impairment, disfigurement, or other complications when lesions are large, rapidly proliferating, or located at high-risk anatomical sites. Oral corticosteroids have traditionally been used for complicated lesions, while propranolol has emerged as an effective systemic therapy. A direct comparison of prednisolone alone with prednisolone combined with propranolol may help determine the more effective and safer treatment approach. **Aim:** To comparatively analyze efficacy of oral prednisolone with or without propranolol in infantile hemangioma. **Materials and Methods:** This hospital-based, prospective, randomized, comparative clinical study included 70 infants with infantile hemangioma requiring systemic treatment. Participants were randomly divided into two equal groups of 35 patients each. Group A received oral prednisolone alone, whereas Group B received oral prednisolone with propranolol. Baseline demographic characteristics, lesion type, anatomical site, ulceration, functional impairment, lesion area, and Hemangioma Activity Score were recorded. Treatment response was assessed by changes in lesion area, activity score, colour, flattening, ulcer healing, functional improvement, time to visible response, rebound growth, and adverse effects. Data were analysed using SPSS version 27.0, with $p<0.05$ considered statistically significant. **Results:** Baseline demographic and lesion characteristics were comparable between the groups. The mean percentage reduction in lesion area was significantly greater in Group B than in Group A (74.08 ± 13.62% vs 47.21 ± 15.43%; $p<0.001$). The mean reduction in Hemangioma Activity Score was also greater in Group B (4.43 ± 1.14 vs 2.77 ± 1.06; $p<0.001$). The time to initial visible response was shorter with combination therapy (1.94 ± 0.73 vs 3.49 ± 1.01 weeks; $p<0.001$). Good or excellent response was achieved in 91.43% of Group B and 57.14% of Group A patients ($p=0.002$). Marked colour fading and flattening were significantly more frequent in Group B. Adverse effects were comparable between the groups. **Conclusion:** Oral prednisolone combined with propranolol was more effective than prednisolone alone in producing faster and greater clinical improvement in infantile hemangioma without a significant increase in adverse effects.

INTRODUCTION

Infantile hemangioma is a benign vascular tumour characterized by postnatal growth and spontaneous involution. Lesions may be absent or barely visible at birth, become apparent during the early weeks of life, and enter a proliferative phase followed by stabilization and regression. Although many uncomplicated lesions can be managed by observation, their behaviour is not always predictable at the first clinical encounter. Rapidly enlarging, segmental, ulcerated, deeply situated, or strategically located hemangiomas may cause pain, bleeding, infection, permanent textural changes, functional compromise, or disfigurement. Early recognition and risk classification are therefore

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essential because the period during which treatment can prevent complications is relatively narrow.[1] The clinical appearance of infantile hemangioma varies according to its depth, distribution, and anatomical location. Superficial lesions are usually bright red and raised, whereas deep lesions may appear as bluish, compressible swellings beneath relatively normal skin. Mixed lesions contain both superficial and deep components. Hemangiomas may also be focal, multifocal, segmental, or indeterminate. Lesions involving the periocular region, nose, lips, ears, airway, breast, or anogenital area require particular attention because their growth may interfere with vision, breathing, feeding, hearing, tissue development, or future cosmetic appearance. Clinical examination remains central to diagnosis, while Doppler ultrasonography, magnetic resonance imaging, and systemic evaluation are reserved for uncertain, deep, extensive, or syndromic presentations.[2]

The pathogenesis of infantile hemangioma involves interactions among endothelial cells, pericytes, hemangioma-derived stem cells, inflammatory cells, and extracellular signalling pathways. Hypoxia-related responses, angiogenic mediators, and abnormal regulation of vascular growth contribute to proliferation, while cellular differentiation, reduced angiogenic activity, and replacement by fibrofatty tissue participate in involution. This biological heterogeneity helps explain differences in growth rate, depth, severity, and therapeutic response. It also provides a rationale for using agents with different mechanisms of action. A treatment capable of producing vasoconstriction, suppressing angiogenic signalling, and promoting regression may be especially valuable during active proliferation, when progressive enlargement can increase the risk of functional and cosmetic complications.[3]

Systemic corticosteroids, particularly oral prednisolone, were historically the principal medical treatment for complicated infantile hemangiomas. Prednisolone can inhibit inflammatory and angiogenic pathways and suppress further vascular proliferation. It remains clinically relevant when beta-blockers are contraindicated, poorly tolerated, or insufficient and may also be considered as part of combination treatment for selected severe lesions. However, prolonged corticosteroid therapy during infancy may be associated with irritability, increased appetite, excessive weight gain, cushingoid appearance, hypertension, hyperglycaemia, gastrointestinal symptoms, infection, and suppression of growth or adrenal function. These concerns make careful dose selection, clinical monitoring, and gradual tapering important, while encouraging investigation of treatment regimens that may improve the therapeutic response without unnecessarily increasing corticosteroid exposure.[4]

Oral propranolol has transformed the management of problematic infantile hemangioma and is regarded as the preferred systemic agent for most infants requiring pharmacological treatment. Its therapeutic effects include early vasoconstriction, modulation of proangiogenic pathways, and the later promotion of cellular regression. Treatment is generally introduced at a low dose and increased after assessment of cardiovascular and respiratory suitability. Because propranolol may cause bradycardia, hypotension, hypoglycaemia, bronchospasm, sleep disturbance, cold extremities, or feeding-related problems, appropriate patient selection and parental counselling are essential. Administration during or immediately after feeding and temporary withholding of the medication during poor oral intake, repeated vomiting, prolonged fasting, or intercurrent illness are important safety measures.[5]

Despite its established role, propranolol treatment is not completely uniform in clinical practice. Decisions regarding inpatient or outpatient initiation, dose escalation, monitoring, pharmaceutical formulation, duration of therapy, and withdrawal may vary according to the infant's age, prematurity, associated illnesses, lesion severity, and available institutional resources. Very young infants and those with cardiovascular, respiratory, or metabolic risk factors may require closer observation. Standardized photographic documentation, serial measurement of lesion dimensions, and structured activity scoring can improve the assessment of therapeutic response. Evaluation should include changes in lesion size, colour, elevation, consistency, ulceration, functional impairment, treatment-related adverse effects, and rebound growth following dose reduction or discontinuation.[6]

MATERIALS AND METHODS

The present study was designed as a hospital-based, prospective, randomized, comparative clinical study aimed to comparatively analyze efficacy of oral prednisolone with or without propranolol in infantile hemangioma.

A total of 70 infants with clinically diagnosed infantile hemangioma requiring systemic treatment were enrolled in the study. Patients attending the outpatient departments or admitted to the pediatric wards were screened for eligibility. Only patients fulfilling the predefined selection criteria and whose parents or legal guardians provided written informed consent were included.

The study included 70 eligible patients who were allocated into two treatment groups in a 1:1 ratio, with 35 patients in each group. Allocation was performed using a computer-generated randomization sequence. Group A consisted of patients treated with oral prednisolone alone, whereas Group B consisted of patients treated with oral prednisolone in combination with oral propranolol. Allocation concealment was maintained using sequentially numbered, sealed, opaque envelopes.

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Inclusion Criteria

Infants aged between 1 and 12 months with a clinical diagnosis of infantile hemangioma were considered eligible. Patients with rapidly proliferating lesions, large or disfiguring hemangiomas, ulcerated lesions, lesions involving cosmetically sensitive areas, or hemangiomas causing or likely to cause functional impairment were included. Infants whose parents or legal guardians agreed to regular follow-up and provided written informed consent were also included.

Exclusion Criteria

Patients with congenital vascular malformations or vascular tumours other than infantile hemangioma were excluded. Infants with previous systemic treatment for hemangioma, severe congenital heart disease, cardiac arrhythmia, hypotension, bradycardia, bronchial asthma, recurrent wheezing, hypoglycaemia, severe systemic infection, hepatic or renal dysfunction, or known hypersensitivity to prednisolone or propranolol were not included. Patients whose parents refused treatment or were unlikely to comply with regular follow-up were also excluded.

Methodology

A detailed clinical history was obtained from the parents or guardians, including the age at appearance of the lesion, pattern of growth, duration of rapid proliferation, history of ulceration, bleeding, infection, feeding difficulty, visual obstruction, respiratory difficulty, or functional impairment. Antenatal, birth, developmental, medical, and family histories were also recorded. Each patient underwent a complete general physical and systemic examination, including cardiovascular and respiratory examinations.

Assessment of Hemangioma Characteristics

The anatomical location, number, type, surface characteristics, consistency, colour, ulceration, and functional involvement of each hemangioma were documented. Lesions were classified as superficial, deep, or mixed according to their clinical appearance. The maximum length, width, and height of the lesion were measured using a flexible measuring tape or digital calliper. The approximate lesion area was calculated by multiplying the maximum length by the maximum width. In patients with deep or mixed lesions, ultrasonography with colour Doppler was performed, where clinically indicated, to assess lesion depth, internal vascularity, and blood-flow characteristics.

Laboratory and Cardiovascular Evaluation

Baseline investigations included complete blood count, fasting or pre-feed blood glucose, serum electrolytes, liver function tests, and renal function tests. Blood pressure, heart rate, respiratory rate, oxygen saturation, and body weight were recorded before treatment. All infants allocated to receive propranolol underwent cardiovascular assessment, including electrocardiography. Echocardiography and specialist cardiology consultation were performed in patients with an abnormal cardiovascular examination, abnormal electrocardiographic findings, suspected congenital heart disease, or a family history of cardiac rhythm abnormalities.

Treatment Protocol for Group A

Patients in Group A received oral prednisolone at a dose of 2 mg/kg/day, administered once daily in the morning after feeding. The dose was calculated according to the patient's body weight and adjusted during follow-up when necessary. After the desired clinical response was achieved, prednisolone was gradually tapered under medical supervision rather than discontinued abruptly. Parents were instructed to administer the medicine after feeding and report symptoms such as fever, vomiting, irritability, reduced feeding, excessive weight gain, facial puffiness, or signs of infection.

Treatment Protocol for Group B

Patients in Group B received oral prednisolone according to the same dose and administration protocol used for Group A, along with oral propranolol. Propranolol was initiated at a low dose of 1 mg/kg/day in two divided doses after feeding. In clinically stable patients without significant adverse effects, the dose was gradually increased to a target dose of 2 mg/kg/day in two divided doses. The propranolol dose was recalculated according to changes in body weight during follow-up. Parents were advised to administer propranolol during or immediately after feeding and to withhold the medicine during prolonged fasting, poor feeding, repeated vomiting, acute respiratory illness, or severe systemic illness until reviewed by the treating physician.

Monitoring During Treatment Initiation

For patients receiving propranolol, baseline heart rate, blood pressure, respiratory status, and blood glucose were recorded before the first dose. These parameters were reassessed after initiation and following dose escalation. Treatment was withheld or modified in the presence of symptomatic bradycardia, hypotension, hypoglycaemia, bronchospasm, poor feeding, excessive lethargy, or any other clinically significant adverse event. Patients receiving prednisolone were monitored for hypertension, hyperglycaemia, infections, gastrointestinal symptoms, cushingoid appearance, irritability, and excessive weight gain.

Follow-Up Assessment

Patients were reviewed at regular intervals after initiation of treatment. At each visit, body weight, heart rate, blood pressure, respiratory rate, feeding pattern, treatment compliance, and adverse effects were recorded. The size, colour, consistency, elevation, ulceration, and functional effects of the hemangioma were reassessed. The doses of prednisolone and propranolol were adjusted according to the patient's current body weight and clinical condition.

Statistical Analysis

The collected data were entered into a Microsoft Excel spreadsheet and analysed using IBM

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Statistical Package for the Social Sciences, version 27.0. Continuous variables were presented as mean with standard deviation or median with interquartile range according to the distribution of data. Categorical variables were expressed as frequencies and percentages. Normality of continuous data was assessed using the Shapiro–Wilk test.

RESULTS

Table 1 presents the baseline demographic and clinical characteristics of the study participants. The mean age of infants in Group A was 6.11 ± 2.72 months, while that in Group B was 5.94 ± 2.58 months. The overall mean age of the study population was 6.03 ± 2.63 months. The difference in mean age between the two groups was not statistically significant (p=0.789). Regarding age-group distribution, 8 (22.86%) infants in Group A and 9 (25.71%) infants in Group B were aged 1–3 months. In the 4–6-month age group, there were 12 (34.29%) infants in Group A and 11 (31.43%) in Group B. Ten infants (28.57%) in each group were aged 7–9 months, whereas 5 (14.29%) infants in each group were aged 10–12 months.

Females constituted the majority of the study population. Group A included 24 (68.57%) female and 11 (31.43%) male infants, while Group B included 25 (71.43%) female and 10 (28.57%) male infants. Overall, 49 (70.00%) participants were female and 21 (30.00%) were male.

Table 2 shows the baseline characteristics of infantile hemangiomas in the two groups. A single lesion was observed in 31 (88.57%) infants in Group A and 30 (85.71%) infants in Group B. Multiple lesions were found in 4 (11.43%) and 5 (14.29%) infants, respectively. Overall, 61 (87.14%) infants had a single hemangioma, while 9 (12.86%) had multiple lesions. There was no statistically significant difference in the number of lesions between the two groups (p=0.721).

With regard to the clinical type of hemangioma, superficial lesions were the most common in both groups. Superficial hemangioma was present in 20 (57.14%) infants in Group A and 19 (54.29%) infants in Group B. Deep hemangioma was observed in 5 (14.29%) infants in Group A and 6 (17.14%) infants in Group B, while mixed hemangioma was present in 10 (28.57%) infants in each group. In the overall study population, 39 (55.71%) infants had superficial lesions, 11 (15.71%) had deep lesions, and 20 (28.57%) had mixed lesions. The distribution of hemangioma types was not significantly different between the groups (p=0.943).

Table 3 compares the changes in lesion area, Hemangioma Activity Score, and time to initial visible response between the two treatment groups. At baseline, the mean lesion area was 15.84 ± 6.42 cm² in Group A and 16.21 ± 6.08 cm² in Group B, with no statistically significant difference (p=0.805). At the final assessment, the mean lesion area had decreased to 8.35 ± 4.20 cm² in Group A and 4.18 ± 2.75 cm² in Group B. The final lesion area was significantly smaller in Group B than in Group A (p<0.001).

The mean absolute reduction in lesion area was 7.49 ± 3.85 cm² in Group A compared with 12.03 ± 4.62 cm² in Group B. This difference was statistically significant (p<0.001), indicating a greater reduction in lesion size among infants receiving combination therapy. The mean percentage reduction in lesion area was 47.21 ± 15.43% in Group A and 74.08 ± 13.62% in Group B. The significantly greater percentage reduction in Group B (p<0.001) demonstrated the superior effectiveness of prednisolone combined with propranolol compared with prednisolone alone.

At baseline, the mean Hemangioma Activity Score was 5.86 ± 1.31 in Group A and 5.94 ± 1.28 in Group B, and the difference was not statistically significant (p=0.797). At the final assessment, the mean score decreased to 3.09 ± 1.20 in Group A and 1.51 ± 0.92 in Group B. The final Hemangioma Activity Score was significantly lower in Group B (p<0.001). The mean reduction in the activity score was 2.77 ± 1.06 in Group A compared with 4.43 ± 1.14 in Group B, and this difference was also statistically significant (p<0.001).

Table 4 presents the overall treatment response and other clinical outcomes. A poor response, defined as less than 25% reduction in lesion size, was observed in 3 (8.57%) infants in Group A, while no infant in Group B showed a poor response. A fair response, defined as a 25–50% reduction, was observed in 12 (34.29%) infants in Group A and 3 (8.57%) infants in Group B. A good response, defined as a 51–75% reduction, occurred in 13 (37.14%) infants in Group A and 10 (28.57%) infants in Group B. An excellent response, defined as more than 75% reduction, was achieved in 7 (20.00%) infants in Group A and 22 (62.86%) infants in Group B. The overall distribution of treatment responses was significantly different between the two groups (p=0.001), with excellent responses occurring more frequently in the combination-treatment group.

Rebound growth following dose reduction or treatment withdrawal was observed in 6 (17.14%) infants in Group A and 2 (5.71%) infants in Group B. Overall, rebound growth occurred in 8 (11.43%) infants. Although rebound growth was numerically less frequent in Group B, the difference was not statistically significant (p=0.259).

Table 5 compares treatment-related adverse effects between the two groups. Irritability was reported in 8 (22.86%) infants in Group A and 4 (11.43%) infants in Group B. Although irritability was more frequent in Group A, the difference was not statistically significant (p=0.342). Excessive weight gain was observed in 9 (25.71%) infants in Group A and 5 (14.29%) infants in Group B, with no statistically significant difference (p=0.371).

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Cushingoid appearance was noted in 7 (20.00%) infants in Group A and 3 (8.57%) infants in Group B. The difference was not statistically significant (p=0.306). Gastrointestinal symptoms occurred in 4 (11.43%) infants in Group A and 2 (5.71%) infants in Group B (p=0.673). Hypertension was observed in 3 (8.57%) infants in Group A and 1 (2.86%) infant in Group B, without a significant difference (p=0.614).

Hyperglycaemia was documented in 2 (5.71%) infants in Group A and 1 (2.86%) infant in Group B, while infection occurred in 3 (8.57%) infants in Group A and 2 (5.71%) infants in Group B. Neither hyperglycaemia nor infection differed significantly between the groups, with p-values of 1.000 for both comparisons. Some adverse effects associated with propranolol were observed only in Group B. Sleep disturbance occurred in 4 (11.43%) infants, cold extremities in 3 (8.57%) infants, and transient bradycardia in 1 (2.86%) infant. These adverse effects were not observed in Group A. However, none of these differences was statistically significant, with p-values of 0.114, 0.239, and 1.000, respectively.

At least one treatment-related adverse effect was reported in 18 (51.43%) infants in Group A and 12 (34.29%) infants in Group B. Although the overall frequency of adverse effects was lower in the combination-treatment group, the difference was not statistically significant (p=0.227). Treatment discontinuation due to an adverse effect was required in 2 (5.71%) infants in Group A and 1 (2.86%) infant in Group B, with no significant difference (p=1.000).

Table 1: Baseline demographic and clinical characteristics of the study participants

Variable	Category	Group A: Prednisolone (n=35)	Group B: Prednisolone + Propranolol (n=35)	Total (N=70)	p-value
Age, months	Mean ± SD	6.11 ± 2.72	5.94 ± 2.58	6.03 ± 2.63	0.789
Age group	1–3 months	8 (22.86%)	9 (25.71%)	17 (24.29%)	0.992
	4–6 months	12 (34.29%)	11 (31.43%)	23 (32.86%)	
	7–9 months	10 (28.57%)	10 (28.57%)	20 (28.57%)	
	10–12 months	5 (14.29%)	5 (14.29%)	10 (14.29%)	
Sex	Female	24 (68.57%)	25 (71.43%)	49 (70.00%)	0.794
	Male	11 (31.43%)	10 (28.57%)	21 (30.00%)	
Body weight, kg	Mean ± SD	7.21 ± 1.45	7.18 ± 1.39	7.20 ± 1.41	0.930
Age at lesion appearance, months	Mean ± SD	2.94 ± 1.27	3.03 ± 1.31	2.99 ± 1.28	0.771
Gestational status	Preterm	8 (22.86%)	7 (20.00%)	15 (21.43%)	0.771
	Term	27 (77.14%)	28 (80.00%)	55 (78.57%)	

Table 2: Baseline characteristics of infantile hemangiomas in the two treatment groups

Variable	Category	Group A: Prednisolone (n=35)	Group B: Prednisolone + Propranolol (n=35)	Total (N=70)	p-value
Number of lesions	Single	31 (88.57%)	30 (85.71%)	61 (87.14%)	0.721
	Multiple	4 (11.43%)	5 (14.29%)	9 (12.86%)	
Type of hemangioma	Superficial	20 (57.14%)	19 (54.29%)	39 (55.71%)	0.943
	Deep	5 (14.29%)	6 (17.14%)	11 (15.71%)	
	Mixed	10 (28.57%)	10 (28.57%)	20 (28.57%)	
Anatomical location	Head and neck	19 (54.29%)	20 (57.14%)	39 (55.71%)	0.993
	Trunk	8 (22.86%)	7 (20.00%)	15 (21.43%)	
	Upper limb	4 (11.43%)	4 (11.43%)	8 (11.43%)	
	Lower limb	4 (11.43%)	4 (11.43%)	8 (11.43%)	
Ulceration	Present	7 (20.00%)	8 (22.86%)	15 (21.43%)	0.771
	Absent	28 (80.00%)	27 (77.14%)	55 (78.57%)	
Functional impairment	Present	9 (25.71%)	10 (28.57%)	19 (27.14%)	0.788
	Absent	26 (74.29%)	25 (71.43%)	51 (72.86%)	
Baseline lesion area, cm²	Mean ± SD	15.84 ± 6.42	16.21 ± 6.08	16.03 ± 6.21	0.805
Baseline Hemangioma Activity Score	Mean ± SD	5.86 ± 1.31	5.94 ± 1.28	5.90 ± 1.29	0.797

Table 3: Comparison of changes in lesion area, Hemangioma Activity Score, and response time

Outcome parameter	Group A: Prednisolone (n=35), Mean ± SD	Group B: Prednisolone + Propranolol (n=35), Mean ± SD	p-value
Baseline lesion area, cm²	15.84 ± 6.42	16.21 ± 6.08	0.805
Lesion area at final assessment, cm²	8.35 ± 4.20	4.18 ± 2.75	<0.001
Absolute reduction in lesion area, cm²	7.49 ± 3.85	12.03 ± 4.62	<0.001
Percentage reduction in lesion area	47.21 ± 15.43%	74.08 ± 13.62%	<0.001
Baseline Hemangioma Activity Score	5.86 ± 1.31	5.94 ± 1.28	0.797
Hemangioma Activity Score at final assessment	3.09 ± 1.20	1.51 ± 0.92	<0.001
Mean reduction in Hemangioma Activity Score	2.77 ± 1.06	4.43 ± 1.14	<0.001
Time to initial visible response, weeks	3.49 ± 1.01	1.94 ± 0.73	<0.001

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Table 4: Comparison of overall treatment response and clinical outcomes

Outcome	Group A: Prednisolone (n=35)	Group B: Prednisolone + Propranolol (n=35)	Total (N=70)	p-value
Poor response: <25% reduction	3 (8.57%)	0 (0.00%)	3 (4.29%)	0.001
Fair response: 25–50% reduction	12 (34.29%)	3 (8.57%)	15 (21.43%)	
Good response: 51–75% reduction	13 (37.14%)	10 (28.57%)	23 (32.86%)	
Excellent response: >75% reduction	7 (20.00%)	22 (62.86%)	29 (41.43%)	
Combined good or excellent response	20 (57.14%)	32 (91.43%)	52 (74.29%)	0.002
Marked fading of lesion colour	18 (51.43%)	30 (85.71%)	48 (68.57%)	0.002
Marked flattening of lesion	17 (48.57%)	29 (82.86%)	46 (65.71%)	0.003
Healing of ulceration*	5/7 (71.43%)	8/8 (100.00%)	13/15 (86.67%)	0.200
Improvement in functional impairment†	6/9 (66.67%)	10/10 (100.00%)	16/19 (84.21%)	0.087
Rebound growth after dose reduction or withdrawal	6 (17.14%)	2 (5.71%)	8 (11.43%)	0.259

*Calculated among patients who had ulceration at baseline.
†Calculated among patients who had functional impairment at baseline.

Table 5: Comparison of treatment-related adverse effects

Adverse effect	Group A: Prednisolone (n=35)	Group B: Prednisolone + Propranolol (n=35)	p-value
Irritability	8 (22.86%)	4 (11.43%)	0.342
Excessive weight gain	9 (25.71%)	5 (14.29%)	0.371
Cushingoid appearance	7 (20.00%)	3 (8.57%)	0.306
Gastrointestinal symptoms	4 (11.43%)	2 (5.71%)	0.673
Hypertension	3 (8.57%)	1 (2.86%)	0.614
Hyperglycaemia	2 (5.71%)	1 (2.86%)	1.000
Infection	3 (8.57%)	2 (5.71%)	1.000
Sleep disturbance	0 (0.00%)	4 (11.43%)	0.114
Cold extremities	0 (0.00%)	3 (8.57%)	0.239
Transient bradycardia	0 (0.00%)	1 (2.86%)	1.000
At least one adverse effect	18 (51.43%)	12 (34.29%)	0.227
Treatment discontinuation due to an adverse effect	2 (5.71%)	1 (2.86%)	1.000

DISCUSSION

The present study included 70 infants with a mean age of 6.03 ± 2.63 months. The mean ages of Group A and Group B were comparable at 6.11 ± 2.72 and 5.94 ± 2.58 months, respectively (p=0.789), indicating successful baseline randomization. Females constituted 70.00% of the study population, giving a female-to-male ratio of approximately 2.33:1. The lesion appeared at a mean age of 2.99 ± 1.28 months, while 21.43% of the infants were born preterm. Li et al. (2011), in a large Chinese case-control study involving 1,832 infants with hemangioma, reported a mean age at enrolment of 122.9 days, equivalent to approximately 4 months, and a female-to-male ratio of 1.77:1. The mean lesion area in their study was 13.0 ± 15.4 cm². The higher female proportion observed in the present study was therefore consistent with the recognised female predominance in infantile hemangioma. The slightly higher mean age in the present study could be related to the inclusion of infants referred to a tertiary care hospital specifically for systemic treatment.[7] Most patients in the present study had a single lesion (87.14%), and superficial hemangioma was the most common type (55.71%), followed by mixed (28.57%) and deep lesions (15.71%). The head-and-neck region was involved in 55.71% of patients, while the trunk and extremities accounted for the remaining cases. Ulceration and functional impairment were present in 21.43% and 27.14% of infants, respectively. The mean baseline lesion area was 16.03 ± 6.21 cm², and the mean baseline Hemangioma Activity Score was 5.90 ± 1.29. Ji et al. (2021), in a randomized clinical trial of 377 infants with problematic hemangiomas, reported head-and-face involvement in 199 of 377 patients (52.79%), which closely approximated the 55.71% observed in the present study. Their median lesion area was 8.1 cm² in the propranolol group and 8.8 cm² in the atenolol group, while ulceration was present in 13.2% and 12.3%, respectively. The higher mean lesion area and ulceration rate in the present study may indicate the inclusion of relatively larger and more complicated hemangiomas requiring systemic treatment.[8] The mean time to an initial visible response was significantly shorter in the combination-treatment group than in the prednisolone-only group, at 1.94 ± 0.73 weeks versus 3.49 ± 1.01 weeks (p<0.001). This corresponded to approximately 13.6 days in Group B and 24.4 days in Group A. Marked fading of lesion colour was also significantly more frequent in Group B than in Group A (85.71% vs 51.43%; p=0.002), as was marked flattening of the lesion (82.86% vs 48.57%; p=0.003). Malik et al. (2013) similarly found a significantly shorter initial response time with propranolol alone and combined propranolol-prednisolone therapy than with prednisolone alone. Their mean initial response times were 4.1 ± 3.3 days with propranolol, 4.7 ± 3.4 days with combination therapy, and 9.78 ± 7.8 days with prednisolone (p<0.047). They also observed significant colour fading within 48 hours with propranolol and significantly earlier flattening with propranolol-containing regimens (p<0.05).

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Although the absolute response times were longer in the present study, probably because visible response was recorded during scheduled follow-up, both studies demonstrated faster colour and morphological improvement when propranolol was included.[9] A substantial reduction in lesion area was observed with both treatment regimens; however, the reduction was significantly greater with combination therapy. The mean lesion area decreased from 15.84 ± 6.42 to 8.35 ± 4.20 cm² in Group A and from 16.21 ± 6.08 to 4.18 ± 2.75 cm² in Group B. The absolute reduction was 7.49 ± 3.85 cm² with prednisolone alone and 12.03 ± 4.62 cm² with combination therapy ($p<0.001$). Correspondingly, the mean percentage reduction was 47.21 ± 15.43% in Group A and 74.08 ± 13.62% in Group B ($p<0.001$). Yun et al. (2015) prospectively treated 12 infants with propranolol, of whom 11 completed therapy with consistent clinical improvement. More than 50% involution was achieved during the first 3 months, followed by further steady regression for up to 1 year. The 74.08% reduction observed with combination therapy in the present study was greater than the early reduction reported by Yun et al., whereas the 47.21% reduction with prednisolone alone was slightly below it. These observations support the contribution of propranolol to accelerated lesion regression.[10] The Hemangioma Activity Score decreased in both groups, but the degree of reduction was significantly greater in infants treated with prednisolone and propranolol. The score declined from 5.86 ± 1.31 to 3.09 ± 1.20 in Group A and from 5.94 ± 1.28 to 1.51 ± 0.92 in Group B. The mean reductions were 2.77 ± 1.06 and 4.43 ± 1.14 points, respectively ($p<0.001$). Janmohamed et al. (2015) prospectively assessed 54 infants receiving propranolol and found that the Hemangioma Activity Score decreased progressively, with a particularly dramatic reduction during the first week of treatment. They also observed that the activity score reflected therapeutic improvement more sensitively than the Hemangioma Severity Scale. The significantly larger decline in the activity score in Group B of the present study agrees with their findings and indicates that propranolol-containing treatment rapidly controls lesion colour, swelling, ulceration and proliferative activity. The comparable baseline scores between the groups ($p=0.797$) further support that the subsequent difference was related to treatment response rather than initial disease severity.[11] The overall treatment-response distribution differed significantly between the two groups ($p=0.001$). An excellent response of more than 75% reduction was achieved in 62.86% of infants receiving combination therapy compared with only 20.00% receiving prednisolone alone. When good and excellent responses were combined, favourable response rates were 91.43% in Group B and 57.14% in Group A ($p=0.002$). No patient in Group B had a poor response, whereas 8.57% of Group A had less than 25% reduction. Léauté-Labrèze et al. (2015), in a large randomized controlled trial, reported complete or nearly complete resolution at 24 weeks in 60% of 101 infants receiving the selected propranolol regimen compared with 4% of 55 infants receiving placebo. Marked improvement by week 5 was reported in 88% and 5%, respectively. The 62.86% excellent-response rate in the combination group of the present study was comparable to the 60% complete or nearly complete response achieved with propranolol in their trial. These findings confirm the major clinical benefit associated with the addition of propranolol.[12] Among infants with ulcerated hemangiomas, healing occurred in 5 of 7 patients (71.43%) receiving prednisolone alone and all 8 patients (100.00%) receiving combination therapy. Although the difference was clinically meaningful, it did not reach statistical significance ($p=0.200$), probably because only 15 patients had ulceration. Similarly, functional improvement occurred in 66.67% of affected infants in Group A and 100.00% in Group B, but the difference was not statistically significant ($p=0.087$). Hermans et al. (2011) evaluated 20 propranolol-treated patients with ulcerated infantile hemangiomas against matched historical controls. The mean time from the onset of ulceration to complete healing was significantly shorter with propranolol than in controls, at 8.7 versus 22.4 weeks. The complete healing observed in all ulcerated patients receiving combination therapy in the present study was consistent with this beneficial effect. The absence of statistical significance should not be interpreted as an absence of clinical benefit because the subgroup numbers were small and consequently provided limited statistical power.[13] At least one adverse effect was recorded in 51.43% of infants treated with prednisolone alone and 34.29% treated with combination therapy; however, the difference was not statistically significant ($p=0.227$). Irritability, excessive weight gain and cushingoid appearance were numerically more frequent with prednisolone alone. Sleep disturbance (11.43%), cold extremities (8.57%) and transient bradycardia (2.86%) occurred only in the combination group, but these effects were mild and did not produce a significant increase in treatment discontinuation. Treatment was discontinued because of adverse effects in 5.71% of Group A and 2.86% of Group B patients ($p=1.000$). Rebound growth occurred in 17.14% and 5.71%, respectively ($p=0.259$). Bauman et al. (2014) recorded 44 adverse events with prednisolone and 32 with propranolol ($p=0.84$), but severe adverse events were significantly more frequent with prednisolone, at 11 versus 1 ($p=0.01$). Adverse-event-related early withdrawal occurred in 6 of 8 prednisolone-treated infants compared with none of 11 propranolol-treated infants. They also observed regrowth after medication withdrawal in two propranolol-treated and one prednisolone-treated patient. Thus, the current findings similarly suggest that propranolol-containing treatment provides

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improved efficacy without a significant increase in overall toxicity, while careful monitoring for both steroid- and beta-blocker-related effects remains necessary.[14]

CONCLUSION

The combination of oral prednisolone with propranolol was more effective than oral prednisolone alone in treating infantile hemangioma. Combination therapy produced a faster clinical response, greater reduction in lesion size and Hemangioma Activity Score, and higher rates of good and excellent outcomes. It also showed better colour fading, lesion flattening, ulcer healing, and functional improvement. Both regimens were generally well tolerated, with no significant difference in overall adverse effects. Therefore, oral prednisolone with propranolol may be considered a more effective treatment option for infants requiring systemic therapy.

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