*Original Research Article*

Comparative Study of Effectiveness Between Oral Propranolol and Combined Oral Propranolol with Prednisolone in The Treatment of Infantile Hemangioma

# ABSTRACT

***Background****: The most prevalent benign vascular tumor found within pediatric patients is infantile hemangioma since its birth frequency stands at 2-3% that progressively surges to 10% by the first birthday. The therapeutic advantage of administering combined propranolol and corticosteroids compared to propranolol as a standalone treatment for Infantile hemangiomas remains an ambiguous matter.* *However, the efficacy of propranolol in treating IH patients is not universal. Systemic corticosteroids have known side effects such as water retention, hypertension and hyperglycemia, which could counter the adverse effects of propranolol like hypotension, bradycardia, hypoglycemia.* ***Objective****: To compare the clinical outcomes and safety profile of oral propranolol monotherapy versus combined oral propranolol and prednisolone in the treatment of infantile hemangioma.* ***Methods****: An observational study was conducted at BSMMU from October 2018 to August 2019, involving 62 patients with IH up to 4 years of age. Patients were divided into two groups: Group A (n=31) received oral propranolol alone, while Group B (n=31) received combined oral propranolol and prednisolone. Treatment outcomes were assessed using Visual Analogue Scale (VAS) for color changes and percentage of size regression.* ***Results****: Both groups showed improvement in color clearance and size regression. In Group A, 22.6% showed excellent color clearance versus 6.5% in Group B. Mean size regression was 68.05% in Group A and 59.35% in Group B, though the difference was not statistically significant. However, Group B experienced significantly more adverse effects (61.3%) compared to Group A (25.8%) (p=0.005).* ***Conclusion****: This research shows that propranolol treatment alone provides similar results as prednisolone combination treatment for infantile hemangioma but produces less adverse side effects. The regular care of infantile hemangioma does not require prednisolone administration with propranolol.*

***Keywords:*** *Infantile Hemangioma, Propranolol, Corticosteroids, Combination Therapy, Treatment Outcome.*

# INTRODUCTION

Hemangioma is the most common benign vascular tumor in pediatric patients. It is characterized by a bright red surface which usually present within two weeks of birth. The incidence of hemangioma is 2% to 3% which increases to 10% at one year of age. The prevalence raises to 22% to 3o% in pre term and low birth weight infant [1]. A hallmark of IH is its predictable life cycle. There are three phases of life cycle of infantile hemangioma. During the proliferative phase, rapid growth of tumor occurs which typically lasts up to 10-12 months of age. [2]. The involution phase of hemangioma occurs from age 1 to 7 years during which period the tumor slowly regresses. This phase shows fading color of the tumor from crimson to a dull purple, which accompanied by deflation of tumor mass. Final involute phase of the tumor continued until the age 10-12 years [3]. Most hemangiomas do not require any intervention other than observation. Although, most IHs have a self-limiting course, some may result in complications like ulceration, bleeding, destruction and distortion of local tissue structure, obstruction of vital structure and high output cardiac failure. In order to not leave disfigurement and psychological sequelae, it is suggested that active treatment should be taken rather than observation. Many parents seek treatment rather than follow up or wait. IHs are sensitive to medication before 4 years of age. [4] Corticosteroids have been

the mainstream for treating IHs for many years. They used to be the first-line treatment for severe, multiple hemangiomas, potentially disfiguring hemangiomas involving vital structures as well as for patients with congestive heart failure, consumptive coagulopathies and thrombocytopenia prior to the discovery and subsequent wide clinical use of propranolol. [5]. Corticosteroids inhibit the expression of VEGF- by hemangioma derived stem cells and thus angiogenesis. The overall response rate is 80-90 % with initial improvement in the color and tension of the usually noted within one week [6]. The main side effects of the systemic corticosteroids therapy are the cushinoid face, disturbance of growth, and susceptibility to serious infections. Furthermore, complications also include appetite changes, behavior changes, polyuria, thrush, hypertension, adrenal suppression and gastrointestinal discomfort. Propranolol is a non-selective beta-blocker stands as the first-line agent for hemangiomas that impair function or cause permanent disfigurement [7]. In 2008, Leaute-Labreze et al in 2008 found propanolol as a treatment option for hemangiomas of infancy by accident. However, the efficacy of propanolol in treating IH patients is not universal. Propanolol inhibits the growth and induces regression of IHs by its potential mechanism of inducing vasoconstriction, decrease expression of vascular endothelial growth factor and matrix metalloproteinase, and or triggering of apoptosis [8]. [9] had shown that oral propranolol was effective in the treatment of IH beyond the proliferative phase. The most important advantages of oral propranolol over glucocorticoids are efficacy and safety. The side effects included hypotension, bradycardia, bronchospasm, hypoglycemia, cold extremities etc. [8].

1. had shown in his research that propranolol was more clinically effective than oral prednisolone in the treatment of infantile hemangioma. Propranolol was better tolerated with minimal adverse effects, compared with oral prednisolone.
2. stated in his study that efficacy of propranolol was found 100% and adverse effect of propranolol are rare so it can be continued until complete regression. Oral prednisolone and propranolol have shown excellent results individually for the treatment of infantile hemangioma. However, the combination of the two drugs in lower doses may be used for the treatment of infantile hemangioma to avoid the complications associated with high doses of both drugs. [12]. As systemic corticosteroids have known side effects such as water retention, hypertension and hyperglycemia, which could counter the adverse effects of propranolol [13]. Aly et al in 2015 [14] stated that combining propranolol with short course corticosteroids gives faster response in the treatment of complicated infantile hemangioma with limited adverse events.

 This research aims to study the therapeutic outcomes and security aspects between oral propranolol single-drug therapy and oral propranolol administered with prednisolone treatment for infantile hemangioma.

# OBJECTIVES

## General Objective

* + Comparison of the outcome of infantile hemangioma treated with propranolol with or without corticosteroid.

## Specific Objectives

* + To compare the changes of color of hemangioma between propranolol monotherapy and combination therapy with prednisolone.
	+ To compare the regression of size and rapidity of changes of lesion between oral propranolol and combined propranolol with prednisolone.
	+ To evaluate the adverse effect of propranolol alone and combination with corticosteroid therapy.

# METHODOLOGY

**Study Design:** Observational study. **Study Place:** Outpatient department, Department of Pediatric Surgery, BSMMU. **Study duration:** October,2018 to August,2019. **Study Population**: Clinically diagnosed Infantile hemangioma up to 4 years of age. **Sampling Technique:** Purposive sampling was taken for data collection.

**Inclusion criteria:**

* + All patients (up to 4years of age because the IHs are sensitive to medications during this period) of clinically diagnosed Infantile hemangioma of either sex attending OPD, pediatric surgery of BSMMU with absolute or relative indication for treatment.

**Diagnostic criteria of infantile hemangioma:**

* + It appears as a red or pink spot, may be formative at birth
	+ Mostly appears within two weeks of life
	+ Usually raised, crimson colored mass
	+ Grows rapidly within 1st month of life
	+ Grows less rapidly up to 1 year of age
	+ Regression starts usually after 1 year of age
	+ Which is non-compressible

**Exclusion criteria:**

* + Cardiovascular disorders contraindicating propranolol use.
	+ Asthma, Bronchiolitis, Bronchopulmonary dysplasia, Family history of atopy, and low birth weight infant.
	+ Visceral hemangioma.
	+ Patients who were previously treated.

**Data processing and analysis:** 1. All the data were compiled and sorted properly and the numerical data were analyzed statistically by using Statistical Package for Social Sciences (SPSS) software supplied by BSMMU and application of standard statistical tools. 2. Results were expressed as percentage, proportion, ratio, mean+ SD 3. Results were published in the form of tables and diagrams, and will be followed by discussions of the findings.

# RESULT

This prospective study was carried out at Bangabandhu Sheikh Mujib Medical University, Dhaka on commonest Treatment was initiated in outpatient settings. A total 62 patients with proliferating and involuting infantile hemangioma treated with propranolol alone and propranolol with prednisolone. Aim of this study to see the comparison of outcome of infantile hemangioma treated with propranolol with or without corticosteroid. This study is statistically compared through tables and graphs.

## Age distribution:

Bar diagram shows distribution of patients of hemangioma by age among two groups. The age of the patients in this study group ranges from 2 months to 48 months. In Group A (n=31), 61.3% patients (n-19) were in <12 months age group and 38.7% patients (n=12) were >12 months of age. Mean age in this group was 13.11. In Group B (n=31), 58.1% patients (n=18) were in <12 months age group and 41.9% patients(n=13) were >12 months of age. Mean age in this group was

17.82. unpaired student t-test was done. P value was 0.195 which was not statically significant.

Percentage (%)

**Age distribution (n=62)**

70

61.3

60

58.1

50

41.9

40

38.7

<12 months

>12 months

30

20

10

0

**Group A (n=31)**

**Group B (n=31)**

***Figure-1:*** *Bar diagram showing the age distribution in two groups*

## Sex distribution:

In Group A (n=31), male patients were 13(41.9%), female patients were 18(58. 1%). Male and female ratio in this group was 1:1.4 In Group B (n=31), male patients were 17(54.8%)), female patients were 14(45.2%). Male and female ratio in this group was 1.2:1 The Male (n=30) and female (n=32) ratio in this study was M: F= 1:1.1 Chi-square test was done. P value was 0.309 which was not statically significant.

Percentage (%)

**Sex distribution (n=62)**

70

60

58.1

54.8

50

45.2

41.9

40

30

Male

Female

20

10

0

**Group A (n=31)**

**Group B (n=31)**

***Figure-2:*** *Bar diagram showing the sex distribution of the study patients in two groups*

## Frequency of pre-treatment color status by VAS in two groups:

In Group-A, maximum patients visual analogue scale were 4 and in Group-B, maximum patients visual analogue scale were 5.

## Table-1-: Frequency of pre-treatment color by VAS in two groups

|  |  |  |
| --- | --- | --- |
| **VAS score** | **Group A (Propranolol) (n=31) No. (%)** | **Group B (Propranolol prednisolone) (n=31)****No. (%)** |
| No. | % | No. | **%** |
| **2** | 3 | 9.68 | 0 | **0.00** |
| **3** | 1 | 3.23 | 1 | **3.23** |
| **4** | 10 | 32.26 | 9 | **29.03** |
| **5** | 8 | 25.81 | 12 | **38.71** |
| **6** | 4 | 12.90 | 6 | **19.35** |
| **7** | **5** | **16.13** | **3** | **9.68** |

**Status of the patient of IHs by color changes according to Visual Analogue Scale (VAS)**

The first noticeable effect on both groups were the changes in color and its consistency followed by regression of size. Color changes of IHs were analyzed by Visual Analogue Scale (VAS). In Group-A, 7 patients (22.6%) had excellent color clearance,6 patients (19.4%) had good,14 patients (45.2%) had fair and 4 patients (12.9%) had poor color clearance. In Group-B,2 patients (6.5%) had excellent color clearance,6 patients (19.4%) had good,17 patients (54.8%) had fair and 6 patients (19.4%) had poor color clearance. Which was statistically not significant.

## Table-2: Comparison of percentage of color clearance between two groups (n=62)

Here is the table format for the percentage of color clearance of IH data you provided:

|  |  |  |  |
| --- | --- | --- | --- |
| **Percentage of Color Clearance** | **Group A (Propranolol) (n=31) No. (%)** | **Group B (Propranolol + Prednisolone) (n=31) No. (%)** | **p- value** |
| **Excellent (80%-100%)** | 7 (22.6%) | 2 (6.5%) | 0.325ns |
| **Good (51-79%)** | 6 (19.4%) | 14 (45.2%) |
| **Fair (25-50%)** | 4 (12.9%) | 6 (19.4%) |
| **Poor (< 25%)** |  |  |
| **Total** | 31 (100%) | 31 (100%) |

Data were expressed as frequency, percentage Chi-square test, ns= not significant

## Status of regression of size of IHs in both group:

Table-3 shows mean of percentage of regression of size in both group. In Group-A, mean percentage of regression of size was 68.05 and In Group-B, mean percentage of regression of size was 59.35. Statistically which was not significant.

## Table-3: Comparison of percentage of regression of size of IH between two groups (n=62)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Group A (Propranolol) (n=31)Mean±SD | Group B (Propranolol prednisolone) (n=31) Mean±SD | p-value |
| Percentage of regression of size of IH | 68.05±24.05 | 59.35±21.68 | 0.140ns |

Data were expressed as mean±SD Unpaired student t-test, ns= not significant

## Table-4 shows comparison of overall regression of size between two group.

In Group-A, excellent was 13 in no (41.9%), good was 10(32.3%), fair was 7(22.6%) and poor was 1(3.2%) In Group-B, excellent was 7 in no (22.6%), good was 13(41.9%), fair was 10(32.3%) and poor was 1(3.2%) P value was 0.437 which was not significant.

## Table-4: Comparison of overall regression of size between two groups (n=62)

|  |  |  |  |
| --- | --- | --- | --- |
| **Percentage of Regression of Size of IH** | **Group A (Propranolol) (n=31) No. (%)** | **Group B (Propranolol + Prednisolone) (n=31) No. (%)** | **p- value** |
| **Excellent (80%-100%)** | 13 (41.9%) | 7 (22.6%) | 0.437ns |
| **Good (51-79%)** | 10 (32.3%) | 13 (41.9%) |
| **Fair (25-50%)** | 1 (3.2%) | 1 (3.2%) |
| **Poor (< 25%)** |  |  |
| **Total** | 31 (100%) | 31 (100%) |

Data were expressed as frequency, percentage Chi-square test, ns= not significant

## Observation of adverse effects following treatment in both groups:

In this study, no serious adverse effects were occurred. In Group-A,3 patients (9.7%) developed gastroenteritis in the form of diarrhea and vomiting,3 patient (9.7%) had sleep disturbance,2 patients (6.5%) had ulceration In Group-B,1 patient (3.2%)had gastroenteritis,5 patient (16.1%) developed sleep disturbance,2 patients (6.5%) became hypertensive and 3 patient (9.7%)s developed cushinoidfacies,5 patients (16.1%) were irritable,3 patients (9.7%) developed fungal infection.

## Table-5: Comparison of post intervention adverse effects between two groups (n=62)

|  |  |  |
| --- | --- | --- |
| **Post Intervention Adverse Effects** | **Group A (Propranolol) (n=31) No. (%)** | **Group B (Propranolol + Prednisolone) (n=31) No. (%)** |
| **Gastroenteritis** | 3 (9.7%) | 1 (3.2%) |
| **Sleep disturbances** | 3 (9.7%) | 5 (16.1%) |
| **Hypertension** | 0 (0.0%) | 2 (6.5%) |
| **Cushingoid Facies** | 0 (0.0%) | 3 (9.7%) |
| **Local Ulceration** | 2 (6.5%) | 0 (0.0%) |
| **Irritability** | 0 (0.0%) | 5 (16.1%) |
| **Fungal Infection** | 0 (0.0%) | 3 (9.7%) |
| **Hypotension** | 0 (0.0%) | 0 (0.0%) |
| **Bradycardia** | 0 (0.0%) | 0 (0.0%) |
| **Bleeding** | 0 (0.0%) | 0 (0.0%) |
| **Skin Allergy** | 23 (74.2%) | 12 (38.7%) |
| **No Adverse Effects** | 0 (0.0%) | 0 (0.0%) |
| **Total** | 31 (100%) | 31 (100%) |

Table-6 shows comparison of adverse effect between two groups In Group-A, different adverse effect was found in 8 patients (25.8%) In Group-B, different adverse effect was found in 19 patients (61.3%) P value was 0.005 which was significant.

## Table-6: Comparison of adverse effects between two groups (n=62)

|  |  |  |  |
| --- | --- | --- | --- |
| **Adverse effects** | **Group A (Propranolol) (n=31)****No. (%)** | **Group B (Propranolol prednisolone) (n=31)****No. (%)** | **p-value** |
| **Present** | 8(25.8%) | 19(61.3%) | **0.005s** |
| **Absent** | 23(74.2%) | 12(38.07%) |
| **Total** | **31(100.0%)** | **31(100.0%)** |  |

Data were expressed as frequency, percentage Chi-square test, s= significant

**Status of patients of IH by pulse rate in both groups:** Table-8 shows mean pulse rate in different follow-up in both groups. In Group-A, mean pulse rate was 110.97 at pre-treatment period and 98.10 was at post treatment follow-up. In Group-B, mean pulse rate was 113.84 at pre-treatment period and 109.35 was at post treatment follow-up.

## Table-7: Comparison of pulse rate in different follow up between two groups (n=62)

|  |  |  |  |
| --- | --- | --- | --- |
| **Pulse rate (/min)** | **Group A (Propranolol) (n=31)****Mean±SD** | **Group B (Propranolol+prednisolone) (n=31)****Mean±SD** | **p-value** |
| **Pre-treatment** | 110.97±18.07 | 113.84±17.89 | **0.532ns** |
| **2nd week** | 104.90±15.91 | 112.39±15.62 | **0.066ns** |
| **1st month** | 102.00±14.59 | 107.48±20.78 | **0.234ns** |
| **2nd month** | 100.13±13.26 | 106.13±19.04 | **0.155ns** |
| **3rd month** | **98.10±12.79** | **109.35±13.44** | **0.001s** |

Data were expressed as mean±SD

Unpaired student t-test, s= significant, ns= not significant

Table-8 shows Changes of pulse rate from pre-treatment to post-treatment within group: In Group-A, mean pulse rate per minute change from pre-treatment was between 6.06-12.87 (5.47%-11.6%) during the period of subsequent follow-up. Maximum changes of pulse rate was seen at 3rd month follow-up. In Group-B , mean pulse rate per minute change from pre-treatment was between 1.45-7.71 (1.48%-7.86%) during the period of subsequent follow-up. Maximum changes of pulse rate was seen at 2nd month follow-up.

## Table-8: Changes of pulse rate from pre-treatment to post-treatment within group (n=62)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Pulse rate (/min)** | **Follow up** | **Mean±SD** | **Mean****difference** | **%****changes** | **p-value** |
| **Group A****(Propranolol)** |  |  |  |  |  |
| **Pre-treatment** |  | 110.97±18.07 |  |  |  |
| **Post treatment** | 2nd week | 104.90±15.91 | -6.06 | -5.47% | **<0.001s** |
| 1st month | 102.00±14.59 | -8.97 | -8.08% | **<0.001s** |
| 2nd month | 100.13±13.26 | -10.84 | -9.77% | **<0.001s** |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | 3rd month | 98.10±12.79 | -12.87 | -11.60% | **<0.001s** |
| **Group B (Propranolol+prednisolone)** |  |  |  |  |  |
| **Pre-treatment** |  | 113.84±17.89 |  |  |  |
| **Post treatment** | 2nd week | 112.39±15.62 | -1.45 | -1.48% | **0.215ns** |
| 1st month | 107.48±20.78 | -6.35 | -6.47% | **0.083ns** |
| 2nd month | 106.13±19.04 | -7.71 | -7.86% | **0.039s** |
| **3rd month** | **109.35±13.44** | **-4.48** | **-4.57%** | **0.001s** |

Data were expressed as mean±SD. Paired t-test, s= significant, ns= not significant

Glycemic status of patients in both group: Table-9 shows mean blood glucose level of children of both group during the period of subsequent follow-up. There was no data which support hypoglycemia. In Group-A, minimum blood glucose level was 4.3 and maximum was 6.2 In Group-B, minimum blood glucose level was 4.8 and maximum was 6.6.

## Table-9: Comparison of blood glucose level in different follow up between two groups (n=62)

|  |  |  |  |
| --- | --- | --- | --- |
| **Blood glucose (mmol/L)** | **Group A (Propranolol) (n=31) Mean±SD** | **Group B (Propranolol+prednisolon e) (n=31)****Mean±SD** | **p-value** |
| **2nd week** | 5.23±0.40 | 5.45±0.28 | **0.016s** |
| **1st month** | 5.17±0.30 | 5.46±0.31 | **<0.001s** |
| **2nd month** | 5.08±0.32 | 5.45±0.29 | **<0.001s** |
| **3rd month** | 5.17±0.31 | 5.44±0.30 | **0.001s** |
| **Range** | **4.30 -6.20** | **4.80-6.00** |  |

Data were expressed as mean±SD Unpaired student t-test, s= significant

**Table-10: Classification of vascular anomalies**

|  |  |
| --- | --- |
| Vascular Tumors | Vascular malformations |
| HemangiomaInfantile hemangioma Congenital hemangioma* Rapidly involuting congenital hemangioma (RICH)
* Non involuting congenital hemangioma (NICH)

Kaposifrom hemangioendotheliomaKaposiform lymphatic malformationTufted angiomaCutaneovisceral angiomatosis with thrombocytopeniaAngiosarcoma Kaposi sarcomaPyogenic granuloma | Slow-flow* Capillary
* Lymphatic
* Venous

Fast flow* + Arterovenous fistula
	+ Arteriovenous malformation

Complex-combined* Capillary lymphatico- venous (Klippel Tranaunay)
* Capillary- arteriovenous (Parkes Weber)
* Lymphatico-venous (Rare)
 |

# DISCUSSION

In this prospective study, total 76 patients of clinically diagnosed infantile hemangioma were recruited. Among them 8 patients were excluded and 1 patient refused to participate.5 patients were lost their follow-up. So, at last 62 patients were followed up for analysis. In Group-A 31 patients were treated with oral propranolol and in Group-B, 31 patients were treated with combined oral propranolol and prednisolone. In Group-A, mean age was 13.11 months and in group -B, mean age was 17.82 months. The ratio of male and female in my study was 1:1.1. Usually, this demographic variation does not affect its treatment outcome. The first noticeable effects of the treatment of hemangioma were changes of color. Color changes of IHs were analyzed by visual analogue scale. In my study, In Group- A-Excellent response was found 22.6% where 6.5% in Group-B. Good response was 19.4% in Group-A and 19.5% was in Group-B. Fair response showed in 45.2% in Group-A and 54.8% in Group-B. Poor response was 12.9% in Group-A and 19.4% in Group-B., overall color changes showed better in Group-A comparable to Group-B but statistically not significant. Aly et al in 2015 [14] found significant color changes in combination group. It may be for longer treatment duration than me. Regarding regression of size of IHs are very important to measure the percentage of regression. Overall regression was seen in all patient. In Group-A, mean percentage of regression of size was 68.05. In Group-B, mean percentage of regression of size was 59.35. which was not statistically significant. Aly et al in 2015 [14] found significant response to treatment with combining propranolol with

prednisolone may be their more follow up time. Sharma et al in 2013 [15] also found no significant difference in regression of size of the lesions in both group of their study which was similar to my study. After discontinuation of the therapy 2 patients in group-A and 3 patients in Group-B developed recurrence of IH which began to grow slowly. Repeat therapy was administered for the beneficial result and to prevent relapse. In further follow up there was no significant difference in improvement between two groups. In order to obtain a considerable improvement treatment was continued beyond the follow up period. One case series reported a recurrence rate of 19% after discontinuation of propanol therapy (Bagazgoitia, Hernandez-Martin, Torrelo.,2011) [16]. Regarding the adverse effect of either monotherapy by propranolol or combined treatment with prednisolone none of the patients were excluded from the study as there were no severe side effects. Although the most commonly reported, serious adverse effects of propranolol in IH has been hypoglycemia and bradycardia, I did not encounter any documented cases of hypoglycemia and bradycardia. Propranolol is generally well tolerated in my study. All patients were hemodynamically stable. Price et al in 2011[18] found one of 68 patients (1%) had hypoglycemia, and 2(3%) had a non-specific skin eruption. Then they discontinued in the latter 2 patients and then restarted at a later date, without recurrence. Therefore, their adverse effects were determined unlikely to be related to propranolol therapy. On the other hand, despite reports of successful corticosteroid therapy in the treatment of IHs evidence for the efficacy and safety are scant. Moreover, Systemic corticosteroid have known side effects. In my study in Group B, faced more side effects but all are not severe. Pan, (2018) [12] in his study also found more side effects in combination therapy. Among them 1 had transient decreased of blood pressure, 2 patients presented a lower heart rate after initial dose of drug, 1 patient presented with lethargy, refusal to take feed and excessive regurgitation of feeds 1 week following initiation of treatment, 1 patient had sleep disturbance and rash involving the face and trunk and 1 patient suffered from hypoglycemia induced seizure during an episode of gastroenteritis. He found more serious side effects may be dose of drug related. Status of the patients of IHs by pulse rate at pre-treatment and post-treatment follow up in both groups were measured. Mean pulse rate per minute change from pre- treatment was between -6.06 to -12.87 during subsequent follow up in Group-A. In Group-B Mean pulse rate per minute change from pre-treatment was between -5.7 to -11.6 during subsequent follow up. There was no significant differences between two groups. Pulse rate was not dropped in any patients below 84 beats/min. No patient developed bradycardia according to age variation. No fall of blood pressure was seen in 62 patients. Haque (2014) [19] at Dhaka shishu hospital found mean pulse rate per minute change from pre-treatment is between value -11.00 to -12.31 in patients treated with propranolol during subsequent follow-up which was slightly differ from my studies. Accurate dose of propranolol usually well tolerated and shows less drop of pulse. Mean blood glucose levels of the patients of group A and group B were compared. None of the patients suffered from hypoglycemia or hyperglycemia. In my study, lowest blood glucose level was 4.3 mmol/L and highest 6.2 mmol/L in Group-A and lowest blood glucose level was 4.8 mmol/L and highest 6.0 mmol/L. Mean blood glucose level was slightly higher in Group-B than Group-A. Haque (2014)

[19] at Dhaka shishu hospital also found similar mean blood glucose level in propranolol group. In my study, all patients were given a starting dose of 1 mg/kg/day in divided doses and titrated to a target dose of 2-3 mg/kg/day according to clinical response. Sharma et al in 2013 [15] used propranolol at a dose of 3 mg/kg/day in their study. Various dosage schedules have been descried for oral prednisolone, which ranges from 1-5 mg/kg/day either as daily or alternative day regimen (Sharma et al.,2013) [15]. In my study, patients of Group-B were given oral prednisolone at a dose of 2-3 mg/kg/day in two divided doses. Haque et al in 2014 [19] used prednisolone at 2 mg/kg/day in their study. Sharma et al (2013) used prednisolone at a dose of 5 mg/kg/day on alternate day basis (i.e., 10 mg/kg/day on alternate days) in their study. According to present study, both the groups showed considerable improvement. But combination therapy was not well tolerable. Hence due to well tolerability of propranolol there was no need of additional use of prednisolone.

# CONCLUSION & RECOMMENDATION

This study concludes that there is no significant difference in the effectiveness between oral propranolol alone and combination therapy with prednisolone in the treatment of infantile hemangioma. However, there was more side effects in combination therapy. Hence there is no need of additional use of prednisolone with propranolol.

**Ethical Approval and Consent:**

* + Ethical clearance for the study was taken from the Institutional Review Board (IRB) of BSMMU prior to the commencement of this study.
	+ After the research protocol is approved by the committee, permission for the study was taken from the Department of Pediatric Surgery, BSMMU.
	+ The aim and objectives of the study along with its intervention, risks and benefits of this study were explained to parents of study subjects in an easily understandable local language.
	+ An informed written consent was taken from all the parents of the participants without exploiting any of their weakness.
	+ Privacy, anonymity and confidentiality of data information identifying any patient were maintained strictly.
	+ Each patient enjoyed every right to participate or refuse or even withdraw from the study at any point of time.
	+ Due respect was be given to all the subjects.
	+ Signed informed written consent was taken from subject
	+ Research data were coded
	+ Data were stored in a locked cabinet
	+ Only research personnel was allowed to access data
	+ There was minimum physical, psychological, social and legal risk
	+ Proper consent was taken •Privacy of patient was maintained

# STUDY LIMITATION

* Single center study.
* Relatively small numbers of patients.

**Disclaimer (Artificial intelligence)**

No generative AI technologies were used in writing or editing this manuscript

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