

## Original Article

## Alternative treatment modality for periocular infantile hemangioma

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## ABSTRACT

**Background:** Capillary hemangiomas are the most common tumors of the eyelids and orbit in children. They typically appear at or shortly after birth, with approximately 90% being clinically obvious by 2 months of age. Complications include functional sequelae like anisometropia, amblyopia, visual axis impairment; cosmetic sequelae like scarring, ulceration, bleeding, displacement of the globe, proptosis and even optic nerve compression. Therapeutic options include corticosteroids, beta-blockers, pulse dye laser, topical imiquimod, interferon- $\alpha$ , vincristine, cyclophosphamide and surgery.

**Aim:** The aim of our study is to investigate the efficacy of intralesional triamcinolone and combination of intralesional triamcinolone with topical timolol in treatment of periocular infantile hemangioma & its recurrence.

**Method:** This prospective study was performed in 24 patients with periocular hemangiomas requiring intervention. Patients were arranged in two groups: Triamcinolone acetonide intralesional injection alone & combination of triamcinolone acetonide intralesional injection with timolol maleate local application. Patients were followed up for three months. The size of the hemangioma was measured in mm<sup>2</sup>.

**Result:** In Group 1, 66.66% of patients showed good response while in group 2, 88.89% of patients showed good response. Group 2 showed less recurrence rate than group 1. None of the patients developed local side effects during or after injection.

**Conclusion:** Beta blocker and intralesional steroid both are relatively safe and effective for the periocular capillary hemangioma. Beta blocker with intralesional steroid has less chances of recurrence than beta blocker and steroid alone.

**Keywords:** Infantile hemangioma, Triamcinolone acetonide, Timolol maleate.

## INTRODUCTION

Capillary hemangiomas are the most common tumors of the eyelids and orbit in children [1]. These benign vascular tumors affect 4-10% of infants, which termed as infantile hemangioma (IH) [2-3]. They typically appear at or shortly after birth, with approximately 90% being clinically obvious by 2 months of age [4]. The exact etiology of capillary hemangiomas remains unclear, but likely to involve a combination of angiogenesis and vasculogenesis. IHs are more likely to occur in low birth weight, premature infants following maternal infertility treatment [5]. It exhibit an initial phase of progressive growth followed by spontaneous regression, and 70% regress completely by the age of 7 years, but it may induce complications

if they left untreated [6]. Complications include functional sequelae like anisometropia, amblyopia, visual axis impairment; cosmetic sequelae like scarring, ulceration, bleeding, displacement of the globe, proptosis and even optic nerve compression [7,8].

So treatment should be based on the basis of individual circumstances, such as size and location of the tumor, complications, the phase at the time of evaluation, the involvement of other organs, and psychological factors [9]. Therapeutic options include corticosteroids, beta-blockers, pulse dye laser, topical imiquimod, interferon- $\alpha$ , vincristine, cyclophosphamide and surgery [8]. Eventhough corticosteroids have been the mainstream treatment

for IHs for many years, the effectiveness of corticosteroids is limited to the proliferative phase of IH growth. There are various routes of administration (topical, intralesional, oral and intravenous), but it is associated with varying degrees of adverse effects like growth retardation, infections, and pain [2,10-15]. The efficacy of propranolol, a non-selective beta-blocker, in the treatment of IHs has been demonstrated [16]. Numerous reports have suggested that other beta-blockers such as nadolol and timolol are effective for treatment of IH [17-24].

The aim of our study is to investigate the efficacy of intralesional triamcinolone and combination of intralesional triamcinolone with topical timolol in treatment of periocular infantile hemangioma & its recurrence.

## MATERIAL AND METHODS

During our prospective study period we encountered 24 patients with periocular hemangiomas requiring intervention. Patients were divided in groups without any randomization. Sampling method was non-randomized and so No matching was done. The indications for intervention in our study were vision threatening capillary hemangioma, rapidly progressive or recurrently bleeding hemangioma and cosmetically unacceptable hemangioma.

Prior to inclusion, all patients were subjected to a detailed cardio-respiratory evaluation, including history-taking, detailed clinical examination, and a 12-lead electrocardiogram, including calculation of heart rate, voltages, and intervals. Any child with cardiovascular problems, bronchial asthma, or diabetes mellitus was excluded. Children who had had previous treatment for hemangioma were also excluded. This study does not include systemic drug administration, thus ethical clearance is not taken.

Patients were arranged in two groups:

Group 1: Triamcinolone acetonide intralesional injection (40 mg/ml)

Group 2: Triamcinolone acetonide intralesional injection (40 mg/ml) + Timolol maleate eye drops (0.5%) local application

15 patients were included in group 1 and 9 patients in group 2. The volume of injected drug depended on the size of the lesion (0.2 ml injected per cm of lesion diameter), with a maximum of 1 ml. Patients had intralesional injection under topical anesthesia with cardiovascular and respiratory monitoring during and

after injection. In addition, dilated fundus examination was done during injection, with careful examination of the central retinal artery.

Patients were followed up weekly for the first month, 2 weekly for second month, 4 weekly for a period of three months. The size of the hemangioma was measured by clinical examination and documented by serial photography. The area was then calculated in mm<sup>2</sup> and measured serially. The response to therapy was graded as excellent, good, fair and poor according to the final outcome achieved at the time treatment was stopped. [Table 1]

Table 1: Grading of response to treatment

Excellent	Complete resolution achieved
Good	Sustained plateau, with >50% reduction in size of hemangioma
Fair	Sustained plateau, with <50% reduction in size of hemangioma
Poor	No response or worsening of hemangioma

Changes in each group were analyzed using repeated measures analysis of variance. Differences between the groups were analyzed using the *t*-test for independent samples. Statistical analyses were carried out using Stat Lab, SPSS for windows.

## RESULTS

Total 24 patients of periocular capillary hemangioma were included in study (mean 9.50 months) with most common site upper eyelid (62.50%). [Table 2]

Table 2: Change in Size of hemangioma after treatment

	Group 1	Group 2
Mean Size before treatment	19.66 +/- 4.53	24.33 +/- 9.81
Mean size after 3 month of treatment	11.06 +/- 5.53	12.11 +/- 5.62
T test	4.710 (P < 0.05)	3.243 (P < 0.05)

All two groups show significant improvement in size of capillary hemangioma after the treatment according to unpaired *t* test. [Table 3]

In Group 1, 66.66% of patients showed good response while in group 2, 88.89% of patients showed good response.

Table 3: Response to Treatment

Response	Group 1	%	Group 2	%
Poor	2	13.34	0	0
Fair	3	20	1	11.11
Good	10	66.66	8	88.89
Excellent	0	0	0	0
Total	15	100	9	100

#### Outcome of intralesional steroid treatment

13 of 15 patients in the intralesional steroid group showed regression of hemangioma. Onset of regression varied from 1 to 12 weeks after the intralesional steroid so that all 13 patients showed evidence of regression by the end of the 12 week.

Regression started with a change in the hemangioma color from intense red to purple-blue with palpable softening of the lesion. After this response, hemangioma continued to improve as regards regression of their size, flattening of the lesion, and more evident blanching of the color.

At the end of the follow-up period, no patient ( $n = 0$ ) showed complete resolution of the lesion, 66.66% ( $n = 10$ ) showed a good response, and 20.00% ( $n = 3$ ) showed a fair response. Five patients (33.33%) showed recurrence to treatment

#### Outcome of intralesional steroid plus topical timolol treatment

8 of 9 patients in the intralesional steroid plus topical timolol group showed regression of hemangioma. Onset of regression varied from 1 to 8 weeks after the initiation of treatment. All of 8 patients showed evidence of regression by the end of the 12 week.

The clinical course of regression was change in color and regression in size and depth of the lesion.

At the end of the follow-up period, no patient ( $n = 0$ ) showed complete resolution, 77.77% ( $n = 7$ ) showed a good response, and 11.11% ( $n = 1$ ) showed a fair response. Two patients (22.22%) showed recurrence to treatment.

None of the patients developed local side effects during or after injection. Patients in the both group had no significant change in heart rate or blood pressure during or after injection. [Figure 1 & 2]

Figure 1: Pre-treatment infantile hemangioma



Figure 2: Post-treatment infantile hemangioma



#### DISCUSSION

Our study aimed at to find efficacy of different treatment modalities of capillary hemangioma. In our study, combination treatment of intralesional steroid and topical  $\beta$ -blocker was effective than intralesional steroid alone. Topical timolol eye drop was not associated with significant cardiovascular changes or local adverse effects. Recurrence rate was higher in only intralesional steroid group.

Leaute-Labreze et al have revolutionized use of  $\beta$ -blocker for the management of infantile haemangioma [16]. They reported two children who were on propranolol for cardiac problems, but who coincidentally also had facial infantile haemangiomas, had significantly reduced in size after treatment. They then successfully treated nine other children with facial infantile haemangiomas using propranolol.

Qin et al performed study in 58 infants with infantile hemangioma using low dose propranolol, reported a good to excellent result in 67% of patients [25]. All of these patients were younger than 5 months at the time of starting treatment. This may be explained by that, in the early months of life, capillary hemangioma

is in its active proliferative phase when there are high levels of pro-angiogenic factors. Later on, there may be a shift of balance towards pro-apoptotic factors, reducing the chance of rebound growth. This suggests that combination treatment of intralesional steroid and topical  $\beta$ -blocker is better than single drug intralesional injection or systemic therapy.

Despite the promising results, this study had some limitations that should be noted, such as relatively small number of patients.

## CONCLUSION

Beta blocker and intralesional steroid both are relatively safe and effective for the periocular capillary hemangioma. Beta blocker with intralesional steroid has less chances of recurrence than beta blocker and steroid alone.

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