

# 0.5% Timolol eye drop monotherapy as a first-line treatment for capillary hemangioma

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**Purpose:** To evaluate the efficacy and safety of 0.5% Timolol eye drop monotherapy as a first-line treatment for capillary hemangioma.

**Methods:** Retrospective, consecutive, clinical case series

**Results:** Medical records, including consequent photographs of children with capillary hemangioma treated consecutively with 0.5% timolol solution from October 1<sup>st</sup>, 2017 to July 31<sup>st</sup>, 2018 were reviewed.

11 cases of capillary hemangioma, age 0-8 months, were treated with 0.5% Timolol eye drops applied to the lesions twice a day as monotherapy for at least one month. General physical examination, included vital signs, respiratory rate, skin lesions, and eye examination before treatment were performed at every follow-up visit.

Eight of 11 cases showed improvement in size, thickness, and coloration of the lesions without any complications. All 8 cases showed clinical improvement within 2 months of treatment. One case had relapsed after treatment cessation and got better after re-treatment. One case was lost to follow up. One case failed the monotherapy and needed additive treatment with propranolol and vinblastine.

**Conclusion:** 0.5% Timolol eye drop monotherapy can be used safely as a first-line treatment for capillary hemangioma, especially uncomplicated cases.

**Conflicts of interest:** The authors report no conflicts of interest.

**Keywords:** Capillary hemangioma, 0.5% Timolol eye drop, Monotherapy, First-line treatment, Efficacy

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## Introduction

Capillary hemangioma is the most common benign tumor in children. Despite their benign and self-limited nature, some hemangiomas can cause complications such as ulceration, infection, disfigurement, scarring, bleeding, vision

impairment, and difficult breathing<sup>1</sup>. Since 2008, systemic beta-blockers such as oral propranolol have been used to treat capillary hemangiomas and has been proved superior to previous therapies<sup>2</sup>. Although the systemic use of beta-blockers may cause severe side effects, such as bradycardia and hypoglycemia. An intensive vital sign screening, serum glucose level should be monitored, and cardiologist consultation is needed<sup>3</sup>. Recently, a topical beta-blocker as 0.5% timolol maleate, a basic anti-glaucoma medication, both eye drop solution and eye gel<sup>4,5,6</sup>, has been reported as an effective

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treatment for capillary hemangioma, especially superficial lesion without report of serious complications in many countries but no reported data from Thailand about the use of 0.5% Timolol eye drop applied topically on the lesion as monotherapy first-line treatment for capillary hemangioma.

### Purpose

To evaluate efficacy and safety of 0.5% Timolol eye drop monotherapy as a first-line treatment for capillary hemangioma

### Methods

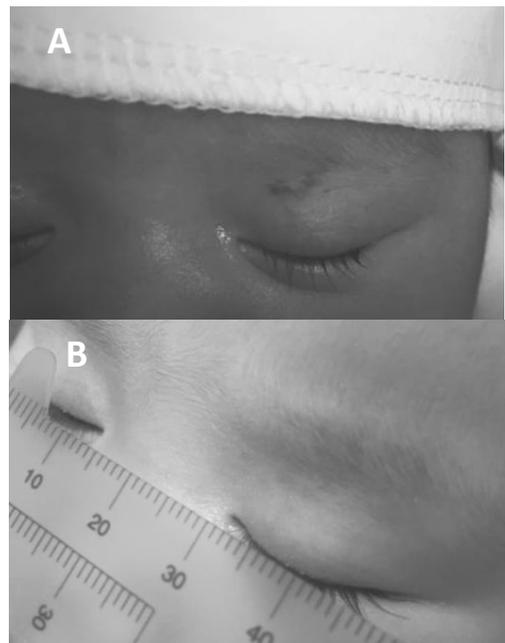
The medical records of all capillary hemangioma cases from October 1st, 2017 to July 31<sup>st</sup>, 2018 were reviewed and included only cases who received 0.5% Timolol eye drop monotherapy topical application twice daily as a first-line treatment. The collected data included demographics, lesion location, size-color-thickness of the lesion with serial photographs of the lesion treated consecutively with 0.5% Timolol solution, treatment duration, treatment side effects, follow-up time, and disease regression (recorded as none, complete, or incomplete regression, graded as good or fair response).

### Results

During the study period, we had 11 cases of capillary hemangioma, ages between 0-8 months, who were treated with 0.5% Timolol eye drop applied to the lesions twice a day as monotherapy for at least one month. General physical examination, including vital signs, respiratory rate, skin lesions, eye examination before treatment was performed at every follow-up visit. The parents of all 11 cases were informed about risks and benefits before starting the treatment and signed consent. The follow-up schedules were 1 – 3 months depending on parent availability with both pediatricians and ophthalmologists. None of the cases reported systemic or localized side effects during the treatment.

All 8 of 11 cases showed improvement in size, thickness, and coloration of the lesions, but had differences in treatment duration as shown in table 1. All 8 cases showed clinical improvement within 2 months treatment initiation. One case relapsed after treatment cessation and improved after re-treatment. One case failed to follow up.

One case failed the monotherapy and needed additive treatment with propranolol and vinblastine. (Table1 and Figure 1-5) None had systemic or localized side effects.



**Figure 1** A 2-month-old girl with a capillary hemangioma on the left upper eyelid (case 1 from table 1)

A. Before treatment

B. 2 months after topical 0.5% Timolol treatment



**Table 1** Summary of treatment capillary hemangioma with 0.5% Timolol eye drop monotherapy

Patient No.	Sex	Age at Treatment	Lesion location	Treatment Duration (months)		Response	Side effects	Follow-up (months)	Other treatments
				improve	total				
1	F	2	Left upper eyelid	2	4	Complete regress	No	6	
2	F	4	Left thigh	2	2	Fair	No	Loss F/U	
3	F	6	Sternum	2	4	Good	No	4	
4	M	3	Left upper eyelid	2	2	Good	No	2	
5	F	1	Left upper eyelid	2	2	Good	No	2	
6	F	8	Scalp	1	4	Good	No	4	
7	F	1	Midface (lip/lid/forehead)	2	10	Complete regress	No	12	
8	F	4	Right axilla	2	2	Good	No	2	Terramycin (ulcerative hemangioma)
9	F	8	Right forearm	2	12	Good	No	12	
10	F	0	Left lower eyelid	1	1	No	No	2	Propranolol Vinblastine
11	M	8	Left chest	2	4	Good	No	4	

**Figure 2** A 4-month-old girl with an ulcerative capillary hemangioma on the right axilla (case 8 from table 1)

**A.** Before treatment

**B.** 2 months after topical 0.5% Timolol treatment together with terramycin



**Figure 3** An 8-month-old girl with a capillary hemangioma on the right forearm (case 9 from Table 1)

**A.** Before treatment

**B.** 2 months after topical 0.5% Timolol treatment  
**C.** 2 months after topical 0.5% Timolol treatment



**Figure 4** A newborn girl with a capillary hemangioma on the left lower eyelid (non-responsive case) (case 10 from table 1)

**A.** Before treatment

**B.** 2 months after topical 0.5% Timolol treatment combined with oral propranolol. The tumor did not respond to beta-blockers and Vinblastine was added to treat the lesion.



**Figure 5** An 8-month-old boy with a capillary hemangioma on the left chest (case 11 from table 1)  
**A.** Before treatment  
**B.** 4 months after topical 0.5% Timolol treatment

## Discussion

Timolol -an inexpensive generic drug that has a low side effect profile-could be beneficial for treating capillary hemangioma even in a newborn with stable vital signs as a first-line treatment in an outpatient setting with less monitoring required than systemic beta-blockers. Topical eye drops, applied over the entire lesion twice-daily, can be used safely and effectively even in ulcerative hemangioma as in this study. Ng MSY et al.<sup>7</sup> revealed similar therapeutic efficacies for both 0.5% Timolol eye drop with 0.5% timolol ophthalmic gel-form. Although, not all cases have good responses. From this study, we found that responsive lesions started a regression in color and/ or thickness within 2 months.

In non-responsive cases, further investigations and management should be performed. The exact mechanism of action of beta-blockers for the treatment of capillary Hemangioma remains unknown. The possible explanation may include vasoconstriction due to decreased release of nitric oxide, which results in the early visible change in color and softening of the hemangioma.<sup>9</sup>

Growth arrest is attributable to the blocking of proangiogenic signals, including vascular endothelial growth factor, basic fibroblast growth factor, matrix metalloproteinases and endothelial nitric oxide synthase<sup>10</sup>. Topical timolol

was found to be systemically absorbed with low serum levels<sup>8</sup>, thus before starting treating the lesions with topical beta-blocker medication, the parents should be informed of risks and benefits of the treatment and complications that may ensue and how to observe their children.

In conclusion, our data suggests that we can safely use 0.5% Timolol eye drop, an inexpensive generic drug, as a first-line monotherapy for capillary hemangioma cases in outpatient settings, although treatment providers need to discuss risk, benefits, and further management if the patient has a poor response to this treatment with the parents before initiating therapy. We can evaluate the treatment efficacy in two months. Non-responsive cases need other adjunctive treatments. This is the first study to report the use of 0.5% timolol eye drop topical application monotherapy as a first-line treatment for capillary hemangioma in Thailand even though it was limited by retrospective design, small sample size, and short observation period. Further prospective randomized controlled trials with larger sample sizes and longer observation periods are needed to confirm the efficacy and safety of topical timolol eye drop for the treatment of capillary hemangioma.

## Conclusion

0.5% Timolol eye drop monotherapy can be used safely as a first-line treatment for capillary hemangioma, especially in uncomplicated cases.

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