A stylized, colorful illustration of a landscape. The foreground features rolling green hills with a brown path. On the left, there is a green tree, a purple flower, and an orange flower. A red bird is flying in the sky above the tree. The background consists of layered blue and white waves, suggesting a sky or water. The overall style is flat and modern.

TOPICAL TIMOLOL IN INFANTILE HEMANGIOMA

Dr. Nguyen Thi Thuy

Definition

- Infantile hemangioma: common neoplasms composed of proliferating endothelial-like cells.

Management

- Many choices:
 - Corticosteroid: topical, oral, or intralesional
 - Beta-blocker
 - Laser
 - Surgery
 - ...

Management

- No guidelines about management of infantile hemangioma
- Beta-blocker, especially topical propranolol, is very efficient in treatment of superficial cutaneous hemangioma, with minimal side-effects.

BETA-BLOCKERS

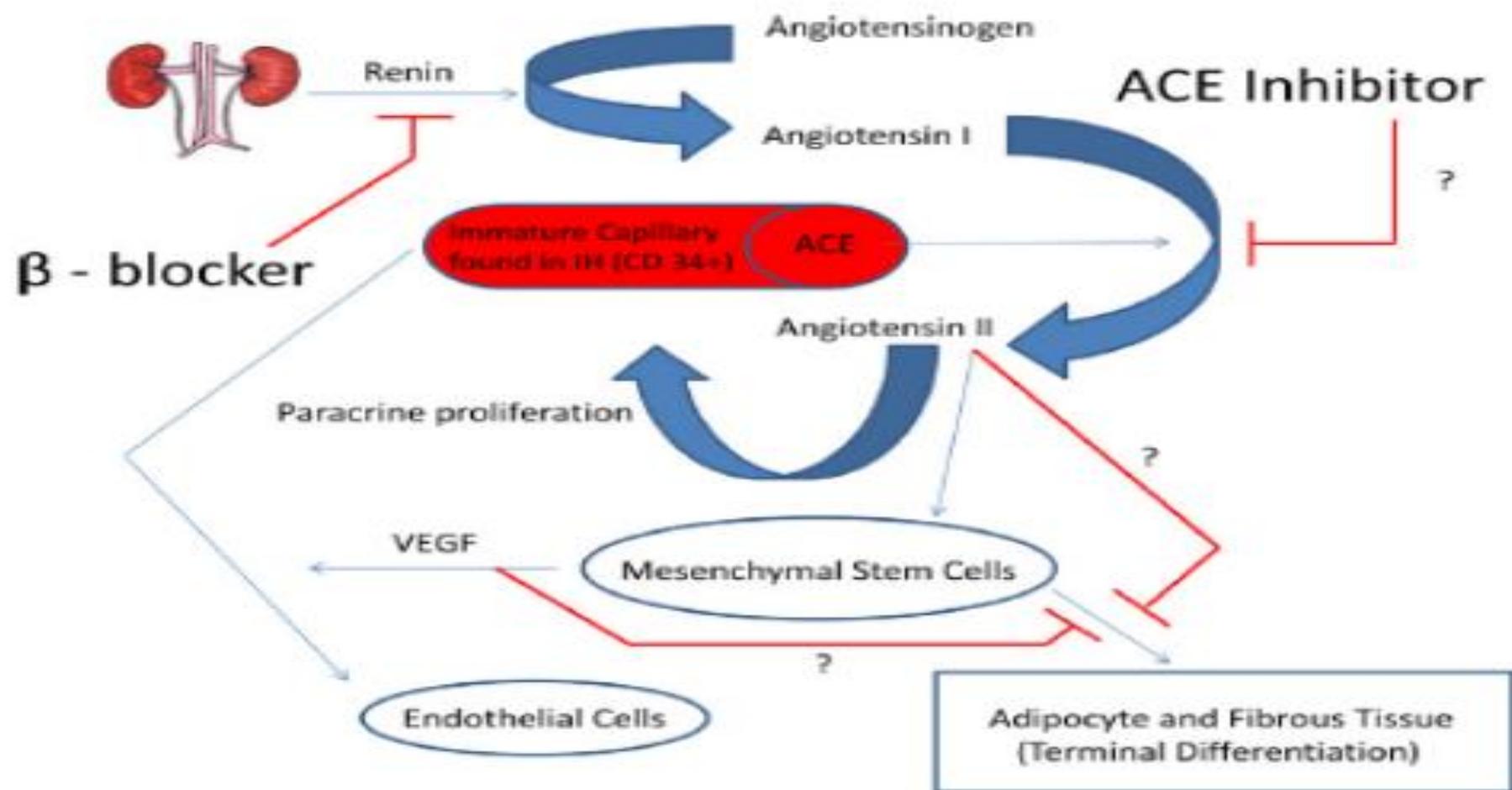


Figure 1 Proposed mechanism of action of beta-blockers in the treatment of IH. A CD34⁺ population of ICC found in IH are thought to express ACE in addition to the angiotensin II receptor. Local angiotensin I (A1) is converted by ACE to angiotensin II (A2). A2 presumably promotes: (a) the release of VEGF from MSC within IH, and (b) a paracrine-like proliferation of ICC. It is thought that VEGF not only prevents the terminal differentiation of MSC into fibrofatty tissue, but also facilitates the maturation of ICC into endothelial cells. Beta-blockers inhibit the upstream release of renin, thereby blocking the entire sequence of events illustrated previously. Note that in this proposed schematic, inhibition of VEGF release would lead to normal terminal differentiation of MSC into fibrofatty tissue, the clinically observed endpoint of IH. ACE, angiotensin-converting enzyme; IH, infantile hemangioma; ICC, immature capillary cells; VEGF,

Research studies

- 2010: S. Guo and N. Ni report first case



Figure 1. Before topical treatment, a large capillary hemangioma involved the child's left upper eyelid, inducing mechanical blepharoptosis and covering her left pupil.



Figure 2. After a few weeks of treatment with topical β -blocker eyedrops, the hemangioma was significantly reduced in size, thickness, and color. The mechanical blepharoptosis also improved significantly, clearing the visual axis.

1 0
pia. The child's mother was instructed to apply timolol maleate, 0.5%, ophthalmic solution twice daily, 2 drops onto the surface of the hemangioma with a gentle spread using a finger. The child was not receiving systemic medication and was followed up by her pediatrician during the treatment period. After 5 weeks of treatment, the hemangioma was significantly reduced in size, thickness, and color, clearing the visual axis (Figure 2). Topical β -blocker treatment was discontinued at 7 weeks and repeat retinoscopy results at 11 weeks improved to $+4.00 - 1.50 \times 180^\circ$ OS. The child has been followed up for 4 months and tolerated the topical treatment well. No local or systemic adverse effects were noted.

Research studies

- 2011: N. Ni et al – 7 cases
- 2012: A.Oranje et al - 20 cases
- 2013: Rivi. S et al - 2 cases
- Decreased significantly in size and colour, and nearly no side-effects.

KHẢO SÁT TÁC DỤNG CỦA DUNG DỊCH TIMOLOL MALEATE 0,5% DÙNG TẠI CHỖ TRÊN TRẺ NHỮ NHỊ BỊ U MÁU VÙNG DA ĐẦU

Phan Ngọc Quỳnh Anh*, Hoàng Văn Minh*

TÓM TẮT

Mở đầu: U máu nhũ nhi là dạng lành tính thường gặp nhất ở trẻ sơ sinh, phát triển trong một năm đầu, sau đó thoái triển tự nhiên trong khoảng 2-7 năm sau. Tuy nhiên, u máu thường không thoái triển hoàn toàn, trẻ có thể còn lại di chứng của u máu như mô sợi, sẹo, và/hoặc giãn mạch. Hiện nay có nhiều phương pháp điều trị u máu, gần đây nhất là dùng dung dịch timolol thoa tại chỗ. Do đó, chúng tôi thực hiện đề tài “Khảo sát tác dụng của timolol 0,5% dùng tại chỗ trên bệnh nhi bị u máu vùng da đầu”.

Đối tượng và phương pháp nghiên cứu: Nghiên cứu tiến cứu mô tả hàng loạt ca trên bệnh nhi dưới 9 tháng tuổi có u máu vùng đầu đến khám lần đầu tiên tại Trung tâm U máu – Bệnh viện Đại học Y Dược – Cơ sở 3. Trẻ được cho thoa dung dịch nhỏ mắt timolol maleate 0,5% hai lần/ngày trong ít nhất 6 tháng. Kết quả được đánh giá dựa trên thang điểm Investigator’s global assessment, bảng điểm tổng quan của phụ huynh và 100-mm visual analog scale (VAS). Mỗi trẻ được đo mạch, huyết áp, chiều cao và cân nặng vào lần đầu tiên và sau mỗi 4 tuần tái khám. Kết thúc quá trình điều trị, Cha Me/Người giám hộ trẻ sẽ được yêu cầu đánh giá về kích thước u máu, tăng và giảm sắc tố, khả năng ảnh hưởng đến hoạt động của trẻ mức độ tin tưởng điều trị, các tác dụng phụ nếu có, khả năng mọc tóc vùng được thoa thuốc.

Kết quả: Tổng cộng 14 trẻ được điều trị với timolol thoa tại chỗ. Sau 6 tháng, tỉ lệ u máu đáp ứng rất tốt là 21,4% (3/14), đáp ứng tốt là 28,7% (4/14), đáp ứng trung bình là 21,4% (3/14), đáp ứng ít là 14,3% (2/14), đáp ứng rất ít là 1/14 (7,1%) chỉ 1 trường hợp u máu không giảm mà còn tăng kích thước, trường hợp này chiếm tỉ lệ 1/14 (7,1%). Không có tác dụng ngoại ý nào đáng kể ảnh hưởng đến trẻ.

Kết luận: U máu nhũ nhi vùng da đầu được điều trị bằng phương pháp thoa timolol maleate 0,5% đạt kết quả khả quan và an toàn sau sáu tháng điều trị. Cần những nghiên cứu với quy mô lớn hơn để đánh giá và đưa ra khuyến cáo chung.

Infantile haemangioma: topical timolol

Evidence summary [ESUOM47] Published date: August 2015

Summary

Limited evidence from 2 small randomised controlled trials (RCTs) and several observational studies suggests that topical timolol reduces the redness of superficial haemangiomas and may reduce their size or volume, but the clinical significance of these changes is unclear. The number of adverse events seen in the studies was low. However, systemic absorption has been shown with timolol used topically to treat infantile haemangiomas and larger studies would be useful to provide more safety data.

Oral propranolol combined with topical timolol for compound infantile hemangiomas: a retrospective study

Jing Ge, Jiawei Zheng , Ling Zhang, Weien Yuan  & Haiguang Zhao

Scientific Reports **6**, Article number: 19765 (2016) | [Download Citation](#) 

Abstract

Compound infantile hemangiomas (IHs) are problematic and usually require intervention. This retrospective study aimed to introduce a combined therapy of oral propranolol and topical timolol, and evaluate its efficacy and safety. Eighty-nine infants with compound IHs were treated with oral propranolol 2 mg/kg/day divided 2 times per day and timolol maleate 0.5% gel 3 times per day, for at least 3 months. Two observers evaluated the hemangioma independently at 0, 1, 3, 6, 9 months after the initiation of treatment. Changes in the hemangioma score values were evaluated using paired t test. Rebound growth and adverse effects were recorded. After treatment was completed, this combined therapy achieved clinical response in 100% of the patients (89/89). Significant positive effects were demonstrated at 1, 3, 6 months ($p < 0.001$), but not obvious after 6 months ($p = 0.06$). The response of IHs to the therapy was depending on the age at initial treatment. The average treatment duration was 6.48 (5.77–7.19) months. One patient (1.1%) relapsed after cessation of 6-month treatment, and 7 children (7.8%) developed side effects. Our study suggested that oral propranolol combined with topical timolol treatment is very effective and well-tolerated for compound IHs, which can be used as a first line treatment.

Conclusion

This retrospective study revealed that oral propranolol combined with topical timolol treatment is very effective and safe for compound IHS, which can be used as a first line treatment. Future prospective trials involving a larger number of patients and a longer follow-up period should be addressed to determine whether this combined therapy fulfils its therapeutic promise.

Pediatrics

August 2016

Article

Topical Timolol Maleate Treatment of Infantile Hemangiomas

Katherine Püttgen, Anne Lucky, Denise Adams, Elena Pope, Catherine McCuaig, Julie Powell, Dana Feigenbaum, Yulia Savva, Eulalia Baselga, Kristen Holland, Beth Drolet, Dawn Siegel, Kimberly D. Morel, Maria C. Garzon, Erin Mathes, Christine Lauren, Amy Nopper, Kimberly Horii, Brandon Newell, Wei Song, Ilona Frieden, on behalf of the Hemangioma Investigator Group

Abstract

BACKGROUND: There has been a dramatic increase in the off-label use of ophthalmic timolol maleate, a β -blocker used for infantile hemangioma (IH) treatment as a topical counterpart to oral propranolol. Its safety and efficacy in a pediatric population with IH have not been evaluated in a large cohort. Our goal was to retrospectively assess timolol's effectiveness, discern characteristics associated with response, and document reported adverse events.

METHODS: A multicenter retrospective cohort study of 731 patients treated with topical timolol was completed at 9 centers. Inclusion required an IH suitable for timolol in the treating physician's judgment and access to clinical details including photographs. Logistic regression analysis and descriptive statistics were performed. Primary outcome measures were efficacy assessed by using visual analog scales for color and for size, extent, and volume from review of digital photographs taken as standard of care.

RESULTS: Most IHs were localized (80.1%) and superficial (55.3%). Risk of disfigurement was the most common indication for therapy (74.3%). Duration of therapy ($P < .0001$), initial thinness ($P = .008$), and subtype ($P = .031$) were significant predictors of response. Best response occurred in superficial IHs <1 mm thick. Fifty-three (7.3%) required subsequent therapy with systemic β -blocker. Adverse events were mild, occurring in 25 (3.4%) patients. No cardiovascular side effects were documented.

CONCLUSIONS: Timolol seems to be a well-tolerated, safe treatment option with moderate to good effectiveness, demonstrating best response in thin, superficial IHS regardless of pretreatment size. Timolol can be recommended as an alternative to systemic β -blockers and watchful waiting for many patients.



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PMID: [28702374](#)

Topical Application of 0.5% Timolol Maleate Hydrogel for the Treatment of Superficial Infantile Hemangioma

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The therapeutic options for infantile hemangiomas (IHs) have been greatly altered since the introduction of oral propranolol for successful treatments of IHs. Recently, there is an increase in the application of topical timolol maleate for treating superficial IHs. In the present study, we developed a new formulation of timolol maleate 0.5% hydrogel and treated 321 patients with superficial IHs to evaluate its efficacy and safety in the treatment of superficial IHs. This new timolol hydrogel was applied three times daily with a mean duration of 7.1 months. Response to treatment was assessed according to cosmetic improvement by using visual analog scale (VAS). The average VAS improvement after treatment was 76.4, with 126 patients (39.3%) achieving excellent responses, 159 patients (49.5%) achieving good responses, 33 patients (10.3%) achieving fair responses, and three patients (0.9%) achieving poor responses. Age at treatment initiation ($P = 0.0349$) and lesion thickness ($P = 0.0147$) were significantly associated with therapeutic efficacy. No severe side effects were observed in all patients. In conclusion, this new topical timolol maleate 0.5% hydrogel appears to be a proper candidate for treating superficial IHs, and our study provides supportive evidence and experience of topical timolol maleate in treating superficial IHs.

The Role of Topical Timolol in the Treatment of Infantile Hemangiomas: A Systematic Review and Meta-analysis

Maham Khan, Aaron Boyce, David Prieto-Merino, Åke Svensson, Emma Wedgeworth, Carsten Flohr

DOI: 10.2340/00015555-2681

Abstract

To date the efficacy and safety of topical timolol in the treatment of infantile hemangioma has not been reviewed and analysed systematically. We collated all published data on the efficacy and safety of topical timolol in the treatment of infantile hemangioma. A total of 31 studies with 691 patients were included. The fixed effects pooled estimate of the response rate defined as any improvement from baseline of infantile hemangioma after treatment with topical timolol was significant (RR = 8.96; 95% CI 5.07–15.47; heterogeneity test $p = 0.99$), and the treatment was overall well tolerated. However, the quality of evidence was low to moderate. Topical timolol is an effective treatment for small infantile hemangioma, with no significant adverse effects noted. However, there is still a need for adequately powered randomised controlled trials.

Topical Timolol Maleate 0.5% for Infantile Hemangioma: Its Effectiveness Compared to Ultrapotent Topical Corticosteroids - A Single-Center Experience of 278 Cases

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Keywords: Superficial infantile hemangioma · Ultrapotent corticosteroids · Timolol maleate 0.5% solution/gel

Dermatology 2016;232:566-571

Abstract

Background: Infantile hemangioma (IH) may have implications on parental distress and cosmetic disfigurement. To date, ultrapotent corticosteroids are used as a treatment of choice for superficial IH. However, due to their side effects and sometimes lack of IH regression, it is necessary to find alternative topical therapies. Timolol maleate 0.5% solution and gel are nonselective β -blockers that could inhibit proliferation and trigger regression of IH. **Objective:** To evaluate the efficacy of topical ultrapotent corticosteroids and timolol maleate 0.5% solution and gel for superficial IH. **Patients and Methods:** The study design was prospective. Two hundred and seventy-eight patients diagnosed as having superficial IH were enrolled from the outpatient clinic of the Department of Dermatology and Venereology, Dr. Sardjito Hospital, Yogyakarta, Indonesia, from January 2009 to December 2014. Patients were divided into three groups: A = treated with topical ultrapotent corticosteroid, B = timolol maleate 0.5% solution and C = timolol maleate 0.5% gel. Patients were followed for 6 months to evaluate the lesion. Lesion size was measured from scaled photodocumentation with the software program ImageJ®. **Results:** There were significant differences in IH size after treatment with timolol maleate 0.5% solution compared with ultrapotent corticosteroids ($p < 0.001$) and timolol maleate 0.5% gel compared with ultrapotent corticosteroids ($p < 0.001$). There was no significant difference in IH lesions after treatment with timolol maleate 0.5% solution versus gel ($p = 0.744$). **Conclusion:** Timolol maleate 0.5% solution and gel were significantly superior to topical ultrapotent corticosteroids in size reduction of superficial IH.



Trước
05/09/12



Sau
02/12/13



Trước
01/02/13



Sau
12/12/13

19/04/2016



04/8/2016



27/10/2016



09/03/2017



12/10/2017



Sau 3 tháng



CONCLUSION

- Topical timolol is may be a good choice for management of superficial IH. It is efficient and safe for children and almost has no remarkably side-effects.
- We need more further studies for it.

THANK

YOU!