Topical Beta Blockers in Small Infantile Hemangioma: State of the Art?

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Introduction

Infantile hemangiomas (IH) are benign forms of endothelial proliferation in the first 8 weeks of life [1-11]. Leaute-Labreze et al. published the first spontaneous cases of IH treated with beta blockers in 2008 due to their cardiac disease in the New England Journal of Medicine. This was a revolutionary new understanding of treatment in infantile hemangioma (IH). Not only systemic but also topical beta blockers seem to be an effective treatment option for small infantile hemangioma. Efficacy and safety of topical beta blockers in the treatment of infantile hemangioma (IH) were proved in systematic reviews and meta-analysis [11]. We present the cases of two children with infantile superficial hemangiomas (IH) treated in our pediatric department. Both parents signed a written consent document to prepare treatment of 2 patients with topical timolol as different studies and clinical analysis have recommended the „off-label“ treatment of topical timolol for infantile hemangiomas with great success [1-4, 6-11].

Case Report

Topical timolol, in a concentration as 0.5% gel, was applied on the hemangioma surface in the morning and the evening put it carefully on the hemangiomal surface. This method was performed for the period of two weeks in each patient. Before start of the therapy, photo documentation of both hemangiomas were taken (Picture A and C). After two weeks, the children were observed for a follow-up and once again, photo documentation was taken (Picture B and C). We observed a clearly-visible change in color from fully red to shade grey and partially color similar to skin color; the skin impressed with a palpable softness of the hemangiomal surface.

Figure A: Patient 1 before treatment with topical timolol.
Infantile hemangiomas must be treated during the proliferative phase [5], especially in the first year of life, as local complications such as ulceration, bleeding and necrosis can lead to scars that are difficult to repair cosmetically in later life. The hemangiomas can even lead to deformities if they are located in the area of the lip, the tip of the nose or the ear. Therefore, early treatment and therapy is of the utmost importance.

Propanolol, a non-selective beta blocker, has been shown to be an effective treatment compared to corticosteroids. The therapeutic effects of propanolol in infantile hemangiomas are the vasoconstriction of the vascular tissue, the reduced expression of the genes of the vascular endothelial growth factor (VEGF) and the basic fibroblast growth factor (bFGF) by downregulating the RAF / mitogen-activated protein kinase pathway as well as the apoptosis of the capillary endothelial cells inside the hemangioma [1].

In a meta-analysis done by Khan et al. in 2017, the treatment with topical timolol 0.5 % was well tolerated and authors came to the result, that topical timolol is an effective treatment in infantile hemangioma. Nevertheless, there is at the moment a very small guidance of optimal dosage and time of application [11].

Timolol is very similar to propanolol. It is available as a topical gel for the treatment of glaucoma in both children and adults. Our cases and multiple studies before suggest that topical timolol gel is effective and safe for the treatment of infantile hemangiomas, and is a viable alternative to systemic propanolol for smaller hemangiomas [6-11]. Further prospective

Blood pressure and heart rate were normal and no complications were found or reported by the parents at home and the examination of both children was without any new aspects, which impresses to finish the local beta blocker therapy.

Discussion
Infantile hemangiomas occur in 5 to 10% of children and are the most common benign soft tissue tumors in childhood. Most hemangiomas resolve spontaneously and only a few require systemic treatment, e.g. B. with beta blockers or interferon. 10% of
studies are needed to determine the efficacy and safety of timolol maleate, 0.5%

References