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**Sue Woodward**, Lecturer, Specialist and Palliative Care, Florence Nightingale School of Nursing and Midwifery, King's College London

## COMMENT

# Children's haemangiomas: use of new topical therapies

Infantile haemangiomas, a type of vascular birthmark, occur in 5–10% of light-skinned children and they are the most common soft-tissue tumors in infancy. Most haemangiomas regress spontaneously and only a few need to be treated systemically. However, 10% of the infantile haemangiomas need to be treated during the proliferative phase (Enjolras and Gelbert, 1997) as local complications, such as ulceration, hemorrhage and necrosis, can lead to scars that are difficult to repair. When haemangiomas are located on the lip, nasal tip or ear, they can even lead to deformities (Khunger and Pahwa, 2011).

For the therapy of infantile haemangiomas, propranolol, a non-selective beta blocker, has proved to be an effective alternative to corticosteroids. The suspected therapeutic effects of propranolol in infantile haemangiomas are vasoconstriction, decreased expression of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) genes by down regulating the RAF/mitogen-activated protein kinase pathway and the apoptosis of capillary endothelial cells (Pope and Chakkittakandiyil, 2010). However, propranolol must be applied systemically and, therefore, side effects, such as hypoglycemia, bronchospasm and hypotension may occur (de Graaf M, 2011).

It is for this reason that topically applicable drugs for the treatment of infantile haemangioma are needed. Quite similar to the non-selective beta-blocker propranolol, is timolol. Timolol is available as a topical gel for the treatment of glaucoma. Topical timolol gel is proposed as an alternative to systemic propranolol in the treatment of infantile haemangiomas and several studies indicate that it is safe and effective to use (Guo and Ni, 2010; Khunger and Pahwa, 2011).

Two children with infantile superficial haemangiomas were presented in our pediatric day center at Ped Mind Institute. With the written consent of both parents, we treated both children with 0.5% timolol maleate gel (Nyogel, Novartis) as several studies have suggested the 'off-label' use of topical timolol for successfully treating infantile haemangiomas (Leaute-Labreze, 2008; Guo and Ni, 2010; Pope and Chakkittakandiyil, 2010; Khunger and Pahwa, 2011)

Timolol gel was rubbed carefully on the haemangiomas two times a day, for a period of 2 weeks. Photos were taken before the start of therapy and again, after 2 weeks, when the parents presented their children for follow up. We observed a significant change in color from dark red to a lighter shade of red and in some places, a shade even to the regular skin colour. This change is associated with a palpable softening of the lesion. The therapy with timolol gel

is scheduled to continue for a period of 4 months or until the haemangiomas disappear.

These cases and several other studies indicate that topical timolol gel is an effective and safe treatment for infantile haemangiomas and provides a real alternative to systemic propranolol. No side effects have been reported in either our cases, or those discussed in the other previously mentioned studies. During therapy with systemic propranolol, however, side effects such as hypoglycemia, bradycardia and hypotension have been reported (Lawley and Seyfried, 2009). Although Timolol is similar to propranolol, its systemic effects on children currently remain unclear. It is important, especially for the nursing staff who work closely with children, to monitor the treatment of infantile haemangioma with topical timolol.

It is, moreover, important to mention a limitation of our study; as it only involved two patients, general recommendations cannot be made. To fully determine the efficacy and safety of timolol maleate, 0.5% gel in the treatment of haemangiomas, further prospective studies are needed.

For infantile haemangioma topical timolol gel is an effective option. However, until there are large, randomized, placebo-controlled studies that clearly determine the role of timolol gel in the therapy of infantile haemangioma, nurses should closely observe the treatment course for possible side effects. **BJN**

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## Anne Weißenstein

Research Assistant, Ped Mind Institute (PMI), Medical and Finance Centre. Epe, Germany.

## Gloria Villalon

Research Assistant, Ped Mind Institute (PMI), Medical and Finance Centre. Epe, Germany.

## Elisabeth Luchter

Research Pediatrician, Ped Mind Institute (PMI), Medical and Finance Centre. Epe, Germany.

## Stefan Bittmann

Head of Ped Mind Institute (PMI), Medical and Finance Centre. Epe, Germany.