

Successful treatment of infantile haemangioma with propranolol

Anne Weissenstein, Elisabeth Luchter and Stefan Bittmann

We report the case of a 4-month-old baby with a large infantile haemangioma of the left shoulder treated successfully with systemic propranolol.

Therapy results were documented by photography. The baby was treated for 4 weeks with oral propranolol with a dosage of 8 mg/day. There was a significant change in colour from dark red to a lighter shade of red and partially even to skin colour. No side-effects occurred during the therapy. Clear guidelines for beta-blocker treatment for infantile haemangiomas are necessary. Beta blockers seem to be the treatment of choice in paediatric haemangioma.

Introduction

The incidence of infantile haemangiomas is 5% to 10% of light-skinned children and they are the most common soft-tissue tumours of infancy (Walter et al, 1999). They occur mostly within the first year of life and female infants are three to four times more likely to suffer from haemangioma as male infants (Frieden et al, 2005).

Haemangiomas are neoplastic proliferations of endothelial cells, which grow after birth and regress spontaneously (Mendiratta and Jabeen, 2010) and only a few need to be treated systemically. However, 10% of the infantile haemangiomas need to be treated during the proliferative phase, as local complications such as ulceration, haemorrhage and necrosis can lead to scars that are difficult to repair (Enjolras and Gelbert, 1997). The haemangiomas can lead to deformities when they are located in areas of the lip, nasal tip or the ear, and can even be life-threatening when present in upper airways and the liver by inducing acute respiratory failure and congestive heart failure (Pope and Chakkittakandiyil, 2010).

For the therapy of infantile haemangiomas, propranolol, a non-selective beta blocker, has

proven to be an effective treatment alternative to corticosteroids or interferon, which have many potential side-effects. The suspected therapeutic effects of propranolol in infantile haemangiomas are vasoconstriction, and 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 (Khunger and Pahwa, 2011).

We present a case of a 4-month-old baby born with a large infantile haemangioma of the shoulder, which was treated successfully with oral propranolol.

Patient and methods

A baby at the age of 4 months with infantile superficial haemangioma was presented in our paediatric day centre. The haemangioma extended over the whole left shoulder and had a dark red colour. After obtaining informed consent from the parents, treatment with propranolol was commenced (8 mg/day over 4 weeks orally as single daily dose). At 4 weeks, a picture of the haemangioma was taken (*Figure 1*).

A physical examination was done before the start of the therapy and the blood pressure was taken. There was no contraindication to the treatment. The follow-up examination,

which included an electrocardiography as well as the measurement of blood pressure, was inconspicuous.

Results

Propranolol was applied at a dosage of 8 mg/day orally for a period of 4 weeks. Before the start of the therapy, pictures of the haemangioma were taken. After 2 and 4 weeks, the parents presented their baby for a follow-up and again pictures were taken.

The pictures were presented to two independent paediatricians with the request for an objective assessment. Both paediatricians confirmed a significant change in colour from dark red to a lighter shade of red and partially even to skin colour (*Figure 1*). No side-effects were reported by the parents. **Further therapy with oral propranolol is planned for a period of 6 months until the haemangiomas completely disappear.** [AQ2: correct? Reworded slightly]

Discussion

The vast majority of infantile haemangiomas do not require any medical or surgical intervention. Medical care of clinically significant haemangiomas has been limited to a few medications, including glucocorticosteroids (topical, intralesional and oral), interferon alpha and, rarely, vincristine and topical imiquimod.



Figure 1: Regression of haemangioma 4 weeks after oral propranolol

Anne Weissenstein is ?????, Elisabeth Luchter is ?????, Stefan Bittmann is ?????? [AQ1: Please give current job titles]

Since 2008, topical and oral beta blockers have been used to treat infantile haemangioma as 'off-label use'. Beta blockers have serendipitously been shown to induce involution of infantile haemangiomas and many reports have described the early regression of infantile haemangiomas after oral or systemic Beta blocker treatment (Lawley et al, 2009; Guo and Ni, 2010; Pope and Chakkittakandiyil, 2010; Khunger and Pahwa, 2011; Ni et al, 2011; Weissenstein et al, 2012a; Weissenstein et al, 2012b).

An expert panel has developed provisional recommendations for the use of topical beta blockers, including in patients with PHACE syndrome (posterior fossa abnormalities, haemangioma, arterial lesions, cardiac abnormalities/aortic coarctation and eye abnormalities) (Khunger and Pahwa, 2011). PHACE syndrome is associated with a higher risk of neurological and cognitive impairment (Khunger and Pahwa, 2011). Pope and Chakkittakandiyil (2010) described a series of six children and Ni et al (2011) described seven children with superficial capillary haemangiomas of the eyelid. All children were treated successfully with timolol gel as a form of topical beta blocker and no side-effects have occurred in these studies. In 2012, Weissenstein et al (2012a, 2012b) reported twice about the early regression of infantile haemangioma.

Different authors have discovered the positive effect of oral beta blockers in a small study group. Guo and Ni (2010) described a case of a child with a capillary haemangioma. However, Lawley et al (2009) have reported on the side-effects of propranolol, such as hypoglycemia, bradycardia and hypotension. Blood sugar, electrocardiogram and blood pressure were proven before starting the therapy (Lawley et al, 2009). However, it is known that for children it is necessary to obtain the permission from both parents and an ethics commission.

It is very important to underline the need for caution with the off-label use of oral and systemic beta blockers in the treatment of infantile haemangioma. The results are promising and clear guidelines from paediatricians are necessary and to **anticipate** [AQ3: anticipate what?]

Conclusion

The use of topical and oral beta blockers seems to be the treatment of choice for infantile haemangioma for the future. **We are confident that** [AQ4: OK? Originally, you wrote 'will', which sounded strange if the studies haven't

yet been done yet] controlled trials with a large number of cases will deliver a conclusion that beta blockers are the first choice therapy in infantile haemangioma. **BJN**

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