

Propranolol in the Treatment of Infantile Haemangioma; A case series of three African Infants

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Abstract

Observation: Haemangioma is the commonest vascular tumour in infancy. Although not obvious at birth, haemangiomas usually appear within the first two to four weeks of life. They go through phases of proliferation and involution. Most haemangiomas do not require treatment, some however do. Treatment may be in form of parenteral steroid, interferon, vincristine, Imiquimod, surgical resection and laser therapy. Of recent propranolol was discovered serendipitously to be effective. It was found to induce accelerated involution of haemangiomas without significant side effects. Since that initial report by Leaute-Labreze et al in 2008, there has been an outburst of case reports and case series describing its excellent efficacy.

We present here 3 African children with haemangiomas that were given propranolol with impressive outcome.

Introduction

Infantile haemangioma is a benign developmental vascular tumour that appears during the first months of life. They are the commonest vascular tumours in childhood affecting up to 12% of infants by the end of first year of life [1]. Since most of these tumours resolve spontaneously, treatment is often not necessary. Medical or surgical intervention is only indicated in about 10% of cases due to clinical or aesthetic reasons like very large tumours, presence of a complication or location in a cosmetically unacceptable site [2].

Before now, corticosteroids were the mainstay of therapy [3]. However, since the discovery of the efficacy of propranolol in treating complicated infantile haemangioma by Leaute-Labreze et al in

2008, it is rapidly gaining ground as the most preferred first-line therapy in treating complicated infantile haemangiomas [4,5,6]. In this paper, we report our experience with propranolol in 3 infants with infantile haemangioma.

Case Report

Case 1: A 3 month-old child, the product of a full term uneventful pregnancy, delivered by spontaneous vaginal delivery presented with a huge left neck and facial haemangioma. No skin abnormality was observed at birth.

At the age of 4 weeks, the mother noticed mild swelling of the left neck with overlying hyperpigmentation. At presentation, there was a huge swelling extending from the left side of the neck to the left side of the face almost obliterating the left eye (**Figure 1a**). It measured 15cm x 17cm, was



Figure 1a. 3 month-old child with a huge left neck and facial haemangioma (before treatment)



Figure 1b. 3 month-old child with a huge left neck and facial haemangioma (after 3 months on propranolol)



Figure 2a. 5-month old baby with right facial haemangioma (before treatment)



Figure 2b. 5-month old baby with right facial haemangioma (after 2 months on propranolol)

soft in consistency, warm, non-tender with overlying erythematous plaque, patches and macules.

After careful history and physical examination to ascertain risk factors or contraindications to using propranolol, propranolol was initiated at a dose of 0.5mg/kg/day divided in two doses. The first dose of the medication was started in the hospital under observation. Subsequently, the mother was told to feed the infant 2-3 hourly in order to prevent asymptomatic hypoglycaemia and, to promptly report any usual changes noticed while at home. The dose of propranolol was then increased gradually, to the maximal dose of 2mg/kg/day. By 3 months, the lesion had resolved almost completely (**Figure**

1b). Thereafter, the dose of propranolol was gradually tapered over 2 weeks and stopped.

Case 2: Case two was a 5-month old product of full term pregnancy, who presented with a plaque-like bright red infantile haemangioma on the right cheek extending to the medial canthus and upper lid of the right eye. The lesion had been growing rapidly over the previous 4 weeks (**Figure 2a**). The parents were afraid that it may obliterate the right eye. After careful history and physical examination, and ruling out contraindications to the use of propranolol, the child was started on propranolol using the same protocol as above. By 2 months, 80% of the lesion had resolved (**Figure 2b**). The



Figure 3a. 3 months old baby with haemangioma of right labium majora (before treatment)



Figure 3b. 3 months old baby with haemangioma of right labium majora (after 4 weeks on propranolol)

child is still on oral propranolol and regular follow up.

Case 3: This was a 3 months old female child with right labium majora haemangioma. She presented with a progressively enlarging mass on the right labium majora (**Figure 3a**). Propranolol was also stated following the same protocol as above. By 2 months, 90% of the lesion had gone (**Figure 3b**). As at the time of writing this paper, the child is still on oral propranolol and regular follow up.

Discussion

Infantile haemangioma is the commonest tumour of infancy [7,8,9]. Prevalence ranges from 1-3% at birth to 12% by the end of first year [4,10]. They are benign developmental vascular tumours that arise as a result of endothelial hyperplasia forming readily visible blood vessels. These vessels fail to anastomose with deeper cutaneous blood vessels forming islands of cutaneous embryonic angioblastic tissue.¹¹ Risk factors include prematurity, low birth weight, female sex, chorionic villus sampling [7,8]. Infantile haemangiomas are usually absent at birth but become apparent in 90% of cases during the first month increasing to 100% by the ninth month. Approximately 65% of these tumours are superficial, 15% are mixed and 20% are deep. These tumours can occur anywhere but about 60% occur on the head and neck region like in all our patients. There is usually a precursor lesion at birth in the form of macular area of hyperaemia or pallor in more than 80% of cases. However, in 20% of cases no

precursor lesion could be seen, as in one of our patients [7,8,9,10].

Typically, these tumours are characterised by a proliferative phase during which the tumour rapidly increases in size and lasts for 3-18 months. This is now followed by an involutonal phase that lasts for 1-5 years [8,9].

Corticosteroids (oral, topical or intralesional) were the first line treatment while other treatment modalities like interferon, imiquimod and surgery are reserved for resistant cases [9,10].

Propranolol is a non-selective B-blocker used in the treatment of hypertension, arrhythmias, thyrotoxicosis and migraine. In 2008, Labreze et al noticed the regression of a facial haemangioma in a child being treated for obstructive cardiomyopathy [4]. Since then, B-blockers like propranolol (oral or topical), topical timolol and acebutalol have been used off-licence to treat complicated haemangiomas.

Possible mechanism of action of propranolol may include constriction of existing blood vessels, inhibition of growth of new vessels, triggering of apoptosis, decreasing the release of vascular endothelial growth factor and basic fibroblast growth factor [11]. Propranolol is most effective when used during the growth phase of haemangioma although it may still be effective afterwards [11]. There is no universally acceptable protocol for administering propranolol [11,12]. However, most literatures advocate the use of 2-3mg/kg/day. The potential side effects of

propranolol are hypoglycemia, hypotension, bradycardia and heart failure. However, these major side effects were not observed in those with haemangioma treated with propranolol [11, 12] The most frequently reported side effects are somnolence and reflux in minority of patients [12].

Conclusion

Propranolol appears to be a very effective, readily available, cheap and relatively safe modality of treatment for complicated infantile haemangioma. However, large multicentre studies are needed to elaborate on these as well as adequate dosing, protocol and duration of therapy.

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