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Clinical Paper

Treatment of Infantile Haemangioma – Perspective of a Regional Surgical Centre

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INTRODUCTION

Infantile haemangioma affects up to 1 in 10 infants, representing the commonest benign tumours of infancy[1]. It is commoner in people of Caucasian ethnicity, premature babies and those who underwent chorionic villous sampling[2,3].

Classification of vascular anomalies follows the International Society for the Study of Vascular Anomalies (ISSVA) classification of vascular malformations, which is based on the published work of Mulliken and Glowacki in 1982[4,5]. In this widely-accepted classification system, infantile haemangiomas are considered benign vascular tumours.

The natural course of haemangioma is reasonably well understood. Lesions typically present soon after birth and undergo rapid proliferation in the first year of life. This is followed by gradual involution in the following five to 10 years. Most haemangiomas are asymptomatic, spontaneously involute and do not require treatment, but they can cause significant issues with airway obstruction, ocular compression, ulceration, scarring or functional impairment[6].

Treatment with propranolol, a non-selective beta-blocker, was reported by Léauté-Labrèze et al in 2008[7]. Since then, further articles have reported its efficacy in inducing regression in the proliferative phase. McGee et al in 2013 demonstrated the safety and efficacy of propranolol therapy in the Northern Irish population, which at that time was reserved for problematic haemangiomas[8]. Marqueling et al published a systematic review finding treatment response in 98% of patients[9].

This study aims to investigate response to propranolol therapy and surgery in patients treated by our unit over a four-year period.

Since our previous publication, there have been no nationally agreed guidelines for the use of oral propranolol in the treatment of infantile haemangiomata[8].

METHODS

Medical records of all patients treated by the department of Plastic Surgery in the Royal Belfast Hospital for Sick Children were retrospectively reviewed between January 2013 and February 2017. A proforma was designed to collect relevant information on patient demographics, indication for propranolol, dosing regimen and observed outcomes. In addition, we collected data on referrals for surgical treatment and the types of surgical treatment undertaken.

A database was created from the information collected. This was used to delineate simple demographics, referral patterns, therapeutic efficacy of propranolol therapy and surgical treatment.

RESULTS

Demographics

37 patients with 50 haemangioma lesions were identified and all notes were retrieved. 7 were male and 30 were female, indicating a male:female ratio of over 1:4.3. Mean age at time of first appointment was 2 years and 1 month (range 1 month to 10 years and 7 months).

The majority of haemangiomas manifested in the head and neck region, followed by the trunk, upper limb, lower limb and external genitalia (Table 1). 10 patients had

Table 1

Patient and lesion demographics

		N (%)
Total patients		37
Mean age at first appointment (months, range)		25 (1-127)
Gender	Male	7
	Female	30
Region	Head and neck	31
	Trunk	11
	Upper limb	4
	Lower limb	2
	External genitalia	1
	Intraoral	1

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haemangiomas in multiple locations, with seven patients in two locations and three patients in three locations.

Current practice

Propranolol therapy

The standard work-up prior to commencement of propranolol therapy has remained unchanged. All patients underwent this assessment and the decision for commencement of propranolol therapy was mutually made between clinician and patient's parents. They were monitored closely when starting therapy and at points of dose escalation.

Of the 37 patients, 28 were referred for assessment of treatment with propranolol therapy. Propranolol therapy was thought to be unsuitable for nine patients because the haemangioma had progressed beyond the proliferative phase. Hence, 19 patients received propranolol therapy.

The age at start of treatment was 9.4 months. The commencement dose was 1mg/kg in 15 patients and 2mg/kg in two patients.

Efficacy and duration of therapy

Objective response was observed in all patients by comparing clinical photographs during outpatient clinics. Three patients were on dose reduction after successful involution and seven patients had successfully stopped propranolol therapy at the time of the study. Five patients were currently still on treatment with propranolol. The mean duration from commencement of propranolol therapy until the decision for dose reduction was made was 372.4 days (n=9, range 133-651 days), requiring an average of 5.8 outpatient clinic appointments (range 2-13 appointments). The mean number of days required until dose reduction was 278.3 days (n=8, range 133-406 days). The total number of clinical appointments required until dose reduction was 3.9 (range 2-6 sessions).

Adverse effects

Oral propranolol therapy was prematurely stopped in two patients due to potential side effects; one patient was reported to have nightly wheeze and cough and another suffered from sleep disturbances. Alternate therapies commenced on these patients were topical Timolol and surgical excision and split skin grafting respectively.

Surgery

In our centre, patients are usually referred for surgical treatment in the event of poor response to propranolol therapy or if debulking is required after involution of haemangiomas. Within the study period, eight patients (24.3%) were referred for consideration of surgery (Table 2). Of these, five patients received surgery in the form of debulking. Conservative treatment was decided for the remaining three patients until they express concern or experience psychosocial harm due to the involuted haemangiomas. Two patients required a single-stage procedure, while two patients required two-stage and three-stage debulking excisions each. One patient was still awaiting surgery at the time of this study.

The mean age of patients who were referred for surgery was 5.3 years (range 3-10). The mean age of patients who underwent surgery was 5.4 years (range 3-10).

DISCUSSION

We found that patients who were older tended to be referred for and treated with surgery. This was consistent with the predictable course of IH, where 50% tended to regress by age 5 and 70% by age 7. With the increasing use of and body of evidence showing the safety and efficacy of propranolol therapy in encouraging accelerated involution, we can anticipate younger patients being referred for surgical treatment in the future.

As before, this case series contributes to the evidence of the efficacy and safety of oral propranolol therapy. We believe that this case series has also shed some light into the trend of surgical treatment of infantile haemangioma. This is consistent with recent findings by Tangtatco et al[10].

New nationally agreed guidelines have yet to emerge. Several regional guidelines, protocols and patient information booklets are readily available from a simple online search

TABLE 2

Summary of patient referred for surgery

Patient	Age (years)*	Reason for referral	Surgery offered?	Stages required	Patient satisfaction
27	5.1	Adverse effects to propranolol therapy	Yes	Awaiting surgery	Yes
28	5.2	Involuted	Yes	2	Yes
30	3.2	Involuted	Yes	3	Yes
33	5.9	Involuted	No	N/A	Yes
34	6.9	Involuted	No	N/A	Yes
35	4.5	No response to propranolol therapy	Yes	1	Yes
36	4.9	Involuted	No	N/A	Yes
37	10.8	Involuted	Yes	1	Yes

*Age at time of first outpatient appointment

including Great Ormond Street Hospital and Nottingham.[11,12] The American Association of Paediatrics published a conference consensus on the initiation and use of propranolol for Infantile Haemangiomas[13]. Consensus amongst dermatologists in Spain and paediatricians in South Australia have been published[14,15].

Treatment alternatives not frequently used in our centre include topical Timolol and laser therapy. The National Institute for Clinical Excellence (NICE) has produced guidance for the use of topical Timolol based on several studies finding positive response in reduction in redness, size and volume, with minimal adverse effects[16].

Chinnadurai et al systematically reviewed the use of a variety of lasers for the treatment of infantile haemangiomas[17]. This review highlighted the effectiveness of longer pulsed dye laser for cutaneous haemangiomas. Laser therapy alone and with beta-blockers were also found to have greater effects on mixed superficial and deep haemangiomas, compared with beta-blockers alone. The authors however found the strength of evidence to be insufficient to low. Limited conclusions were drawn on the effectiveness of neodymium-doped yttrium aluminium garnet (Nd:YAG) and carbon dioxide (CO2) lasers.

CONCLUSION

This study shows the efficacy of propranolol therapy with minimal adverse reactions. Limitations to this study are that this is a single centre study. Surgery, which was performed on a small number of patients, continues to be the mainstay of treatment in patients who do not meet indications for propranolol therapy or poor responders.

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