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Paediatrics

MANAGEMENT OF INFANTILE HEMANGIOMAS WITH ORAL PROPRANOLOL

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ABSTRACT

Introduction: Infantile hemangioms (IH) are the commonest tumors of infancy. They pass through an initial phase of evolution followed by spontaneous resolution. However good number of them need treatment for various reasons. Among many available modalities of treatment, oral Propranolol has recently come up as a safe and effective mode of treatment of IH.

Aim: To evaluate and assess the efficacy of oral propranolol therapy in IH.

Material & Methods: All children presenting to Pediatric surgery OPD from March 2013 till March 2017 with IH were treated with oral Propanolol and the response was evaluated.

Results: The incidence of IH was highest among age group of 2-8 months. Males were slightly more affected than females. Head and neck region was the most commonly affected area. Oral propranolol therapy showed excellent results in more than 95% of patients. Conclusion: Oral Propanolol is a safe and highly effective option in the treatment of IH, even in very small infants and with prolonged therapy.

KEYWORDS : infant, involution, vascular malformation.

INTRODUCTION:

Infantile Haemangiomas (IH) are the most common tumours of infancy. The incidence in newborns is 1-3%, and this increases to 10% by the age of 1 year. Their natural history includes an evolving phase consisting of rapid proliferation during the first year of life and slow involution over next 5-10 years. Treatment for IH may be necessary to a) prevent or improve functional impairment or pain, b) prevent or improve scarring or disfigurement, and c) avoid life-threatening complications. Conventional treatment include intra-lesional and systemic corticosteroids, chemotherapy (interferon alpha and vincristine), laser ablation, liquid nitrogen cryotherapy and surgical excision. Recent interest in the use of propranolol in the treatment of IH followed a 2008 report's incidental finding.

AIM:

To study the role of oral Propranolol in treatment of IH in pediatric patients.

MATERIAL & METHODS:

The study was carried out in the Pediatric Surgery OPD of Himalayan Institute of Medical Sciences, Dehradun. All patients who presented with a diagnosis of IH between March 2013 and March 2017 were included in the study. Patients with extreme lesions involving vital organs like eyes and nose, and patients receiving any kind of treatment elsewhere were excluded from the study. Patients with haemangiomas over head and neck region underwent an USG abdomen to rule out hepatic haemangiomas. A detailed history was also obtained in these patients for seizure disorders to rule out CNS involvement. A total of 42 patients were included in the study among the age group of 2-26 months. After a thorough clinical examination, they were started with oral Propanolol at 2mg/kg/day in two divided doses. The first dose was given in the OPD itself. Patients were then observed for 4-5 hours for bradycardia, hypotension, and any breathing difficulty. Parents were counselled to report in cases if child was excessively jittery, irritable or if there were any wheeze. Patients were then followed up after 2-3 weeks according to the feasibility of follow-up. Response was assessed at the end of 3-4 weeks in the form of 1) decreased vascularity (fading of the color of lesion), 2) lesions becoming softer, and 3) lesions started shrinking. If there was no response at the end of 3-4 weeks, the dose of Propanolol was increased to 3mg/kg/day. The results were then analysed.

RESULTS:

Incidence was seen highest in age group 9-14 months (38.1%), followed by 15-20 months (26.2%) (table 1). Male children were slightly more affected than the female ones. Head & neck was the most common region involved, followed by trunk and extremeties, in that order (table 2). Approximately 27% patients already had some complication, ulceration being the commonest, follwed by bleeding. Out of a total 42 patients, 39 (92.86%) showed excellent results (fig. 1). 19 patients (45.23%) showed regression within first 2 weeks of treatment while in 12 patients (28.57%), the response was seen within 4 weeks (table 3). The dose of Propanolol was increased to 3 mg/kg/day in 8 patients (19.04%) who did not show respone at the end of 4 weeks. In rest of the 3 patients (7.1%), steroids were required as an adjunct treatment. Patients were followed up for 6-18 months depending on their feasibility to come for it as most of these patients come from far off places. Treatment was continued for 4-8 months. A gap of one week was provide every 6-weeks. There were no side-effects observed during the follow-up and in no patient was treatment stopped or changed due to intolerance of the drug.

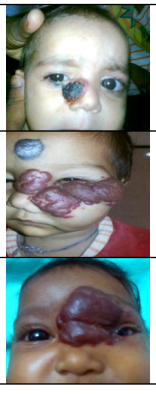
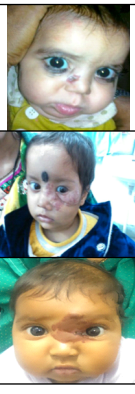
Pre-treatment	Post-treatment
	

Table 1: Age- and sex-wise distribution

Age group (months)	No. of patients (M/F)	%
2-8	9 (5/4)	21.4
9-14	16 (10/6)	38.1
15-20	11 (5/6)	26.2
21-26	6 (3/3)	14.3

Table 2: Area-wise distribution

Site of involvement	No. of patients	%
Head and Neck	17	40.4
Trunk	12	28.6
Extremities	8	19.1
Multifocal lesions	5	11.9

Table 3: Response to therapy

Follow Up duration	No of patients responded	%
2 weeks	19	45.23
4 weeks	12	28.57
> 4 weeks	8	19.04
No response	3	7.1

DISCUSSION

Hemangiomas are the most common tumors of infancy.[1] Traditionally, this term has been applied to benign tumors of vascular tissues and vascular malformations. Hemangiomas are classified as capillary, cavernous, and mixed lesions. The incidence in newborns is 1-3%, and this increases to 10% by the age of 1 year (2). Clinically, they are characterized by a typical evolution profile, consisting of a rapid proliferation during the first year of life and slow involution that usually is completed by 5 to 10 years of age (3). In contrast to hemangiomas, vascular malformations are hamartomatous lesions composed of dysplastic vessels lined by non-proliferating endothelium. They almost never regress and may expand in size (4). Complications of hemangiomas are cosmetic and functional, and depend on their location, size, and the rapidity of its initial growth. Some type of complication is found in up to 40% of lesions, the commonest being ulceration (21%) and bleeding (7.5%) (5). Treatment for IH may be necessary to a) prevent or improve functional impairment or pain, b) prevent or improve scarring or disfigurement, and c) avoid life-threatening complications. Accepted treatments include intralesional and systemic corticosteroids, chemotherapy (vincristine and interferon alpha), liquid nitrogen cryotherapy, laser ablation and surgical excision (6).

Recent interest in the use of propranolol in the treatment of IH followed a 2008 report by Leìauteì-Labreỉze following an incidental finding while treating a patient with dilated cardiomyopathy (7). Several mechanisms of action for propranolol have been suggested. Results from combined grayscale and color Doppler ultrasound imaging suggest that propranolol reduces vessel density (8). Propranolol has a dose-dependent cytotoxic effect on cultured hemangioma endothelial cells via the hypoxia-inducible factor 1á pathway, leading to decreased secretion of VEGF (9).

There have been other studies as well which have shown the similar promising results as our study. Quinn et al in 2009 in a case series of 58 patients showed good to excellent response in 89% patients (10). Hogeling et al in a randomized control trial observed 20 patients for a period of 6 months and concluded that there was a significant difference in reduction in size of IH in patients who were given propranolol in first 2 weeks as compared to patients who were given other treatment (11). Talaat et al in 2011 observed regression of IH in almost all cases who were given proapnolol at a dose of 2mg/kg/day for approximately 6.5 months (12). Celik et al in 2012 in a case series of 67 patients observed regression in all patients and total involution in 7 patients (13).

CONCLUSION

Though many treatment modalities are available, oral Propanolol is a safe and highly effective option in the treatment of IH, even in very small infants and with prolonged therapy. This study matches the results published in literature. After proper evaluation and workup, almost all patients can be started with oral Propanolol therapy and results can be seen as early as 2 weeks.

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