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# Duration of treatment of problematic infantile hemangioma with oral propranolol: a single institutional review

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#### Abstract:

**Aims:** To study the use of propranolol as a single therapy in problematic infantile hemangioma with special reference to the total duration of treatment and its short term outcome(s).

**Methods:** Single institutional retrospective study of patients of problematic infantile hemangioma treated with propranolol between January 2016 to December 2017. Assessment was done by change in colour, redness & size. Accordingly, outcome was graded as excellent, good/partial and no response.

**Results:** 17 girls and 9 boys with problematic infantile hemangioma were initiated treatment with propranolol at the mean age of 7 months(range 2-24 months) for a mean duration of 12 months(range 6-18 months). Head and neck was the most common site(65%). Complete/excellent response was seen in 16 patients(61.6%), good/partial response in 8(30.7%) and no response in 2 patients(7.7%). Rebound was seen in 3 patients(12%).

Conclusions: Use of oral propranolol in problematic infantile hemangioma is safe, feasible and effective with very few adverse effects at the recommended dosage of 2-3 mg/kg/day in divided dosage. Treatment should continue till the complete regression of the lesion for at least 12 months substantiated by the fact that all the 3 cases of rebound had received treatment for lesser duration and showed excellent response to longer duration of treatment.

**Keywords:** Propranolol, problematic infantile hemangioma, duration.

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# I. Introduction

Infantile hemangioma is one of the most common benign tumours of infancy and childhood with an approximate incidence rate of 4-10%. Treatment with oral propranolol, a non selective b- blocker, has become the 1st choice option in the last decade or so. However the total duration of treatment with oral propranolol remains a topic of debate. (1,2) In this article, we report our study findings of 26 consecutive patients of problematic infantile hemangioma treated with oral propranolol as 1st line drug with special reference to the duration of treatment.

# II. Materials and methods

All the clinical data regarding 26 consecutive patients with problematic infantile hemangioma treated with oral propranolol on outpatient basis in a single institution between Jan 2016 to December 2017 were collected , reviewed and analysed. Variables noted were sex, age of presentation, duration of treatment and short term outcomes : response, recurrence and rebound if any. Prior to treatment of problematic infantile hemangioma with oral propranolol, proper evaluation with complete hemogram , blood sugar , chest x-ray , echocardiogram and Doppler ultrasound of the local region was completed. Infants with cardiovascular diseases, bronchospasm and hypoglycaemia were excluded. Informed consent of the parents after proper counselling was obtained. Propranolol was administered orally at 2 mg/ kg/ day in two divided doses. Blood pressure and heart rate of the patients were monitored in the first 4-6 hrs in the outpatient department.

Response was graded as excellent (75-100%), good (50-75%) and poor response (<50%) in terms of decreased in size and change in color assessed photographically and by follow up ultrasound at the same institution. Rebound or recurrence if any were noted. (2)

# III. Results

A total of 26 patients diagnosed with problematic infantile hemangioma were treated with oral propranolol in the study period in a single institution on outpatient basis. 17 were females and 9 males, thus the female: male ratio is almost 2:1.

The distribution of hemangiomas location wise is: (a) head and neck - 17 (65.4%), trunk - 4 (15.4%), extremity - 3 (11.5%) and perineum - 2 (7.7%).

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An oral dose of propranolol at 2 mg/ kg /day in two divided doses was administered to the 26 patients. The mean age of initiation of treatment was 7 months ( range 1 m- 2 yr). The mean duration of treatment was 1 yr ( range 6 months - 18 months).

16 patients (61.6%) showed complete or excellent (75-100%) response whereas 8 patients (30.7%) good or partial (50-75%) response. 2 patients (7.7%) showed poor or no response, therefore needed an alternative treatment mode. Rebound (2,3) was seen in 3 patients (12%) on follow up. The patients had received treatment for 6-8 months. On longer treatment with oral propranolol itself for another 6-12 months, the patients showed excellent/ complete response.

## **IV. Discussion**

Infantile hemangioma is one of the most common benign tumors in the infancy due to hyperplasia of vascular endothelial cells induced by upregulation of vasculogenic and angiogenesis peptides. After an initial latent period, it shows proliferation reaching its peak in 2-3 months lasting usually up to the 1st yr of life and then shows involution. (1,2,4)

Approximately 10-15% are problematic infantile hemangioma (bleeding, disfigurating, ulcerating or potentially function threatening), hence require treatment. Since first reporting of its efficacy in 2008, oral propranolol has become the 1st line of treatment in problematic infantile hemangioma. The mechanism of action proposed is vasoconstriction, downregulation of vasculo- and angio-genesis. (2)

The female :male ratio was 2:1 as found in the large systematic analyses. Overall most common location was head and neck as reported in large prospective studies. Also, 61.6% showed excellent response, 30% good/partial response which was within the range of response reported by various large prospective studies. (2)

Since the proliferative phase of infantile hemangioma usually lasts for the 1st year of life, the total duration of treatment must be greater than this period to show optimum results. Treatment for 6 months and less, falling short of the age at which the proliferation enters into a plateau has the highest risk for rebound. (4) Rebound is probably due to early withdrawal of treatment and prolonged proliferative phase (in some cases upto 2 yrs e.g. with deep component, regional or segmental distribution). Also, the fact that all cases that showed rebound had received less than optimum duration of treatment and all cases showed regression on longer treatment with oral propranolol alone provides the indirect evidence. Gradual tapering of dosage vs abrupt stoppage of treatment has not been found to be a significant risk factor.(5) Doppler ultrasound has been found to be accurate for assessment of treatment response. (6) CT and MRI are other important diagnostic modalities but not used due to cost, anesthetic requirements and radiation hazards.

Regression of the lesion has been found to have a strong correlation with the duration of treatment and stoppage of treatment is recommended when regression rate is minimum. Dhaybi et al reported a rebound rate of approximately 7% when propranolol was stopped at 1 yr of age, whereas Holmes reported a considerable high rebound rate of 24% when treatment was terminated at 6.5 months of age.(3,7)

### V. Conclusion

Use of oral propranolol in problematic infantile hemangioma is safe, feasible and effective with very few adverse effects at the recommended dosage of 2-3 mg/kg/day in divided dosage. Treatment outcome can be assessed by serial photography and ultrasound. Treatment should continue till the complete regression of the lesion for at least 12 months. Earlier discontinuation or stoppage of treatment is responsible for the cases of rebound.

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