Journal of Paediatric Surgeons of Bangladesh (2016) Vol. 7 (1): 11-14
Official organ of the Association of Paediatric Surgeons of Bangladesh

Journal of Paediatric Surgeons of Bangladesh

Original Article

THE STUDY OF PROPRANOLOL TREATMENT FOR HEMANGIOMA OF INFANCY- A HOSPITAL BASED OBSERVATIONAL STUDY

KHATUN M[1], SAYED MMA[2], PERVIN M[3]

Abstract

Background: Infantile haemangiomas are the most common tumours of infancy, regularly encountered in dermatology and paediatric practices.

Methods: One hundred patients from Dhaka Medical College Hospital were treated with oral propranolol for IHs between May 2015 and December 2015.

Results: Majority 25(69.45%) patients belonged to age ≤6 months, the mean age was found 4.2±5.0 months. Males were predominant (80.6%). Male female ratio was 4.14:1. Regarding facial segments 10(27.8%) patients had S3. Two (6.0%) patients had trunk lesions. Eyelid was found 6(17.0%). Ulcerated hemangioma was found in 4(12.0%). Mean severity scores were significantly reduces from 4 to 32 weeks when compare with baseline and different follow up.

Conclusion: Majority hemangioma patients belonged to age ≤6 months, mean severity scores were significantly reduced from 4 to 32 weeks when compared with baseline and different follow up.

Introduction:

Infantile haemangiomas are the most common tumours of infancy, regularly encountered in dermatology and paediatric practices. Due to the natural history of spontaneous involution, the majority of haemangiomas do not require treatment.[1] Infantile hemangiomas (IHs) are common neoplasms composed of proliferating endothelial-like cells. Despite the relative frequency of IH and the potential severity of complications, there are currently no uniform guidelines for treatment.[2] Haemangiomas are the most common benign tumour of infancy, with a postnatal incidence of around 5%.[3] In the latest International Society for the Study of Vascular Anomalies classification, infantile haemangiomas (IHs) are morphologically subdivided into focal or localized, segmental, indeterminate and multifocal IHs.[4] They typically develop during the first month after birth and follow a characteristic evolution from early rapid proliferation to a stabilization and a slow involution phase, which often takes years. Around 20% of IHs need medical attention due to complications, for instance bleeding, ulceration or threat to vision.[5] Propranolol is a novel treatment for infantile hemangiomas that has shown great promise in case series and is rapidly becoming a first-line treatment.[6] Infantile haemangiomas are benign tumours comprising of proliferating vascular endothelial cells, which usually appear at or shortly after birth, and can grow rapidly. They usually stop growing when the infant is 6 months old, but large haemangiomas may continue to grow for 18 months.

1. Dr. Masuda Khatun, Associate professor, Department of Dermatology and Venereology, Dhaka Medical College.
2. Dr. M.M.Abu Sayed, Senior Consultant, National Institute of Cancer Research and Hospital.
3. Dr. Monira Pervin, Associate Professor, Departent of Virology, Dhaka Medical College

Correspondence to : Dr. Masuda Khatun, Associate Professor, Department of Dermatology and Venereology, Dhaka Medical College, Dhaka

Materials and methods:

One hundred patients from Dhaka Medical College Hospital (DMCH) were treated with oral propranolol for IHs between May 2015 and December 2015. We included in our study cases of children younger than 4 years old with IHs that were considered to require treatment because of one of the following reasons: eyelid involvement with ocular risk of occlusion or compression; airway obstruction; or large IHs with considerable aesthetic derangement or ulceration. Patients previously treated with corticosteroids or surgery was also considered candidates for inclusion if prior modalities had failed. Exclusion criteria included PHACES (Posterior fossa malformations, Hemangioma, Arterial anomalies, Cardiac defects, Eye abnormalities, Sternal clefts) syndrome, history of cardiac abnormalities, history of hypoglycemia, and history of asthma or bronchospasm. While the study focused on infants, patients over 1 year of age were enrolled if IHs showed signs of continued proliferation or did not show any signs of resolution since infancy. All parents signed an informed consent as a requirement for authorization of treatment by the oral propranolol in Department of Dermatology.

Results:

Majority 25(69.45%) patients belonged to age ≤6 months, the mean age was found 4.2±5.0 months. Males were predominant (80.6%). Male female ratio was 4.14:1. Majority 26(72.2%) patients beginning of treatment d"6 months. Thirteen (37.0%) patients had superficial, 15(42.0%) had mixed, 8(22.2%) had deep, 11(30.0%) had segmental and 26(72.0%) had focal. Regarding facial segments 10(27.8%) patients had S3. Two (6.0%) patients had trunk lesions. Eyelid was found 6(17.0%). Regarding previous treatments, (9.0%) patients had surgery. Ulcerated hemangioma was found in 4(12.0%) (Table-I). Mean severity scores were significantly reduces from 4 to 32 weeks when compare with baseline and different follow up (Figure 2 and table-II).

Table-I

Demographic characteristics of the Study population (n=36)

Demographic characteristics Age (month)	Number of patients	Percentage
≤ 6	25	69.4
>6	11	30.6
Mean ±SD	4.2	±5.0
Range (min-max)	1	-26
Gender		
Male	29	80.6
Female	7	19.4
Age at the beginning of treatment (month)		
≤6	26	72.2
>6	10	27.8
Superficial	13	37.0
Mixed	15	42.0
Deep	8	22.2
Segmental	11	30.0
Focal	26	72.0
Facial segments		
S1	8	22.2
S2	5	13.9
S3	10	27.8
Frontonasal	8	22.2
Other locations		
Limbs	2	5.0
Gluteal/genital	1	3.0
Trunk	2	6.0
Special locations		
Eyelid	6	17.0
Parotid	2	6.0
Nasal tip	3	9.0
Previous treatments		
Surgery	3	7.0
Corticosteroids	2	5.0
Ulcerated hemangiomas	4	12.0

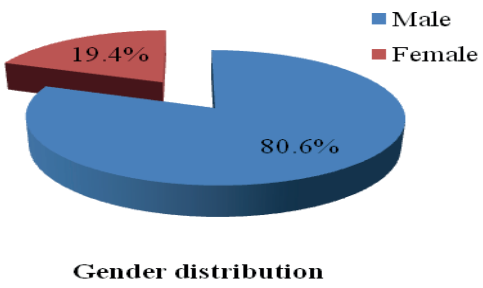

Fig.-1: *Pie chart showing gender distribution of the patients.*

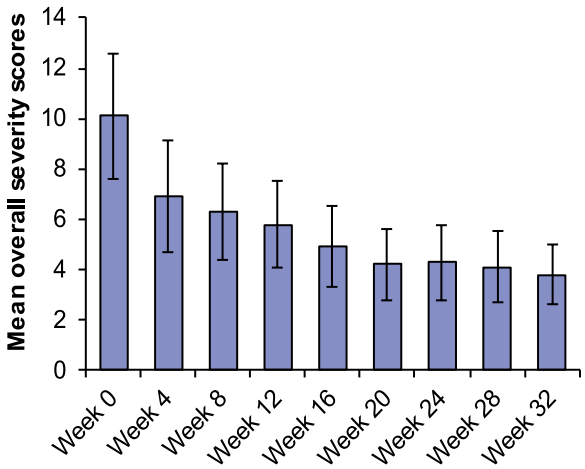

Fig.-2: *Bar diagram showing overall severity scores of IHs treated with propranolol over time.*

Table-II

Comparison of overall severity scores of IHs treated with propranolol over time baseline and different follow up

Follow comparison	P value
Week 0 vs Week 4	<0.001
Week 0 vs Week 8	<0.001
Week 0 vs Week 16	<0.001
Week 0 vs Week 20	<0.001
Week 0 vs Week 24	<0.001
Week 0 vs Week 28	<0.001
Week 0 vs Week 32	<0.001

Mean severity scores were significantly reduces from 4 to 32 weeks when compare with baseline and different follow up (Figure 2 and table 2).

Discussion:

In current study showed that the Majority 25(69.45%) patients belonged to age ≤6 months, the mean age was found 4.2±5.0 months. Males were predominant (80.6%). Male female ratio was 4.14:1. Majority 26(72.2%) patients begun treatment at 6 months. Thirteen (37.0%) patients had superficial, 15(42.0%) had mixed, 8(22.2%) had deep, 11(30.0%) had segmental and 26(72.0%) had focal. Regarding facial segments 10(27.8%) patients had S3. Two (6.0%) patients had trunk lesions. Eyelid lesion was found in 6(17.0%). Regarding previous treatments, 9.0% patients had surgery. Ulcerated hemangiomas were found in 4(12.0%). In a study Wedgeworth et al.[7] observed that the majority (92.9%, 1018) of patients had focal IHs and were female (76.1%). The median age at initiation of propranolol was 17 weeks (range 0.5–396). Hogeling et al.[8] study observed that the majority of 12(63.16%) patients belonged to age >6 months. Female was 14(73.68%). Segmental was 3(15.8%), focal IH was 16(84.21%), previous oral corticosteroid treatment was 4(21.05%).[9] Seventy-one patients (15 male and 56 female, age range 1-45 mos) entered the study. Fifty patients started therapy before 6 months of age, and in 21 patients the treatment began after 6 months (mean age 5.8 months, range 1-45 months). Five patients had subglottic IHs causing significant airway obstruction. Facial IHs were divided according to embryological segments as suggested by Haggstrom et al.[10] as follows: frontonasal, frontotemporal, maxillary, and mandibular. In 21 patients, the IH was segmental and was focal in 50 children. Propranolol had been the only treatment administered to 63 patients, whereas four patients had been previously treated with corticosteroids and four with surgery. In both instances, such treatments had failed to achieve significant improvement.

The current study observed that the mean severity scores were significantly reduced from 4 to 32 weeks when compared with baseline and different follow up. Bagazgoitia et al.[9] study observed that At 4 weeks of treatment, the average score was 6.8 ($p < 0.001$ compared to the initial value). At 8 weeks of treatment, the average score was 5.6 ($p < 0.001$ compared to the 4 wks value); at 12 weeks, the average score was 4.8 ($p < 0.05$ compared to the 8 wks value); at 16 weeks it was 4.4 ($p < 0.01$ compared to the 8 wks value); at 20 weeks it was 3.9 ($p < 0.01$ compared to the 12 wks value); at 24 weeks it was 3.9 ($p < 0.01$

compared to the 12 wks value); at 28 weeks it was 3.5 ($p < 0.01$ compared to the 16 wks value); and at 32 weeks it was 3.2 ($p < 0.01$ compared to the 16 wks value). At 20 weeks of treatment, a mean score of 4 was achieved, thus indicating an average reduction of 60%. After this initial response, less impressive size reductions were obtained after 20 weeks of treatment. Eight of 71 (11%) IHs had experienced a reduction of at least 50% in the severity score at 4 weeks, 24 of 71 (34%) at 8 weeks, and 42 of 71 (59%) at 16 weeks. We observed that the reduction of the IH was more marked during the first 10 weeks of treatment, and the effect of propranolol on IHs seems to stabilize after week 20. The mean duration of treatments was 20.0 weeks, and only 15 patients continued treatment for more than 32 weeks, achieving some further lesion reduction. Hogeling et al.[8] significant decrease in IH redness and elevation occurred in the propranolol group at weeks 12 and 24 (P =.01 and .001, respectively).

Conclusion:

In conclusion, in the series of patients in this observational study, oral propranolol 2 mg / kg / day was a well-tolerated and effective treatment for IHs. Majority Hemangiomas patients belonged to age ≤6 months, mean severity scores were significantly reduced from 4 to 32 weeks when compared with baseline and different follow up.

References:

1. Smithson SL, Rademaker M, Adams S, Bade S, Bekhor P, Davidson S, Dore A, Drummond C, Fischer G et al. Consensus statement for the treatment of infantile haemangiomas with propranolol. Australasian Journal of Dermatology 2017: 1-5.
2. Drolet BA, Frommelt PC, Chamlin SL, Haggstrom A, Bauman NM, Chiu YE, Chun RH, Garzon MC, Holland KE, Liberman L, MacLellan-Tobert S, Mancini AJ, Metry D .Initiation and use of propranolol for infantile hemangioma: report of a consensus conference. Paediatrics 2013; 131(1): 128-40.
3. Munden A, Butschek R, Tom WL. Prospective study of infantile haemangiomas: incidence, clinical characteristics and association with placental anomalies. Br J Dermatol 2014; 170:907–13.
4. Dasgupta R, Fishman SJ. ISSVA classification. Semin Pediatr Surg 2014; 23:158–61.
5. Hemangioma Investigator Group, Haggstrom AN, Drolet BA, Baselga E et al. Prospective study of infantile hemangiomas: demographic, prenatal, and perinatal characteristics. J Pediatr 2007; 150:291–4.
6. Hogeling M, Adams S, and Wargon O, A Randomized Controlled Trial of Propranolol for Infantile Hemangiomas. Paediatrics 2011; 128(2): e259- e266
7. Wedgeworth E, Glover M, Irvine AD, Neri I, Baselga E, Clayton TH, Beattie PE, Bjerre JV, Burrows NP, Foelster-Holst R, Hedelund L, Hernandez-Martin A and Audrain H. Propranolol in the treatment of infantile haemangiomas: lessons from the European Propranolol In the Treatment of Complicated Haemangiomas (PITCH) Taskforce survey. British Journal of Dermatology 2015; 1-8.
8. Hogeling M, Adams S and Wargon O. A Randomized Controlled Trial of Propranolol for Infantile Hemangiomas. Paediatrics 2011; 128:e259–e266.
9. Bagazgoitia L, Torrelo A, Gutierrez JCL, Hernandez-Martinn A, Luna P, Gutierrez M. Propranolol for Infantile Hemangiomas. Paediatric Dermatology 2011; 28(2): 108–114.
10. HaggstromAN, Lammer EJ, SchneiderRAet al. Patterns of infantile hemangiomas: new clues to hemangioma pathogenesis and embryonic facial development. Paediatrics 2006; 117: 698–703.