A Comparison of Propranolol with Steroid in the Treatment of Hemangioma in Children In Terms Of Regression in Size

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ABSTRACT

OBJECTIVE: To compare the efficacy of Propranolol with steroid (oral prednisolone) in treating the children with cutaneous haemangioma in terms of frequency of size reduction.

STUDY DESIGN: A Randomized Comparative Trial

PLACE AND DURATION: Department of Pediatric Surgery at Children Hospital PIMS Islamabad from 9th July 2013 to 9th Jan 2014.

METHODOLOGY: Total 60 children having cutaneous haemangiomas at any site were studied. Patients were randomly divided and in Group A 30 patients were given oral propranolol while 30 patients in Group B were given oral prednisolone for treating haemangiomas. Patients had an age range one month to 12 years. Patients were followed for one month to see >75% Regression in size of haemangioma in each dimension for each group.

RESULTS: The >75% regression in size in Group A was 93.3% (n=28) and in Group B was 0% (n=0) with p value 0.000.

CONCLUSION: Oral propranolol is more effective treatment of haemangioma than oral steroid used for same duration in terms of size reduction with no major side effects of treatment.

KEY WORDS: Infantile, Cutaneous haemangioma, Size regression, Propranolol, Steroid, Efficacy.

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INTRODUCTION

A common vascular tumor i.e. infantile haemangioma is composed of endothelial cells and has a characteristic natural history. Incidence is about 4 to 10%[1] in newborn infants while it increases to 23% in premature infants. Caucasian children have higher incidence of hemangiomas[2]. Vascular malformation present at birth must be differentiated from haemangiomas, but they grow with child's age. Haemangiomas are diagnosed on history and examination (about 95% of cases) and 30 to 50% of newborns have birthmark[3]. The growth of the haemangiomas at the early phase can be rapid and unpredictable and influence of haemangiomas on children is variable. Haemangiomas around an orifice can cause obstruction of vital structures which leads to vision and hearing loss or respiratory and gastrointestinal obstruction. Haemangioma cases with large and multiple lesions are associated with complications like cardiac failure, cosmetic and psychosocial morbidity as inferiority complex, unsociable, stubbornness, and low self-confidence in children. They may cause structural abnormalities as ulceration, necrosis, and infection. Mainstay in haemangiomas treatment is to prevent complications, to prevent disfigurement and adequately treat ulceration, thereby minimizing scarring, infections and pain. Therefore, these infantile haemangiomas may need systemic, surgical, or laser treatment for avoiding these adverse effects[3-6]. Several therapies have been prescribed for treatment of haemangiomas including oral prednisolone, intra-lesional steroids, laser therapy, and cyclophosphamide. Somehow previous therapies for haemangiomas are associated with risks and complications. Laser penetration is minimal in cutaneous haemangiomas so proved ineffective. However, oral steroids cause Cushingoid features and cryotherapy causes ulceration in haemangioma cases so newer drug oral propranolol is introduced for treating haemangiomas. As fewer complications are associated with propranolol treatment than steroid and other therapies[7]. Trials have shown that oral propranolol reduces the size of infantile haemangiomas more than steroids used for same duration[4,5,7,8]. Research on oral propranolol effectiveness in Pakistan is lacking[9]. Our study may help to improve handling the infantile haemangiomas regarding choice of a better drug with fewer

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side effects. There is need for surveillance and further research to set standard protocols and decrease haemangioma complications to reduce burden on health care resources. This study would also help in minimizing patient miseries. Objective of our study is to compare the efficacy of Propranolol with steroid (oral prednisolone) in treating the children with cutaneous haemangioma in terms of frequency of size reduction.

METHODOLOGY

This randomized comparative trial was done in Pediatric Surgery at Children Hospital Pakistan Institute of Medical Sciences Islamabad from 9th July 2013 to 9th Jan 2014. Sixty children who fulfilled the inclusion criteria were admitted via emergency and OPD. All cases with age one month to twelve years belonging to either sex group, presenting in emergency and OPD department were included with cutaneous haemangiomas at any site on body (eyelid, tip of nose, genital, inguinal fold, and knee etc.). Children on other treatments of haemangiomas, hypersensitivity to drugs under study, and risk of aggravation of diseases such as asthma, Raynaud syndrome, cardiac failure, impaired renal or liver functions, diabetes mellitus (IDDM) by drugs used in study and visceral haemangiomas were excluded from study on basis of history. Diagnosis of haemangioma was made on basis of history and clinical examination and confirmed by doing Doppler ultrasonography. Age, sex, socioeconomic status, history and clinical findings including baseline length, width and height of haemangiomas in cm were recorded on proformas. Parents of patients were counseled regarding risks and benefits of drugs under study. Permission from hospital ethical committee was taken and Informed consent signed. Patients were divided into two groups by non-Probability consecutive sampling randomly. Keeping level of significance at .05 and power of test at 80% with anticipated population equal to 82%[3] and 29%[3] sample size was calculated by WHO calculator, n=60 patients (n=30 in each group). 30 Patients in Group A received oral propranolol 2mg/kg/day in 2 divided doses in 1st week and then 3mg/kg/day for next three weeks. 30 patients in Group B received oral prednisolone 1mg/kg/day in 1st week and 2mg/kg/day for next two weeks with gradual tapering in 4th week. Vital signs were checked in first 24 hour period in both groups and pretreatment data and size of haemangioma was recorded by single post graduate resident final year. Patients in both groups were followed every week in OPD for 4 weeks regularly to see changes in skin and regression in size of haemangioma as measured in centimeters of length; width and height (volume) from first visit (baseline size) to post treatment follow up with any complications noted in both groups. Regression/ clearance of 75% or more was defined by a correlating percentage of decrease in volume, a cosmetically acceptable result by physician / parent and a lack of need for further treatment. Single observer senior registrar followed the cases after treatment and observed all the changes in each follow up till final visit at 4th week which coincided with culmination of study. **Data Analysis:** Data was analyzed on Statistical Package for Social Sciences (SPSS) version 16. Chi square test was applied on qualitative variables and independent sample t-test was applied on quantitative variables. p-value ≤0.05 was considered significant.

RESULTS

Total number of children included in study was 60 and they were divide in two groups. The mean ± SD age of the study patients in group A was 21.4 ± 21.6 months ranging from 3 to 84 months (7 years) and for group B was 17.4 ± 17.5 months ranging from 0.5 to 84 months (7 years) (Table - I). Out of total 60 patients 31% (n=19) were males while remaining 68% (n=41) were females. The regression in size of > 75% in Group A was 93.3% (n=28) while in 6.7% (n=2) patients there was <75% regression at 4th week. While in Group B >75% regression in size was noted in 0% (n=0) cases while <75% regression was observed in 100% (n=30) cases at 4th week post treatment. There were no complications observed in Group A while in Group B there was weight gain seen in 6.6% (n=2) cases only (Fig. - 1).

DISCUSSION

Haemangiomas are one of the commonest benign vascular tumors which occur in infants. Incidence is about 4 to 10%[1] in newborn infants while it increases to 23% in premature infants. Caucasian children have higher incidence of hemangiomas[2]. Male to female ratio is about 1:5. Haemangiomas grow rapidly up to two years of age in size, depth and elevation

Table-I: Age Distribution in Propranolol and steroid Groups (N=60)

N	Minimum	Maximum	Mean ± Std. Deviation
Age in Group A (n=30)	3.0 month	84.0 months	20.43 ± 21.65
Age in Group B (n=30)	0.5 month	84.0 months	20.43 ± 21.65
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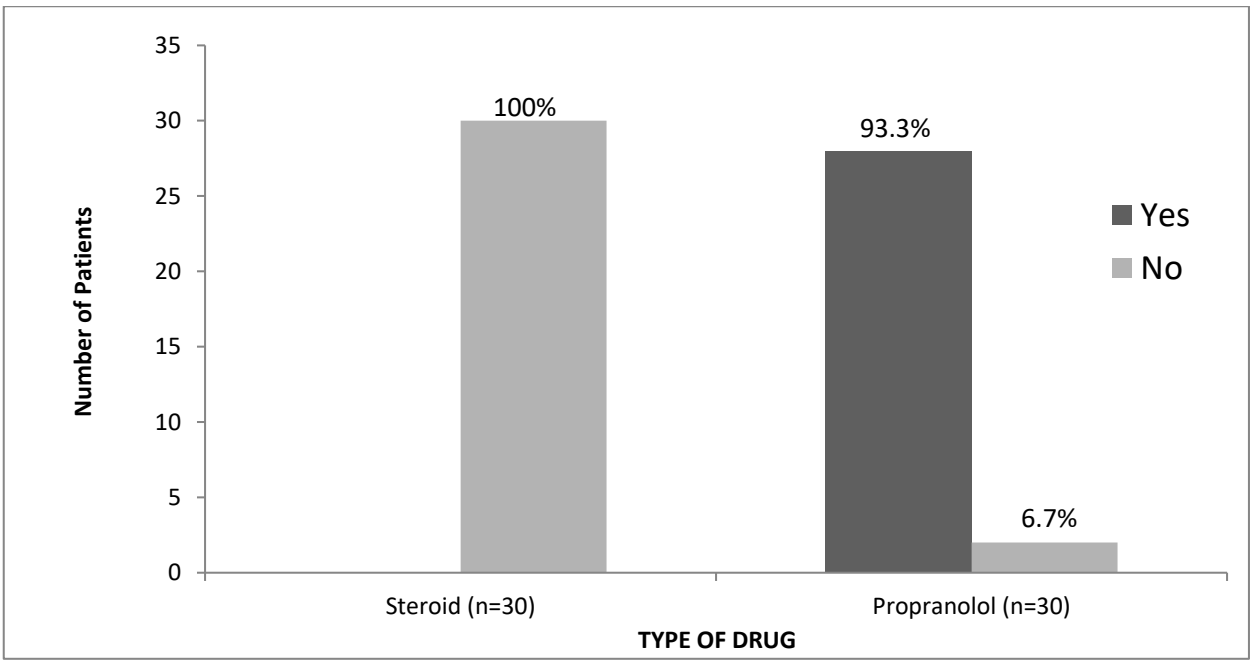

FIGURE- 1: Regression in size of haemangioma (> 75%) in Propranolol and steroid Groups at 4th Week (N=60)

above skin surface but afterwards they regresses in size with 60% disappearing by 5 years of age[10]. Haemangiomas show complications like ulceration, massive growth, disfigurement, impairment of vital sensory organs (eye obstruction leads to irreversible amblyopia) and in these cases treatment is necessary[11]. 10 % of haemangiomas require medical intervention including those involving the peri-orbital area, central face, airway, skin folds, ano-genital area that are sites of high risk for ulceration, dysfunction, or disfigurement[12,13]. Controversy still exists about various different options available for haemangiomas such as medical drugs, laser, cryotherapy and surgery. As laser penetration is limited in cutaneous haemangiomas making it less useful. Oral prednisolone had been in use for treating haemangiomas for 30yrs but is more effective drug in younger 6months patients than older children and associated with irritability, Cushingoid face and delayed growth. Oral propranolol used to treat haemangiomas has dramatic effect on shrinkage in size and promising results with minimal complications as hypoglycemia in some studies[5]. Research on propranolol effectiveness in Pakistan is lacking. Our study will help to show the effectiveness of propranolol in size reduction of cutaneous haemangiomas. The mean age of patients in our study i.e. 20.4 months in propranolol group and 17.48 months in steroid group is comparable to other studies[14-16]. Price[3] et al showed 82% patients who received propranolol had clearance of 75% or more compared to 29% patients who received oral steroids ($p<0.01$). The number of ulcerations was also significantly lower in propranolol group than in steroid group[3,17-20]. Same effects of size regression >75% was seen with propranolol in our study with no side effects of drug. Naouri et al[4] in their study proved that propranolol is highly effective and safe new therapy for ulcerated infantile haemangiomas. In our study none of the cases showed any side effect of propranolol while Holland et al[5] showed that symptomatic hypoglycemia appeared during treatment with propranolol for infantile haemangiomas in three cases. In a study Jalil S[9] compared the effectiveness of oral and intra-lesional steroids in reduction of size of haemangioma. The results were, 32% haemangiomas showed greater than 50% size reduction in oral steroid group while in intra-lesional steroid group 44% haemangiomas showed greater than 50% size reduction. So steroid helped to reduce the size of haemangiomas. In our study when compared the steroid group had similar regression in size with no patient reaching >75% regression level. Goldenberg[21] reported the successful treatment of a refractory left orbital and periorbital haemangioma, while Fay et al[22] showed the successful use of propranolol as primary therapy for a deep intra-conal Infantile haemangiomas. Haider et al[23] reported a series of 17 patients with peri-ocular Infantile haemangiomas showing 100% arrest of progression, more than 50% regression in 10 patients, and moderate regression in 6 patients. Missoi and colleagues[24] demonstrated even more favorable results with reduction in size (median 61%) in all 17 patients with peri-ocular IH treated with oral propranolol. Large haemangiomas, especially those appearing on the face, could cause anxiety and psychological distress. Complications such as ulceration and infection are quite common.[23] This is why emphasis has been given in literature for many decades as health care authorities are trying to treat infantile haemangiomas complications precisely. Our study may help to improve handling the infantile haemangiomas regarding choice of a better drug that was not widely tested previously for haemangioma treatment with minimal complications so far. There is need for surveillance and further research to set standard protocols and to reduce morbidity of patients landing with complications of disease. Our study might be in the first few drops in the ocean of vast research that will prove its worth in times to come.

CONCLUSION

Oral propranolol is more effective in the treatment of haemangioma than oral steroid used for same duration in terms of frequency of size reduction with no major side effects.

CONTRIBUTION OF AUTHORS

Rahman BU: Conceived idea, wrote Introduction and Data collection.
Bibi A: Literature search and wrote Discussion.
Ghafoor A: Wrote the Methodology
Taimur M: Formulated Data, analyzed Data, Wrote Results.

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