

Propranolol, Use in Facial Haemangioma in Children

MUHAMMAD AMIR HANIF KHAN, IRAM UZMA KHALID, MUTEE ULLAH MAJID, RAFIQ AHMAD KAMRAN

^{1,2,4}Assistant Professor

³Senior Registrar

Department of Paediatric Surgery, Nishtar Medical University & Hospital, Multan

Correspondence to Dr. Muhammad Amir Hanif Khan Email: mamirhanif114@gmail.com

ABSTRACT

Aim: To determine the efficacy of propranolol in the treatment of facial haemangiomas.

Study design: Prospective cross sectional study.

Place and duration of study: Department of Paediatric Surgery, Nishtar Medical University, Multan during January 2017 to June 2019.

Methods: In this study the cases of both genders with age less than 2 years were included. Facial haemangiomas were diagnosed clinically. Baseline pulse rate, blood pressure and blood glucose levels were recorded. Then these cases were started with propranolol at a dose of 1 mg per kg per day. If tolerated well, the dose was increased to 2 mg per kg in two divided doses. It was continued for 6 months. These cases were then assessed at the end of 3rd and 6th months regarding outcome. It was assessed by consultant on the basis of visual and photographic assessment. The drug was labelled effective if regression was more than 50%.

Results: In this study there were total 35 cases suffering from facial haemangiomas. Out of these 22 (62.85%) were males and 13 (37.15%) females. The mean age of the subjects was 4.13±1.22 months. Efficacy with propranolol was noted in 27 (77.14 %) of the cases. Poor sleep with irritability was noted in 2 (5.71%) cases, hypotension in 1 (2.86%) case and diarrhoea in 1 (2.86%) case.

Conclusion: Propranolol is effective in facial haemangiomas and has minimal side effect profile.

Key words: Propranolol, Haemangiomas, Children

INTRODUCTION

Haemangioma are vascular tumors occurring in infancy. They are considered as the most common benign tumors of infancy¹. They are benign but sometimes pose concern due to cosmetic problems. Its prevalence varies, usually 4-10% of infants suffer from it². Its incidence is more in female, premature and low birth weight babies³.

Haemangiomas can be found anywhere in the body but highest number is seen in the head and neck region⁽²⁾. Among different variants focal haemangiomas are commonly seen over head and neck⁴. Sometimes they are not evident at birth but over the next few weeks become visible. They rapidly progress during the first year of the life. Thereafter they involute over the next 2-10 years⁵. There are no major complications associated with this in ninety per cent of the cases⁶. However 10% can result in different complications warranting treatment⁷.

The diagnosis is usually clinical. It does not need any diagnostic modality and treatment is offered in problematic cases. There are number of agents that had been tried for this ailment with different degree of efficacy and side effects⁽⁸⁾. The most commonly used drugs are systemic corticosteroids, interferon-alpha, vincristine, pulse dye laser, liquid nitrogen cryotherapy and excisional surgery⁴.

Propranolol is a beta blocker and is used in number of diseases like tetralogy of fallot, arrhythmias, hypertension and thyrotoxicosis⁴. It is being used in the management of haemangiomas and certain studies have proved it be effective as well⁽⁹⁾. Side effects or complications of propranolol are usually low¹⁰. In a paediatric surgical unit of

a hospital where paediatric cardiology facilities are not available, it was a challenge to start propranolol therapy. There is also deficiency of local data in this regard. We decided to conduct the study with minimal involvement of cardiologist to ascertain the efficacy of propranolol in treatment of facial haemangiomas and to assess its side effects in our local settings.

PATIENTS AND METHODS

This cross sectional study was carried out at Department of Paediatric surgery, Nishtar Medical University, Multan during January 2017 to June 2019. In this study the cases of both genders with age less than 2 years were included. Facial haemangiomas were diagnosed clinically. Data like age, sex, weight, lesion location, size were noted along with photographic record of lesions. Any patient with a cardiovascular disorder, asthma, syndrome or associated visceral lesions was not included in the study. Base line pulse rate, blood pressure and blood glucose levels were recorded. Then these cases were started with propranolol at a dose of 1 mg per kg per day in two divided doses. Pulse rate and blood pressure were recorded hourly for four hours. Daily glucose levels were checked. If no abnormality was detected the dose was increased to 2mg per kg in two divided doses. Patients were followed up in outpatient department after every month for four months. Then the dose was tapered to 1 mg per kg in sixth month with stoppage at the end of sixth month. These cases were assessed at the end of 3rd and 6th months regarding outcome. It was assessed by tumor size and divided in two groups: effective (regression more than 50%) and not effective (regression less than 50%).

Statistical analysis: The data was analysed by SPSS 23.0. Categorical data was presented as frequencies and

Received on 17-08-2019

Accepted on 27-01-2020

percentages and numerical as mean and standard deviation.

RESULTS

In this study there were total 35 cases suffering from facial haemangiomas. Out of these 22(62.85%) were females and 13(37.15%) males. The mean age of the subjects was 4.13±1.22 months as shown in table I. Efficacy with propranolol was noted in 27(77.14%) of the cases as shown in figure I. it was found to be not effective in 8(22.86%) patients. Poor sleep with irritability was noted in 2(5.71%) cases. Hypotension was seen in 1(2.86%) case and diarrhoea was also observed in 1(2.86%) case as shown in table II. None of the patients suffered from hypoglycemia.

Table I: Study variables (n= 35)

Variables	Mean ± SD	Range
Age (months)	4.13±1.22	1-12
Weight (kg)	3.23±1.02	2.5-5
	Number	Percentage
Female	22	62.85
Male	13	37.15

Figure I: Efficacy of propranolol (n= 35)

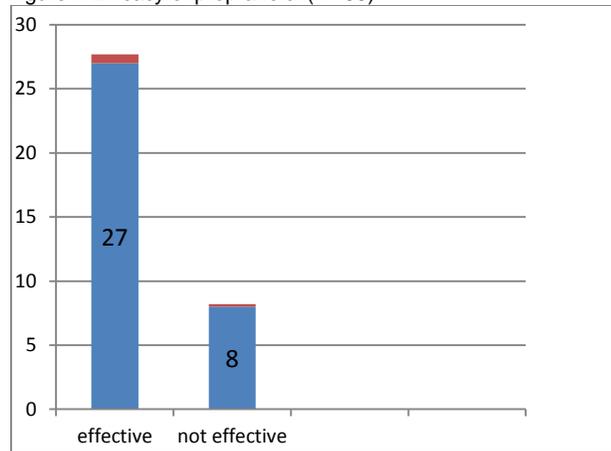


Table II: Side effects of propranolol (n= 35)

Side effects	Number	Percentage
Poor sleep	2	5.71
Hypotension	1	2.86
Diarrhoea	1	2.86
None	31	88.71

DISCUSSION

Infantile Haemangiomas are usually benign disorder. It rapidly grows after birth but there is spontaneous regression in most of the cases⁵. Focal haemangiomas can be found anywhere in body but they are most commonly found over head and neck region¹¹. Sometimes they can cause cosmetic or functional impairment. This situation may need treatment¹². Propranolol is used in number diseases in cardiology, medicine and plastic surgery⁽⁴⁾. It is becoming first line of treatment in infantile haemangiomas, with a good safety profile¹³.

Infantile haemangiomas are common in female babies and our study also had the same division. Same

finding was shared by Bota et al². The propranolol is available in tablet form of 10 mg. It was started at a dose of 01mg per kg in two divided doses in liquid form after dissolving it in water. Before starting the dose base line pulse rate, blood pressure and glucose levels were recorded. After starting the medication these parameters were re-checked to ascertain safety¹⁴. If everything was within normal limits, the dose was increased to 02mg per kg. Some studies have stated a dose of 2-3mg per kg in three divided doses⁴, however generally 2mg per kg is considered suitable for infantile haemangioma¹³. There was a possibility to reduce the dose in case of any complication but it was not required. The dose was continued upto sixth month and initially tapered to 1 mg per kg and stopped at the end of sixth month.

The tumor size was assessed at the end of 3rd and sixth month and patients were divided into two groups. In the present study, regression and not regression of the haemangioma were taken as variable to see the efficacy of the drug. If tumor size reduced more than 50% it was labelled at regression and drug was found effective. It was seen in 27(77.14%) patients. Other 8(22.86%) showed no regression i.e., regression less than 50% of the size. According to a study done by McGee P et al, they found that the efficacy in the form of reduction in size of the haemangiomas by giving propranolol was seen in 22 (91.6%) out of 24 cases¹⁵. Our study showed rather less effectiveness. It seems to be due to keeping the regression size at 50%. Eghbali et al found effectiveness in 78% patients¹⁶. Alsmman et al found effectiveness in 75% cases if size reduction of 50% was set as acut-off point⁵.

The side effects related to propranolol were observed in 4(11.29%) cases. Other 31(88.71%) patients remained free of any side effects. The side effects were of mild in nature and none resulted in termination of therapy. Irritability with poor sleep, hypotension and diarrhoea were seen but got better with time. These findings were almost similar to Eghbali et al and Grzesik et al^{13,16}. McGee P et al also did not find any significant side effect profile. Only one out 24 cases had bradycardia, for that the dose was reduced to 01 mg per kg¹⁴.

The total duration for propranolol was 6 months. This duration is generally accepted for its use as described by Leaute-Labreze et al¹⁴. More than 50% reduction was seen in 27(77.14%) cases. We did not follow up patients beyond six months but studies have shown further reduction in size over the time¹⁷. Furthermore, relapse after stoppage of therapy is also very rare¹⁸. None of our patients reported back with complaints of rebound increase in size. In another study by Aletaha M et al they reported a case series of three cases and found a significant reduction in the size of the haemangiomas within 2 months and there was again a linear and sustained response to the reduction in size of these during the remaining follow up periods¹⁹. El-Sabbagh also reported that none of his patients required a second course⁴.

CONCLUSION

Propranolol is effective in treatment of facial haemangiomas in children at a dose of 2mg per kg. There is acceptable safety profile at this dose.

REFERENCES

1. Beth A. Drolet, Nancy B. Esterly IJF. Haemangiomas in children. *N Engl J Med.* 1999;341(3):173–81.
2. Bota M, Popa G, Blag CL, Leucua DC, Tătaru A. Infantile hemangiomas: A 7-Year experience Of a single-center. *Clujul Med.* 2017;90(4):396–400.
3. Garzon MC, Epstein LG, Heyer GL, Frommelt PC, Orbach DB, Baylis AL, et al. PHACE Syndrome: Consensus-Derived Diagnosis and Care Recommendations. *J Pediatr.* 2016 November ; 178: 24–33.e2. doi:10.1016/j.jpeds.2016.07.054.
4. El-Sabbagh AH. Oral Propranolol: A Useful Treatment for Infantile Hemangioma. *J Biomed- ical Sci Eng.* 2015;8:441–50.
5. Alsmman AH, Mounir A. Combined oral propranolol with intralesional injection of triamcinolone acetonide in treatment of infantile periocular hemangiomas. *Clin Ophthalmol.* 2017;11:2177–81.
6. Menapace D, Mitkov M, Towbin R, Hogeling M. The changing face of complicated infantile hemangioma treatment. *Pediatr Radiol [Internet].* 2016;46(11):1494–506. Available from: <http://dx.doi.org/10.1007/s00247-016-3643-6>
7. Darrow DH, Greene AK, Mancini AJ, Nopper AJ, Cohen BA, Antaya RJ, et al. Diagnosis and management of infantile Hemangioma. *Pediatrics.* 2015;136(4):e1060–104.
8. Baselga E, Roe E, Coulie J, Muz FZ, Boon LM, McCuaig C, et al. Risk factors for degree and type of sequelae after involution of untreated hemangiomas of infancy. *JAMA Dermatology.* 2016;152(11):1239–43.
9. Hoeger PH, Harper JI, Baselga E, Bonnet D, Boon LM, Atti MCD, et al. Treatment of infantile haemangiomas: recommendations of a European expert group. *Eur J Pediatr.* 2015;174(7):855–65.
10. Guo X, Zhu X, Liu D, Gong Y, Sun J, Dong C. Continuous delivery of propranolol from liposomes-in-microspheres significantly inhibits infantile hemangioma growth. *Int J Nanomedicine.* 2017;12:6923–36.
11. Bruckner AL, Frieden IJ. Hemangiomas of infancy. *J Am Acad Dermatol.* 2003;48(4):477–96.
12. Lawley LP, Siegfried E, Todd JL. Propranolol treatment for hemangioma of infancy: Risks and recommendations. *Pediatr Dermatol.* 2009;26(5):610–4.
13. Grzesik P, Wu J. Current perspectives on the optimal management of infantile hemangioma. *Pediatr Heal Med Ther.* 2017;Volume 8:107–16.
14. Léauté-Labrèze C, Hoeger P, Mazereeuw-Hautier J, Guibaud L, Baselga E, Posiunas G, et al. A randomized, controlled trial of oral propranolol in infantile hemangioma. *N Engl J Med.* 2014;372(8):735–46.
15. McGee P, Miller S, Black C, Hoey S. Propranolol for infantile haemangioma: A review of current dosing regime in a regional paediatric hospital. *Ulster Med J.* 2013;82(1):16–20.
16. Eghbali A, Hajjani S, Sedeh BS, Pakniyat A, Mansouri V, Bagheri B. A 24-week treatment of pediatric hemangioma with oral propranolol. *Iran J Pharm Res.* 2017;16(2):808–13.
17. Chen YZ, Bai N, Bi JH, Liu XW, Xu GQ, Zhang LF, et al. Propranolol inhibits the proliferation, migration and tube formation of hemangioma cells through HIF-1 α dependent mechanisms. *Brazilian J Med Biol Res.* 2017;50(12):1–7.
18. Buckmiller LM. Propranolol treatment for infantile hemangiomas. *Curr Opin Otolaryngol Head Neck Surg.* 2009;17(6):458–9.
19. Aletaha M, Salour H, Bagheri A, Raffati N, Amouhashemi N. Oral propranolol for treatment of pediatric capillary hemangiomas. *J Ophthalmic Vis Res.* 2012;7(2):130–3.