

## Research Article

# Assessment of propranolol efficacy on pediatric haemangioma: an experimental study

Afshin Fathi, Mehrdad Mirzarahimi\*

Department of Pediatrics, Ardabil University of Medical Science, Ardabil, Iran

**Received:** 12 October 2015

**Accepted:** 18 November 2015

**\*Correspondence:**

Dr. Mehrdad Mirzarahimi,

E-mail: [m.mirzarahimi2014@gmail.com](mailto:m.mirzarahimi2014@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

**Background:** Hemangioma is the most common vascular tumor in infancy. Recent studies show Propranolol efficacy on hemangioma treatment due to its rapid effect and a few side effects. The aim of this study was to assess the efficacy of Propranolol on pediatric haemangioma.

**Methods:** This quasi-experimental study was done on 20 children referred to Bu-Ali hospital. Treatment indications were multiple hemangioma, organ malfunction and enlarging hemangioma. Treatment of patients was started with 1 mg/kg/day and then increased to 3 mg/kg/day and continued for 6 months. Collected data analyzed by statistical methods in SPSS-19.

**Results:** Patients mean age was  $23.2 \pm 11.2$  months. 65% of them were female and 35% were male. The mean size of damages was  $4.9 \pm 3.3$  cm. 70% of patients had acceptable response with more than 50% and 30% had partial response with less than 50% decrease in size. This effect is similar to corticosteroid effect (about 84%) but with less side effects.

**Conclusions:** This study showed that Propranolol has acceptable effect on decreasing size of hemangioma and could be recommended as a first choice of hemangioma treatment.

**Keywords:** Hemangioma, Propranolol, Treatment effect, Infants, Ardabil

### INTRODUCTION

Hemangiomas, including infantile hemangiomas, are the most common vascular tumors in children with a prevalence of about 10% in Western countries and less than this rate in the Asia and Africa.<sup>1,2</sup>

Although hemangiomas often recover themselves in ages 7 to 10 years, but can disrupt vital sensory activities among the people.<sup>3-5</sup>

Hemangioma can be small and limited to the skin or as a great waste associated with serious complications and involving many organs such as the eyes, lungs and air passages, liver, gastrointestinal tract or even the brain.<sup>6</sup>

The most common complication of Hemangiomas is injury which was commonly associated with bleeding, pain, infection and leaving scarring.<sup>7</sup>

First line treatment of hemangioma despite having certain side effects was long term use of oral corticosteroids. More than thirty years glucocorticoids are used for the treatment of infantile hemangiomas. Systemic steroids can be useful for hemangioma of infancy and can have different and non-obvious effects. The rate of Steroids was about 84%.<sup>8</sup>

Recent studies showed the positive effects of propranolol on hemangiomas.<sup>9-12</sup>

Propranolol is a beta receptor inhibitor drug that act randomly. It was discovered in 1950 by James Black.<sup>13</sup> In recent studies, the beneficial effect of oral propranolol in improving hemangioma of infancy period is evident.<sup>14</sup>

Propranolol side effects include bradycardia, hypotension and hypoglycemia.<sup>12,15</sup>

Hypoglycemia in infants is often asymptomatic, but can occasionally cause neurological symptoms.<sup>16</sup>

As well as both large and small hemangiomas can be associated with heart disease with high output that propranolol can be cover the signs of heart failure.

So for optimization of treatment with propranolol recommending for doing a primary ecocardiology and blood sugar control before treatment and four week after is necessary.

More hemangioma hase size about 0.5-5 cm but they may be reaching to 20 cm diameter. The damages can be superficial or deep. More superficial damages are purple. Approximately 50-60% of hemangioma arent fully recovered and associated with changes such as the skin telangiectasia, dilated superficial veins, scars or dents or hypopigmentation.<sup>17-18</sup>

The aim of this study was to assessment of Propranolol efficacy on less than 15 years pediatric hemangioma.

## METHODS

This is a quasi-experimental study that has been done on 20 infants and neonates in pediatrics clinic.

Of the patients admitted to the hospital, and identify children with hemangiomas and children with multiple hemangioma, hemangioma in sensitive areas or children who were hemangioma large (greater than 5 cm) that they are low probability of spontaneous recovery , were referred to the Hematology and Oncology for follow-up treatment.

Initially, all patients were evaluated for vital signs and blood sugar and echocardiography was performed and those patients who have no heart problems and were eligible for treatment were treated with propranolol.

Also, of all the patients before treatment, ultrasound of the abdomen and pelvis was performed to assess the presence of visceral hemangiomas cell.

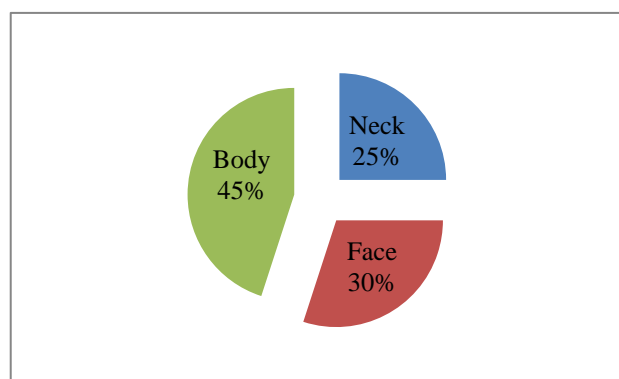
Firstly treatment starts with 1 mg/kg body weight and after two week increase to 3 mg/kg. In first week patients evaluated by sugar and heart rate that in case of existence signs of hypoglycemia and bradycardia therapy was stopped. Treatment followed for 6 months and after response patients followed for relapse. According to the decreasing in the size of hemangioma, the response to

treatment classified in four group very good (more than 70%), good (50-75%), moderate (25-50%) and week (<25%).

Collected data analyzed by statistical methods such as chi-square and t-test and descriptive statistical methods such as table and graph. P<0.05 considered as significant.

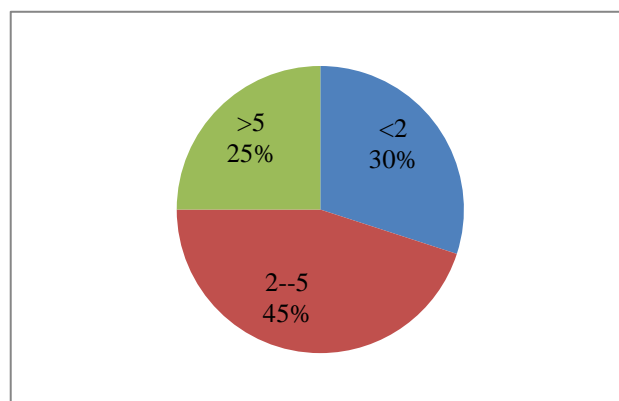
## RESULTS

The mean age of patients was 23.2±11.2 months (range from two month-5 year). 7(35%) were in age group 13-24 months. 65% of infants were girl and rest of them were boy. 45% of infants have hemangioma in Body (Figure 1).



**Figure 1: The areas of hemangioma distribution.**

9 patients (45%) have hemangioma in size 2-5 cm. The mean of hemangioma in these patients were 4.9±3.3 (Figure 2).



**Figure 2: Size of hemangioma in infants.**

The indication of patients for treatment were Beauty problems (13 cases, 65%), speedy growth of hemangioma (4 cases, 20%) and impaired organ function (3 cases, 15%). To search for hemangiomas in other parts of the body, ultrasound of the abdomen, pelvis, and liver were taken from all patients and in none of the cases was observed. Echocardiography was performed in these patients and in only two patients had abnormal echocardiography (one case PFO and one case TR) and in

other patients had normal. For all patients, blood sugar and heart rate were done and no side effects were observed in treatment with beta-blockers. The mean of damages in study start time was  $4.9 \pm 3.3$  cm and this rate decreased significantly in end of study and reach to  $1.8 \pm 1.1$  cm ( $p=0.001$ ).

Also results showed that 14 patients (70%) have acceptable response to treatment which from them 15% has very well and 55% have good response. Results showed that there wasn't any significant relation between sex and response of patients. The mean age of patients with very good response was 25 months and with good response was 22.8 months. There wasn't any significant difference between age of patients and size of damages and response rate of patients to treatment.

## DISCUSSION

Hemangioma is tumors of endothelial cells and the most common type of tumor in infants<sup>19</sup> which the sex ratio f/m was varied from 2/1 to 5/1.<sup>20</sup>

The mean age of patients in this study was  $23.2 \pm 11.2$  months. Other studies in other places showed that the mean age of infants were under one year old which wasn't similar to our study that this result can be related to the delay in parent's referred to treatment of infants.<sup>19,21-26</sup>

65% of infants were girl and 35 % were boy which was similar to other studies.<sup>26-28</sup>

In this study most of patients (70%) have significant damage decreasing and a few of them (30%) have week response to propranolol. After compare the result of this study with other studies seen that most of patients in all studies have very good or good response to propranolol and there was significant relation between damages size and propranolol use. ( $p=0.001$ ) and only a few of patients not response to propranolol. So, this treatment can be one of the usual treatments for hemangioma which has been increased in the recent years.<sup>19,21-26</sup>

There weren't any side effects related to propranolol drug use. In other studies, it was found that beta blockers have fewer side effects than corticosteroids for patients and these drugs are safer than cortisone.<sup>19,21-26,29-30</sup>

Some of studies compared the propranolol with prednisolone in hemangioma treatment and most of them resulted that the propranolol is better than prednisol in decreasing hemangioma damages.<sup>28-30</sup>

## CONCLUSION

The use of propranolol in children has sufficient reduction in size of the hemangioma. Due to the lower side effects of the propranolol than corticosteroids, propranolol is recommended as a first-line therapy in the

treatment of hemangioma. In this study we use only the propranolol for treatment hemangioma and we not use placebo group or another group for compare the results between them. It is recommended that another study in this subject must be done in the future and determine the effect of propranolol in higher doses.

## ACKNOWLEDGMENTS

The result of this study financially supported by Ardabil University of Medical Science and we thanks all persons help us.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Kilcline C, Frieden IJ. Infantile hemangiomas: how common are they? A systematic review of the medical literature. *Pediatr Dermatol.* 2008;25(2):168-73.
2. Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. *Plast Reconstr Surg.* 1982;69:412-22.
3. Chiller KG, Passaro D, Frieden IJ. Hemangiomas of infancy: clinical characteristics, morphologic subtypes, and their relationship to race, ethnicity, and sex. *Arch Dermatol.* 2002;138:1567-76.
4. Frieden IJ, Haggstrom AN, Drolet BA, Mancini AJ, Friedlander SF, Boon L. Infantile hemangiomas: current knowledge, future directions: proceedings of a research workshop on infantile hemangiomas, April 7-9, 2005, Bethesda, Maryland, USA. *Pediatr Dermatol.* 2005;22:383-406.
5. Bennett ML, Fleischer AB Jr, Chamlin SL, Frieden IJ. Oral corticosteroid use is effective for cutaneous hemangiomas: an evidence-based evaluation. *Arch Dermatol.* 2001;137:1208-13.
6. Kliegman RM, Behrman RE, Jenson HB, Stanton BF. *Nelson textbook of pediatrics.* 18<sup>th</sup> ed. Philadelphia, PA: Saunders Elsevier; 2007.
7. Chamlin SL, Haggstrom AN, Drolet BA, Baselga E, Frieden IJ, Garzon MC, et al. Multicenter prospective study of ulcerated hemangiomas. *J Pediatr.* 2007;151(6):684-9.
8. Akhavan A, Zippin JH. Current treatments for infantile hemangiomas. *J Drugs Dermatol.* 2010;9(2):176-80.
9. Léauté L. Propranolol for Severe Hemangiomas of Infancy. *N Engl J Med.* 2008;358(24):140-9.
10. Propranolol In Pediatric Hemangioma; available at: [www.health-forums.com/alt-support-cancer/propranolol-pediatric-heman](http://www.health-forums.com/alt-support-cancer/propranolol-pediatric-heman). 2011.
11. Léauté-Labrèze C, Dumas de la Roque E, Hubiche T, Boralevi F, Thambo JB, Taïeb A. Propranolol for

- severe hemangiomas of infancy. *N Engl J Med* 2008;358(24):2649-51.
12. Shayan Yasaman R. Use of propranolol in treating hemangiomas. *Canadian Family Physician* March 2011;57:3302-3
  13. Burns CM, Rutherford MA, Boardman JP, Cowan FM. Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycemia. *Pediatrics*. 2008;122:65-74.
  14. Sehgal VN. *Textbook of clinical dermatology*, 4<sup>th</sup> ed, Jaypee, New denli. 2004;220-224.
  15. Habif TP. *Clinical dermatology*. London: Mosby. 2009;691-93.
  16. Melo-Gomes JA. Problems related to systemic glucocorticoid therapy in children. *J Rheumatol Suppl*. 1993;37:35-9.
  17. Zimmermann AP, Wiegand S, Werner JA, Eivazi B. Propranolol therapy of infantile haemangiomas: review of the literature. *Int J Pediatr Otorhinolaryngol*. 2010;74(4):338-42.
  18. Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. *Plast Reconstr Surg*. 1982;69:412-22.
  19. Menezes MD, McCarter R, Greene EA, Bauman NM. Status of propranolol for treatment of infantile hemangioma and description of a randomized clinical trial. *Ann Otol Rhinol Laryngol*. 2011;120(10):686-95.
  20. Eichenfield LF, Frieden IJ, Esterly NB. *Textbook of Neonatal Dermatology*. Philadelphia, Pa: WB Saunders Co. 2001:324-353.
  21. Fridman G, Grieser E, Hill R, Khuddus N, Bersani T, Slonim C. Propranolol for the treatment of orbital infantile hemangiomas. *Ophthal Plast Reconstr Surg*. 2011;27(3):190-4.
  22. Buckmiller LM, Munson PD, Dyamenahalli U, Dai Y, Richter GT. Propranolol for infantile hemangiomas: early experience at a tertiary vascular anomalies center. *Laryngoscope*. 2010;120(4):676-81.
  23. Haider KM, Plager DA, Neely DE, Eikenberry J, Haggstrom A. Outpatient treatment of periocular infantile hemangiomas with oral propranolol. *J AAPOS*. 2010;14(3):251-6.
  24. Kim LH, Hogeling M, Wargon O, Jiwane A, Adams S. Propranolol: useful therapeutic agent for the treatment of ulcerated infantile hemangiomas. *J Pediatr Surg*. 2011;46(4):759-63
  25. Kunzi-Rapp K. Topical propranolol therapy for infantile hemangiomas. *Pediatr Dermatol*. 2012;29(2):154-9.
  26. Xu G, Lv R, Zhao Z, Huo R. Topical propranolol for treatment of superficial infantile hemangiomas. *J Am Acad Dermatol*. 2012;67(6):1210-3.
  27. Chung SH, Park DH, Jung HL, Shim JW, Kim DS. Successful and safe treatment of hemangioma with oral propranolol in a single institution. *Korean J Pediatr*. 2012;55(5):164-70.
  28. Pope E, Chakkittakandiyil A, Lara-Corrales I, Maki E, Weinstein M. Expanding the therapeutic repertoire of infantile haemangiomas: cohort-blinded study of oral nadolol compared with propranolol. *Br J Dermatol*. 2013;168(1):222-4.
  29. Bertrand J, McCuaig C, Dubois J, Hatami A, Ondrejchak S, Powell J. Propranolol versus prednisone in the treatment of infantile hemangiomas: a retrospective comparative study. *Pediatr Dermatol*. 2011;28(6):649-54.
  30. Xu SQ, Jia RB, Zhang W, Zhu H, Ge SF, Fan XQ. Beta-blockers versus corticosteroids in the treatment of infantile hemangioma: an evidence-based systematic review. *World J Pediatr*. 2013;9(3):221-9.

**Cite this article as:** Fathi A, Mirzarahimi M. Assessment of propranolol efficacy on pediatric haemangioma: an experimental study. *Int J Res Med Sci* 2015;3:3604-7.