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Emir Čokić, Jasmina Alajbegović-Halimić, Tarik Halimić, Almina Merdić

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Authors:

Emir Čokić¹, Jasmina Alajbegović-Halimić², Tarik Halimić³, Almina Merdić⁴

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Affiliations:

¹Dom Zdravlja Visoko; BiH, ²Privatna oftalmološka ordinacija "Prof. dr. Jasmina Alajbegović-Halimić"; BiH, ³Klinika za očne bolesti SKB Mostar; BiH, ⁴Dom Zdravlja Visoko; BiH

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Corresponding author: Emir Čokić Email: emir_alfac@hotmail.com The association between binocular vision and anisometropic amblyopia in children. **Introduction**: Anisometropic amblyopia is the second most common cause of amblyopia in children population, as a result of unequal refractive errors between the eyes. Eye with the more dominant refractive error has less chance to achieve binocular vision and signal from that eye is being suppressed.

Aim: To evaluate the presence of binocular vision in children with anisometropic amblyopia before and after the treatment, then establish how is binocular vision affected by the magnitude of anisometropia, depth of amblyopia, pattern of fixation and type of refractive error.

Patients and methods: Retrospective study was conducted in Pediatric Department of Clinic for Eye Disease of KCUS, in a period from 2016. to 2017. There were 100 patients with diagnosed anisometropic amblyopia.

Results: Anisometropia in average was $1,9\pm1,7D$. During the first evaluation most of the patients didn't have stereopsis(62%), on the follow-ups 81% had stereopsis. Patients with intact binocular vision showed smallest differences in visual acuity $2,7\pm1,9$, in anisometropia $1,2\pm0,9D$ also; statistically significant higher frequency of myopia and astigmatism with myopia, and foveolar fixation. Patient who developed binocular vision during the therapy had higher values of difference in visual acuity($4,4\pm2,7$) and anisometropia $1,9\pm1,6D$. Patients who haven't established binocular vision even after the therapy have the highest values in differences in visual acuity and anisometropia, $7,1\pm2,2$ and $3,6\pm3,1D$; highest frequency of hyperopia, eccentric fixation, and severity of amblyopia.

Conclusion: Children with greater depth of amblyopia, higher magnitude of anisometropia have less chance to achieve binocular vision even with treatment.

Key words: amblyopia, anisometropia, stereopsis, binocular vision.

INTRODUCTION

Amblyopia is term that derives from Greek and it means "dullness of vision". It represents a decrease in visual acuity without any noticable structural abnormalities. Amblyopia excludes manifest nor latent diseases both of the eve and visual pathways [1]. It is considered to be a primarily cortical phenomenon that occurs due to a unequal competitive impulses from both eyes in primary vision cortex (Area 17). The prevalence of amblyopia in general population is 2-3%, and it is the most common cause of vision loss amongst children. Term that is often used for ambliopic eye is "lazy eye" [2]. This problem occurs mostly before child's second year, but it can manifest even in the seventh year. Left eye is "lazy" in more than a half cases because there are more righthanded people, which means there are more people with dominant right eye [3]. Critical period for amblyopia to occur is so called "sensitive period" while afferent

visual system is still plastic and able to form and rearrange synapses. Visual acuity of children matches adults in the age of 5-6 years. Duration of this sensitive period is individual for each person and many factors interfere. That is why early detection and therapeutic treatment of amblyopia is crucial in prevention of development of amblyopia [1]. There are three types of amblyopia: strabismic, anisometropic, and third group represents the mixture of previous two. Anisometropic amblyopia is the second most common cause of amblyopia in children population, as the result of unequal refractive errors between the eyes. Although they occur mostly at the same time, anisometropia is considered to be a precursor and the cause of amblyopia [4]. Eye with greater deprivation of vision in terms of refractive anomaly proceces blurred images and the signals are being inhibited and supressed. That is how anisometropic amblyopia affects binocular vision. That is why anisometropic amblyopia can be unnoticed in children for a long time. Refractive anomaly in both eyes can be of a different type, or same type of anomaly but different values. Patients with myopia have, in general, smaller levels of anisometropia and depth of amblyopia, unlike patients with hyperopia or astigmatismus [4]. Both eves are used to observe world around us, but our brain use signals from them to create one, synchronic picture. That is possible due to the motoric and sensoric coordination. Binocular vision is cortical ability of fusion of two monoocular information into one. Binocular vision is not inborn ability, instead it is developed around fifth or sixth year of life. It is of extreme importance that this period of development is not affected by any kind of disturbance. Sooner the problem occurs, consequences are more difficult to deal with [5]. The gold standard for diagnosing anisometropic amblyopia is complete examination of 4 year old child by ophthalmologist. Screening of visual acuity is one of the most effective and useful screenings [6]. Amblyopia is characterized by deprivation of visual acuity, loss of stereopsia(binocular vision), eccentric fixation etc. Depth of amblyopia is defined by loss of visual acuity. Mild amblyopia has best corrected visual acuity in values from 0,4 to 0,8. By medium amblyopia we consider visual acuity from 0,1 to 0,3 and severe with visual acutiv that is less than 0,1 [7-8]. In regular terms eve has foveolar fixation and usually amblyopia, if occurs, is mild or medium depth. When eye has an eccentric fixation depth of amblyopia increses [9]. Treatment of every child should be individual and adjusted, but gold standard in therapy is still occlusion of better eye with adequate correction of refraction error. Part-time occlusion is preferred by both children and ophthalmologists[2]. With this kind of treatment almost 79% of children show better results and significant improvement in just 4 months. But improvement in visual acuity doesn't mean necessarily improvement in binocular vision. New approaches in treatment use video games or movies for children, which force them to use both eyes, with more information that are given to the amblyopic eye. [10-11].

We wanted to evaluate the presence of binocular vision in children with anisometropic amblyopia before and after the treatment, and evaluate how is binocular vision affected by the magnitude of anisometropia, depth of amblyopia, pattern of fixation, type of refractive error.

MATERIAL AND METHODS

The study was conducted as clinical, descriptive and retrospective study, including a total of 100 patients who were followed and examined during 2016. and 2017 at the Eye Clinic, University Clinical Center Sarajevo. All patients have been diagnosed with anisometropic amblyopia and they were adequately treated and followed. Data for the study were obtained from medical records: personal data, data from the first examination and follow up (presence of amblyopia, visual acuity, refractive error, binocular vision, type of fixation, treatment method). Results were compared from first examination and follow-up. In cases with astigmatisms spherical equivalent was used. To examine binocular vision we divided patients into three groups:

• Children who had binocular vision at first examination.

• Children who didn't have binocular vision at first examination, but who established binocular vision after the treatment which was noticed at the follow-up examination.

• Children who even after the treatment haven't established binocular vision.

Results of the analysis are presented in tables and charts by number of the cases, percentage, mean, median, standard deviation, standard error, cut off values. To test the difference and impact of certain parameters following tests were used: chi-square test, analysis of variance ANOVA, Sperman's rank correlation coefficient, ROC curve analysis. Results of these tests were considered statistically significant with p<0,05 or at the 95% confidence level. The analysis was conducted using the statistical package IBM Statistics SPSS v 23.0.

RESULTS

Sample included a total of 100 children with criteria for anisometropic amblyopia, who were examined and followed at Eye Clinic, University Clinical Center Sarajevo during 2016. and 2017. Sample included 52 females (52%), and 48 males (48%). The analysis of age shows that mean age is 8,5±3,2 with youngest patient who had 3 years, and oldest with 17 years. Visual acutiy was better on the right eye with average 0,62±0,31. Visual acuity on the left eye was, in average, 0,53±0,32, no statistical significance. Distribution of refractive errors showed that most commonly children had hyperopia with 53%, then myopia with astigmatismus in 22%, hyperopia with astigmatismus in 14%, and myopia as the rarest with 11%. Magnitude of anisometropia was in average 1,9±1,7D with lowest value od 0,25D and highest with 9D. As for the presence of binocular vision on the first examination, 62% didn't have, 35% had, and in 3% doctor was unable to determine. On the followup, 81% established binocular vision, 12% didn't have, and 7% were unclear to determine. Sample was divided into three groups (Table I).

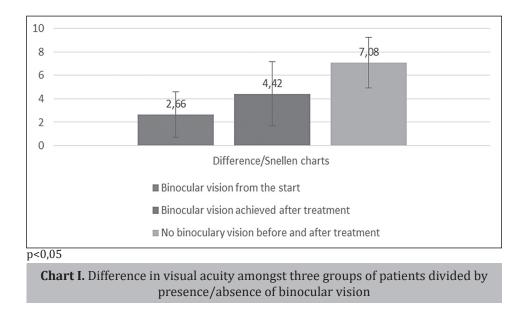
Precisely 62% had foveolar fixation while 38% had some kind of eccentric fixation. On the first examination most of the children had mild amblyopia 49%, moderate 43% and 8% had severe amblyopia. Analysis of difference in visual acuity amongst eyes showed that patients with higher difference showed less possibility of achieving binocular vision after treatment. This difference was statistically significant (p<0,05) Chart I.

Amongst patients with no binocular vision on the first examination we determined Cut-off value(AUC-Area under the Curve; ROC. Receiver Operating Curve). For difference in visual acuity value of area under the curve was 0,778 with confidence interval 0,657.0,871 and

Table I. Three groups of patients according to the presence of binocular vision before and after treatment

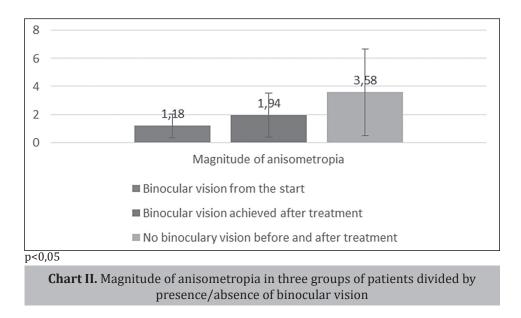
Binocular vision			
Patients who had binocular vision from the start			
Patients who established binocular vision on the follow-up			
Patients with no binocular vision even after the treatment			
Total	100		

NS- non significance



Z=4,081 so we can conclude with p<0,0001 that this analysis is reliable. With Cut-off difference in visual acuity <8 we can, with sensivity of 92,5%, claim that patients will have improvement and establisment of binocularvision. Analysis of magnitude of an isometropia

showed that patients with higher magnitude have less chance of achieving binocular vision(p<0,05) and cutoff value was determined <5,25D with sensivity of 98,11% Chart II.



Considering type of refractive error we noticed statistically significant difference in achieving binocular vision (p<0,05). Patients who established binocular vision after treatment had more often myopia and myopia with astigmatismus. Patients with foveolar

fixation had better results compared to the patients with some kind of eccentric (p<0,05). Correlation between depth of amblyopia and binocular vision is showed in.

		Binocular vision		
			Binocular vision from the start	Binocular vision achieved after treatment
Depth of amblyopia (without correction)	Mild	N	25	22
	Mika	%	71,4	41,5
	Moderate	Ν	10	26
	Moderate	%	28,6	49,1
	Severe	Ν	0	5
	Severe	Severe %	0,0	9,4
Total		N	35	53
		%	100,0	100,0

Table II. Connection between depth of amblyopia and binocular vision

p<0,05

Permanent loss of binocular vision is correlated with severe and moderate amblyopia while patients with mild amblyopia in most cases achieve binocular vision. Correlation analysis shows that there is direct correlation between depth of amblyopia and presence/ absence of binocular vision.

DISCUSSION

In this retrospective study we observe a total of 100 children with anisometropic amblyopia. Gender structure of respondents indicated the higher representation of females (52%), but there was no statistically significant difference. Mean age is $8,5\pm3,2$ years. Donahue et al. found that younger children with anisometropic refractive anomaly have less prevalence of amblyopia and if amblyopia occurs then it is mostly mild. The same study showed that amblyopia is rare in children younger than 2 years even if they have anisometropia. Moderate and severe amblyopia is found only in children older than 4 years. Anisometropic amblyopia is often unrecognized by parents and doctors because it has no obvious signs. It is estimated that only 15% of children have correct diagnosis before fifth year of life [1].

Respondents showed better visual acuity on the right eye. Other studies confirmed the same, anisometropic amblyopia occurs predominantly on the left eye [12]. One of the possible explanations is visual dominance of the eye we choose when we look through the telescope. fMRI scan showed that signals from the dominant eye activate bigger area of the visual cortex [12].

Considering the type of refractive anomaly, hyperopia was dominant with 53%, then myopia with astigmatismus in 22%, hyperopia with astigmatismus in 14%, and last myopia with 11%. Levi M et al. found that prevalence of amblyopia is lower amongst patients

with myopia. On the other hand children with hyperopia have faster and more significant loss of visual acuity. With magnitude of anisometropia 3D almost 40% of hyperopia patients will show some signs of amblyopia, while myopia patients in only 15% of all cases [13].

Average value of anisometropia in our sample was $1,9\pm1,7$. Different authors use different parameters. Value that has been used as a borderline for anisometropia is difference in value of the spherical equivalent between eyes 1D [14]. In fact, we can use every difference between refraction anomalies between eyes as anisometropia, but borderline value is estimated by its clinical significance. Some authors use different values considering different refraction errors. In case of myopia 2D, hyperopia 1D, myopia with astigmatismus 1,5D etc [4,15].

Dorn et al. found that almost 50% of patients with anisometropic amblyopia have intact binocular vision. Element of binocular vision which is mostly damaged is steropsis. Without stereopsis it is hard for children to participate in sports, to do some kind of exercises etc. Stereopsis is mostly affected in strabismic amblyopia, where only 10% of children have binocular vision, while in anisometropic amblyopia this ratio is up to 50%. Sometimes it is hard to determine does a child have binocular vision [16-17].

Difference in visual acuity between eyes directly affects binocular vision. Patients with smallest differences mostly have unaffected binocular vision. But some studies found that there are people who are essentialy stereo blind. With those cases excluded, we came to cutoff value of visual acuity 0,8. Which means that even moderate amblyopia, if properly treated, is reversible [16].

Patients with intact binocular vision had smallest magnitudes of anisometropia. With greater magnitude,

chance of intact stereopsis got smaller. Weakley followed patients during 42 months and concluded following: myopic anisometropia greater than 2D, or hyperopic anisometropia greater than 1D has statistically significant effect on presence of binocular vision and depth of amblyopia [18].

Chen et al. found that magnitude of anisometropia directly affects binocular functions as fusion, stereopsis. With greater magnitude, chance of supressing signal from one eye, is getting higher, especially with anisometropia that is greater than 3D. It is estimated that 93,33% of patients whose magnitude was smaller than 3D, have intact fusion and 80% stereopsis. Critical value is, according to Chen et al, 6D. When magnitude is

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greater only 16,67% have intact fusion and just 8,33% stereopsis. Cut-off value in our study 5,25D is close to what this survey found [19].

CONCLUSION

The analysis of patients with anisometropic amblyopia revealed that children with greater depth of amblyopia, higher magnitude of anisometropia have less chance to achieve binocular vision. All these parameters were statistically significant. We found that hyperopia is most common refractive error, but children with myopia and myopia with astigmatisms showed better results in achieving binocular vision.

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