

## THE PRINCIPLES OF ANISOMETROPIC AMBLYOPIA TREATMENT

*Markovska Cheleva V.*

Eye Clinic, University "Ss. Cyril and Methodius", Skopje, Republic of Macedonia

### Abstract

**Aim:** Prospective examination of the methods of treatment of anisometropic amblyopia without strabismus.

**Material and method:** 52 patients (from 6 to 11 years old) with anisometropic amblyopia without strabismus were included in this study. After the prescription of spectacles on the second visit, if there was no improvement of the visual acuity of the amblyopic eye and if there is still deference of two or more lines on the vision chart between the eyes, occlusion was prescribed for at least 6 hours a day of the sound eye.

**Results:** 28 patients from all 52, (53%) were female and 24 patients (47%) were male. The age of the patients was average 9,2 years. Average visual acuity on the amblyopic eye at baseline was approximately 0,33 with correction before the patching treatment. There were 7 patients (13,7%) which resolved the amblyopia only with spectacles without patching. Average time for resolution of amblyopia was 8,2 months (range 3 to 16 months). The visual acuity of 20/20 achieved 43% patients with hypermetropic anisometropic amblyopic eye and 3,8% patients with astigmatic anisometropic amblyopia.

**Conclusion:** Early screening of preschool children for detection of anisometropic and other types of amblyopia is important for the on time treatment of the amblyopic eye.

**Key words:** amblyopia, anisometropic, therapy, patching and occlusion, recurrence

## ПРИНЦИПИ НА ЛЕКУВАЊЕ НА АНИЗОМЕТРОПНА СЛАБОВИДОСТ

### Апстракт

**Цел:** Проспективно иследување на методите на третман на анизометропна слабовидост без кривогледство.

**Материјал и метод:** Во иследувањето беа вклучени 52 пациенти (на 6 до 11-годишна возраст) со анизометропна слабовидост без кривогледство. По препишување на рефракција со очила при повторниот контролен преглед, ако нема подобрување на видната острина на слабовидото око и ако сеуште постои разлика од две или повеќе линии на таблата за видната острина помеѓу очите, се препишува оклузија на водечкото око најмалку 6 часа на ден.

**Резултати:** Од 52 пациенти кои беа лекувани, од женски пол беа 28 (53%) и 24 (47%) од машки пол. Средната возраст на пациентите беше 9,2 години. Средната вредност на видната острина на слабовидото око изнесуваше 0,33 со наочари пред да започне лекувањето. Кај 7 пациенти (13,7%) амблиопијата беше решена само со очила без затварање. Средно време на решавање на слабовидоста беше 8,2

месеца (од 3 до 16 месеци). Видна остринa од 1,0 со наочари или 20/20 се постигна кај 43% од пациентите со хиперметропична анизометропија на слабовидото око и кај 3,8% пациенти со астигматична анизометропна слабовидост.

Заклучок: Раниот скрининг на предшколските деца за откривање на анизометропната слабовидост и другите видови на слабовидост е важен за навремено лекување на истата.

**Клучни зборови:** слабовидост, анизометропна, терапија, затворање на доминантно око, реверзибилност.

## **Introduction**

Amblyopia means a blunt sight on Greek and has been describe by the Hippocrates. Hippocrates definition for amblyopia is: "When the doctor sees nothing and the patients see nothing, the diagnosis is amblyopia". The more appropriate modern definition of amblyopia comes from Von Norden: "Unilateral or bilateral decries of visual acuity caused by form visual deprivation and/or abnormal binocular interaction for which no structural cause can be detected by the physical examination of the eye and which is appropriate cases, is reversible by therapeutic measures" (1).

Anisometric amblyopia is only one type of amblyopia. Apart from anisometric amblyopia there are strabismic amblyopia, deprivation form of amblyopia and ametropic amblyopia. A difference in refractive error between the two eyes (anisometropia) is common case of amblyopia. This type of amblyopia is the only one type with identifiable amblyogenic factor in 37% of cases. Also it is present concomitantly with strabismus in an additional 24% of clinical populations (2).

Amblyopia is correctable, assuming that is promptly recognize and vigorously treated. Anisometric amblyopia is a preventable form of blindness, as that anisometric amblyopia treatment must be intensified and individualized. It is generally accepted after the prescription of the refraction; occlusion of the non-amblyopic eye is the mainstay of amblyopia (1, 3, 4). In fact, occlusion therapy has been mainstay since 18th century (5).

Basic research in animal models has shown that the major pathologic changes are in the visual cortex of dysfunctional brain, in amblyopia. Functional imaging studies confirm processing abnormalities in area VI of humans and hint at deficits within higher cortical areas (3, 6).

Aim: Prospective examination of the methods of treatment of anisometric amblyopia without strabismus.

## **Material and methods**

The methods of the treatment are, using spectacles in the beginning and occlusion of the sound eye after refraction. This was a prospective study of anisometric amblyopia treatment in patients without strabismus. The treatment starts with refractive correction of visual acuity with spectacles and after the refraction continues with occlusion of the sound eye. The patients were treated in the Department of Strabology at the University Eye Clinic in Skopje, Republic of Macedonia from January 2010 to December 2016.

Prospectively study was done on children with anisometric amblyopia in from 6-year to 11-year-old in the period of 5 years. There were 52 patients with anisometric amblyopia without strabismus. Clinical date included patient age, gender, uncorrected

## THE PRINCIPLES OF ANISOMETROPIC AMBLYOPIA TREATMENT

visual acuity, best-corrected visual acuity (BCVA), cover test, fixation test, binocular motility, slit-lamp and fundus examinations. The spherical equivalent was calculated according the cycloplegic refraction results with Cyclopentolate 1% eye drops. Anisometropic amblyopia was defined as refractive difference more than 2 diopters sph. (hypermetropic or myopic) between eyes with best vision acuity correction with glasses or astigmatism difference  $\geq 1,50$  D cyl. Also amblyopia was defined as a BCVA difference of two lines of the chart or more, between the amblyopic and sound eye. The visual acuity was measured at Snellen charts. Patients with at least 12 months' follow-up examination and treatment were included in the study. The best visual acuity in the amblyopic eye was from  $\leq 0,5$  to  $\geq 0,1$  c.c. The visual acuity in the sound eye was  $\geq 0,5$  c.c. Inter eye acuity difference was  $\geq 2$  lines.

Spherical and astigmatic errors were fully corrected in each patient. On the second visit, depending of visual acuity improvement ( $\geq 2$  lines difference between sound and amblyopic eye persisted) the patient was required to patch the sound eye 6 hours per day. Patching was prescribed after the non-improvement of the best visual acuity after two months.

Visit schedule during the first months was on 4 weeks, 8 weeks, 16 weeks and 24 weeks. After 3 months subsequent patching hours was prescribed depending of:

- if  $\leq 0,66$  and  $\leq 2$  line improvement, increased up to all or all but one walking hours (max 12 hours per day)
- if  $\geq 0,66$  and  $\geq 2$  line improvement, we decrease patching to a minimum of one hour a day.

Visit schedule from 6 months to 1 year was on 3 months and from 1 year to 2 years was minimum at 6 months. Masked outcome exams were performed from the Orto optician at 6, 12 and 24 months.

Patients with at least 12 months' follow-up examination and treatment were included in the study.

From the examined group and from the research were excluded all the anisometropic amblyopic patients with eye abnormality, strabismus, previous operations, cataract, previous eyeglass prescription, ocular trauma, previous occlusion or penalization therapy or patients with neurological disease.

### Results

28 patients from all 52, (53%) were female, and 24 patients (47%) were male. The age of the patients had mean of 9,2 years. There were 17 patients (32%) in the group 6 to 7 years old, 10 patients (20%) in the group 7 to 8 years old, 9 patients (17,5%) in the group 8 to 9 years old, 9 patients (17,5%) in the group 9-10 years old, 6 patients (11%) in the group 10-11 years old and 1 patient (2%) in group of 11 to 12 years old.

Amblyopic eye visual acuity without refraction was: 0,1 c.c. 6 patients (11,5%), 0,20 c.c. 14 patients (26.9%), 0,25 c.c. 17 patients (32.6%), 0,33 c.c. 9 patients (17.3%), 0,40 c.c. 4 patients (7.6%), 0,50 c.c. 2 patients (3,8%).

Mean amblyopia visual acuity at baseline was approximately 0,33 c.c.

There were 7 patients (13,4%) which resolve the amblyopia only with spectacles without patching. All patients got the BVAC after two months after the refraction prescription, or the difference between the visual lines was one line and there was no

need for occlusion. Treatment of anisometropic with spectacles alone in the beginning and in some cases can be a successful option. Mean time for resolution of amblyopia was 8,2 months (range 3 to 16 months).

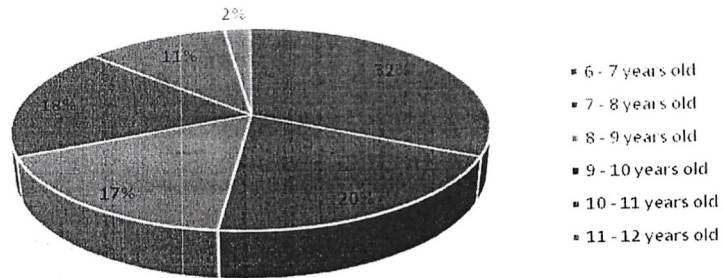


Figure 1 Representation of patients' age

The number of hours prescribed was 6 hours per day and it was the maximum for (37,7%) 17 patients. For 28 patients (62.2%) patching time during follow up was increased from lesser amount to 8 hours or more hours a day, patching 8hours for 22 patients (48,8%), patching 10 hours for 3 patients (6,6%), 12 hours patching for 2 patients (6,6%).

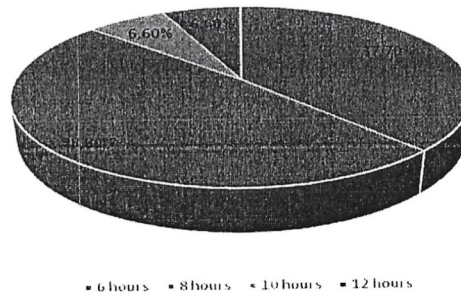


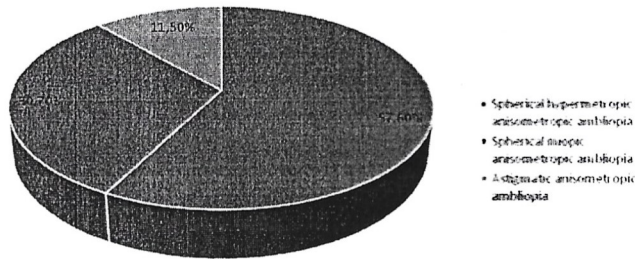
Figure 2 Percentage of patients with the max hours of patching prescribed

There were 2 patients (6,6%) who should have been, but were not prescribed at least 12 hours per day of patching as dictated by the protocol for incomplete response to lesser amount of patching because of complaining of the child and his parents.

A spectacle occlude was prescribed as a substitute for patching in 3 patients who could not tolerate the skin patches.

Spherical anisometropia had 32 patients (61,5%). Myopic spherical anisometropia had 12 (37,5%) of them and 20 (62,5%) patients had hypermetropic amblyopia. The rest from all has astigmatic anisometropia 20 patients (38,4%).

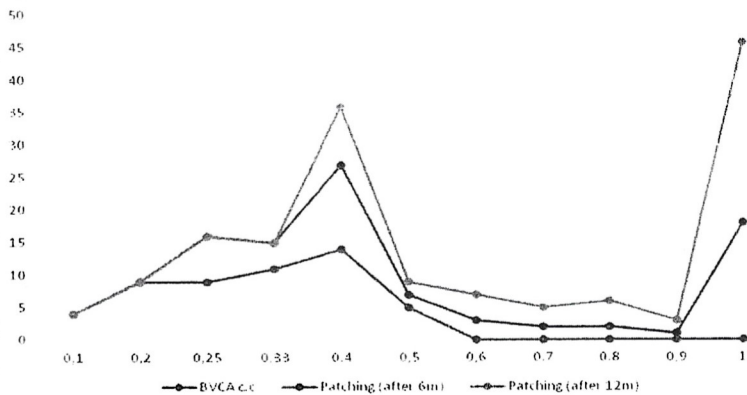
## THE PRINCIPLES OF ANISOMETROPIC AMBLYOPIA TREATMENT



**Figure 3** Representation of different types of anisometropic amblyopia

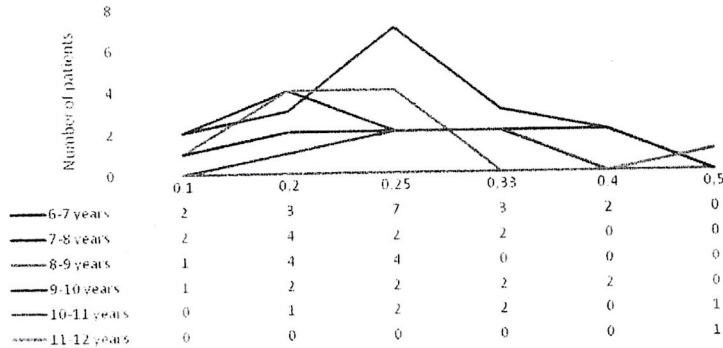
The visual acuity of 20/20 achieved 43% patients with hypermetropic anisometropic amblyopic eye. None of the myopic anisometropic patients with amblyopic eye and without strabismus achieved 20/20 visual acuity. And only 2 patients (3,8%) with astigmatic anisometropic amblyopia achieved visual acuity 20/20.

Best visual acuity of the amblyopic eye with glasses was: 0,1 c.c. 4 patients (7,6%), 0,20 c.c. 9 patients (17,3%), 0,25 c.c. 9 patients (17,3%), 0,33 c.c. 11 patients (21,1%), 0,40 c.c. 14 patients (26,9%), 0,50 c.c. 5 patients (9,6%). The visual acuity after 6 months of patching was: 0,25 c.c. 7 patients (13,46%), 0,33c.c 4 patients (7,69), 0, 40 c.c. 13 patients (25,0%), 0,50 c.c. 2 patients (4,6%), 0,60 c.c. 3 patients (5,7%), 0,70c.c 2 patients (3,8%), 0,80c.c. 2 patients (3,8%), 0,90 c.c. 1 patients (1,9%), 1,0c.c. 18 patients 34,6%. The visual acuity after 12 months of patching was: 0, 40 c.c. 9 patients (15,3%), 0,50 c.c. 2 patients (4,6%), 0,60 c.c. 4 patients (9,30%), 0,70 c.c. 3 patients (6,9%), 0,80c.c. 4 patients (7,69%), 0,90c.c. 2 patients (3,8%), 1,0c.c. 28 patients 53,8%.



**Figure 4** Best visual acuity of the amblyopic eye with glasses and after patching (6 and 12 months)

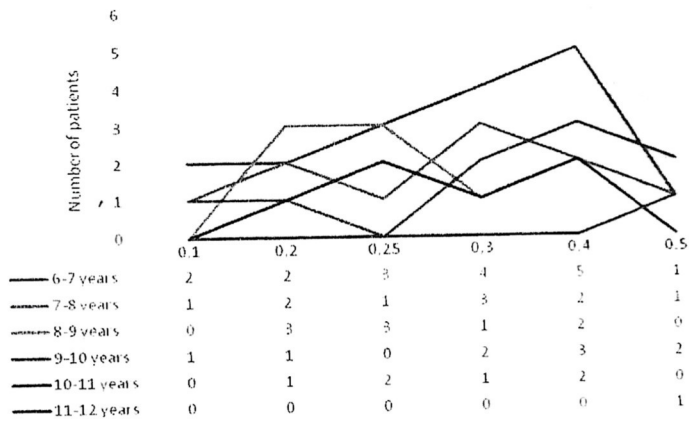
The BVAC after prescription of glasses in the group of 6-7 years old patients was: 0,1 c.c. (2 patients), 0,20 c.c. (3 patients), 0,25 c.c. (7 patients), 0,33 c.c. (3 patients), 0,40 c.c. (2 patients). In the group of 7-8 years old patients the BVAC was: 0,1 c.c. (2 patients), 0,20 c.c. (4 patients), 0,25 c.c. (2 patients), 0,33 c.c. (2 patients). The BVAC in the group of 8-9 years old patients was: 0,1 c.c. (1 patient), 0,20 c.c. (2 patients), 0,25 c.c. (2 patients), 0,33 c.c. (2 patients), 0,40 c.c. (2 patients). In the group of 9-10 years old patients BVAC was: 0,20 c.c. (1 patient), 0,25 c.c. (2 patients), 0,33 c.c. (2 patients), 0,50 c.c. (1 patient). The BVAC in the group of 10-11 years old patients was: 0,25 c.c. (1 patient), 0,33 c.c. (2 patients), 0,40 c.c. (2 patients), 0,50 c.c. (1 patient). In the group of 11-12 years old patients was only one with vision acuity of 0,50 c.c.



**Figure 5** Visual acuity after the prescription of glasses per age group of patients

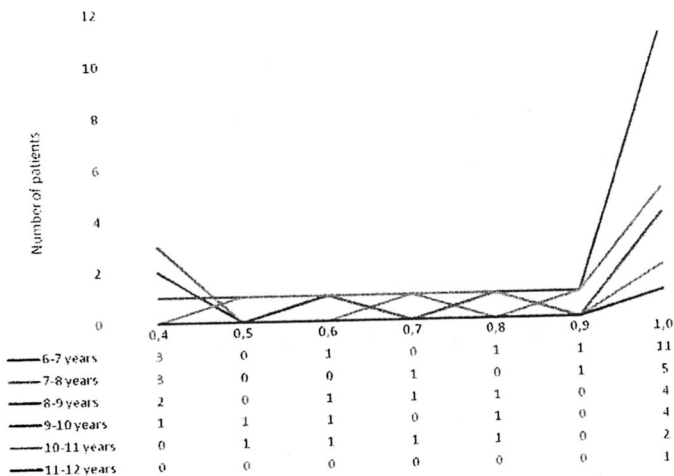
The BVAC after 6 months in the group of 6-7 years old patients was: 0,10 c.c. (2 patients), 0,20 c.c. (2 patients), 0,25 c.c. (3 patients), 0,33 c.c. (4 patients), 0,40 c.c. (5 patients), 0,50 c.c. (1 patient). In the group of 7-8 years old patients the BVAC was: 0,10 c.c. (1 patient), 0,20 c.c. (2 patients), 0,25 c.c. (1 patient), 0,33 c.c. (3 patient), 0,40 c.c. (2 patients), 0,50 c.c. (1 patient). The BVAC in the group of 8-9 years old patients was: 0,20 c.c. (3 patients), 0,25 c.c. (3 patients), 0,33 c.c. (1 patient), 0,40 c.c. (2 patients). In the group of 9-10 years old patients BVAC was: 0,10 c.c. (1 patient), 0,20 c.c. (1 patient), 0,33 c.c. (2 patients), 0,40 c.c. (3 patients), 0,50 c.c. (2 patients). The BVAC in the group of 10-11 years old patients was: 0,20 c.c. (1 patient), 0,33 c.c. (2 patients), 0,40 c.c. (1 patient). In the group of 11-12 years old patients was only one with vision acuity of 0,50 c.c.

# THE PRINCIPLES OF ANISOMETROPIC AMBLYOPIA TREATMENT



**Figure 6** Visual acuity after 6 months per age group of patients

The BVAC after 12 months in the group of 6-7 years old patients was: 0,40 c.c. (3 patients), 0,60 c.c. (1 patient), 0,80 c.c. (1 patient), 0,90 c.c. (1 patient), 1,0 c.c. (11 patients). In the group of 7-8 years old patients the BVAC was: 0,40 c.c. (3 patients), 0,70 c.c. (1 patient), 0,90 c.c. (1 patient), 1,0 c.c. (5 patients). The BVAC in the group of 8-9 years old patients was: 0,40 c.c. (2 patients), 0,60 c.c. (1 patient), 0,70 c.c. (1 patient), 0,80 c.c. (1 patient), 1,0 c.c. (4 patients). In the group of 9-10 years old patients BVAC was: 0,40 c.c. (1 patient), 0,50 c.c. (1 patient), 0,60 c.c. (1 patient), 0,80 c.c. (1 patient), 1,0 c.c. (4 patients). The BVAC in the group of 10-11 years old patients was: 0,50 c.c. (1 patient), 0,60 c.c. (1 patient), 0,70 c.c. (1 patient), 0,80 c.c. (1 patient), 1,0 c.c. (2 patients). In the group of 11-12 years old patients was only one with vision acuity of 1,0 c.c. after 12 months of treatment.



**Figure 7** Visual acuity after 12 months per age group of patients

Only 11,54% (6 patients) of all the patients (52 patients) developed recurrence of lower visual acuity over an average follow up period of 24 months $\pm$ 12months, compared to the achieved BVAC (within up to 12 months of treatment). Nonetheless, the best achieved vision acuity was restored by additional successful treatment with updated spectacles or patching.

## **Discussion**

As the Von Norden definition, we have the obligation to treat amblyopia by the most appropriate means until the best possible visual acuity result is achieved and to continue the treatment by supportive therapy to prevent occurrence. There are some controversies for the sensitive periods for treatment of the anisometropic amblyopia but the most authors agree that the most successful time is up to 10 or 12 years old.

Children with anisometropic amblyopia usually are diagnosed later, than the other types of amblyopia as amblyopia with strabismus which is easily recognized (7-9) Hussein et al (10) concluded that the type, amount of refractive error, and the difference in refractive power between the eyes are significant risk factors for the unsuccessful treatment. The hypermetropic anisometropia is more severe and more frequent than the myopic anisometropia (11) as it was in our study. The Kim et al (12) reported that there is no significant difference in the frequencies of amblyopia between spherical and cylindrical anisometropia patients, and hyper anisometropia patients have a higher risk to develop amblyopia compared to the myopic anisometropia. In our study there was no statistical difference between the groups of spherical or cylindrical anisometropic amblyopia probably from the small number of the patients in the groups.

There are some papers in which the authors, Kivlin and Flynn, examined 67 patients up to age 13 years, with mean initial vision 20/70. After the median duration of patching of 8 months, 70% got the better vision than 20/40. They conclude that older children improved their vision as well with the glasses alone as initial therapy. There were bad vision acuity results if anisometropia was greater than six diopters (13). From our study we have concluded that better outcome of the amblyopia depends on the initial age of treatment and BCVA of the sound eye at the beginning of the treatment. Hussein et al (10) found that an initial visual acuity in the amblyopic eye of 20/200 or worse was a risk factor of treatment failure and they can achieve a significant improvement in vision but the final vision may be less than 20/40.

Children with anisometropic amblyopia who started the initial treatment later, respond less favorably to treatment (1). Hussein et al (10) conclude that treatment started on age 6 or greater was a risk factor to achieve success on visual improvement. In the current study the initial age of treatment was 6 years, as that we could not conclude that the visual improvement is in correlation with the age. In the literature, some practitioners are reported to favor full time occlusion (1,3) while others just a few minutes' occlusion each day (14). But from our examination we have concluded that the more rapid improvement with patching was most pronounced when 8 or more hours a day were prescribed.



## THE PRINCIPLES OF ANISOMETROPIC AMBLYOPIA TREATMENT

Lee et al (15) in a study of patients with anisometropic amblyopia with and without strabismus, demonstrated that patients with  $\geq 4$  lines of difference in the BCVA between sound and amblyopic eye at the beginning had a high success rate with patching therapy. The improving of the vision acuity of the sound eye is more rapid when the occlusion of the amblyopic eye is more than 8 hours a day.

Future issues for better understanding of the problems of the anisometropic amblyopia is better classification of amblyopia and valuation of the time occlusion as part-time, full time or alternate occlusion.

In conclusion, eyes with worse initial visual acuity of  $<20/40$ , high anisometropia, and a difference between the eyes (sound and amblyopic) of  $\geq 4$  lines, were less likely for success treatment success. In fact, the depth of amblyopia correlates with the degree of anisometropia in untreated anisometropic amblyopic cases. As that it is very important early screening of preschool children for detection of amblyopia and especially anisometropic amblyopia without strabismus which otherwise may go undetected, being asymptomatic at early age.

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