Treatment of Ametropic Amblyopia and the Significance of Cycloplegia in Childhood

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SUMMARY

Aims: This retrospective study evaluates the effect of full cycloplegic spectacle correction on best corrected visual acuity (BCVA), interocular difference in BCVA, and the presence of stereopsis in children previously treated for ametropic amblyopia (isoametropic or anisometropic type).

Material and Methods: We analyzed data from 43 children aged 4–12 years (mean 6.42 ±2.06 years) who had been previously diagnosed and treated for amblyopia. All underwent a complete ophthalmologic examination including cycloplegic refraction, BCVA, and stereopsis testing. The primary intervention was full correction of the refractive error based on cycloplegic refraction. The patients were monitored at 3-month intervals, and the effect of treatment was assessed after 12 months. The statistical analysis included a Shapiro-Wilk test, paired t-test or Wilcoxon test, and linear regression for evaluating the impact of age and prior occlusion therapy.

Results: Average BCVA improved significantly from 0.41 to 0.65 ($p < 0.0001$), with 65% of amblyopic eyes improving by ≥ 2 lines on the Snellen chart. Interocular difference was reduced by 41%, and stereopsis improved from 14% to 72%. The mean difference between non-cycloplegic and cycloplegic spherical equivalents prior to treatment was 2.26 D ($p < 0.0001$), supporting the diagnostic value of cycloplegia. The minimal change in cycloplegic refraction over the course of one year ($p > 0.05$) indicated refractive stability. A regression analysis detected an insignificant negative trend between age and BCVA improvement ($p = 0.069$).

Conclusion: Full spectacle correction based on cycloplegic refraction leads to a statistically significant improvement in BCVA and stereopsis. Routine use of cycloplegia is essential for precise diagnosis and optimal visual outcomes in pediatric amblyopia management.

Key words: amblyopia, anisometropia, children, cycloplegia, cycloplegic refraction

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INTRODUCTION

Sight is the most effective and most widely used human sense. It enables us to orient ourselves within our environment, to recognize color, size, distance, depth, capacity, direction, motion, and space within our surroundings. It provides more than 80% of the information we receive about the world. Incapacity or deficiencies of visual perception have a dramatic impact on every practical activity.

Amblyopia is the most common cause of visual morbidity in childhood. It is distinguished by a deficit of BCVA (best corrected visual acuity), although abnormalities in amblyopia go beyond monocular BCVA and may also have an influence on a higher level of visual processing, which leads to a deficit of spatial vision and perception of motion. Amblyopia therefore refers to impaired monocular and binocular vision. The critical period, or maximum neuroplasticity limit of the visual cortex for the treatment of amblyopia in children, is at maximum up to the age of three years. Amblyopia in children is difficult to correct by training after the age of six years. The primary goal is therefore to ensure timely diagnosis of this disorder, with subsequent appropriate treatment. If treatment is not commenced sufficiently in time, the patient is at risk of suffering a lifelong handicap.

Previous estimates of the global prevalence of amblyopia have been within the range of 0.2% to 5.3%, in which the estimated percentages differed because of differences in the definition of amblyopia, geographical localization, and the heterogeneity of the studies [5]. Recent meta-analyses published in 2018 and 2022 estimated the overall global prevalence of amblyopia at 1.36% and 1.75% respectively, with the highest prevalence determined in European countries [1,2].

To date no standards or directives for the treatment of amblyopia have been processed in Slovakia. A considerable number of foreign authors and studies also do not lay down unequivocally clear and uniform guidelines for addressing this specific issue. We believe that this study may provide valuable information for our colleagues in local ophthalmology clinics and assist them in addressing the spectrum of patients who suffer from this ocular pathology.

The aim of the study is to present a retrospective analysis of the applied spectacle correction of refractive error in relation to cycloplegic refraction in pediatric patients treated for the ametropic form of amblyopia. In the following step, we evaluated the effect of treatment of amblyopia following full correction of the amblyogenic refractive error.

MATERIAL AND METHOD

In this study we present a retrospective evaluation of the effect of treatment of ametropic amblyopia primarily by means of spectacle correction. In the observation period from 2016 to 2021 we examined 51 children aged between 4 and 12 years old at our center, who had been diagnosed with amblyopia at another center. The children were from various regions of Slovakia.

Following the initial examination at our center, we had to exclude eight children from the cohort; three patients with a not fully corrected non-amblyogenic refractive error and five children with presence of microstrabismus. After the inclusion and exclusion criteria had been considered, the remaining subjects in the cohort were 43 children with amblyopia with a mean age of 6.42 ±2.06 years. The cohort of patients comprised 20 boys (7.05 ±2.22 years) and 23 girls (5.82 ± 1.74 years). In five cases the etiology was isoametropic amblyopia, and in 38 children anisometropic amblyopia.

The inclusion criteria for selection of the patients into the cohort were as follows: age of 4–12 years, treated ametropic form of amblyopia (isoametropic or anisometropic), interocular difference in BCVA of ≥ 2 rows on the Snellen chart.

Exclusion criteria: age of under four and over twelve years, non-amblyogenic refractive error, strabismus and other ocular pathologies.

The initial treatment of amblyopia in these children was performed at several different ophthalmological centers in Slovakia. The minimum and maximum known period of treatment at a different center was 6–12 months. In all 51 children (100%), amblyopia was treated by means of spectacle correction of the refractive error, in 39 children (76.5%) treatment also included occlusion, and 20 children (39.2%) also underwent pleoptic therapy and conventional visual exercises.

The baseline moment was when the subjects underwent the first ophthalmological examination at our center. After the signature of an informed consent form by the subject's legal representative, all children at our center underwent a complete pediatric ophthalmological examination. For the requirements of the study we focused on focometry, binocular and monocular vision with the subject's own correction, a cover test, a Lang Stereotest I, and cycloplegic refraction.

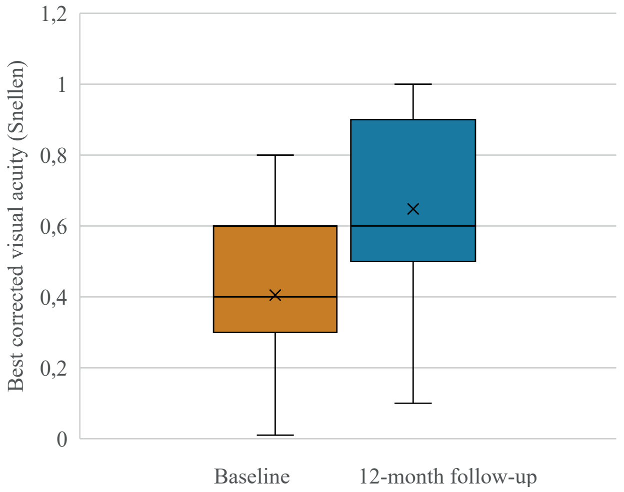
To induce cycloplegia in the patients, we instilled the preparation Cyclogyl gtt. 1% (Alcon, USA). Upon application we adhered to the established protocol of our center, i.e., three drops were applied at five-minute intervals. We subsequently measured refraction 45 minutes after application of the last drop. Refraction was measured using the autorefractometer ARK-1 (Nidek, Japan). We examined distance BCVA with the aid of a pictorial or Snellen chart (LCD optotype CX-1000, Topcon, Japan).

The patients were observed every three months, while the cycloplegia examination was repeated every six months. We evaluated the individual data after one year of observation, and subsequently after more than 12 months of observation. In the study we analyzed correction of amblyogenic refractive error by means of spectacle correction in relation to cycloplegic refraction, change in the difference of distance BCVA between the amblyopic and contralateral eye, change of distance BCVA in the amblyopic eye, and stereopsis.

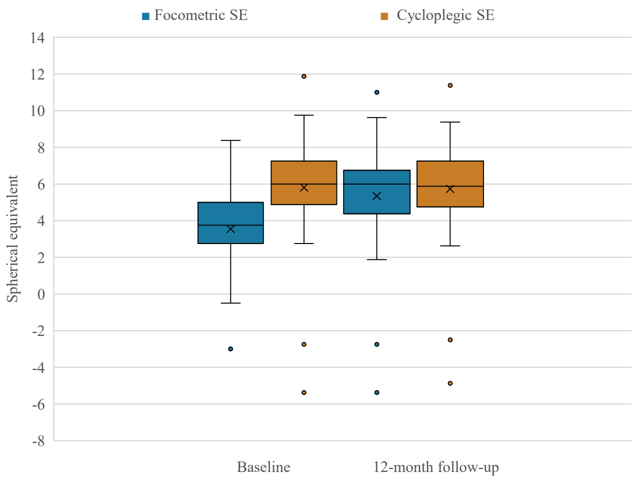
A Shapiro-Wilk test was used to verify the normality of the differences. In the case of data with a normal distribution a paired t-test was used, while in the case of abnormally distributed data a Wilcoxon test was applied. For evaluation of the differences between spectacles and cycloplegic refraction, paired tests were used according to the distribution of the differences. For explanation of the influence of age, occlusion and pleoptic therapy on the result of treatment, a linear regression analysis was applied. The value of $p < 0.05$ was considered statistically significant.

RESULTS

In the children with anisometric amblyopia the mean value of anisometropia was 2.55 D. In the smaller group of children with isoametropic amblyopia the mean spherical equivalent of ametropia was 7.18 D. We observed the correction of amblyogenic refractive error in relation to cycloplegic refraction, the change in the difference of BCVA between the amblyopic and contralateral eye, and the change of stereopsis.



Graph 1. Visual acuity (BCVA) at baseline and at the 12-month follow-up
BCVA – best corrected visual acuity



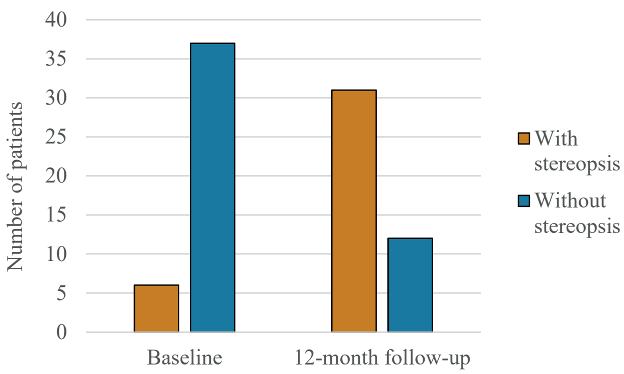
Graph 2. Difference in spherical equivalent (SE) between focometric refraction (prescribed spectacle correction) and cycloplegic refraction at baseline and at the 12-month follow-up
SE – spherical equivalent

The amblyogenic refractive errors appearing in the cohort were as follows: 10 eyes with hypermetropia, 1 eye with myopia, 1 eye with myopia and astigmatism, and 31 eyes with hypermetropia and astigmatism.

After 12 months of treatment with full cycloplegic spectacle correction, we recorded a significant improvement of BCVA in the amblyopic eye. The mean value of BCVA increased from 0.41 to 0.65, which represents an improvement by approximately 2.4 lines on the Snellen chart ($p < 0.0001$). Graph 1. Out of the total number of amblyopic eyes, BCVA improved by 2 or more lines in 28 eyes (65%). The mean difference in BCVA between the amblyopic and contralateral eye decreased from the initial value of 0.49 to 0.29, meaning that a reduction of the interocular difference was achieved by 41%.

As part of the evaluation of the precision of refractive correction, we compared spectacle correction prescribed at another center with cycloplegic refraction determined at our center (spherical equivalent (SE) 3.55 ±2.02 vs. 5.81 ±2.83), as well as spectacle correction prescribed at our outpatient clinic with the values of cycloplegic refraction (SE 5.38 ±2.81 vs. 5.58 ±2.79). The difference between the SE values was significantly reduced after 12 months of treatment from 2.26 D to 0.38 D ($p < 0.05$), which confirms the higher degree of accordance and stability of the refractive finding upon correction determined on the basis of cycloplegic refraction [7,8], and underlines the importance of cycloplegia for precise determination of amblyogenic refractive error. Graph 2.

At the beginning of the observation, 6 children (14%) were recorded with stereopsis. After 12 months of refractive treatment the number of patients with stereopsis had increased to 31 (72%). This pronounced increase in binocular function can be attributed to precise correction of refractive error, and probably also to the young age of many of the patients at the commencement of correction [3,6]. Graph 3.



Graph 3. Presence of stereopsis at baseline and at the 12-month follow-up

DISCUSSION

In this retrospective analysis we evaluated the effectiveness of refractive correction on visual acuity, refractive parameters, and stereopsis in children with ametropic amblyopia. The results confirm that spectacle correction alone based on cycloplegic refraction leads to a statistically significant improvement of BCVA. The mean improvement of 0.24 corresponds to approximately two to three lines on the Snellen chart. This finding is in accordance with the PEDIG meta-analysis, in which an improvement by ≥ 2 lines was achieved in 75% of children following the application of correction without any further interventions [5].

A comparison of SE between spectacles and cycloplegic refraction before treatment demonstrated a statistically significant difference – cycloplegia detected on average 2.26 D higher hypermetropia ($p < 0.0001$). After one year, the difference between the methods was smaller (0.38 D), but still statistically significant (p = 0.0043). These findings confirm that cycloplegia is essential to ensure precise diagnosis of refractive errors in children [6].

Change of SE during treatment was minimal in the case of cycloplegia and was not statistically significant (p = 0.7422), which indicates stability of the refractive error.

We also recorded a significant increase in the number of children with stereopsis – from the original percentage of 14% to 72% after treatment, which exceeds the usually stated values in the literature upon refractive correction alone [3]. A regression analysis indicated a negative trend between patient age and BCVA improvement (p = 0.069), which is in accordance with the literature, indicating the reduced plasticity of the visual system with increasing age [4].

In our study on 43 children aged 4–12 years, we determined that the amblyogenic refractive error had not been fully corrected at the beginning of the study in a single patient. The mean difference between spectacles and cycloplegic refraction was 2.26 D. Following full correction after 1 year, BCVA improved on average by 2.4 lines. As many as 65% of eyes improved by 2 or more lines due to correction alone, in which 14% achieved vision of 1.0. After more than 12 months, we also indicated several patients for occlusion and pleoptic therapy, after which the improvement increased to a mean of 3.5 lines. At the same time, the interocular difference was reduced from 4.9 to 1.9 lines, and stereopsis was present in 86% of children.

These results confirm that spectacle correction alone may be an effective modality of treatment, and in some cases, it is sufficient as the sole therapeutic intervention. The studies conducted by Cotter et al. [5] and Chen et al. [6] reached similar conclusions, although in their cohorts the percentage of success was slightly higher – which could be attributed to the lower patient age and lesser degree of anisometropia.

In our study, the resulting effect may also be influenced by further factors such as the late determination of the diagnosis, instability of fixation, unsuitable selection of spectacle frames, imprecise optic centration, low level of compliance on the part of parents, or inexpert reduction of the prescribed correction.

In their meta-analysis, Asper et al. [9] state that refractive correction is effective across all types of amblyopia and should therefore be the first line of treatment. Our results also confirm that upon application of a thorough procedure, this correction may lead to a significant improvement of BCVA and binocular functions.

In the three cases where BCVA remained on the level of 0.2 after one year, this concerned older patients with a pronounced degree of anisometropia. However, it is of interest that despite their poor vision, stereopsis was demonstrated in two of these patients. This aspect has not yet been investigated in detail in the literature, and merits further attention.

CONCLUSION

Our analysis confirmed that full correction of refractive error based on cycloplegia leads to a statistically significant improvement of BCVA. More than 65% of children attained an improvement by ≥ 2 lines, while stereopsis was restored in more than 70% of patients.

The significant differences between spectacles and cycloplegic measurement before treatment indicate that the routine use of cycloplegia when examining children with amblyopia is essential. Well applied cycloplegia is therefore of key importance in determining refraction in children. Cycloplegia should be performed on children at minimum once per year in the case of any ocular pathology. In children with strabismus, anisometropia, and amblyopia it should be performed more frequently, above all in the first measurements of cycloplegic refraction and specification of precise spectacle correction. It is necessary to be aware that the relationship between cycloplegia and mydriasis is not directly proportionate. Well applied mydriasis is not a guarantee of good cycloplegia and conversely, partial mydriasis does not constitute evidence of the ineffectiveness of cycloplegia.

At the outset of the therapeutic procedure, we consider it to be of crucial importance to commence treatment with precise correction of the amblyogenic refractive error, which may itself bring about an improvement of visual acuity, reduce the need for occlusion therapy, and at the same time contribute to better compliance on the part of children and their parents, which may then have a positive influence on the subsequent course of treatment. Nevertheless, it remains essential to ensure thorough monitoring and individual adjustment of therapy.

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