Research Square

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A novel strategy for degree design in amblyopia with anisometropia and ametropia

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Research Article

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Abstract

Objective

To propose a novel strategy for degree design in amblyopia with anisometropia and ametropia.

Methods

28 patients with refractive amblyopic eye visual acuity ranging from 20/666 to 20/29 (45 eyes) were provided with optical correction followed by the maximum plus to maximum visual acuity (MPMVA) and amblyopic training. After which, the patients were supposed to test acuity improvement at the 3-month, 6-month, and 12-month visit.

Results

At the initial 3-month visit and 6-month visit, visual acuity improvement from the spectacle-corrected baseline acuity averaged 1.5 ± 1.00 lines and 2.0 ± 1.10 lines respectively. Moreover, the data demonstrated that the age and baseline acuity both inversely related to the visual acuity improvement ($P = 0.093$, $P < 0.001$, at 3-month visit; $P = 0.080$, $P < 0.001$, at 6-month visit). And it showed there are no relationship between type of anisometropia and ametropia and acuity improvement at 3-month visit ($P = 0.315$), while they were relevant at 6-month visit ($P = 0.025$).

Conclusion

From another point of view, we proposed a new notion to reveal secret of amblyopia. The study directed by the principle based on the new notion showed that getting the degree to MPMVA and following by amblyopic training in amblyopia with anisometropia and ametropia can improve visual acuity effectively.

Introduction

As defined in the Ambiyopia PPP-2017, “Amblyopia is a unilateral or, less often, bilateral reduction of best-corrected visual acuity (BCVA) that usually occurs in the setting of an otherwise normal eye. It is a developmental disorder of the central nervous system that results from the abnormal processing of visual images, which leads to reduced visual acuity. Less commonly, amblyopia occurs in association with a structural abnormality involving the eye or visual pathway. Patients with amblyopia experience a reduction in visual acuity that cannot be attributed only to the effect of the structural abnormality; such eyes may also have a deficit in contrast sensitivity and accommodation. Often the fellow eye is not normal but has subtle structural and functional deficits.”[1] By cause, it can be classified to follows: strabismic amblyopia, refractive amblyopia, visual deprivation amblyopia, and occlusion amblyopia (reverse amblyopia).[1] In which, refractive amblyopia is the most common.

In refractive amblyopia, there are three main methods of amblyopia matching in degree design: full corrected, best visual corrected and under corrected.[2] Someone think that under correction by + 1.00 ~ + 2.50DS can fit the strong regulation of child. Others think that the regulation in child with hyperopia is decline in which patient can get better recovery by full correction.[2] So, different doctors will prescribe different degree design following different principle, and the degree of under correction also varies from different doctors. Based on the current inconsistent prescribing situation, this study propose a novel strategy for degree design in amblyopia with anisometropia and ametropia in order to make people think from another point and unify the degree design in refractive amblyopia.

Methods

This study was conducted by Shandong Provincial Hospital. The protocol and informed consent forms were approved by institutional review boards. The parent or guardian (referred to subsequently as “parent”) of each study patient gave written informed consent and each patient gave assent to participation.

PATIENT SELECTION

We enrolled patients age 3 to 13 years with a history of anisometropia or ametropia amblyopia, no ocular cause for reduced acuity, and no myopia more than a spherical equivalent of -3.00 D in the amblyopic eye.

BASELINE EXAMINATION

Visual acuity was measured in each eye with the patient wearing optimal optical correction. To be included in the study, it was necessary for the spectacle-corrected amblyopic eye visual acuity to be between 20/25 and 20/2000 inclusive. And cycloplegic refraction should be tested (using 1% cyclopentolate, performed according to the investigator’s usual routine with retinoscopy and subjective refraction)

PRESCRIPTION OF SPECTACLES

Spectacles were prescribed based on a cycloplegic refraction using cyclopentolate 1%. Anisometropia and ametropia were corrected following the maximum plus to maximum visual acuity (MPMVA).

AMBLYOPIC TRAINING

After wearing glasses, patients were supposed to do amblyopic training with the frequency of twice or three times a day that one should be taken before sleeping. The introduction of the training program is available at http://www.sunvisionmed.com/.

FOLLOW-UP SCHEDULE

Follow-up visits were conducted after 3 months, 6 months, and 12 months. At every visit, visual acuity was measured in each eye and if amblyopic eye visual acuity had not improved at least one line from the

prior visit, the amblyopic eye was retested.

STATISTICAL METHODS

Patients eligible at the baseline visit but with incomplete follow up were excluded from analyses. For each patient, the maximum acuity improvement was calculated as average and standard deviation (SD). The proportion of patients whose amblyopia resolved (improve 2 or more lines) was computed. The associations of age, baseline amblyopic eye visual acuity, and degree of anisometropia and ametropia with the maximum improvement and resolution of amblyopia were assessed using analysis of Pearson correlation. Analyses were conducted using SPSS statistics 26.

Results

Between January 2019 and January 2021, 28 patients with refractive amblyopic eye visual acuity ranging from 20/666 to 20/29 were provided with optical correction and amblyopic training. The mean age of the patients at study entry was 6.2 ± 2.3 years; the mean visual acuity measurement in the amblyopic eye at study entry was 0.50 logMAR (approximately 20/66). Table 1 provides the baseline characteristics of the cohort.

Table 1
Baseline Demographic and Clinical Characteristics (N = 28, n = 45)

Age	n
3 year	4
4 year	5
5 year	9
6 year	12
7 year	8
8 year	1
9 year	1
10 year	2
11 year	1
12 year	0
13 year	2
Mean (SD) years*	6.2 (2.3)
Best-Corrected Distance Visual Acuity in Amblyopic Eye	
20/666	1
20/200	3
20/133	3
20/100	9
20/80	4
20/66	4
20/50	6
20/40	8
20/33	5
20/29	2

* SD = Standard Deviation
† logMAR = logarithm of the minimum angle of resolution
‡ D = diopter

Age	n
Mean (SD) logMAR†, Snellen equivalent	0.5 (0.28), 20/66
Refractive Error in Amblyopic Eye	
-3.00D‡ to 0	1
0	5
0 to + 3.00D	10
+ 3.00D to + 5.00D	8
≥+5.00D	21
* SD = Standard Deviation	
† logMAR = logarithm of the minimum angle of resolution	
‡ D = diopter	

VISUAL ACUITY IMPROVEMENT

At the initial 3-month visit, visual acuity improvement from the spectacle-corrected baseline acuity averaged 1.5 ± 1.00 lines. 13 (65%) of the 20 refractive amblyopic eyes with spectacle-corrected baseline acuity of 20/666 to < 20/66 had improvement of 2 or more lines of acuity, while in 8 (32%) of the 25 eyes with spectacle-corrected baseline acuity of ≥ 20/66, meaning the worse the baseline acuity is, the easier the acuity gets improvement ($P < 0.001$) (Table 2). 16 (53.3%) of the 30 refractive amblyopic eyes with baseline age of 3 to < 7 years had improvement of 2 or more lines of acuity, while in 5 (33.3%) of the 15 eyes with baseline age of 7 years or older, meaning the younger the patient is, the easier the acuity gets improvement ($P = 0.093$) (Table 2). And visual acuity improvement is not related to type of anisometropia and ametropia (sphere only, cylinder only, both) compared between different baseline refractive error in amblyopic eye ($P = 0.315$) (Table 2).

Table 2
Improvement at 3 months in Amblyopic Eye Visual Acuity

		Improvement in Amblyopic Eye Acuity from Baseline to 3 months				
		<=0 lines (no improvement or worsened)	1 line	2 lines	≥ 3 lines	Mean (SD) lines*
Overall N = 28, n = 45		8	16	12	9	1.5 (1.00)
Baseline Amblyopic Eye Visual Acuity	20/666 to < 20/66 n = 20	2	5	6	7	1.9 (0.99)
	≥ 20/66 n = 25	6	11	6	2	1.2 (0.88)
Baseline Age	3 to < 7 years n = 30	5	9	10	6	1.6 (0.99)
	≥ 7 years n = 15	3	7	2	3	1.3 (1.01)
Baseline Refractive Error in Amblyopic Eye	-3.00D‡ to 0 n = 1	1	0	0	0	0 (0)
	0 n = 5	2	1	1	1	1.2 (1.17)
	0 to + 3.00D n = 10	0	5	3	2	1.7 (0.78)
	+ 3.00D to + 5.00D n = 8	2	4	0	2	1.25 (1.09)
	≥+5.00D n = 21	3	6	8	4	1.6 (0.95)
* SD = Standard Deviation						
‡ D = diopter						

At the 6-month visit, visual acuity improvement from the spectacle-corrected baseline acuity averaged 2.0 ± 1.10 lines. 17 (85%) of the 20 refractive amblyopic eyes with spectacle-corrected baseline acuity of 20/666 to < 20/66 had improvement of 2 or more lines of acuity, while in 13 (52%) of the 25 eyes with spectacle-corrected baseline acuity of ≥ 20/66, meaning the worse the baseline acuity is, the easier the acuity gets improvement (P < 0.001) (Table 3). 21 (70%) of the 30 refractive amblyopic eyes with baseline age of 3 to < 7 years had improvement of 2 or more lines of acuity, while in 9 (60%) of the 15 eyes with baseline age of 7 years or older, meaning the younger the patient is, the easier the acuity gets improvement (P = 0.080) (Table 3). And the data also showed that the higher the degree of refractive

errors, the more obvious the improvement of visual acuity (P = 0.025) (Table 3), which different from the result at the 3-month visit.

Table 3
Improvement at 6 months in Amblyopic Eye Visual Acuity

		Improvement in Amblyopic Eye Acuity from Baseline to 6 months				
		<=0 lines (no improvement or worsened)	1 line	2 lines	≥ 3 lines	Mean (SD) lines*
Overall N = 28, n = 45		6	9	9	21	2.0 (1.10)
Baseline Amblyopic Eye Visual Acuity	20/666 to < 20/66 n = 20	2	1	3	14	2.45 (0.97)
	≥ 20/66 n = 25	4	8	6	7	1.64 (1.05)
Baseline Age	3 to < 7 years n = 30	3	6	6	15	2.1 (1.04)
	≥ 7 years n = 15	3	3	3	6	1.8 (1.17)
Baseline Refractive Error in Amblyopic Eye	-3.00D‡ to 0 n = 1	1	0	0	0	0 (0)
	0 n = 5	1	2	0	2	1.6 (1.2)
	0 to + 3.00D n = 10	0	4	3	3	1.9 (0.83)
	+ 3.00D to + 5.00D n = 8	2	2	1	3	1.6 (1.22)
	≥+5.00D n = 21	2	1	5	13	2.4 (0.95)
* SD = Standard Deviation						
‡ D = diopter						

At the 12-month visit, 18 patients missed the visit making the amblyopic eyes were only 16 left (Table 4). Because there were too many missing patients, the data were no longer statistically evaluated.

Table 4
Improvement at 12 months in Amblyopic Eye Visual Acuity

		Improvement in Amblyopic Eye Acuity from Baseline to 12 months				
		<=0 lines (no improvement or worsened)	1 line	2 lines	≥ 3 lines	Mean (SD) lines*
Overall N = 10, n = 16†		0	1	2	13	2.75 (0.56)
Baseline Amblyopic Eye Visual Acuity	20/500 to < 20/66 n = 8	0	0	1	7	2.9 (0.33)
	≥ 20/66 n = 8	0	1	1	6	2.6 (0.70)
Baseline Age	3 to < 7 years n = 13	0	1	2	10	2.7 (0.61)
	≥ 7 years n = 3	0	0	0	3	3 (0)
Baseline Refractive Error in Amblyopic Eye	-6.00D‡ to 0 n = 0	0	0	0	0	0 (0)
	0 n = 2	0	0	1	1	2.5 (0.5)
	0 to + 3.00D n = 2	0	0	0	2	3 (0)
	+ 3.00D to + 5.00D n = 2	0	0	0	2	3 (0)
	≥+5.00D n = 10	0	1	1	8	2.7 (0.64)

* SD = Standard Deviation

† 18 patients who missed the 12-month visit are not included

‡ D = diopter

Discussion

According to the definition proposed in 2017, amblyopia is a developmental disorder. But in the definition, the description is too disordered and illogical. So we proposed a more distinct notion to explain what amblyopia is:

During the period of visual development, due to the visual signal afferent disorder, insufficient effective stimulation in fovea macula, or macular dysplasia, the development of binocular visual function is lower

than that of normal children of the same age or the difference of binocular vision is more than 2 lines, which is called amblyopia.

In this notion, there are there core elements:

1. The important period of visual development. It can be divided into critical period (from born to 3 years old) and sensitive period (from 3 to 12 years old). In the two periods, visual development is not mature and has strong plasticity. The younger the child is, the stronger the plasticity is, the easier to form amblyopia, and the better the therapeutic effect is. That's why success rates of amblyopia treatment decline with increasing age.[3, 4] Which can be also provided by the data in our study.
2. Visual signal: Light, shape, and color.
3. Effective (intense, sustained, and stable) stimulation in fovea macula. That is, sustained and stable clear imaging focusing on the central fovea of macula in retina.

In this notion, we concentrate on the development of visual centre, also called "Brain Vision". It can be explained that visual acuity depends on optical imaging of the retina, which has positive correlation with diopter, conduction of the optic nerve, which can lead different visual acuity with same diopter, and analysis of the cerebral cortex, which make difference in diopter with same visual acuity, and problems at any point can affect vision development. This is also a guide to many emerging treatments, such as perceptual learning, transcranial magnetic stimulation (TMS), and so on.[1, 5–7] And the amblyopic training program in our study is designed according to this principle.

Based on the new notion, we can divide amblyopia into 3 classes:

(1) Afferent disorder of visual signal: At the critical stage of infant visual development, because of afferent disorder of visual signal, stimulation of macula is insufficient, which will lead poor development of visual centre, and then cause amblyopia. This kind of amblyopia mainly caused by congenital cataract, opacitas corneae, infectious or non-infectious endophthalmitis, vitreous hemorrhage and ptosis.

(2) Abnormal focus site of visual signal: At the critical and sensitive stage of visual development, because visual signal focus deviates from macular area, the weak intensity of visual signals in the central fovea will affect the development of visual centre, and then cause amblyopia, like strabismus and nystagmus.

(3) Poor macular focusing of visual signal: At the critical and sensitive stage of visual development, because of failure to match corrective glasses in time, the image of the retina remains blurred, and stimulation of macula is insufficient, which then lead poor development of visual centre, and cause amblyopia. This kind of amblyopia is mainly caused by anisometropia and ametropia. In anisometropia patients, because the size of binocular retinal imaging is different, it's difficult for visual centre to fuse the different images, so that it will actively inhibit the image in the eye with high diopter causing insufficient stimulation of macula in the eye, and then forming amblyopia. The degree of anisometropia is positively correlated with the probability and severity of amblyopia. In patients with ametropia, hyperopia will make

the light focus behind the retina, and astigmatism can lead a zonal focusing on the retina, both of which can cause low intensity of visual signals in the fovea and increase risk of amblyopia. While myopia often has a good focus when looking near, and make the stimulation of macular visual signal close to normal, which decrease the risk of amblyopia.

So, based on the new classification, the basic treatment of amblyopia can be directed:

1. Afferent disorder of visual signal: Etiological treatment. The first stage is to remove afferent disorders through early surgery or other treatment. Only after removing afferent disorders, the visual signal can reach the central fovea, and then stimulate the development of cerebral optic cortex, avoiding amblyopia.
2. Abnormal focus site of visual signal: In this condition, the focus site of visual signal should be corrected to the central fovea firstly. After which, the visual signal can stimulate central fovea effectively, and then promote visual development. For example, when a patient is diagnosed with strabismus, the first thing to do is to correct the eye position by wearing glasses or surgery.
3. Poor macular focusing of visual signal: In order to make the light focus on the retina, refractive correction must be performed. According this principle, we consider to get the maximum plus to maximum visual acuity (MPMVA), in which condition, the image can be clearly presented on the retina.

And after the primary principle, the following steps are similar which can be divided into daily life training and professional amblyopia training. Daily life training, which means to promote use of the amblyopic eye by occluding or blurring the fellow eye in daily life, mainly contains patching and pharmacological treatment.[1, 7–9] Professional amblyopia training mainly contains perceptual learning, video gaming, dichoptic training, transcranial magnetic stimulation, acupuncture, et al.[1, 9], meaning to promote cerebral development, elevate visual acuity, and improve visual function by special training. And only after a combination of the above steps, amblyopia can be better improved.

So, according to the treatment principle of amblyopia with poor macular focusing of visual signal, we designed this study. According to the result, we can see that the treatment following the principle is effective. But we have to say it was a pity that there was no contrast group. And the studies that therapy the refractive amblyopia by full correction and under correction were short of the amblyopic training in our study, which made there is no comparability between these studies.

Conclusion

Though there is absent of comparability between our study and these studies which were performed degree design to treat amblyopia caused by anisometropia and ametropia, this study showed that getting the degree to MPMVA and following by amblyopic training in amblyopia with anisometropia and ametropia can improve visual acuity effectively.

The new notion reveals secret of amblyopia from another point of view. And based on the new notion, the image can be the most clear which can stimulate visual development most effectively only when the degree designed to MPMVA. So, we believe that the degree design directed by the principle of new notion is a new strategy compared by full correction and under correction. And further randomized controlled study is ongoing.

Abbreviations

MPMVA: Maximum plus to maximum visual acuity

Declarations

Declaration of interest and funding

There are no conflicts of interest and no funding.

Authors' contributions:

Chuanyu Wang: statistical analysis, drafting of the manuscript

Zhiwei Li: data collection

Guoying Mu: conceptualization and study design, study supervision

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