World Journal of Medical and Surgical Ophthalmology

The Effect of Induced Anisometropia and Binocular Visual Function

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Abstract

Background To determine the effect of experimentally induced anisometropia on binocular function in healthy adults as a means of assessing the likely effects of uncorrected anisometropia on binocular visual development in childhood.

Design This prospective study was conducted in Department of Ophthalmology, JLN Medical College, Aligarh Muslim University, Aligarh, U.P., India

Patients and Methods:

A total of 30 healthy adults aged between 18-35 years and free of ocular disease participated in the study. One to five diopter (D) of unilateral hypermetropia and myopia was induced in each eye in ID increments. Fusion was assessed with the Worth-Four Dot test for distance (WFDT) and near and Bagolini's lenses (BL); stereopsis with the TNO test, bifoveal fusion with the four-prism diopter base-out test (4PDBOT) and aniseikonia with charts.

Results All subjects showed a decline in binocular function with increasing levels of anisometropia. Significantly increasing foveal suppression as evident on the WFDT and BL, with all subjects definitely suppressing at$\pm$ 3Danisometropia.Aniseikoniawas altered by 2% per 1 D anisometropic Induction. Proportion of cases with monofixation significantly increased up to 3D ($p<0.05$).Stereopsis decreased in proportion to the degree of anisometropia. Three diopters of anisometropia, regardless of type, produced a marked reduction of stereoacuity in all patients.

Conclusions Relatively low degrees of spherical anisometropia (as small as 1D) causes significant abnormalities in high-grade binocular function in adults.The potential amblyogenic effects of even small uncorrected anisometropia on binocularity in children require further investigation, and should be considered in developing guidelines for the empiric correction of refractive errors.

KeyWords Amblyopia, Aniseikonia Anisometropia, Binocular visual function, Worth-Four Dot test

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Submitted: Sunday, February 22, 2015; Accepted: Tuesday, March 17, 2015; Published Saturday, March 28, 2015

Introduction

Anisometropia (even in the absence of strabismus) is well known to be a significant risk factor for the development of amblyopia [1-3]. The exact mechanism of amblyopia remains unclear but Von Noorden and

Ciruffreda suggested that the defocused image and active suppression of more emetropic eye in anisometropia may lead to amblyopia [4, 5]. While the exact prevalence of anisometropia in the general population is not known, a prevalence of 4-4.7% has been described in hospital based data. Up to 25% of infants and approximately 2% to 8% of toddlers shows difference (1D or >1D) in refractive error between the two eyes [6, 7].

Although extremely common in small degrees, significant anisometropia is considered to be when the difference between l the refractive states of the two eyes is of a magnitude of 2.5 Diopter (D) or more [8]. Most of the symptomatology of anisometropia arises from the fact that it leads to aniseikonia. A difference of 5% aniseikonia is the probable limit which can be tolerated [9].

Lubkin V *et al*., [10] demonstrated that aniseikonia *per se* does not appear to have a major causal role in amblyopia. In a clinical setting, it is probable that anisometropia in tandem with aniseikonia is likely to be amblyogenic.

Researches shows that unilateral image blur during the early period of visual development results in loss of binocular functions [11]. Chen and Song found in the patients with previously untreated anisometropic amblyopia that, higher degree of anisometropia is significantly associated with deeper amblyopia; worse contrast sensitivity, fusion and steriopsis functions [12]

Thus, it is important to quantify the effects of anisometropia on binocular vision when establishing guidelines for the emperical management of this potentially amblyogenic stimulus. Current opinion suggests that empirical correction should be considered for an interocularanisometropic difference of: astigmatism>1.5D, myopia>3D and hyperopia>1.5D [13]. However, more research is needed to validate these recommendations. Shrikant *et al*., assessed the impact of transient induced ansometropia and anisekonia on the accommodative and vergence performance of developing infants and children and found that binocularity remain upto $\pm$4D of induced anisometropia and 11% induced aniseikonia [14].

Although anisometropia would likely to be more detrimental in the younger child, it is difficult to clinically elicit the responses in this age group. Therefore, by replacing the child with an adult and presuming the sensory deterioration produced in both age groups is similar, we undertook a prospective study to analyze the adverse effects of increasing anisometropia on the various parameters of the binocular function.

Materials and Methods

After ethical clearance was obtained from the Institutional Ethical Committee, 30 healthy adults aged 18-35 years were included in the study. An informed consent was obtained from all of them. The inclusion criteria were uncorrected Snellen visual acuity of 6/6 in both eyes, no prior anti-amblyopia treatment, no organic ocular pathology, demonstrable stereopsis of 40 arc seconds on the TNO test, absence of strabismus on cover test, patients with phorias <4

Table 1: Number (%) of subjects with Binocular Single Vision (BSV) or suppression (Supp) with Increasing Anisometropia (N=30) on Worth-Four Dot Test for Distance (6 mts)

Anisometropia induced (D)	BSV	Supp	p value*
Hyperopia (Right Eye)			
+1	28 (93.3)	2(6.7)	0.500
+2	12(40)	18(60)	<0.001
+3	0(0)	30(100)	<0.001¯
Hyperopia (Left Eye)			
+1	24 (80)	6 (20)	0.031´
+2	8 (26.7)	22(73.3)	<0.001¯
+3	0(0)	30(100)	0.008ª
Myopia (Right Eye)			
-1	30(100)	0(0)	~
-2	11 (36.7)	19(63.3)	<0.001 ª
-3	0(0)	30(100)	0.001¯
Myopia (Left Eye)			
-1	24 (80)	6 (20)	0.031´
-2	7 (23.3)	23 (76.7)	<0.001¯
-3	0(0)	30(100)	0.016´

*The p value (Mc Nemar) is of the change in the binomial response, as compared to the previous induced refractive error with p set at < 0.05.
¯ highly significant p value.
´Significant p value.
~ No significant change.

prism diopters (PD) and normal fusion responses on Bagolini's lenses (BL) test and Worth-Four Dot Test (WFDT).

All the following tests were conducted on all 30 patients in the Strabismus Clinic of Aligarh Muslim University, Institute of Ophthalmology, J. N. Medical College Aligarh. One to five diopters of hyperopia and myopia was experimentally induced, by placing lenses in a trial frame in front of the right eye and later the left eye. Both WFDT for distance (6 mts) and near (33 cms) and BL were used to assess fusion or the lack of it. Stereoacuity was measured by the TNO test. Four-Prism Diopter Base-Out Test (4PDBOT) was used to assess bifoveal fixation and aniseikonia percentages were recorded with the help of New Aniseikonia Charts of S. Awaya, Handaya Co. Ltd. The statistical analyses were done using SPSS (PC+) version 10 by Wilcoxon test and Mc Nemar test with significant set at ≤ 0.05.

Results

With the WFDT at distance and +1D of induced anisometropia, 2 of 30 subjects gave a suppression response. With +2D of anisometropia, 18 responded with suppression, a highly significant change (Mc Nemar p value< 0.001). With ≥ +3D, all subjects had lost the ability to fuse, with statistically significant changedemonstrated between +2D and +3D.On the other hand, with -1D induction of anisometropia, all subjects continued to fuse, while at-2D, 19 responded with suppression, having lost fusion, again a highly significant change. With ≥ -3D, all subjects lacked fusion

Table 2: Number (%) of subjects with Binocular Single Vision (BSV) or suppression (Supp) with Increasing anisometropia (N=30) on **Bagolini's lenses test**.

Anisometropia induced (D)	BSV	Supp	p value*
Hyperopia (Right Eye)			
	28 (93.3)	2(6.7)	0.500
+2	10(33.3)	20(66.7)	<0.001¯
+3	0(0)	30(100)	0.002¯
+4	0(0)	30(100)	~
+5	0(0)	30(100)	~
Hyperopia (Left Eye)			
+1	23 (76.7)	7 (23.3)	0.016´
+2	6 (20)	24 (80)	<0.001¯
+3	0(0)	30(100)	0.031´
+4	0(0)	30(100)	~
+5	0(0)	30(100)	~
Myopia (Right Eye)			
-1	30 (100)	0(0)	~
-2	10 (33.3)	20 (66.7)	<0.001ª
-3	1 (3.3)	29 (96.7)	0.004ª
-4	0(0)	30 (100)	1.000
-5	0 (0)	30 (100)	~
Myopia (Left Eye)			
-1	24 (80)	6 (20)	0.031´
-2	5 (16.7)	25 (83.3)	<0.001¯
-3	0(0)	30(100)	0.063
-4	0(0)	30(100)	~
-5	0(0)	30(100)	~

*The p value (Mc Nemar) is of the change in the binomial response, as compared to the previous induced respective error with p value set at < 0.05.
¯Highly significant p value.
´Significant p value.
~ No significant change.

(Table 1).For a given value of anisometropia induced there was no statistically significant differences in the responses, between the right eye and the left eye,exceptwith-1D (Mc Nemar p<0.05.

On the BL test, with the induction of +1D of hyperopia, 2 subjects showed suppression response, whereas this number was increased to 20 with +2D.With +3D to +5D, all lacked fusion. With the induction of -1D of myopia all 30 demonstrated fusion. With -2D, this number had increased to 20 and by -4D, all lacked fusion (Table 2).

The difference in response between the right eye and left eye for a given diopter of induction was not found to be statistically significant except with -1D; which was significantly more detrimental to the left eye (McNemar p<0.05).

Stereoacuity levels on TNO test were significantly worse more than 480 arc seconds in 11 patients with +2D as compared to none with +1D .This change was found to be highly significant (Wilcoxon p value <0.001). Stereoaucity continued to deteriorate with increasing hyperopia. Finally, with +5D, all had a stereoaucity worse than 480 arc seconds. Inducing minus

Table 3: Number (%) of subjects ,demonstrating different levels of sterioacuity with increasing anisometropia (N=30) on **TNO Test**.

Anisometropia Induced (D)	Sterioacuityin Arc Secs.				
	120	240	480	>480	P value[a]
Hperopia (Right Eye)					
+1	12 (40)	8 (26.7)	10 (33.3)	0 (0)	<0.001**
+2	5(16.7)	3 (10)	11 (36.7)	11 (36.7)	<0.001**
+3	0 (0)	1 (3.3)	7 (23.3)	22 (73.3)	<0.001**
+4	0 (0)	0 (0)	2 (6.7)	28 (93.3)	0.008**
+5	0 (0)	0 (0)	0 (0)	30 (100)	0.157
Hyperopia (Left Eye)					
+1	9 (30)	5 (16.7)	10 (33.3)	6 (20)	<0.001**
+2	4 (13.3)	1 (3.3)	9 (30)	16 (53.3)	<0.001**
+3	0 (0)	1 (3.3)	4 (13.3)	25 (83.3)	0.002**
+4	0 (0)	0 (0)	1 (3.3)	29 (96.7)	0.025**
+5	0 (0)	0 (0)	0 (0)	30 (100)	0.317
Myopia (Right Eye)					
-1	14 (46.7)	9 (30)	7 (23.3)	0 (0)	<0.001**
-2	0 (0)	5 (16.7)	14 (46.7)	11 (36.7)	<0.001**
-3	0 (0)	0 (0)	5 (16.7)	25 (83.3)	<0.001**
-4	0 (0)	0 (0)	0 (0)	30 (100)	0.025*
-5	0 (0)	0 (0)	0 (0)	30 (100)	1.000
Myopia (Left Eye)					
-1	10 (33.3)	3 (10)	12 (40)	5 (16.7)	<0.001**
-2	1 (33.3)	1 (3.3)	8 (26.7)	20 (66.7)	<0.001**
-3	0 (0)	1 (3.3)	0 (0)	29 (96.7)	0.004**
-4	0 (0)	1 (3.3)	0 (0)	29 (96.7)	1.000
-5	0 (0)	1 (3.3)	0 (0)	29 (96.7)	1.000

a The p value (Wilcoxon) is of the change in the stereoacuity as compared to the previous induced refractive error with p value set at <0.05.
** Highly significant p value.
* Significant p value.

powers in the right eye revealed that by -4D, all subjects had attained a maximum deterioration of the stereoacuity which was worse than 480 arc seconds. For each diopteric hyperopic or myopic induction up to 3D, in either eye, the change in stereopsis was highly significant (Wilcoxon p value <0.001).There was a similar deterioration in the stereoaucity with increasing anisometropic inductions in the left eye (Table 3).

For a given dioptre of anisometropia the stereopsis was significantly different when the induction as compared between the right eye and the left eye. A far greater number of subjects showed a stereoaucity of worse than 480 arc seconds with +1D or -1D over the left eye as compared to the right eye. Such a significant difference was not found when higher grades of hyperopic or myopic inductions in the right eye and the left eye were compared.

On 4PDBOT, with +1D, all demonstrated bifoveal fixation. With +2D, 20 showed monofixation response and this number increased to 30 with +3D.With -2D, 23 subjects showed a monofixation response as compared to none with -1D. With-3D, all showed monofixation response

Table 4: Number (%) of subjects with bifocal fixation or monofixation response with increasing anisometropia (N=30) on **Four –Prism Diopter Base-Out Test**.

Anisometropia induced (D)	Bifoveal fixation	Monofixation	p value *
Hyperopia (Right Eye)			
+1	30(100)	0(0)	NS
+2	10(33.3)	20(66.7)	<0.001**
+3	0(0)	30(100)	0.002**
+4	0(0)	30(100)	NS
+5	0(0)	30(100)	NS
Hyperopia (Left Eye)			
+1	22(73.3)	8 (26.7)	0.008**
+2	0 (0)	30 (100)	<0.001**
+3	0(0)	30(100)	NS
+4	0(0)	30(100)	NS
+5	0(0)	30(100)	NS
Myopia (Right Eye)			
-1	30 (100)	0(0)	NS
-2	7 (23.3)	23 (76.7)	<0.001**
-3	0 (0)	30 (100)	<0.001**
-4	0(0)	30 (100)	NS
-5	0 (0)	30 (100)	NS
Myopia (Left Eye)			
-1	22 (73.3)	8(26.7)	0.008**
-2	5 (16.7)	25 (83.3)	<0.001**
-3	0(0)	30(100)	1.000
-4	0(0)	30(100)	NS
-5	0(0)	30(100)	NS

* The p value (Mc Nemar) is of the change in the binomial response, as compared to the previous induced refrective error with p value set at < 0.05.
** Highly significant p value.
NS. No significant change.

(Table 4). Aniseikonia altered significantly per D increase in hyperopia or myopia, averaging a mean of 2% magnification or minification of the retinal image per diopter.

Discussion

Although the mechanism of amblyopia production due to anisometropia is poorly understood, it remains one of the leading causes of amblyopia. While it is generally agreed that inanisometropia refractive errors should be corrected in patients with established amblyopia or strabismus, it is not clear what levels of anisometropia should be empirically corrected in otherwise healthy children to ensure optimal visual development and maturation. Studies in primates reveal that uncorrected anisometropic stimulus during the critical period can adversely alter the binocular response [15].

Although our study conducted in healthy adults, it is reasonable to assume that the results apply to the children as well. Oguz and Oguz [16] have suggested that the condition of induced anisometropia in adults is optically identical to that experienced by an anisometropic child. In our study, maximum deterioration in the binocular function was achieved with 3D of induced hyperopic or myopic anisometropia.

Suppression was evident on the WFDT for distance and BL and increased in

proportion to the anisometropia. It is likely that the depth of the suppression zone increased with increasing anisometropia. This is also reflected in other studies [17, 18] which suggest that bifoveal fusion becomes increasingly impossible as the anisometropia increases in magnitude. Our results on WFDT for distance are in agreement with those by Dadeya *et al*., [17], who reported in their study on 15 subjects that with 3D of spherical anisometropia, none of their subjects was able to fuse on WFDT for distance.

With the near WFDT, all the 30 subjects demonstrated binocular single vision with all induced anisometropic powers in either eye. These results are similar to those of Tomac and Birdal [19] who reported fusion response in twenty-two of their twenty-five subjects on WFDT for near. They explained the difference between the responses of WFDT for distance and near as being due to the lessening of binocular rivalry at near. As the object gets closer to the eye, its retinal images become larger, thus binocular rivalry diminishes and fusion becomes easier and therefore, a high number of anisometropes show fusion with the near WFDT unless binocularity is too degraded. We agree with Tomac and Birdal [19] on their view that anisometropia induces foveal rivalry. It is this fact which allows the WFDT for near to give a fusion response through peripheral fusion mechanisms while the WFDT for distance shows suppression as it tests for foveal fusion.

Our data showed that clinically acceptable level of 40 arc seconds of stereopsis can still be maintained with 1D of anisometropia. These findings are consistent with that of Lovasik [20] while they differ from the findings of Brooks *et al*., [18] who reported that even 1D of anisometropia has the potential to degrade stereopsis to subnormal levels in visually mature adults. The precise means by which anisometropia leads to the observed decrease in stereoaucity is not clear. Simpson [21] has suggested that foveal suppression in the defocused eye is the cause of decreased stereopsis but other factors, like the contrast and density of fusional detail play an important role as well. The depth of the suppression zone increased with increasing anisometropia, suggesting that fusion requires greater inter-ocular image symmetry as the foveal center is approached. This may account for the deterioration in stereoaucity observed in our study with increasing anisometropia.

Our data on 4PDBOT showed a significant loss of bifoveal fixation with increasing anisometropia upto 3D. This is contrary to the findings of Tomac and Birdal [19] who concluded that even if fusion is weak, almost all patients with anisometropia have bifoveal fusion. However, our findings are consistent with those of Weakley [22] who reported that increasing anisometropia resulted in an increase in monofixation response as compared to bifoveal fusion response.

We also found that with increasing anisometropia, there was a significant alteration in aniseikonia with a mean of 2% per D which is close to what has been described in literature [9]. Aniseikonia is generally thought to reflect disparities in retinal image size

that often accompany anisometropia. Our study is limited by the fact that we have not evaluated astigmatic anisometropia. Moreover its precision could have been improved if we had induced anisometropia in 0.5 diopter steps.

In agreement with Brooks *et al*., we are of the opinion that anisometropia as little as 1D can adversely affect various facets of the binocular function and must be corrected [18]. In children, uncorrected anisometropia has deleterious implications by contributing to the amblyogenic milieu of the developing eye and hence due consideration should be given to the correction of even smaller degrees of anisometropia.

Funding Support

None

Ethical Consideration

Ethical Clearance was obtained from Institute Ethical Committee.

Conflict of Interest

The authors declare that there is no clinical conflict with the subject matter of the paper, nor any commercial or proprietary interest in any product or company.

Authors' Contributions

JR: Conducted the study and prepared the draft manuscript.

RRS: Conceived and designed the study and edited the final manuscript for publication.

AKA: Conceived and designed the study and helped preparing the manuscript.

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