Reliability of Fixation Preference for Detecting Amblyopia in Strabismic Patients

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Purpose: To evaluate the association between fixation preference (FP) and amblyopia in strabismic patients.
Methods: This study includes 50 patients with horizontal, vertical or mixed strabismus of at least 10 prism diopters. Best-corrected monocular visual acuity (VA) was measured using Snellen E-chart and the presence of amblyopia was determined accordingly; FP was evaluated and graded from 0 to 3.
Results: Of 50 patients, including 27 female and 23 male subjects, 29 (58%) patients had FP but 18 (36%) subjects were truly amblyopic. Overall, the sensitivity and specificity of FP for detection of amblyopia was 88.9% and 59.4% respectively. The positive predictive value (PPV) and negative predictive value (NPV) were 55.2% and 90.5% respectively. Sensitivity, PPV and NPV were significantly higher in esotropic as compared to exotropic patients. Strong monocular FP was correlated with more than 3 lines of interocular difference (IOD) in visual acuity (P=0.001).
Conclusion: Although FP is not an ideal method for diagnosis of strabismic amblyopia, it has high sensitivity, PPV and NPV in esotropic patients and in subjects with more than 3 lines of IOD in VA.

Key words: Binocular Fixation Pattern; Fixation Preference; Strabismic Amblyopia

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INTRODUCTION

The prevalence of amblyopia in the general population ranges from 2% to 2.5%.[1] The most common form of amblyopia develops in the constantly deviating eye of a child with ocular misalignment. Constant, nonalternating tropias, typically esodeviations, are most likely to cause significant amblyopia.[2] Reliable evaluation of visual acuity (VA) in preverbal children is important for diagnosis and treatment of amblyopia. On the other hand, subjective responses can be difficult to elicit or may be unreliable in this age group.[3] One of the most common tests for diagnosis of strabismic amblyopia is binocular fixation pattern or the fixation preference (FP) test.[4,5]

Zipf[4] was one of the first authors to study the reliability of the FP test and stated that amblyopic patients with esotropia or exotropia demonstrate strong levels of FP. He found that FP was reliable for detecting amblyopia with large angle deviations, but the test falsely diagnosed amblyopia in approximately 70% of patients with small angle tropias, i.e. less than 10 prism diopters (PD) and equal vision in fellow eyes. Wright et al[5] introduced the use of a 10-PD vertical prism to evaluate FP in patients with straight eyes and in those with small angle deviations. The reliability of this

simple test among pediatric ophthalmologists has been reevaluated by Hakim[6] in a recent study. The results of the latter study were very different from previous reports. The aim of the present study was to evaluate the reliability of the FP test in detecting amblyopia in patients with strabismus.

METHODS

Fifty strabismic patients with heterotropia ≥10 PD who were old enough (≥6 years) to cooperate for subjective assessment of VA were randomly selected from new cases or follow-up patients. A complete ophthalmologic examination including slitlamp biomicroscopy, funduscopy and refraction was performed in all subjects. Best-corrected VA (BCVA) was measured using Snellen E-chart at 6 m distance with standard illumination. Strabismus examinations included unilateral cover (cover-uncover) test with and without correction. All patients with history of strabismus surgery, anisometropic amblyopia and retinal or optic nerve abnormalities were excluded. Written informed consent was obtained from the patients or their guardians.

Amblyopia was defined as the presence of 2 lines of interocular difference (IOD) in BCVA together with BCVA ≤20/32 in the worse eye. FP was evaluated by an independent observer unaware of the level of VA in the study subjects. If the patient did not alternate fixation, the preferred eye was temporarily occluded to force fixation to the nonpreferred eye. After establishment of fixation with the nonpreferred eye, the occluder was removed from the preferred eye to see whether fixation was maintained with the nonpreferred eye. Examinations were repeated until the dominant eye was recognized followed by grading of PF.

Binocular fixation pattern was categorized into four grades based on Zipf's classification;[4,6,7] grade 0: no FP (alternate fixation), grade 1: mild FP (the patient prefers one eye, but maintains fixation by the fellow eye through a blink), grade 2: moderate FP (the patient prefers one eye, but holds fixation by the fellow eye only up to a blink), and grade 3: strong FP (the patient prefers one eye and cannot hold fixation by the fellow eye). Amblyopia was defined as unmaintained fixation according to binocular fixation pattern testing (grades 1, 2 and 3).

Using BCVA as the gold standard, the validity of the FP test for detection of amblyopia was evaluated using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), Youden's J. statistic, and likelihood ratio. Frequency values were tested using Chi-square or Fisher's exact test. Youden's J. statistic is the measurement of the probability of a correct diagnosis of amblyopia by FP test that is invariant by chance alone.

RESULTS

Overall, 50 patients including 27 female and 23 male subjects with manifest strabismus greater than 10 PD and mean age of 12.9±5.1 (range 6 to 20) years were evaluated. The deviations included exotropia (XT) in 27 (54%) patients, esotropia (ET) in 15 (30%) subjects, hypertropia (HT) in 1 (2%) case, combined XT and HT in 3 (6%) subjects, and combined ET and HT in 4 (8%) patients. Mean horizontal deviation was 32.9±16.4 (range, 10-80) PD and only one patient had vertical deviation of 30 PD.

Based on BCVA, 18 (36%) subjects were amblyopic (13 left and 5 right eyes), however 29 (58%) patients demonstrated certain degrees of FP including grade 1 in 7 (14%), grade 2 in 6 (12%) and grade 3 in 16 (32%) patients. Table 1 summarizes reliability values of the FP test for diagnosis of amblyopia using BCVA as the gold standard. Overall, the sensitivity, specificity, PPV and NPV of the FP test for diagnosis of amblyopia were 88.9%, 59.4%, 55.2% and 90.5% respectively. Youden's J. statistic and likelihood ratio were 0.483 and 2.19 respectively. Sensitivity and specificity values were higher in male patients as compared to female subjects ($P<0.05$). Sensitivity ($P=0.45$), specificity ($P=0.91$) and PPV ($P=0.1$) values were also higher in patients older than 10 years of age as compared to younger subjects. Sensitivity ($P=0.005$), specificity ($P=0.04$) and PPV ($P=0.003$) values were significantly higher in esotropic patients as compared to exotropic ones.

Table 2 presents the correlation between

IOD in VA and the grade of FP. Most patients with no FP or mild and moderate FP (grades 0, 1, 2) had no significant or less than 2 lines of IOD in visual acuity, but patients with strong FP (grade 3) had more than 3 lines of IOD in visual acuity (P=0.001).

Table 1 Reliability indices of fixation preference test for diagnosis of strabismic amblyopia based on sex, age and type of deviation

	Sensitivity (95% CI)	Specificity (95% CI)	Youden's J. S. (95% CI)	PPV (95% CI)	NPV (95% CI)	LR
Overall	88.9 (75.28-100)	59.4 (42.35-76.45)	0.483 (0.26-0.706)	55.2 (37.2-73.2)	90.5 (78-100)	2.19
Sex: Female	77.8 (50.6-100)	57.1 (31.2-83)	0.349 (-0.026 to 0.724)	53.8 (26.56-81)	80 (55.2-100)	1.81
Male	100 (-)	61.1 (38.6-83.6)	0.611 (0.124-0.574)	56.3 (31.8-80.8)	100 (-)	2.57
Age: <10 yr	80 (44.7-100)	58.8 (35.48-82.12)	0.388 (-0.033 to 0.809)	36.4 (8-64.8)	90.9 (73.9-100)	1.94
≥10 yr	92.3 (80-100)	60 (30-90)	0.523 (0.236-0.81)	66.7 (45-88.4)	90 (71.4-100)	2.3
Type of HD: ET	100 (-)	20 (0-98.4)	0.2 (-0.151 to 0.551)	77.8 (58.6-97)	100 (-)	1.25
XT	50 (20-80)	69.2 (33.4-100)	0.192 (-0.16 to 0.54)	20 (0-44.8)	90 (76.5-100)	1.62

S, statistics; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio; CI, confidence interval; NA, not applicable; HD, horizontal deviation; ET, esotropia; XT, exotropia.

Table 2 Correlation between interocular difference in visual acuity and grading of fixation preference

Fixation preference grade	Interocular difference in visual acuity			Total
	2 lines	*3-4 lines*	*> 4 lines*	
0	19	2	0	21 (42%)
1	6	1	0	7 (14%)
2	5	1	0	6 (12%)
3	4	1	11	16 (32%)
Total	34	5	11	50 (100%)

DISCUSSION

The fixation preference test is based on the assumption that nonamblyopic strabismic patients will alternate fixation or hold fixation well with either eye during binocular viewing. Conversely, amblyopic patients will show strong fixation preference with the sound eye and will not hold fixation with the amblyopic eye.[5] In this prospective study we evaluated the reliability of the FP test in strabismic patients as an alternative method of measuring IOD in VA for assessment of amblyopia in young strabismic children.

Sensitivity and NPV of FP test were 88.9% and 90.5% respectively indicating that the test can detect significant amounts of true positive cases of amblyopia. Sensitivity, PPV and NPV were higher in esotropic as compared to exotropic patients. Due to the high number of false positive cases, the specificity of this test was low. In a similar fashion, Cotter et al[7] reported a high false positive rate, however they observed no difference in sensitivity, specificity and NPV in esotropic versus exotropic patients in their work.

Zipf[4] in 1976 studied the reliability of FP test and found that the grade of FP is a reliable indicator for the presence of amblyopia in children with esotropia larger than 11 PD, however children with small angles of esotropia may be falsely considered amblyopic according to FP. In 1981, Wright et al[8] induced vertical deviation by placing a 10-diopter vertical prism over one eye. Once the eyes were dissociated, FP was evaluated and used to predict the presence of amblyopia. He found that all amblyopic children with two or more lines of IOD in VA showed abnormal fixation patterns regardless of the presence or amount of deviation, while those without amblyopia showed normal patterns. Conversely, Cotter et al[7] observed that false positive errors still occur despite the precaution of using induced-tropia test for small angle strabismus, and this occurs with large-angle deviations as well.

Hakim[6] reevaluated this test and found that 87% (70/80) of patients diagnosed amblyopic based on FP testing, only 18% (15/80) were truly amblyopic using Snellen E-chart. Laws et al[9] evaluated binocular FP in 53 strabismic children aged 5-13 years using 3 different cutoff values for FP testing. They observed sensitivity and specificity of 78% and 86% respectively

and also reported a PPV of 89% for amblyopia in the presence of a strong FP. They concluded that binocular fixation pattern can be rapidly assessed with minimal equipment and training. Sener et al[10] assessed the reliability of the grading system of standard FP test on 111 strabismic patients with mean age of 10.4 years and large angle heterotropia (>10 PD), and reported that binocular FP had sensitivity of 85% and specificity of 79%.

In the present study, specificity of the FP test was lower and sensitivity was comparable to previous studies. For example, specificity and sensitivity of the test were reported 18% and 100% by Hakim,[6] and 79% and 99% by Cotter et al[7] respectively. This difference is due to the relatively high number of false positive cases. Specificity and sensitivity were determined by Cotter et al according to the type of deviation; sensitivity and specificity of the FP test were 70% and 72% in esotropic patients versus 67% and 84% in exotropic patients, respectively, a difference which was not statistically significant. In our study the difference in sensitivity and specificity was statistically significant according to the type of deviation and was higher with esodevaitions.

According to our findings and previous studies we may conclude that although FP is not an ideal test for detecting strabismic amblyopia in all patients, it has high sensitivity, PPV and NPV in esotropic patients with >10 PD heterotropia and in patients with more than 3 lines of IOD in VA.

REFERENCES

1. Von Noorden GK. Binocular vision and ocular motility. 6th ed. St Louis, Mosby; 2002.
2. American Academy of Ophthalmology. Amblyopia. In: Basic and clinical science course: Pediatric ophthalmology and strabismus. San Francisco: The Academy; 2007-2008: 67-75.
3. Robbin SL, Christian WK, Hertel RW, Granet DB. Vision testing in the pediatric population. *Ophthalmol Clin North Am* 2003;16:253-267.
4. Zipf RF. Binocular fixation pattern. *Arch Ophthalmol* 1976;94:401-405.
5. Wright KW, Edelman P, Walonker F, Yiu S. Reliability of fixation preference testing in diagnosing amblyopia. *Arch Ophthalmol* 1986;104:549-553.
6. Hakim OM. Association between fixation preference testing and strabismic pseudoamblyopia. *J Pediatr Ophthalmol Strabismus* 2007;44:174–177.
7. Cotter SA, Traczy-Hornoch K, Song F, Lin J, Brochert M, Azen SP, et al. Fixation preference and visual acuity testing in a population-based cohort of preschool children with amblyopia risk factors. *Ophthalmology* 2009;116:145-153.
8. Wright KW, Walonker F, Edelman P. 10-Diopter fixation test for amblyopia. *Arch Ophthalmol* 1981;99:1242-1246.
9. Laws D, Noonan CP, Ward A, Chandna A. Binocular fixation pattern and visual acuity in children with strabismic amblyopia. *J Pediatr Ophthalmol Strabismus* 2000;37:24-28.
10. Sener EC, Mocan MC, Gedik S, Ergin A, Sanac AS. The reliability of grading the fixation preference test for the assessment of interocular visual acuity differences in patients with strabismus. *J AAPOS* 2002;6:191-194.