Clues for the Diagnosis of Accommodative Excess and Its Treatment with a Vision Therapy Protocol

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Authors’ contributions

This work was carried out in collaboration among all authors. Author CB designed the study, performed the statistical analysis, wrote the protocol, wrote the first draft of the manuscript and managed the literature searches. Author EZ collected the data, wrote the protocol, managed the literature searches and wrote the first draft of the manuscript. Author IS designed the study, performed the statistical analysis, wrote the protocol, managed the analyses of the study, managed the literature searches and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Accommodative and vergence dysfunctions are the most common vision disorders in the pediatric population with a prevalence of up to 30%, and patients with these dysfunctions usually have symptoms at near distances that could affect academic results. This study is the retrospective assessment of accommodative excess cases and aims to find a pattern in optometric exams to help diagnose accommodative excess without cycloplegic drugs. Furthermore, this study assesses the utility of a vision therapy protocol as accommodative excess treatment.
Methodology: A retrospective study was conducted with 24 patients who were diagnosed with accommodative excess and completed all sessions of the vision therapy protocol. The vision therapy protocol was organized into 8-12 sessions. Statistical analysis was performed using SPSS 23.0. Wilcoxon nonparametric paired tests were used to compare the clinical values between visits.

Results: In total, 24 patients with accommodative excess were included in the retrospective study. The pairwise comparisons of sphere values obtained with the different refraction methods without cycloplegic drugs found statistically significant differences (P< 0.01). Statistically significant differences (P< 0.01) were shown in the sphere values obtained from subjective refraction, visual acuity tests, near point of convergence and stereopsis between the diagnosis visit and the post-vision therapy protocol visit, with better values post-therapy.

Conclusion: Variations in the sphere values could be clues for accommodative excess if a double condition is given, the retinoscopy results are more positive than the subjective refraction findings (>0.60D) and are more positive than the values obtained with an auto refractor (>1.75D).

Keywords: Accommodative excess; vision therapy; pseudomyopia; spasm of the near reflex; accommodative spasm.

1. INTRODUCTION

New technologies have changed the way of life in developed countries in the past 30 years. These technologies lead to higher use of visual functions overall at near distances. In addition, the use of screens (smartphones, laptops, computers, televisions, etc.) is present in both work and personal life and decreases the time spent outdoors using visual functions at far distances [1,2]. This fact could be related to an increase in the incidence of myopia in recent years, especially in urban environments [3-6], with an increase in asthenopia symptoms that are related to accommodative and vergence dysfunction [2,7,8].

It is believed that these dysfunctions are more frequent today and are related to the extended use of visual functions at near distances caused by the increase in the number of years spent at school or the increase in indoor activities [2,9-11]. Accommodative and vergence dysfunctions are the most common visual disorders in the pediatric population, with a prevalence higher than 30% depending on the study consulted [10,11]; the prevalence is between 13% and 30% in the higher education population [12-14], usually with symptoms at near distances that could affect academic results [9,13].

Accommodative excess (AE) is an accommodative dysfunction that is characterized by symptoms such as headache, asthenopia, blurred vision after completing tasks at near distances and other nonspecific symptoms [11,14,15]. AE has a prevalence that varies from 0.8% to 10% depending on the study population [10-14]. The definition of AE can be confused because some studies include the same diagnosis for AE, accommodative spasm and spasm of the near reflex [15,16].

This study follow the clinical criteria proposed by Scheiman & Wick because this is the criteria accepted by other authors [17]. AE could be defined as a condition in which the subject exerts more accommodation than required for the visual stimulus or is unable to relax after the accommodation [15].

Diagnosing AE can be difficult without cycloplegic drugs because many optometrists around the world usually do not use cycloplegic refraction. However, it is possible to find some clues from optometric exams that suggest a diagnosis of AE, such as variable visual acuity findings, variable static and subjective refraction findings, low monocular estimate method or fused cross-cylinder findings, low negative relative accommodation values, high positive relative accommodation values or failure of monocular and binocular accommodative facility with +2.00 Diopters (D) [13,14,18,19]; pseudomyopia is also considered a variable sign of accommodative excess [15].

In all accommodative and vergence dysfunctions, the first option of treatment must be refractive error prescriptions, even for mild refractive errors. If the dysfunction still persists, sometimes vision therapy can be the primary treatment method [16,17,20]. A correct diagnosis of accommodative or vergence dysfunction and a correct prescription for the refractive error are necessary to choose a suitable combination of exercises for vision therapy. A wrong combination of exercises could lead to the failure
of the vision therapy protocol, even when it is the first option for treatment [16,21]. The goal of vision therapy is to restore the balance in visual functions in order to lessen the symptoms during habitual visual activities [20].

For these reasons, the purpose of this study is to retrospectively assess AE cases to find a pattern from optometric exams to help in the diagnosis of AE without cycloplegic drugs. Furthermore, this study assesses the utility of the vision therapy protocol for the treatment of AE.

2. METHODOLOGY

2.1 Study Design

A retrospective study was conducted with patients who were between 7 and 30 years old; were diagnosed with accommodative excess; inclusion criteria were of visual acuity below 20/20 (Snellen chart) with the most positive subjective refraction findings without cycloplegic drugs after discard any pathology and completed the vision therapy protocol. To verify the accommodative excess diagnosis, a complete eye examination and binocular vision assessment were carried out, including a case-history reflecting the full range of symptoms presented by the patient, visual acuity tests, retinoscopy without cycloplegic drugs, autorefraction without and with cycloplegic drugs, refraction without and with cycloplegic drugs, fusion and stereopsis assessments, near and distance cover tests, near point of convergence (NPC) test, monocular and binocular vergence facility tests and accommodative function tests, considering the Scheiman & Wick criteria for AE [17]. The cycloplegic used was adequate instillation of cyclopentolate 1% drop in each eye.

Due to the retrospective nature of the study, some tests were not performed in all patients. Cycloplegic retinoscopy was replaced by cycloplegic autorefraction because it is faster than retinoscopy.

2.2 Materials and Procedures

Monocular and binocular visual acuity was measured under photopic conditions at a distance of 6 meters with the Snellen chart displayed in a CC100XP screen (Topcon, Japan) and recorded on a decimal scale to facilitate statistical analysis. Autorefractor readings were collected with KR8800 and TRK1P (Topcon, Japan). Retinoscopy was measured with a retinoscope Elite (Welch Allyn, USA) and phoropter VT-200 (Topcon, Japan) at a distance of 60 centimeters under scotopic conditions. Refraction was measured with a phoropter and the Snellen chart. Stereopsis was measured with a fusion of vectographic crosses at distance and with the TNO test (OOTECH Lameris, Holland) at a distance of 40 centimeters with red-green spectacles under photopic conditions. The cover test was measured at a distance of 6 meters with the Snellen chart and at a distance of 40 centimeters with the Snellen chart for near distance readings under photopic conditions; an esophoria (at far or near distance); or an exophoria at far distance value equal or above 3 prismatic diopters (Δ) or an exophoria at near distance above 6 Δ were considered out of the normal limits follow the Scheiman & Wick criteria for horizontal phorias. Accommodation facility was measured with flippers ±2.00 diopters at a distance of 40 centimeters under photopic conditions as cycles per minute. NPC was measured with a pen torch at a distance of 40 centimeters under photopic conditions [13]. Complete optometric exploration was carried out to verify the exclusion criteria: previous intraocular/strabismus surgery, ocular or head trauma and any systemic or eye pathology. Refraction value is not an exclusion criteria. Complete binocular vision exam was conducted during the first visit when the patients were diagnosed and during the last visit when the patients had finished the vision therapy protocol.

2.3 Vision Therapy Protocol

The vision therapy protocol was developed in the Ikusgune optometric center (Donostia, Spain). The protocol is organized into sessions and weeks, as shown in Table 1. This protocol has 8 sessions that could be extended to 12, if necessary. The sessions with the optometrist were 45 minutes, and the sessions at home were 4 to 5 times per week and 20 minutes each being supervised by their parents in patients under 14 years old with exercises taught by the optometrist.

2.4 Data Analysis

Statistical analysis was performed using SPSS 23.0 (SPSS, Chicago, Illinois, USA) for Windows. Nonparametric data distribution was verified with the Kolmogorov-Smirnov test (P > .05 indicated that the data were nonparametrically distributed). The results are presented as the means ± standard deviations (SDs) and 95% confidence intervals (CIs 95%).
Table 1. Vision therapy protocol organized by sessions and weeks with exercises with the optometrist and at home

<table>
<thead>
<tr>
<th>Session</th>
<th>Week</th>
<th>Session with the optometrist</th>
<th>Session at home</th>
</tr>
</thead>
</table>
| 1ª      | 1    | Four monocular exercises are taught and performed:  
1. - Positive lens with a dartboard with letters.  
2. - Dartboard with letters and Hart chart.  
3. - Marsden ball with negative lens.  
4. - Monocular flipper ±2.00 D with letter dartboard. | An information sheet is delivered with the necessary material to carry out the exercises. |
| 2ª      | 2    | The previous exercises are performed in order to verify that the patient is performing them correctly.  
Vergence facility exercises are taught and performed with computer applications, anaglyphs and Whetstone stereoscope. | Monocular exercises are maintained. |
| 3ª      | 4    | Monocular exercises are performed in order to verify that the patient is performing them correctly.  
The same vergence facility exercises are performed with computer applications, anaglyphs and Whetstone stereoscope. | Monocular exercises are maintained. |
| 4ª      | 6    | Accommodation facility control with the previous four exercises.  
The exercises are withdrawn if they are performed without difficulty. | Monocular exercises that are performed with difficulty are maintained and combined with binocular flippers and computer applications (Visionary®) for vergence facility improvement. |
| 5ª      | 8    | Exercises performed at home are checked. Exercises with apertures, vectograms and letters with transparent lens and prisms are performed. | The binocular flipper and monocular exercises are stopped if they are performed correctly. Central anaglyphs and computer applications (Visionary®) begin. |
| 6ª      | 10   | Previous exercises are checked, and Brock strings with prisms are added. | Central anaglyphs exercises are stopped. Apertures with flippers are included and the other exercises are maintained. |
| 7ª      | 12   | Aperture and vectogram exercises are performed with flippers. | Binocular exercises that are performed with more difficulty are maintained. |
| 8ª      | 14   | A complete optometric binocular vision evaluation is performed to assess the improvement of the visual system function. If the EA are solved is checked again in 3 months. If the problem persists, the vision therapy protocol is extended for 4 more sessions (two months). | If it is necessary to continue, the binocular exercises that are performed with more difficulty should be maintained. |
The exercises with which the patient has the most difficulty will be performed.

A complete eye examination and binocular vision assessment is performed to assess the improvement of the visual system function. If the EA are solved is checked again in 3 months. If the problem persists, the therapy is considered to be a failure and other treatment or professional help will be considered.
A Wilcoxon nonparametric paired test (P< .05 was considered significant) was used to compare the visual acuity results, autorefractor sphere values, retinoscopy sphere values, subjective refraction with and without cycloplegic sphere values and stereopsis findings achieved after the vision therapy protocol against the baseline values (diagnosis visit) (P< .05 was considered significant). Refractive astigmatism was not analyzed because only one patient had a significant astigmatism (> 1.00 D) and two patients had low astigmatisms of 0.50 D in both visits.

The effects of the refraction method findings, autorefractor sphere values, retinoscopy sphere values, and subjective refraction with and without cycloplegic sphere values were also assessed and compared with the Wilcoxon nonparametric paired test (P< .05 was considered significant).

3. RESULTS

Twenty-four patients with AE (21 women and 3 men) with an average age of 12.9 ± 5.3 years. The AE are considered the primary disorder or as a secondary disorder with convergence insufficiency as a primary disorder according to the Scheiman & Wick criteria for AE [17]. 6 patients with spectacle correction prior to the exam (spherical refraction between -5.75 D to +1.00 D) and 18 patients without correction were included in the retrospective study.

In the diagnosis visit, the results of the cover test at distance were within the normal limits for 95.83% of the patients. However, the results of the cover test at near fixation were out of the normal limits for 41.66% of the patients (25% esophorias and 16.66% exophorias >6 Δ). Moreover, patients with exophoria (70.83%) had NPCs that were farther from the normal value relative to their age (> 7 cm). [17]. The stereopsis was greater than 120° in 70.83% of the patients. In the last visit, after the vision therapy protocol was completed, the results of the cover test at near fixation were within the normal limits in 83.33% of the patients, with 4 patients who had low esophorias, with normal NPC and stereopsis ≤120°. Fourteen patients (58.33%) completed the vision therapy protocol in 8 sessions, and 10 patients completed the vision therapy protocol in 12 sessions (41.67%).

Table 2 shows the mean with the standard deviation and confidence interval (95%) of the sphere values obtained for the three refractions without cycloplegic drugs. The refraction value obtained with autorefractors was more negative than the value obtained with subjective refraction, and the subjective refraction result was more negative than the retinoscopy result. Furthermore, a pairwise comparison (Wilcoxon test) of the sphere values obtained in the three refraction methods without cycloplegic drugs (Table 2) found statistically significant differences (P< .001) between all of one method in the diagnosis visit. In addition, cycloplegic refraction values showed statistically significant differences (P< .001) from the refraction values obtained without cycloplegic drugs, but non-statistically significant differences were found between the refraction methods with cycloplegic drugs (P> .10). In the last visit, after the vision therapy protocol, a pairwise comparison of the sphere values obtained with the three refraction methods found non-statistically significant differences between subjective refraction and retinoscopy (P> .82) but showed differences between autorefractor and the other methods (subjective refraction and retinoscopy) (P< .02).

Table 3 shows the mean with the standard deviation, confidence interval (95%) and statistically significant differences (P< .001) in the sphere values from the subjective refraction, visual acuity test, NPC and stereopsis between the diagnosis visit and post-vision therapy protocol visit. Positive sphere values in the visit post-vision therapy confirms the decrease in accommodation, in agreement with the improvements to visual acuity that reached 6/6 or a superior value in 100% of the patients at the end of the vision therapy protocol.

4. DISCUSSION

Accommodative and vergence dysfunctions have seemed to be on the rise in recent years [9,11]. It is necessary to consider protocols for the screening of these dysfunctions. In addition, AE is an accommodative dysfunction that sometimes could be confused with myopia [15]. AE is usually characterized by symptoms associated with reading or close work such blurry vision at far distances, especially at the end of the day or after reading, difficulty focusing form far to near or headaches and eyestrain after close work [14,15].

Symptoms are clear in AE, for this reason a correct interview is important to suspect an AE diagnosis that is often obtained through refraction with cycloplegic drugs. However, this
study has found some clues from the eye exam that indicate AE dysfunction without cycloplegic refraction, such as a reduced NPC, reduced stereopsis, and retinoscopy findings that are more positive than subjective refraction findings (> 0.60 D) and are significantly more positive than autorefractor findings (>1.75D) \((P<.001)\), compared to other studies that evaluate the cycloplegic effect in patients without accommodative dysfunctions [22-24]. These differences in sphere values were reduced with cycloplegic drugs, and values < 0.50 D were used in all methods to measure the refraction. Moreover, in healthy people, these differences are small, as shown in the study by Jorge et al. [22] to estimate the role of the accommodative response between non-cycloplegia and cycloplegia in objective refraction (autorefraction and retinoscopy) for young adults (21.6±2.66 years). Their results show a spherical equivalent of 0.86 D with an autorefractor that is more positive with and without cycloplegic drugs. Other studies report minor differences of approximately 0.25 D (7-28 years old) between subjective refraction with and without cycloplegic drugs, including the study by Choong and Chen [25] or Kumar and Ghose [23] that had the same examination method as this study. Research

Table 2. Outcomes of the different refraction methods in diagnosis visit (prescription) and post vision therapy protocol

<table>
<thead>
<tr>
<th>Sphere value (D) Mean±SD (CI 95%)</th>
<th>Subjective refraction</th>
<th>Autorefractor</th>
<th>Retinoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis Visit</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without cycloptic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right eye</td>
<td>-0.53±1.57</td>
<td>-1.78±2.80</td>
<td>-0.01±1.47</td>
</tr>
<tr>
<td>With cycloptic</td>
<td>(-1.19 to +0.13)</td>
<td>(-2.98 to -0.58)</td>
<td>(-0.63 to +0.61)</td>
</tr>
<tr>
<td>Right eye</td>
<td>0.36±1.54</td>
<td>0.45±1.54</td>
<td>-</td>
</tr>
<tr>
<td>With cycloptic</td>
<td>(-0.28 to +1.01)</td>
<td>(-0.20 to +1.10)</td>
<td>-</td>
</tr>
<tr>
<td>P-value*</td>
<td>&lt; .001</td>
<td>&lt; .001</td>
<td>-</td>
</tr>
<tr>
<td>Without cycloptic</td>
<td>-0.56±1.57</td>
<td>-2.02±3.09</td>
<td>0.00±1.54</td>
</tr>
<tr>
<td>Left eye</td>
<td>(-1.23 to +0.10)</td>
<td>(-3.33 to -0.71)</td>
<td>(-0.65 to +0.65)</td>
</tr>
<tr>
<td>With cycloptic</td>
<td>0.40±1.51</td>
<td>0.44±1.49</td>
<td>-</td>
</tr>
<tr>
<td>Left eye</td>
<td>(-0.24 to +1.03)</td>
<td>(-0.19 to +1.07)</td>
<td>-</td>
</tr>
<tr>
<td>P-value*</td>
<td>&lt; .001</td>
<td>&lt; .001</td>
<td>-</td>
</tr>
</tbody>
</table>
| P-value*: refraction with and without cycloplegic; D: diopters; SD: Standard deviation; VT: Vision therapy

Table 3. Outcomes for diagnosis visit and post vision therapy protocol (mean ± standard deviation and 95% confidence interval) with their differences

<table>
<thead>
<tr>
<th>Test</th>
<th>Diagnosis visit Mean±SD (CI 95%)</th>
<th>Post-VT visit Mean±SD (CI 95%)</th>
<th>Difference Mean±SD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sphere Right Eye (D)</td>
<td>-0.53±1.57 (-1.19 to +0.13)</td>
<td>0.10±1.42 (-0.50 to +0.71)</td>
<td>0.64±0.88</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Subjective refraction</td>
<td>-0.56±1.57 (-1.23 to +0.10)</td>
<td>0.14±1.39 (-0.45 to +0.72)</td>
<td>0.70±1.00</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Sphere Left Eye (D)</td>
<td>0.84±0.29 (0.72 to 0.97)</td>
<td>1.07±0.10 (1.03 to 1.11)</td>
<td>0.23±0.26</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>VA Right Eye</td>
<td>0.80±0.29 (0.68 to +0.93)</td>
<td>1.05±0.09 (1.02 to 1.09)</td>
<td>0.25±0.28</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>(Snellen 6m)</td>
<td>(0.75 to 1.01)</td>
<td>(1.14 to 1.20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VA Binocular VA</td>
<td>0.8±0.30 (0.8+0.93)</td>
<td>1.17±0.08 (1.02 to 1.09)</td>
<td>0.29±0.31</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>NPC (cm)</td>
<td>12.25±9.64 (+8.18 to +16.32)</td>
<td>6.71±1.49 (+6.08 to +7.34)</td>
<td>-5.54±8.95</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Stereopsis (*)</td>
<td>279.17±322.27 (+147.31 to +411.03)</td>
<td>69.17±41.28 (+51.74 to +86.60)</td>
<td>-218.33±305.77</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

D: diopters; VA: Visual acuity; SD: Standard deviation; NPC: Near point of convergence; VT: Vision therapy
about subjective refraction with and without cycloplegic drugs is limited. The outcomes showed that after a vision therapy protocol, the pairwise comparison found statistically significant differences between autorefractors and the other methods (subjective refraction and retinoscopy) \( (P < .02) \), but these differences are not clinically significant because they are close to 0.30 D.

Other studies do not find a relationship between stereopsis and NPC with AE \[13,14,19\] and NPC could be related to convergence insufficiency \[14,19,26\], which can appear as secondary to accommodative excess \[14,15\]. The outcomes show that half of the patients had exophoria at near distances with an NPC >8 cm; this value is related to convergence insufficiency, which in some cases could exist for patients with AE who are using accommodation to get the convergence needed for near distances. Regardless, patients with AE usually have pseudomyopia that can be verified with objective and subjective refraction \[15\], and cycloplegic refraction is advised for patients whose excessive accommodative response affects the refractive error measurement \[20\].

The diagnosis of accommodative and vergence dysfunctions depends on the symptoms of the patient and some clinical findings. For many patients, a great battery of tests is necessary to ensure the diagnosis of the dysfunction, taking into account that a typical refractive examination excludes the majority of the tests associated with vergence and accommodative dysfunctions. For this reason, optometrists should systematically complement their daily routine with a test that is associated with the detection of accommodative and vergence dysfunctions. The selection process for this test should be elaborate through evidence-based practice \[14,16\]. This study shows a pattern in the sphere values of the different refraction methods and some tests, such as stereopsis, NPC and phoria values that could be altered with the diagnosis of AE or convergence insufficiency.

### 4.1 Vision Therapy Protocol

The AE treatment was the same vision therapy protocol for all patients. This protocol is specific for AE and consists of 8 sessions with the optometrist (45 minutes), and it includes exercises that the patient must do at home (20 minutes at day). Some patients needed four more sessions to restore the balance of the visual system. All patients showed better values (more positive NPC, stereopsis, VA and sphere values) in the eye exam at the end of the vision therapy protocol with statistically significant differences \( (P < .001) \) than in the diagnosis visit, as shown in Table 3. Most of these values were considered important in the AE diagnosis and assessment of the visual function balance recovery by other studies \[14,19\].

Vision therapy is a controversial treatment. Some studies show that vision therapy is an effective treatment for accommodative dysfunction \[11,21,26-29\]. However, Martinez et al. \[30\] conducted a review in this field that included studies from 1986 until 2007 and concluded that previous studies are not rigorous enough to demonstrate that vision therapy is an effective treatment for accommodative dysfunctions. Traditionally, Scheiman and Wick \[17\] recommended a vision therapy protocol with 12 to 24 sessions at the office with home maintenance therapy, depending on the severity of the dysfunction. Nevertheless, Ciuffreda reviewed some studies related to vision therapy in accommodative dysfunctions and found that the treatment length should be less than twelve weeks \[21\].

Currently, research on vision therapy is focused on vergence dysfunctions, although accommodative dysfunction can occur in 60% to 80% of patients with accommodative and vergence dysfunctions \[20\]. Studies on vision therapy for accommodative dysfunctions focus on accommodative insufficiency and infacility \[21,26,30\]. Few studies report the use of vision therapy for AE; thus, this study has a relatively larger sample size and shows the vision therapy efficacy for AE.

### 4.2 Study Limitations

This study has some limitations. This study was a retrospective pilot study with a small sample size. These outcomes should be validated with another sample in a prospective study that includes a control group. Moreover, this future study should include some tests that are considered important in AE, such as cycloplegic retinoscopy, monocular and binocular accommodative facility, monocular estimate method, vergence tests and negative relative accommodation, to analyze the variation before and after the vision therapy protocol.

It was not been possible to analyze the effect of astigmatism because few patients had
astigmatism; however, AE should only affect the sphere values of the refraction, and this interpretation has a better clinical translation than vectorial representations of astigmatism.

5. CONCLUSION

Variations in the sphere values could be clues for accommodative excess if a double condition is finding: the retinoscopy is more positive than the subjective refraction finding (>0.60 D) and more positive than the finding obtained with autorefractors (>1.75D); support to correctly diagnosis of accommodative excess, a complete eye examination, including binocular vision assessment would be necessary.

This vision therapy protocol has demonstrated its effectiveness because all patients showed improvements in their visual acuity, stereopsis result, near point of convergence and accommodation function. Vision therapy should be the first option in the treatment of accommodative excess, as long as the patient has the commitment to perform the exercises at home, and the exercises have achievable objectives.

CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline participant consent and ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


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