THE EUROPEAN SOCIETY OF MEDICINE
Medical Research Archives, Volume 12 Issue 7

RESEARCH ARTICLE

Horizontal Incomitance and Anisocoria in Congenital Esotropia

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OPEN ACCESS

PUBLISHED
31 July 2024

CITATION
Gallegos-Duarte, M., Mendiola-Sántibañez, J., et al., 2024. Horizontal Incomitance and Anisocoria in Congenital Esotropia. Medical Research Archives, [online] 12(7). https://doi.org/10.18103/mra.v12i7.5403

DOI
https://doi.org/10.18103/mra.v12i7.5403

ISSN
2375-1924

ABSTRACT

Introduction: When exploring horizontal version movements, the pathways integrating Slow Eye Movements (SEMs) are analyzed, and when exploring pupil behavior, the pupillary pathway is analyzed. In healthy patients, the horizontal version trajectory is concomitant and the difference in size between both pupils is usually not significant, however, in Congenital Esotropia (CE), differences can be significant.

Objective: Identify if the type of horizontal incomitance is related to the degree of anisocoria in CE.

Materials and Methods: A prospective, cross-sectional, and experimental study was conducted on patients diagnosed with CE from Querétaro, Mexico. Infrared Video-oculography was performed under scotopic conditions (0.3 lux). Signs of congenital stigma such as Dissociated Vertical Deviation (DVD) and Latent Nystagmus (NL) were sought; likewise, the type of Horizontal Incomitance (IH) was classified according to motor behavior. Pupil area was measured using Voxel-based morphometry (VBM) and anisocoria was classified. The results were statistically analyzed.

Results: 53 patients aged 5 to 14 years were recruited: 22 boys and 31 girls. 21 patients presented with DVD and 25 with NL. All patients showed abduction limitations to varying degrees. IH had an incidence of 0.698, NL 0.471, DVD 0.396, Passive Horizontal Incomitance (PHI) 0.377, Active Horizontal Incomitance (AHI) 0.320, and No Horizontal Incomitance (NHI) 0.301.

Discussion: Both anisocoria and incomitance occur in CE. It is the first time the type of horizontal incomitance has been related to the degree of anisocoria. The analysis suggests a relationship between anisocoria and the type of incomitance, establishing differences between forms with and without Ciancia of CE. This contributes to decision-making and guides diagnosis, as well as prognosis.

Keywords: Anisocoria, congenital esotropia, methods, Horizontal Incomitance

Introduction

Eye movements represent one of the most complex interactions of the central nervous system [1]. The pathways integrating Slow Eye Movements (SEMs) are analyzed when exploring horizontal version movements. Physiologically, these movements are governed by laws and controlled at three different neurological levels: the prefrontal cortex, responsible for fine eye movements and voluntary tracking [2], the superior colliculus, responsible for saccades, and finally, the brainstem.

In healthy patients, the horizontal version trajectory is constant and occurs without limitations; however, in CE, the eye that moves from inside to outside travels more slowly than the eye that moves from outside to inside [3-5]. Abduction is usually limited, and nystagmus is present at the end of the movement [6,7]. Analyzing these events allows for a better understanding of the nature of the problem [8].

SEMs can be clinically evaluated by comparing the movement between both eyes during the horizontal version maneuver, that is, slowly moving the gaze from left to right and vice versa (Figure 1). The difference in speed can be observed more accurately through Electrooculography (Figure 2) or Video-oculography (Figure 3) [3,4,6].

In CE, dissociated movements and latent nystagmus are present, which, along with abduction limitation, constitute the congenital stigma of the disease [9,10]. Nystagmus in CE increases in intensity when looking outward according to Alexander's law [11], while it decreases when the eyes turn inward. In this position, not only does the intensity of nystagmus decrease, but also the oscillation and visual confusion [7]. Therefore, the patient tends to rotate the head to maintain a stable image, thus keeping the fixing eye in esotropia and, on the other hand, limiting abduction to reduce nystagmus shaking. This characterizes the Ciancia syndrome, a variety of CE whose deviation is constant and does not vary over time or distance, hence the type of incomitance presented is constant and is called Passive Horizontal Incomitance (PHI) [12,13].

In Mexico, a distinct form of presentation in CE has been identified, which differs from the Ciancia syndrome and is referred to as the 'non-Ciancia' subtype [10]. In these cases, the patient does not rotate the head, there is a pseudo limitation to abduction, the horizontal version movement shows variations in speed and amplitude [3-6,10], and the angle of presentation varies with time and distance, hence it is called Active Horizontal Incomitance (AHI) [4,10,14].

A third group consists of patients with CE who do not manifest incomitance or it is very discreet, hence it is called No Horizontal Incomitance (NHI) [4,10].

Based on the above, three forms of incomitance have been identified during the horizontal version maneuver: PHI, AHI, and NHI [4,5,10].

Furthermore, the presence of anisocoria in children with CE has been described, and its predictive value has been evaluated to determine whether it is a dissociated variety or not [15-18].

The purpose of this study is to identify if the type of horizontal incomitance present in CE is related to the degree of anisocoria.

Materials and Methods:

A prospective, cross-sectional, and experimental study was conducted on a cohort of children from Querétaro, Mexico, diagnosed with CE.

All patients underwent an analysis of eye movements using digitized infrared Video-oculography during the horizontal version maneuver [18]. The study was conducted under mesopic and scotopic conditions (0.3 lux) with infrared light, always maintaining visualization of the light reflex on the cornea through infrared light (Figure 1) [5,19].

Each patient was asked to look at a non-luminous stimulus placed 50 cm away. The stimulus was then slowly moved from left to right and vice versa to stimulate horizontal version movements at a constant speed in the horizontal plane (Figures 1 and 2).

The Video-oculography were analyzed by the same observer who classified Horizontal Incomitance based on the motor behavior observed during the horizontal version maneuver.

Variability in the angle of presentation and the degree of abduction limitation were measured to identify the presence and type of incomitance in motor behavior, whether active or passive (Figure 4).

The presence of Latent Nystagmus (LN) and Dissociated Vertical Deviation (DVD) was identified as these clinical signs, along with abduction limitation, are the most characteristic of the congenital stigma [9,10].

Images were frozen when the patient was looking in the primary gaze position to determine the value of anisocoria by measuring the mathematical difference between the pupil area of both eyes under scotopic conditions of 0.3 lux. The obtained images were processed using the JImage program, and the area of each pupil was calculated separately using Voxel-based morphometry (VBM) and expressed in pixels [18].

The relationship between the type of horizontal incomitance and the degree of anisocoria was statistically analyzed. The results obtained are shown in graphs.

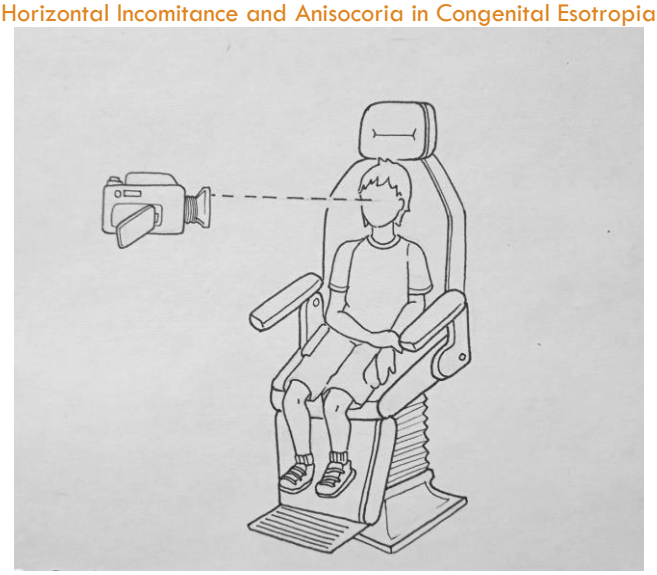

Figure 1.

Video-oculography was performed while maintaining attention in a neutral environment and under scotopic lighting conditions of 0.3 lux. Each patient was asked to look at a white target in front of them to measure anisocoria, and then they were asked to follow an object moving horizontally slowly from left to right and vice versa. The following were used as measurement instruments: a digital camera with infrared light placed at 2 m in manual focus, an opaque and translucent occluder, a fixation object at 50 cm, white, and 5 mm in diameter.

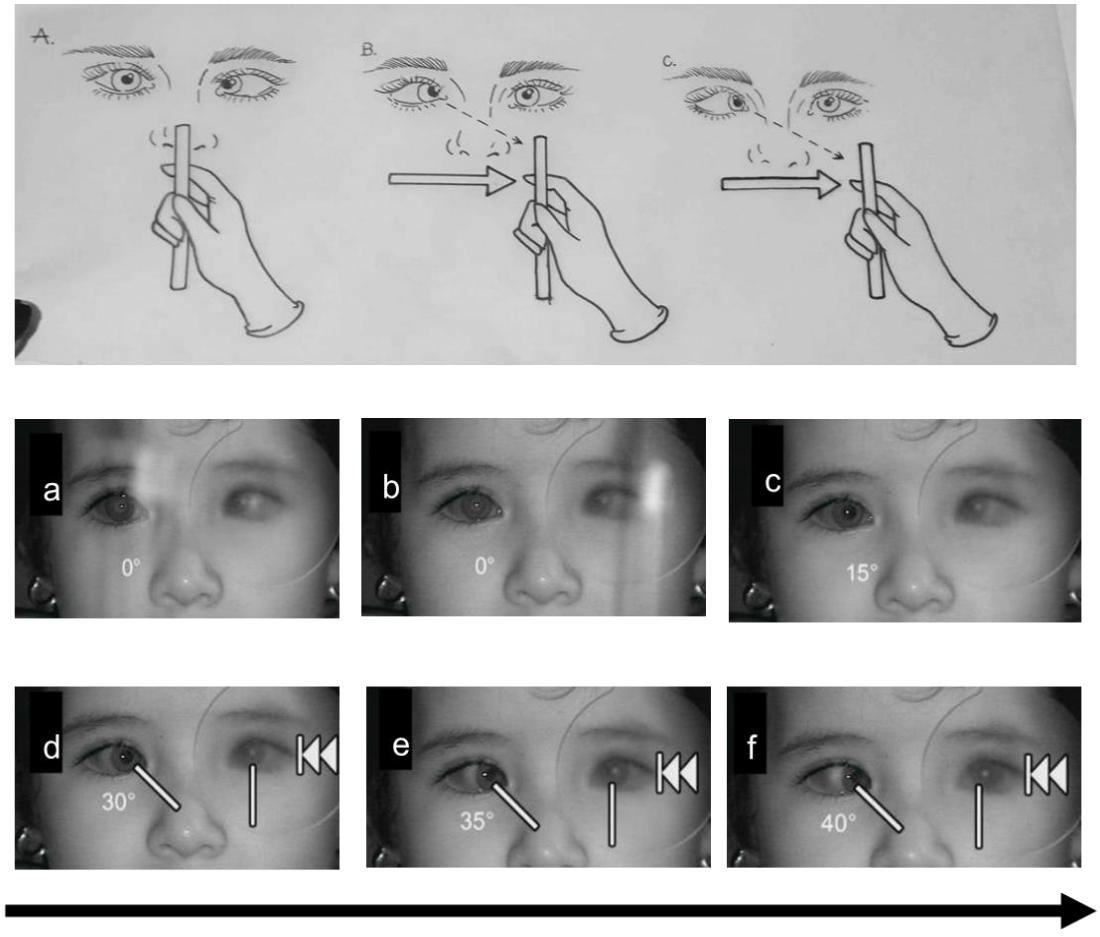

Figure 2.

Graphic explanation of the movement of the fixing eye during the horizontal version maneuver. Below, the photographic sequence shows a 6-year-old girl with CE following an object moving horizontally with her right eye, while the left eye remains occluded with a translucent Spielman occluder.

It can be observed that the left eye remains still (a, b, and c) when the right eye has already traveled 15° of arc (d). At 30°, 40°, and 50°, the right eye, it can be observed that the left eye has barely reached a forward position (d, e, and f) while the movement of the left eye outward is limited [20].

Figure 3.

The sequence shows the position of the eyes during the horizontal version maneuver under scotopic conditions: 1) Dextro version, 2) gaze forward position, 3) Levo version. Note the frontal electrode for Electrooculographic recording (1, 2, and 3) and the translucent Spielman occluder placed transversely to identify lateral gaze nystagmus (1).

Statistical analysis was performed using SPSS Statistics software (v. 20, SPSS Inc.). Also, the GraphPad PRISM v.8 was utilized to render figures. Descriptive statistics were obtained for the total sample. One way ANOVA and the Kruskal-Wallis test were employed for comparisons among groups, according to the data distribution. The Tukey pairwise Comparisons and the Dunn's multiple comparison test were used as post hoc tests. The Shapiro-Wilk test was used to determine data distribution. A p-value of <0.05 was considered to indicate statistical significance.

Results

A total of 53 cases were obtained: 22 patients were boys and 31 were girls. The minimum age was 5 years, and the maximum was 14 years, with a mean age of 8.22.

Three forms of motor behavior were observed: 20 cases presented Passive Horizontal Incomitance (PHI), 17 presented Active Horizontal Incomitance (AHI). In 16 patients, no significant Horizontal Incomitance (NHI) was observed.

Through Video-oculography, it was observed that all patients presented different degrees of abduction limitation, as well as lateral gaze nystagmus, while Horizontal Incomitance (HI) had an incidence of 0.698, Latent Nystagmus (LN) 0.471, Dissociated Vertical Deviation (DVD) 0.396, Passive Horizontal Incomitance (PHI) 0.377, Active Horizontal Incomitance (AHI) 0.320, and No Horizontal Incomitance (NHI) 0.301 (Table 1).

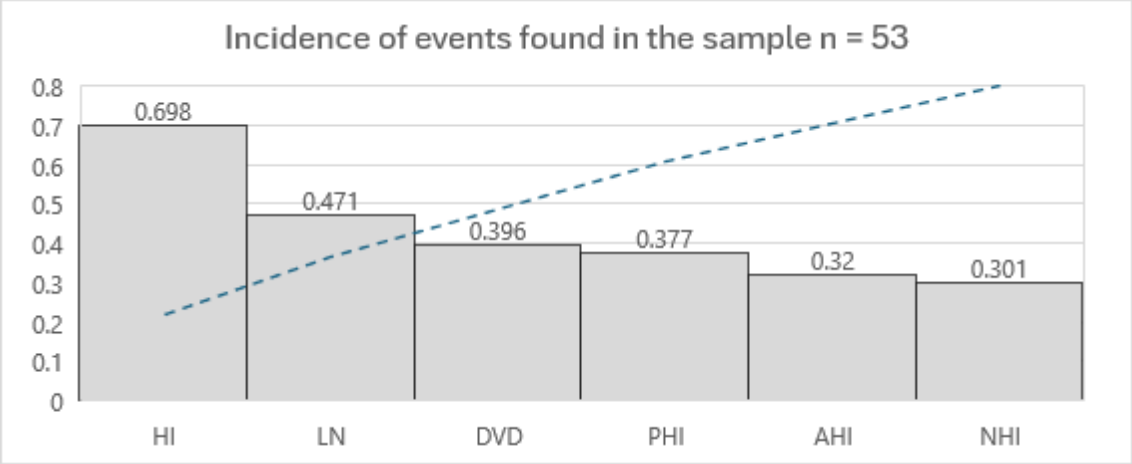

Table 1.

At the top of each column, the incidence of events found in the analyzed sample is displayed. At the bottom of each column, the initials of each of the clinical manifestations found are displayed: Horizontal Incomitance (HI), Latent Nystagmus (LN), Dissociated Vertical Deviation (DVD), Passive Horizontal Incomitance (PHI), Active Horizontal Incomitance (AHI), and No Horizontal Incomitance (NHI) 0.301.

Furthermore, according to the area of anisocoria expressed in pixels, 4 groups were obtained according to their significance: a) non-significant (from 396 to 3096 pixels), b) Slightly significant (from 3096 to 5796), c) Significant (from 5796 to 8496), and d) Very significant (from 8496 to 13896) (Table 2).

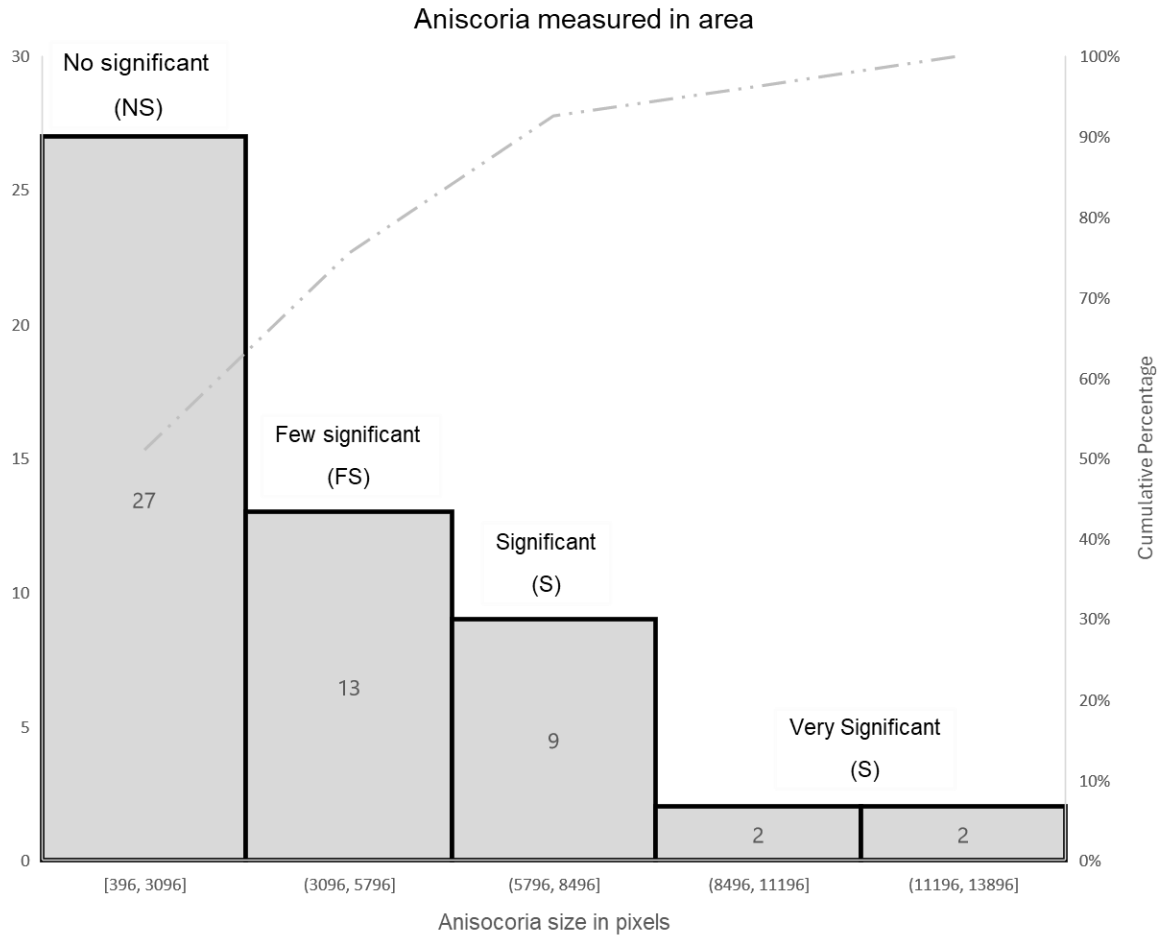

Table 2.
Above each column, the meaning of anisocoria is displayed. The value of anisocoria is expressed in pixels at the bottom of each column. The number of cases is displayed in the body of the column.

Meanwhile, the Kruskal-Wallis correlation analysis displays a significant relationship (p = <0.0001) between anisocoria and the 3 groups of horizontal incomitance (Table 3).

Parameter	PHI (n =20)	AHI (n = 16)	NHI (n = 16)	* *P*-value
Mean ± (SD) Range CI 95%	1760±393-5 5990 3041-4689	3498±847.9 12118 3984-7579	1882±470.5 7334 696.9-2703	<0.0001

Table 3. Parameters obtained.

When comparing the three groups of Horizontal Incomitance using the Tukey test, a statistically significant difference was found between the PHI group and the NHI group (Figures 4 and 5).

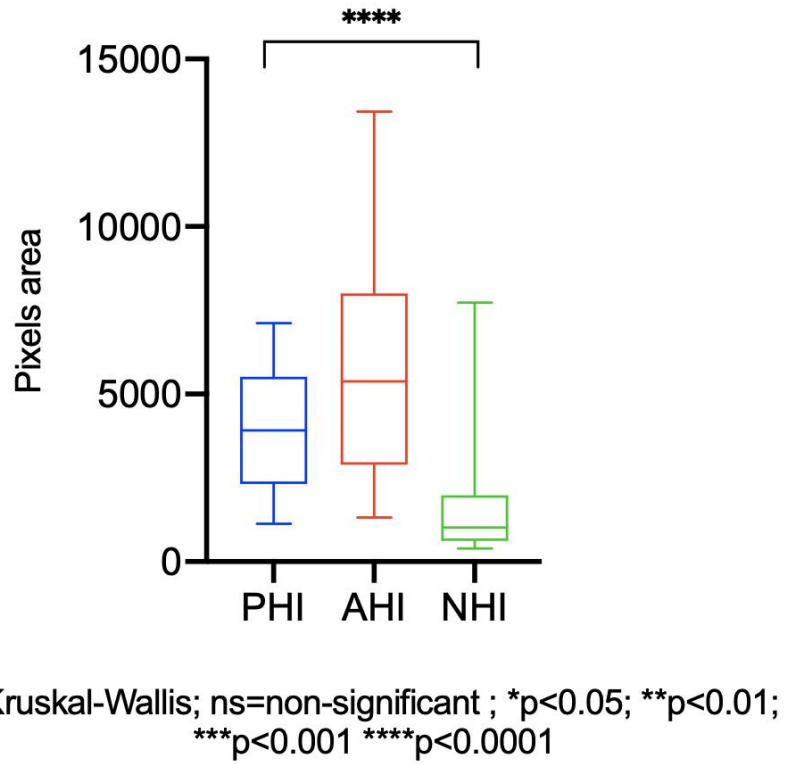

Figure 4. A significant difference (P= 0.0001) was found among groups, evidencing a higher pixels area for the AHI group.

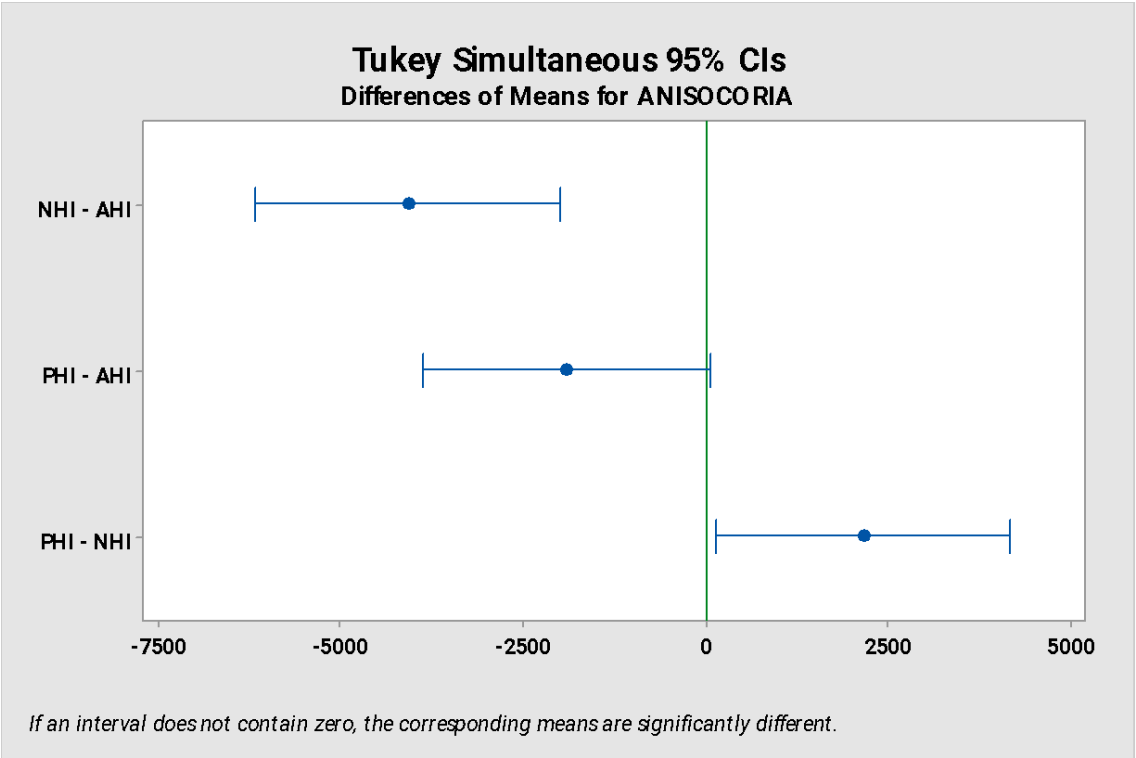

Figure 5. Tukey Pairwise Comparisons Using the Tukey Method and 95% Confidence. A significant difference (P= 0.01) was found between the PHI and NHI groups.

Regarding anisocoria expressed in pixels, it was more significant in the AHI group (Figure 6).

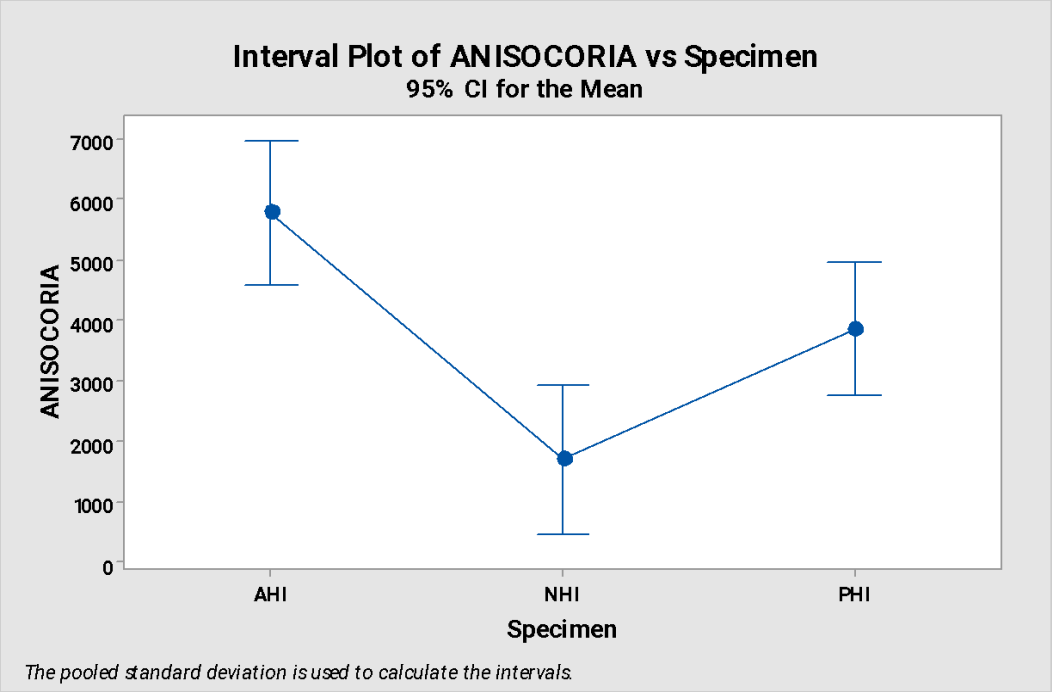

Figure 6. The most significant anisocoria measured in pixels obtained a mean of 5782 in the group of patients with AHI, 3865 pixels in the group of patients with PHI, and 1700 for the NHI group.

Discussion

Until recently, it was thought that congenital strabismus (CS) was of unknown cause. However, by demonstrating that both the pupillary reflex and the vergence reflex are altered, it indicates that, in some way, both the cortical integrator and the mesencephalic integrator may have difficulties in the proper control of these reflexes [26,27].

To understand the pathophysiology of congenital esotropia, it is important to recognize those clinical signs that prove the involvement of the cerebral cortex. One way to demonstrate this is to identify the changes in oculomotor dynamics that occur in this disease [4,5,10].

Traditionally, congenital esotropia (CE) has been classified based on the accommodative phenomenon[23–25]. However, recently a different classification has been proposed, based on the motor behavior observed during the slow movement of horizontal version. This classification has proven useful in differentiating between the Ciancia and non-Ciancia forms of the disease[10,18].

The importance of this study lies in the fact that it is the first time the type of horizontal incomitance has been related to the degree of anisocoria identified under scotopic conditions. The analysis suggests that the combination of both elements helps establish a more precise diagnosis and strengthens the thesis that there is an underlying cortical alteration in the disease.

CE is characterized by alterations in eye position as well as in the dynamics of their movements. A "nasotemporal asymmetry of horizontal pursuit" and an asymmetry of the Look optokinetic nystagmus (OKN) have been reported in both macaques and humans with CE [21,22].

The dynamics of saccadic movements are also altered in these patients, but their analysis is beyond the scope of this study. Traditionally, CE is classified based on the accommodative phenomenon. However, a different classification has recently been proposed based on the motor behavior observed during slow horizontal version movement. This classification has shown its usefulness in differentiating between the Ciancia and non-Ciancia forms of the disease [18,26,27].

Since anisocoria represents a neurological sign, it should always be investigated. Anisocoria in CE also helps differentiate between a dissociated and non-dissociated form of the disease [15,17,18]. In the present analysis, 26 out of 53 patients had anisocoria, of which half, that is, 13 children, had significant or very significant anisocoria.

When comparing the degree of anisocoria among different types of incomitance, it was observed that anisocoria was most significant in patients with AHI, moderately significant in patients with PHI, and insignificant in patients without horizontal incomitance.

In a previous study, the importance of measuring anisocoria under scotopic conditions using the area calculated in pixels instead of using the conventional method based on perimeter was highlighted [18]. Therefore, it was investigated whether the anisocoria obtained using the area method is a method that allows validating the classification of CE based on motor behavior during horizontal version movement [10].

The results are encouraging in the quest to establish greater precision in the classification of CE by contributing to distinguish one form of Ciancia from another non-Ciancia form as well as between a dissociated or non-dissociated strabismus, using more sophisticated and precise measurement methods for research purposes [18].

The data obtained from the exploration of SEMs through video-oculography, together with the measurement of anisocoria in pixels, was relevant. It is expected that this methodology will allow for more precise surgical guidelines to avoid unwanted results [28] and contribute positively to a better understanding of the pathophysiology of this disease that affects 2-4% of children worldwide [4,10,29].

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