Independent Risk Factors for Type III Acute Acquired Concomitant Esotropia: A Matched Case-Control Study

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Abstract

Background: Acute acquired concomitant esotropia (AACE) is a relatively rare subtype of esotropia that can develop in older children (>5 years) and adults. The etiology of AACE is unknown, but there have been case studies describing risk factors. This study applied multiple regression analysis to explore risk factors and the impact of this subtype's surgical design esotropia and to gain insights into pathogenesis.

Methods: Patients with Type III AACE and healthy controls, who were matched for age (±5 years) and refractive diopter (±1 D), were included in this study. All patients were treated between March 2018 to September 2020. We collected information on the number of hours spent performing near work per day, whether the patient wore glasses, and the refractive diopter of both the eyes. We also determined the deviation angles at both near- and far-vision in these individuals. Additionally, we measured the distance from the medial rectus insertion to the limbus in surgical patients.

Results: Patients (n=51) with Type III AACE and sixty healthy control persons (n=60) were included in the study. We found that 99.96% of cases and 91.67% of controls had myopia. Among them, 60.8% of cases and 20.0% of controls did not wear glasses for near work. Twelve cases were treated with a prism, and thirty-nine were treated surgically. The average time devoted to near work per day was 7.24±1.91 (range: 4-12) hours and 3.7±1.29 (range: 2-7) in cases and controls, respectively. In univariate and multivariate logistic regression models, Type III AACE was significantly associated with increased hours of near work per day and near work without wearing glasses.

Conclusions: Increased hours of near work per day and myopic patients performing near work without glasses are independent risk factors of Type III AACE. A satisfactory result can be obtained by optimizing the foot correction with the maximum and the most stable angles before operation.

Introduction

Acute acquired concomitant esotropia (AACE) is a relatively rare subtype of esotropia that can develop in older children (> 5 years), adults, and older adults [1–3]. Burian and Miller [4] in 1958 defined three main types: (1) Type-I AACE (Swan type) occurs due to the disruption of fusion precipitated by monocular occlusion or impaired vision in one eye; (2) Type-II AACE (Burian-Franceschetti type) is defined by large deviation, mild hyperopia, and minimal accommodative element. Type-II AACE may be associated with physical or mental stress; (3) Type III AACE (Bielschowsky type) has unique clinical features that were first reported by Bielschowsky, having onset after adolescence in myopic patients. The esodeviation is usually small at the beginning and present only at distance fixation. Diplopia also appears at near vision as the disease progresses. The incidence rate of Type III AACE is the highest and has dramatically increased due to excessive near work during the COVID-19 lockdown [5]. Type III AACE affects the appearance and causes uncomfortable diplopia, which significantly reduces the quality of life and can even damage visual function.

The exact mechanism underlying this prevalent type of AACE is not fully understood. Several potential risk factors for Type III AACE have been proposed, including fusion dysfunction and disruption, esophoria, myopia, and anatomical structures [1–3, 6–8]. However, uncorrected myopia as a risk factor for Type III AACE is still controversial. Von Graefe et al. [4, 9, 10] holds that the uncorrected myopic individual tends to hold materials excessively close to the eyes, resulting in an imbalance between the converging and diverging forces of the eyes. Celeste Ruatta(2) did not deem uncorrected myopia as the genesis of Type III AACE because their patients usually wore corrective glasses. To date, the sample size of risk factor studies has been relatively small. Most are case series reports and do not provide evidence to explain this problem.

In this study, we designed a retrospective analysis of the clinical characteristics of patients with Type III AACE who were matched by age and diopters to controls. We applied multiple regression analysis to explore risk factors and the impact of this subtype's surgical design esotropia and to gain insights into pathogenesis.

Methods

Patient population

For our retrospective case-control study, we identified our cases from patients with Type III AACE treated in our hospital between March 2018 and September 2020. The patients were followed for more than six months. Our data were extracted from a review of their records. The study conformed with the Declaration of Helsinki and obtained Institutional Review Board approval at the First Affiliated Hospital of Fujian Medical University (IRB No. [2015] 084-1). Informed consent was obtained from the patients or their guardians before operation. The inclusion criteria of the AACE group were: (1) type III AACE with the diplopia presenting at far fixation at the beginning, (2) patient more than five years old, (3) corrected visual acuity greater than 20/25 for both eyes, (4) normal eye movement, (5) normal brain MRI, blood glucose, blood pressure, thyroid function, and neostigmine tests results, and (6) no history of systemic diseases, head injury, neurology, ophthalmic surgery, and strabismus during infancy. The time of close work (≤30cm) which including mobile phone, computer and non-video display terminal (non-VDT) work per day and whether wore glasses in doing the above work were carefully recorded. We identified individuals without AACE to match as cases to age (±5 years) and refractive diopter (±1 D) as the control group. The same senior physician provided the diagnosis, surgical design, and conducted follow-up for all patients.

Clinical tests

All cases underwent cycloplegic refractive error assessment. Patients over 12 years old were given 0.5% tropicamide, while patients under 12 years old were given 1% atropine eye ointment. First, the Hirschberg test was performed to observe the corneal light reflex. Next, we performed the alternate prism cover test for near for all directions of gaze, and (33 cm) and distance (6 m) fixation. We increased the base-out prisms until an exotropia occurred. We then gradually decreased the prism up to the power at which the

eye did not move, which was the objective deviation of esotropia and recorded the significant findings as PD. The simultaneous perception was evaluated with Bagolini glasses. Fusion was assessed with synoptophore; near stereopsis was assessed with the Titmus test.

Treatment

Cases were divided into two groups: a prism correction group (n=12, deviation ≤ 15PD) and a surgery group (n=39, deviation > 15PD). Patients underwent either a unilateral (non-dominant eye) or bilateral medial rectus muscle recession for deviation < 40 PD. A unilateral medial rectus resection combined lateral rectus resection for deviation ≥ 40 PD, or a bilateral medial rectus recession and unilateral lateral rectus resection for deviation > 90PD. Patients who could cooperate for the operation received surface anesthesia combined with local infiltration anesthesia. Cases that opted not to have general anesthesia were anesthetized with intravenous injection of a small dose of sedative and analgesic drugs administered by an anesthesiologist. The distance from the medial rectus insertion to the limbus was measured with a caliper before the muscle was cut. Intraoperative adjustable sutures were placed as a loose knot was tied on the muscle. The case was seated with appropriate refractive glasses for near and distance targets.

Treatments were defined as success when esophoria was ≤8PD after the treatment, and both near and distant diplopia was resolved. The follow-up period was at least six months, and the angle of deviation, diplopia, and visual function were measured at the follow-up visits.

Statistical analyses

SPSS version 26.0 (IBM SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. The age and spherical equivalent between the AACE group and the control group were compared by Wilcoxon signed-rank test. The difference in pre-and post-treatment angle of deviation and visual function was evaluated by the Fisher exact test. The risk factors of Type III AACE were analyzed by univariate and multivariate logistic regression models. $P < 0.05$ was considered statistically significant.

Results

Baseline features

The AACE group included fifty-one patients; thirty-five males (66.7%) and seventeen females (33.3%), with a mean age of onset was 26.94±10.41 (range: 11-56) years. The mean duration of diplopia was 22.85±27.49 (range: 0.1-132) months. Diplopia presented at a distance fixation in the beginning and was more evident than near. Sixty patients were in the control group: thirty-one males (57.9%), twenty-nine females (48.3%). The mean time of near work per day was 7.24±1.91 (range: 4-12) and 3.7±1.29 (range: 2-7) hours in the AACE and control group, respectively. The difference in age and spherical equivalent between the AACE and control groups was no significant (P > 0.05). The comparison of clinical factors between the AACE and control groups was listed in Table 1.

Surgical outcomes

In the AACE group, twelve patients were treated with a prism, and thirty-nine patients were treated with surgery. Deviations and visual function were significantly different pre-and post-treatment ($P < 0.05$); the results are presented in Table 2. Only one patient had long-term near work for more than 10 hours per day after the operation, and his condition recurred one year later. The success rate of the operation was 99.97%. The mean distance from the medial rectus insertion to the limbus was 4.68±0.54 (range:3-5.5) mm in patients treated with the operation.

Risk factors

Single factor logistic regression analysis showed that increased hours of near work per day and near work without glasses were individually associated with increased risk of Type III AACE ($P<0.05$) (Table 3). Multiple logistic regression analysis revealed that the increasing hours of close work per day ($\beta=1.947$, $P<0.001$) and near work without glasses ($\beta=3.007$, $P <0.05$) were independent risk factors for AACE. (Table 4). The comparison of the importance of risk factors in AACE as list in Figure 1.

Discussion

To the best of our knowledge, this is the first case-control study to report the risk factors of Type III AACE. Our study has the most participants in an experimental design, while previous studies were mostly a series of case reports.

Type III AACE is an acquired esotropia that mainly occurs after five years of age, once the visual function has matured [1]. In the present study, the youngest patient was 11 years old, and the oldest was 56 years old. All cases had unique features, such as sudden onset esotropia and horizontal ipsilateral diplopia, an equal angle of deviation in all gazes, without ocular movement abnormality, without paralysis of extraocular muscles, intermittent at the beginning, diplopia only appears at distance fixation. As the disease progresses, diplopia also appears at near fixation, which is represented in the previous reports. Another interesting phenomenon is that all cases did not exhibit anisometropia. We suggest that this is explained by both eyes having the same amount of convergence and divergence, which may result in a more susceptible onset. Normosensorial people overcome ipsilateral diplopia caused by esophoria through negative fusion. If negative fusion is insufficient, esophoria is decompensated, and diplopia occurs. In this study, we analyze the relationship between convergence and divergence to explore why the risk factors lead to Type III AACE.

Multiple logistic regression revealed that uncorrected myopia in near work is an independent Type III AACE risk factor. Because of the strong collinearity between the spherical equivalent and the time of close work per day, the spherical equivalent of myopia was not included in the multiple logistic regression model. Our study found that forty-nine cases (99.96%) were myopic. Thirty-one cases (60.8%) did not wear glasses while performing near work, indicating that uncorrected myopia in near work is one of the leading causes of AACE. The pathogenesis may be an esophoria that existed before the onset of AACE.

Myopic patients with glasses at near fixation can develop accommodative convergence by gradually increasing the distance of the visual target from far to near. At the same time, the patient can develop the ability to diverge. However, stimulative accommodation and accommodative convergence would be reduced if individuals with myopia do not use glasses while performing near work. The ability to diverge is also reduced in those conditions. Esophoria is more likely to be decompensated and lead to diplopia.

Prolonged near work is a separate independent risk factor for Type III AACE. Excessive near work leads to persistent convergence; divergent fusional amplitudes, which are not sufficient to compensate for the deviation; and esophoria, which decompensates at distance fixation. This can explain why diplopia presents at distance fixation at the beginning and is more obvious than near fixation. On the other hand, long-term near work also can lead to persistent tension in the medial rectus, which will evolve into spasticity, denaturation, fibrosis, and is similar to the “rein effect.” Zheng [7] found that the patients with Type III AACE spent a prolonged period performing tasks requiring near vision, ranging from 6–13 hours per day, with a median of 12 hours before the onset of double vision. In that study, seven patients underwent a pathological examination of their lateral rectus muscles, showing that there were no muscle fibers but rather collagenous fibers. The medial rectus can't relax effectively, and the esotropia occurs when the divergent function is unable to compensate.

In the present study, the mean distance from the medial rectus insertion to the limbus was 4.68±0.54 (range: 3-5.5) mm in cases that involved operation. Cai [6] also found that the distance from the insertion location to the limbus of the medial rectus was 4.8±0.4mm in AACE. We suggest that because the medial rectus insertion in Type III AACE patients is more forward than that in unaffected people, the tension of the medial rectus muscle is increased at near fixation. Esotropia is more likely to develop due to the interrupted balance between convergence and divergence.

AACE may be associated with neurological diseases. Some researchers believe that the etiology of AACE may not be related to the risk of intracranial lesions. However, delayed esotropia is still the first symptom of cerebellar tumors in many cases [1]. Buch [11] analyzed forty-eight children and confirmed that AACE of childhood had a small but significant association with intracranial disease. They found that onset older than six years of age, papilledema, a significant angle deviation at a distance (>40%), and the recurrence in a hyperopic child are risk factors for AACE with intracranial disease. It is recommended that every AACE patient should be screened for nervous system diseases. We found no cases of neurological disorders in our study.

The treatment of AACE includes prismatic correction and binocular single vision train, injection of botulinum toxin, and surgery. In this study, thirty-nine cases involved treatment with surgery. The purpose of the operation is to correct esotropia, eliminate diplopia, and motor function, and recover sensory function. However, the optimal design for the operation is controversial. Wan and Savino [12, 13] hold that the target deviation is difficult to correct accurately, and there is a tendency of recurrence after the operation because of the “eating-prism phenomenon.” Ali [8] argued that an additional 10 PD augments the residual esophoria in most AACE cases and the surgical target angle. We suggest that the operation

should be fully corrective and designed according to the maximum preoperative angle. The satisfactory ocular position is exophoria at distance and esophoria at near vision.

The following three proposals aim to reduce surgical under-correction and find the full latent deviation. The angle of strabismus needs to have multiple measurements at different times before operation. The surgical plan would then be designed using the largest and most stable angle. Prism adaptation is another effective measure. We use press-on prisms according to the distance deviation, and the patient wears this prescription for 1-2 weeks. If there is a residual esotropia, the strength of press-on prisms can be increased, followed by another 1-2 weeks adaptation period would be needed. The repetitive process would continue until the power of the prism is stable. The surgical plan relies on the full prism-adapted power. Intraoperative adjustable sutures are also very effective, allowing the use of significant local anesthesia to achieve adjustment of ocular position during operation.

In conclusion, multiple factors are associated with Type III AACE. Increased hours of near work per day and myopic patients close to near work without glasses are independent risk factors. A satisfactory result can be obtained by optimizing the foot correction with the maximum and most stable angles before operation.

This study had some limitations. This was a retrospective analysis, and the hours of near work were imprecise, as they depended on patients' recall. The sample size was relatively small, and the follow-up time was not long enough to observe some complications. In the future, prospective research should be performed to address these limitations.

Abbreviations

AACE: Acute acquired concomitant esotropia; D: diopter; MRI: Magnetic Resonance Imaging; PD: prism diopter; N, number.

Declarations

There were no competing interests in authors.

Ethics approval and consent to participate:

The study conformed with the Declaration of Helsinki and obtained Institutional Review Board approval at the First Affiliated Hospital of Fujian Medical University (IRB No. [2015] 084-1). Informed consent was obtained from the patients or their guardians before operation.

Consent for publication:

Not applicable

Availability of data and materials:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests:

None

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None

Authors' contributions:

WZ designed the study. JZ and JC collected and analyzed the data from the patients. SM and LH prepared the tables and figures. JC, JZ, and LH contributed to writing the manuscript. WZ reviewed and approved the final manuscript published. All authors were involved in the discussion of the manuscript throughout the study period. All authors read and approved the final manuscript.

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Not applicable

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Tables

Due to technical limitations, table 1-4 is only available as a download in the Supplemental Files section.

Figures

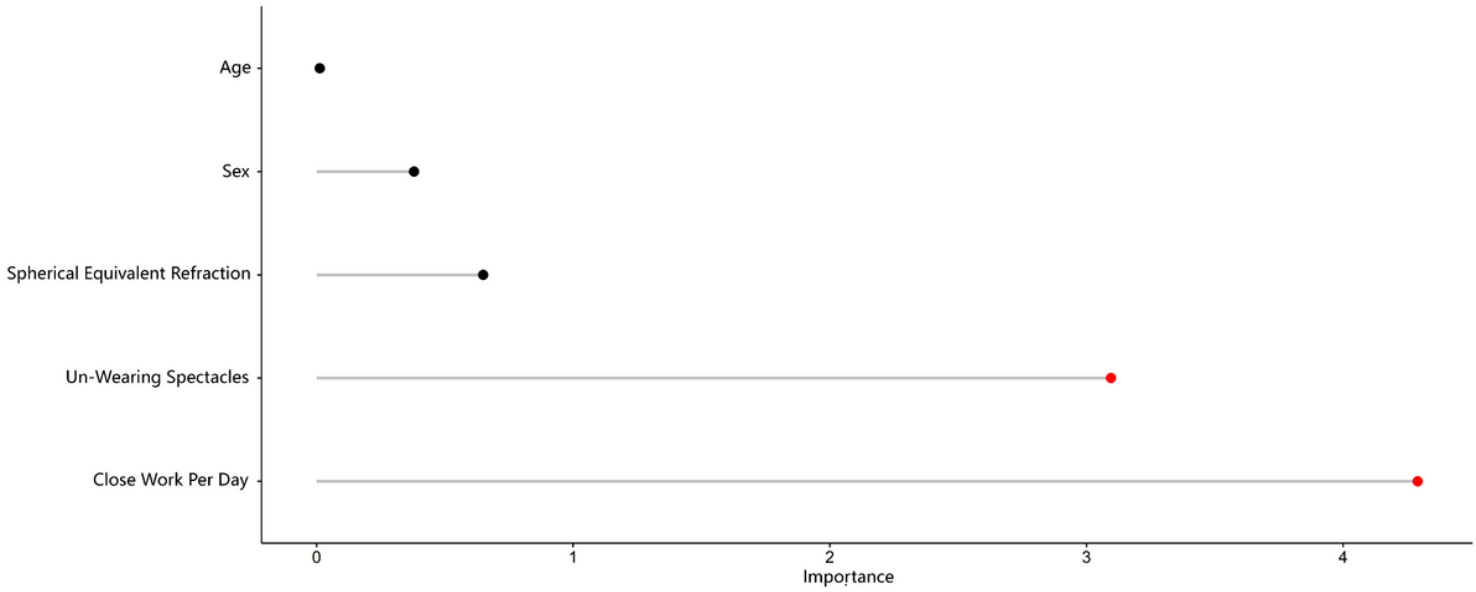

Figure 1

Comparison of the importance of risk factors in AACE: age, sex, spherical equivalent refraction, failure to wear glasses, and amount of near work per day. The red dot represents the difference with statistical

significance, as shown in Table 4

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.pdf
- Table2.pdf
- Table3.pdf
- Table4.pdf