Clinical Research

Clinical features and treatment of near-work-related acquired esotropia

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Abstract

• **AIM:** To investigate the characteristics of near-workrelated esotropia and the clinical efficacy of botulinum toxin type A (BTXA) injection therapy on it.

• **METHODS:** A total of 107 patients aged 15-57y with near-work-related esotropia were taken as the BTXA-treated group, and 30 other peers without near-work-related esotropia were included in the control group. All participants were refractive corrected to analyse the clinical characteristics of near-work-related esotropia. All subjects were examined including Worth4 spot examination, stereoscopic vision, strabismus angle, accommodative convergence to accommodation ratio (AC/A), far and near positive and negative convergence, positive and negative fusion range, positive and negative relative relative accommodation. Clinical efficacy was evaluated at a period of 10mo follow-up.

• **RESULTS:** The distant and near stereopsis were found in 84.9% and 77.5% of patients in the BTXA-treated group, respectively. In the control group, all patients had distant and near stereopsis. The incidence of taking off one's glasses to see close objects was significantly higher in the BTXA-treated group than in the control group (P<0.05). The BTXA-treated group showed a smaller range of infusion (9.84±5.72)° than the control group (22.04±8.71)° (P<0.05). The near esotropia angle of the BTXA-treated group (17.08±11.98)^{\triangle} was significantly smaller than the distant esotropia angle (19.07±11.68)^{\triangle} (P<0.05). Ten months after injection, the diplopia and esotropia of most patients underwent improvements after treatment (P<0.05). • **CONCLUSION:** This study reveals that the accommodation function and the habit of near work without wearing spectacles are associated with near-work-related esotropia, while the length of time for near work and the onset time are independent of near-work-related esotropia. Additionally, BTXA injection therapy plays a vital role in relieving diplopia and restoring eye position.

• **KEYWORDS:** esotropia; near-work; botulinum toxin; accommodation; electromyography

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INTRODUCTION

A cute acquired comitant esotropia (ACE) has a large impact on binocular visual functions of patients. It is common among juveniles and adults^[1]. Diplopia develops suddenly in most patients who also show esotropia without symptoms of ophthalmoplegia or organic lesions. This kind of esotropia usually has a certain binocular visual function^[2]. Diplopia refers to the abnormal phenomenon of two images appearing when two eyes look at one object, which is caused by deviation of the visual axis and projection of the object image onto the macular fovea of one eye and the area outside the fovea of the other eye^[3-6].

With the development of society and the widespread popularity of portable electronic devices, the number of ACE patients has increased. Most of these patients suffer from distant diplopia, with mild or asymptomatic near symptoms that can be relieved after rest. They spend long periods using mobile devices, which eventually results in constant diplopia. This kind of ACE is temporarily being called near-work-related esotropia^[7]. There have been few reported studies on esotropia, and its mechanism remains unknown, including its relation with the duration of near vision, dioptre, accommodation and convergence as well as the difference in binocular visual function, accommodation and convergence amplitude between patients and normal people. This study intends to explore the causes of the occurrence and development of this kind of esotropia and evaluate the therapeutic efficacy of botulinum toxin extraocular muscle injections by analysing the differences

in accommodation and convergence, binocular vision and other functions between these patients and normal people.

SUBJECTS AND METHODS

Ethical Approval This study was conducted following the Declaration of Helsinki and was approved by the Ethics Committee of Beijing Tongren Hospital affiliated with Capital Medical University. All participants signed their informed consent.

Subjects In this study, from April 2015 to November 2018, 107 patients with near-work-related esotropia who were treated in Beijing Tongren Hospital affiliated with Capital Medical University were recruited as participants in the experimental group. Another 30 peers without near-work-related esotropia were included in the control group

Inclusion and Exclusion Criteria Inclusion criteria: 1) bestcorrected visual acuity ≥ 1.0 ; 2) no history of prior esotropia or systemic disease; 3) seeing distant complexes was the first symptom, diplopia is horizontal ipsilateral, and the distance between objects in all directions is equal; and 4) near vision $\geq 4h$ per day (distance between the eyes and the object ≤ 30 cm). Exclusion criteria: 1) patients with other systemic diseases; 2) patients with incomplete data.

Methods The general ophthalmological testing included refraction, best-corrected visual acuity, slit-lamp and fundus exams. The patients' primary characteristics were collected, such as their age, sex, time of onset, main symptoms and occupation. At the same time, the patients' medical history, daily duration of close distance (\leq 30 cm) eye use and habit of taking off glasses to see near objects.

To assess the effect of the treatment from the standpoint of the patients, each participant needed to subjectively assess the severity of their symptoms at each visit before and after treatment on a scale from zero to four. With higher scores, the patients experienced more diplopia: 0 meant no diplopia, neither distant nor near; 1 indicated occasional diplopia only at a distance; 2 meant occasional diplopia, both distant and near; 3 suggested diplopia most of the time; and 4 indicated diplopia in the distance and near all the time (diplopia score 0:4).

For the patients and normal participants over 18 years of age, manifest refraction was performed; for those under 18, cycloplegic refraction with 1% tropicamide was performed first, followed by post-cycloplegic refraction the next day to get the final endpoint. The following data were measured after completing the refractive correction: adjustment amplitude (negative lens method), positive and negative relative accommodation (PRA and NRA, respectively), accommodative convergence to accommodation ratio (AC/A; gradient method), distant and near-horizontal squint angle (prism alternating cover test and Von Graefe method), distant and near-horizontal imaging function, binocular vision function and stereopsis (Worth four-point lamp, Synoptophore and Titmus near stereopsis).

Treatment Botulinum toxin type A (BTXA; Hengli, Lanzhou Institute of Biological Products) injection is a freeze-dried crystalline product; there are 100 units per bottle, where one unit is a 50% lethal dose in a mouse, which is equivalent to 0.04 ng^[5]. All patients were injected with BTXA in the medial rectus of both eyes. Alcaine surface anaesthetic (0.5%) was used before injection. Under the guidance of an EMG magnifier, a monopole needle-like electrode was used for the medial rectus of both eye injections. The dose of each injection was recorded. All patients were reexamined ten months after treatment.

Statistical Analysis The software program SPSS 22.0 (IBM, Chicago, USA) was used to conduct the statistical analysis. The continuous variables of normal distribution were expressed as the mean±standard deviation, the continuous variables of non-normal distribution were expressed as the median (interquartile range), and the categorical variables were expressed as the frequency (%). For two comparisons, each value was compared by a *t*-test when the data conformed to the normal distribution, while the non-normally distributed continuous data were compared using non-parametric tests. The counting data were tested by the Chi-square test. A value of P < 0.05 was considered statistically significant.

RESULTS

General Characteristics A total of 107 patients were included in the experimental group: 52 males (48.6%) and 55 females (51.4%). The average age was 31.06 ± 10.64 (range 15-57)y. There were 30 participants in the control group: 17 females (56.67%) and 13 males (43.33%). The average age was 32.1 ± 7.97 (range 16-53)y. There was no significant difference in age (*P*=0.825) or sex (*P*=0.61) between the two groups (Table 1).

Refraction According to the measurements, the recruited patients did not have presbyopia, and the influence of refractive error was excluded in the patients with glasses. So, both factors could be excluded. After the examination, only 2 of the 107 patients in the experimental group had remarkable overcorrection of myopia, while no remarkable overcorrection of myopia was observed in the control group.

The results of this study showed that the refraction of the two groups conformed to a normal distribution. In the experimental group, the refractive error was -3.63 ± 2.56 D in the right eye and -3.61 ± 2.39 D in the left eye. There was no significant difference in the refraction between the left and right eyes. In the control group, the refractive error was -2.80 ± 2.56 D in the right eye and -2.61 ± 2.39 D in the left eye. There was no significant difference between the two eyes. There was also no significant difference in the refraction between the two groups (Table 2).

Habit of Taking off Glasses to See Near Objects In this study, 79.5% of the patients in the experimental group had a habit of taking off their glasses to see near objects, and 3.2% of the patients in the control group had the same habit. The rate of this habit in the experimental group was significantly higher than that in the control group (P=0.00; Table 3).

Comparison of Accommodation Parameters The results exhibited that the AC/A was $(3.97\pm1.66)^{\triangle}/D$ in the experimental group and $(3.20\pm1.15)^{\triangle}/D$ in the control group (*P*=0.089; Table 4). In the experimental group, the NRA was 2.18±0.61 D in the right eye and 2.25±0.64 D in the left eye; the NRA of both eyes was 2.37±0.73 D. In the control group, the NRA was 2.21±0.44 D in the right eye and 2.18±0.43 D in the left eye; the NRA of both eyes was 2.28±0.40 D (Table 5). It is worth noting that there was a significant difference in the PRA between the two groups (Table 6). In the experimental group, the PRA was -2.59±2.15 D in the right eye and -2.53±2.19 D in the left eye; the PRA of both eyes was -2.27±2.17 D. In the control group, the PRA was -4.21±1.93 D in the right eye and -4.37±1.87 D in the left eye; the PRA of binoculus was -3.73±1.45 D.

The range of ex-fusion was $(-6.49\pm4.22)^{\circ}$ in the experimental group and $(-6.77\pm1.81)^{\circ}$ in the control group (*P*>0.05). The infusion range was $(9.84\pm5.72)^{\circ}$ in the experimental group and $(22.04\pm8.71)^{\circ}$ in the control group (*P*=0.000). The fusion range in the experimental group was smaller than that in the control group (Figure 1).

In the near-work-related esotropia group, 84.9% of the patients had far stereoscopic vision, 15.1% had no distant stereoscopic vision, 77.5% had near stereoscopic vision, and 22.5% had no near stereoscopic vision. In the control group, the number of people with far and near stereopsis was 100%, and there was a significant difference. Distant stereopsis was found in 84.9% of patients in the experimental group; 15.1% of the patients had no distant stereopsis. Additionally, 77.5% of patients had near stereopsis and 22.5% had no near stereopsis in the experimental group. In the control group, all patients had distant and near stereopsis. Based on the above data, the difference between the two groups was statistically significant.

Clinical Follow-up The follow-up results showed that in the near-work-related esotropia group, the duration of looking closely was (9.26 ± 2.97) h, the onset time was (21.13 ± 20.68) mo, the near esotropia angle was $(17.08\pm11.98)^{\triangle}$, and the distant esotropia angle was $(19.07\pm11.68)^{\triangle}$, demonstrating the significant difference between the distant and near squint angles (*P*<0.05). Twenty-seven patients received the BTXA injection treatment. The diplopia score was 3.57 ± 0.39 before treatment and 0.47 ± 0.64 after treatment, which evidenced that the diplopia symptoms of most patients improved. Ten months after treatment, the squint angles of distant and near vision were

 Table 1 General information of age distribution in the near-workrelated esotropia group and the control group

Group	Cases	Male:female	Age range (y)	Mean±SD
Near-work-related esotropia	107	52:55	15-57	31.06±10.64
Control	30	13:17	16-53	32.1±7.97

 Table 2 Refaction in the group of near-work-related esotropia and the control group
 mean+SD

the control group			mean±5D
Group	Right eye	Left eye	Р
Near-work-related esotropia	-3.63 ± 2.56	-3.61±2.39	0.903
Control	-2.80 ± 2.56	-2.61±2.39	0.301
Р	0.120	0.051	

Table 3 Habit of taking off glasses to see near objects of near-

work-related e	esotropia	group and	control	group
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Group	Taking off glasses to see near objects	See near objects without taking the glasses off	Р
Near-work-related esotropia	79.5%	20.5%	0.00
Control	3.2%	96.8%	

Table 4 Comparison of AC/A in near-work-related esotropia

group and control group		me	an±SD, [△] /D
Group	AC/A	t	Р
Near-work-related esotropia	3.97±1.66	1.179	0.089
Control	3.20±1.15		

Table 5 Comparison of NRA values in near-work-related esotropia

group and control group			mean \pm SD, $^{\triangle}$ /D
Group	Right eye NRA	Left eye NRA	Binocular NRA
Near-work-related esotropia	2.18±0.61	2.25±0.64	2.37±0.73
Control	2.21±0.44	2.18±0.43	2.28 ± 0.40
Р	0.837	0.594	0.544

NRA: Negative relative accommodation.

Table 6 Comparison of PRA values in near-work-relate	ed esotropia
groun and control group	mean±SD

Stoup and control Stoup			mean=0D
Group	Right eye PRA	Left eye PRA	Binocular PRA
Near-work-related esotropia	-2.59±2.15	-2.53±2.19	-2.27±2.17
Control	-4.21±1.93	-4.37±1.87	-3.73±1.45
Р	0.001	0.00	0.001

PRA: Positive relative accommodation.

 $(4.07\pm3.86)^{\triangle}$ and $(1.93\pm2.86)^{\triangle}$, respectively. The difference between the pre-treatment and post-treatment values was statistically significant (*P*<0.05).

After 10mo of treatment, the diplopia and esotropia of most patients had improved after treatment (P < 0.05).

DISCUSSION

In the clinical trial, we noticed that the patients were able to describe their symptoms very clearly and precisely; some even listed the specific dates when they were or were not symptomatic. They were well educated and generally anxious. Additionally, convergence spasm, which is often provoked by fixation at near, is associated with certain psychiatric

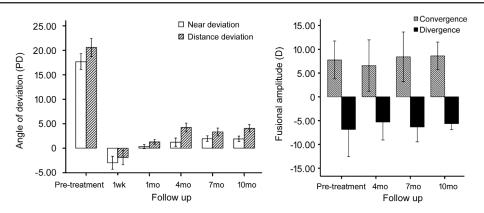


Figure 1 Follow-up results of fusion range after botulinum toxin injection.

conditions^[8]. This made us believe that there might be some predisposing psychological factors to near-work-related esotropia. We then attempted to qualify the personality trait of perfectionism in this group using a scale from 0 to 4, with higher scores tending toward perfectionism (self-serious level score 0:4).

The results of this study revealed that 84.9% of patients in the experimental group had distant stereopsis. Additionally, 77.5% of patients had near stereopsis in the experimental group. In the control group, all patients had distant and near stereopsis. The results showed that there were significant differences. Of the patients with near-work-related esotropia, 89.72% had ametropia of more than -1.0 D. These patients needed little or no accommodation when looking closely at something, but more convergence was still needed to achieve better proximal binocular vision that led to the occurrence of tonic convergence, visual proximity convergence and fusional convergence^[9]. This made the patients unable to relax when adjusting their vision, resulting in distant-look diplopia. In this study, 79.5% of the patients with near-work-related esotropia had a habit of taking off their glasses to see nearby objects, as did 3.2% of the participants in the control group. There was a significant difference between the two groups. Therefore, it was speculated that taking off glasses to see nearby objects is one of the determinants inducing the onset of this kind of esotropia^[10-11]. Most of the patients with ACE suffered acute onset, especially young people and adults^[12-14]. Most patients had good binocular vision before the onset of esotropia and abnormal binocular retinas after the esotropia affected their stereoscopic vision^[15]. Therefore, this examination demonstrated that the visual function of the patients was affected by esotropia. However, several studies have shown that there is no significant correlation between the time of onset and the prognosis of stereoscopic function.

Normally, accommodation of 1 D could cause a set of 3-5 prism dioptors of convergence (AC/A: 3-5)^[16]. The data of the two groups were in the normal range. There was no significant difference between the two groups, but the AC/A of the

experimental group was slightly higher than that of the control group. Although some studies have shown that the AC/A is constant over one's lifetime^[17], it is still worthy of long-term observation.

The PRA and NRA can indirectly evaluate the ability of image sets. The NRA refers to the ability to adjust and relax when a set is fixed, while the PRA refers to the ability to increase the adjustment reserve when a set remains unchanged. If the relative adjustment ability is strong, then the imaging set is large; if the relative adjustment ability is weak, then the imaging set is small. In this study, the PRA of the experimental group was significantly lower than that of the control group, but there was no significant difference in the NRA. According to Yekta et al^[18] mean NRA and PRA is +2.08±0.33 and -2.92±0.76 D in an Iranian young adult population. The maximum expectable normal NRA could be up to +2.5 D, but the maximum PRA depends on different factors. The PRA is usually stopped at -2.5 D by the examining physician to balance the PRA and NRA values, though the true value of the PRA could be even higher^[19]. The NRA of our results was in the same range, while the PRA was higher; this might depend on age, dioptre, gender and other factors^[20]. The PRA in the experimental group was significantly lower than that in the control group. When the binocular set was fixed, the accommodation of the eye increased or decreased separately, and the imaging set was used instead of the accommodative set to maintain the binocular vision, which was called relative adjustment. Combining these results for the NRA and PRA values, it was speculated that patients with a low regulatory reserve for a lengthy period of using near vision experienced a retinal defocus phenomenon, induced regulation and regulatory collection, resulting in esotropia. At the same time, the smaller PRA indirectly reflected the poor imaging aggregation ability of the patients, which was consistent with the symptoms of diplopia^[21].

The range of in-fusion in the experimental group was significantly smaller than that in the control group, but the ex-fusion results showed no significant difference between the two groups. Previous studies have proven that the scope of convergence is negatively related to the encouragement, examination sequence, distance and focal length. This study's results discovered that the fusion range of the experimental group became smaller and that the esotropia angle became larger. The fusion range of the patients with near-work-related esotropia was reduced, and the imaging set was insufficient. Therefore, it was necessary to mobilise other fusion functions, such as tension collection, which resulted in poor eye position control and esotropia, and the binocular visual function of some patients was damaged. The follow-up results of this study showed that there was a significant difference between the distant esotropia angle and the near esotropia angle in the experimental group. This feature was similar to 'divergence insufficient esotropia^{,[14]}. It has been speculated that long-term close vision may lead to medial rectus spasm, which causes the eye position to change when looking far away, bringing about changes in the farsighted eye position, abnormal location of the retina and diplopia^[22].

In this study, all patients suffered from long-distance diplopia, initially long-term close vision after long-term diplopia, which can be relieved after rest and eventually developed into continuous hypermetropia and even diplopia with the aggravation of the course of the disease. Twenty-seven patients received a BTXA extraocular muscle injection. Ten months after treatment, most patients had ameliorated diplopia symptoms. There was also a significant difference in the esotropia angle between ten months before and after treatment, which indicated that the BTXA played an important role in treating the esotropia and reducing the diplopia symptoms. It was confirmed that this kind of esotropia is associated with medial rectus spasm^[23-25]. Ten months after surgery, the diplopia and esotropia of most patients presented an improvement after treatment. The remission of symptoms after the extraocular injection of BTXA could certify this conclusion.

However, this study was a retrospective study. According to the data, we found that there were differences in the aspect of the accommodation function between the patients and the general population. The differences could explain some of the symptoms of the patients, such as esotropia and diplopia, but were insufficient to prove that the accommodation function defect provoked the esotropia or that the esotropia led to the anomaly of the accommodation function. These specific conclusions need further confirmation by prospective cohort studies.

There were still several limitations in this study. First, this study was a case-control study, not a randomised controlled trial. Second, this study was a single-centre clinical study with a small sample size. It is necessary to enlarge the sample size across multiple centres. Third, the clinical follow-up was of short duration. Longer follow-up observation is still needed. In conclusion, this study evidenced that the regulation function and the habit of taking off one's glasses when looking closely are related to near-work-related esotropia; however, the length of time spent looking closely at something and the onset time have nothing to do with it. Therefore, near-work-related esotropia may be inhibited by regulation function training in the early stage of this disease. Additionally, BTXA injections play a significant role in relieving diplopia and restoring eye position.

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