Chinese Medical Journal®

Efficacy of initial dose botulinum toxin A injection in acute concomitant esotropia with different clinical characteristics

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To the Editor: Acute concomitant esotropia (ACE) is an acquired esotropia with a sudden appearance and no pathologic changes on cerebral imaging. There are various treatments for ACE, including extraocular muscle surgery, botulinum toxin A (BTA) injection, prisms, and divergence training.[1] BTA had been used in the treatment of ACE since it was approved by Food and Drug Administration (FDA, USA) in 1989.[2] Some researchers have confirmed that its effect is stable and has unique advantages in the treatment of ACE, such as less trauma, shorter anesthesia time and earlier intervention, etc.[3]

However, previous researches have primarily compared the efficacy of BTA injection versus extraocular muscle surgery, leaving a lack of standard guidelines and expert consensus regarding its specific clinical applications. The initial dose of BTA is 1.25–2.50 IU/mL in its instructions.[1] But it is unknown whether the initial dose could achieve a satisfactory effect for ACE with different clinical features.

The main purpose of this study is to observe the efficacy of the initial dose of BTA in the treatment of ACE with different angles of deviation and durations of disease, and to explore relevant factors that may affect the efficacy.

We selected the ACE patients without other eye diseases that received the BTA injection for the first time at the Eye Center of the First Affiliated Hospital of Zhengzhou University from June 2018 to June 2021. This study was approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University (No.2021-KY-0699-003). Informed consents of subjects were exempted because this is a retrospective study.

All patients have completed routine ophthalmological examinations and professional examinations for strabismus. Unilateral injections of BTA (Onabotulinum toxin A, Botox, 2.5 IU/mL) were made into the medial rectus muscles. Collected cases were grouped by preoperative angles of deviation and durations of disease, respectively. The angles of deviation were measured at 1, 2, 3, and 6 months after the injection. A successful operation was characterized by the angles of deviation ≤10 prism diopters (PD) at 6 months after the injection. The median value of deviation, success rate, and incidence of complications of each group were evaluated.

Continuous variables were represented by median (Q1, Q3) and analyzed by Kruskal–Wallis test and Bonferroni correction. Categorical variables were expressed in frequency and percentage, and the comparison was carried out using a Chi-squared test. The difference is statistically significant with P <0.05, and P <0.017 is statistically different through multiple-testing correction.

A total of 57 patients were selected, including 40 males and 17 females. The age was 3–25 years with a median PD value of 6.00 (4.00, 12.00). The distribution of deviation was +20 PD to +85 PD at a 33 cm distance and +20 PD to +80 PD at a 6 m distance, the median values of which were +60.00 (40.00, 65.00) PD and +50.00 (35.00, 65.00) PD, respectively, with no statistically significant difference (P = 0.909) [Supplementary Table 1, http://links.lww.com/CM9/B586]. Prism at near was selected as the evaluated index. The patients were grouped by the preoperative angles of deviation (<+50 PD: n = 20; +50 PD to <+70 PD: n = 27; ≥+70 PD: n = 10) and the durations of disease (<3 months: n = 18; ≥3 to <6 months: n = 24; ≥6 months: n = 15).

The success rate in this study was 70% (40/57). At 6 months post-injection, the median angle of deviation was +5.00 (0.00, 22.00) PD of all cases, which was significantly smaller than that of +60.00 (40.00, 65.00) PD before the injection (P <0.001).

Among different angles of deviation groups, there was no statistically differences in median angles of deviation at 1, 2, 3 months after injection (P = 0.213, 0.094, 0.090). At 6 months post-injection, the median angles of deviation were +3.50 (0.00, 5.00) PD, +5.00 (0.00, 26.25) PD,

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000002728

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Chinese Medical Journal 2023;136(18)
Received: 11-01-2023; **Online:** 26-05-2023; **Edited by:** Jing Ni

and +35.00 (5.00, 70.00) PD, respectively. There was a statistically significant difference between <+50 PD group and ≥+70 PD group ($P = 0.006$). The success rates of the three groups were 90% (18/20), 70% (19/27), and 40% (4/10), with statistically significant differences between <+50 PD group and ≥+70 PD group ($P = 0.007$). The incidences of postoperative complications in the three groups were 45% (9/20), 44% (12/27), and 10% (1/10), with no statistically significant difference ($P = 0.123$). [Supplementary Table 2, http://links.lww.com/CM9/B586]

Among different durations of disease groups, there were no statistical differences in the median angles of deviation at 1, 2, 3, 6 months post-injection ($P = 0.779$, 0.470, 0.757, 0.862). The success rates of the three groups were 72% (13/18), 71% (17/24), and 67% (10/15), with no statistically significant difference ($P = 0.937$). The incidences of postoperative complications in the three groups were 44% (8/18), 33% (8/24), and 40% (6/15), with no statistically significant difference ($P = 0.759$). [Supplementary Table 2, http://links.lww.com/CM9/B586]

The total incidence of complications was 39% (22/57), all of which disappeared within 3 months after injection. Among these complications, secondary exotropia (64%, 14/22) accounts for the highest proportion, followed by vertical strabismus (36%, 8/22), eye movement disorders (32%, 7/22), and ptosis (14%, 3/22). The deviation of secondary exotropia ranges from –50 PD to –3 PD, and all cases appeared 1 month after injection and recovered 2 months after injection spontaneously except for two cases. The other three complications were also mild and disappeared spontaneously without intervention.

The application instruction of BTA in the treatment of ACE has been a tough problem for a long time. Its instructions and the relationship of dose and efficacy are still under research.[4] The results of this study suggest that BTA is an effective and safe treatment option for ACE, and that the effect of the initial dose of BTA varies depending on the angle of deviation.

The success rate in this study was consistent with previous studies that showed a success rate of 37–70% in esotropia.[5] The efficacy of the <+50 PD group was better than that of the ≥+70 PD group, suggesting that the initial dose of BTA has a better effect in small angles of deviation. Other studies also found that BTA injections were most effective in patients with +30 to +40 PD. [6] This may be due to the fact that the initial dose of BTA is not enough to completely paralyze the muscle in the case of larger angles of deviation and cannot restore its strength to balance.

There was no statistically significant difference for patients with different durations of disease. No difference was found in efficacy for different injection times of BTA in past research,[2] which is consistent with our result. This indicates that the window of injection time of BTA is wide. Some scholars think that the effect of BTA is also related to muscle thickness, area, and strength,[7] as well as refractive status and accommodation power of patients.

Thirty nine percents (22/57) of patients developed one or more complications during follow-up, and 91% (20/22) complications disappeared spontaneously within 2–3 months after injection. Complications disappeared as the toxin wore off, indicating that the complications associated with BTA injection are transient and suggesting that BTA is a safety option for treatment. It is reported that the most common side effect after BTA injection is ptosis.[2] The secondary exotropia accounted for the highest proportion in this study, because it occurred more frequently in small angles of deviation, and these cases account for the majority of subjects.

The major limitation of this study is that it is a retrospective study with a small sample size and a short follow-up period. It is necessary to conduct further research and observe other relevant factors in the future. The results in this article show that a smaller degree of deviation can obtain better results with the initial dose of BTA, and the duration of disease may not be directly related to the treatment efficacy of ACE. These conclusions may provide some help for clinicians in choosing a better treatment plan for different ACE patients.

Acknowledgments

The authors thank the patients for participation in the study.

Funding

This study was supported by grants from Key Program on Basic Research Project of Universities of Henan (No. 22B320016) and Scientific Research Fund of National Health Commission–Henan Province Medical Science and Technology Project (No.SB201901013).

Conflicts of interest

None.

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How to cite this article: Wang Y, Lang LJ, Zhang J, Xu LM, Rong JB, Guo KX, Zhang LX, Li ZG, Zheng GY. Efficacy of initial dose botulinum toxin A injection in acute concomitant esotropia with different clinical characteristics. Chin Med J 2023;136:2249–2250. doi: 10.1097/CM9.0000000000002728