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Original Article

Botulinum toxin type A injections demonstrate remarkable efficacy in treating hemifacial spasm in elderly patients

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Abstract: Objective: To investigate the effectiveness of botulinum toxin type A (BTX-A) injections in elderly patients with hemifacial spasm (HFS). Methods: In this retrospective study, a total of 120 elderly patients diagnosed with HFS were recruited and divided into two groups: a research group (n=65) receiving multi-point BTX-A injections and a control group (n=55) undergoing conventional treatment. Comparative analyses were conducted to evaluate therapeutic efficacy, duration of efficacy, adverse reactions, Hamilton Anxiety Scale (HAMA) scores, and Hamilton Depression Scale (HAMD) scores between the two groups. Furthermore, factors influencing treatment outcomes in elderly HFS patients were investigated. Results: The research group demonstrated significantly higher overall efficacy, prolonged durations of therapeutic efficacy in grades II, III, and IV, a lower incidence of adverse reactions, and more pronounced improvements in HAMA and HAMD scores. Additionally, Cohen grading, HAMA and HAMD scores, and the treatment approach were independently correlated with treatment failure in elderly patients. Conclusion: Multi-point BTX-A injections are highly effective in treating HFS in elderly patients.

Keywords: Hemifacial spasm, botulinum toxin type A, anxiety, depression

Introduction

Facial spasm (or facial tic) is a clinically prevalent cranial nerve disorder characterized by intermittent, involuntary, and recurrent muscle twitching or rigidity on one side of the face. The condition progresses gradually and rarely resolves spontaneously without medical intervention [1]. It primarily affects middle-aged and elderly women. Initially, it manifests as intermittent twitching of the orbicularis oculus muscle, which subsequently extends to other muscles on the ipsilateral side of the face, with perioral muscle twitching being most frequently observed. With the aging of the Chinese population, the incidence of hemifacial spasm (HFS) has been rising among the elderly in recent years [2-4]. Although HFS does not directly endanger patients' lives, the persistent and involuntary muscle twitching significantly impacts daily lives, work, and studies. Chronic episodes often lead to excessive psychological stress, resulting in anxiety and depression [5, 6]. Current treatments for HFS include medications, acupuncture, physiotherapy, nerve blocks, and surgery. While these treatments can alleviate symptoms to varying degrees, they fall short in providing a complete cure and are accompanied by various side effects. Consequently, patients may experience increased psychological burden, which is particularly pronounced in elderly patients who often face multiple comorbidities and declining organ function. Polypharmacy further exacerbates the burden on their liver and kidney functions. Considering these circumstances, optimizing treatment strategies for elderly HFS patients is crucial for improving both clinical outcomes and quality of life.

Botulinum toxin (BTX), secreted by *Clostridium botulinum*, is the most potent biological neuro-

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toxin known [7]. Clostridium botulinum, BTX type A (BTX-A) is the most widely used in clinical practice. Renowned for its high stability, BTX-A is relatively easy to prepare, and can be stored and transported for extended periods under low-temperature conditions [8]. The use of BTX-A injections to treat HFS, particularly in the elderly, has proven to be effective and reliable. It is favored for its safety, stability, efficacy, minimal side effects, and the ability to facilitate rapid recovery, making it the first-line treatment for HFS in clinical settings [9, 10]. Nonetheless, a notable limitation of this treatment is the necessity for repeated injections, as its therapeutic effect typically lasts from 3 to 6 months. Studies suggest that the development of BTX antibodies is primarily linked to the repeated administration of high-dose BTX over short intervals. Conversely, low-dose, multipoint local injections allow the spastic muscles to bind to the BTX more efficiently, with only a minimal amount entering the bloodstream, which can be rapidly cleared by the body, reducing the likelihood of antibody formation [11]. The mechanism by which BTX-A treats HFS is believed to involve its interaction with calcium ions at the presynaptic membrane of the neuromuscular junction, inhibiting acetylcholine release, disrupting neuromuscular conduction, and reducing muscle tension in the affected muscles, ultimately achieving the desired therapeutic outcome [12].

This study aims to investigate the efficacy of local multi-point BTX-A injections in treating HFS in the elderly, as well as its effects on patients' neuropsychological outcomes following symptom improvement.

Materials and methods

Case selection

This retrospective study included 120 elderly patients diagnosed with HFS, who were admitted to the Geriatrics Department and Neurology Outpatient Clinic of Nanjing Pukou People's Hospital between January 2019 and December 2022. Among them, 65 cases who received BTX-A injections constituted the research group, while 55 patients who underwent conventional treatment served as the control group. The study protocol was approved by the Ethics Committee of Nanjing Pukou People's Hospital.

Inclusion criteria: 1. Completion of clinical physical examinations and imaging studies to exclude other conditions, in accordance with the diagnostic criteria for HFS [13]; 2. Clinical manifestations of involuntary twitching of the unilateral or bilateral eyelids and/or facial muscles; 3. No evidence of secondary HFS caused by other etiologies, as confirmed by cranial CT and MRI scans; 4. Treatment-naïve status; 5. No contraindications to the medications used in this study; 6. Availability of complete clinical data.

Exclusion criteria: 1. Allergic constitution, protein allergy, or myasthenia gravis; 2. Severe cardiovascular, renal, hepatic, or pulmonary diseases, infectious diseases, tumors, cerebrovascular diseases, hematological disorders, etc.; 3. Secondary HFS with a known etiology; 4. Pregnant or breastfeeding women; 5. Comorbid psychiatric disorders.

Intervention methods

The control group received routine therapy: Carbamazepine was administered orally starting at an initial dose of 100 mg twice daily, with subsequent gradual titration up to 400-800 mg per day, divided into two or three doses, depending on the patient's response. In the research group, treatment with BTX-A injections was implemented. BTX-A (Henli, a lyophilized crystalline toxin manufactured by Lanzhou Institute of Biological Products Co. Ltd., 100 U per vial) was diluted with 5 ml of 0.9% sodium chloride solution to achieve a concentration of 5 U/ml. The dilution process was performed carefully to ensure slow, gentle manipulation, and the solution was prepared extemporaneously to maintain its integrity. Throughout the dilution, handling, and administration processes, efforts were made to maintain a low-temperature environment to prevent loss of biological activity of BTX-A.

Prior to injection, the injection sites were aseptically prepared using povidone-iodine solution. Subsequently, multi-point injections were administered using a 1-ml tuberculin syringe, with 10 to 25 injection points selected on the face based on the spastic muscles. A low-dosage, multi-point injection strategy was applied, with the total dosage ranging from approximately 40 U to 80 U, individualized according to the patient's clinical condition. For injections at the

eyelid margin, subcutaneous injections of 2 U per site were used. For the remaining facial muscles, intramuscular injections were administered, with a volume of 2 U to 5 U per site. After injection, dry cotton balls were applied to the sites for compression.

After the procedure, patients were closely monitored for 30 minutes to detect any adverse reactions. Patients were explicitly instructed not to cleanse their faces for 2 hours post-injection. A follow-up assessment was scheduled one week after the injection. If residual spasm persisted, additional injections were administered. Regular follow-up visits were conducted every 3 to 6 months, with repeat injections based on symptom recurrence. Emergency medications, specifically 1:1000 epinephrine, were readily available to manage any potential allergic reactions during the injection process.

Data collection and outcome measures

Spasm Severity Grading [14]: Spasm severity was graded according to the Cohen criteria: Grade 0: Absence of spasm. Grade I: Increased blinking, triggered by external stimuli. Grade II: Mild spasm without functional impairment. Grade III: Moderate spasm with mild functional impairment. Grade IV: Severe spasm with significant functional impairments that affect daily life.

Therapeutic efficacy: Patients were followed for 3-6 months after treatment. Efficacy was evaluated by re-grading spasm severity according to the Cohen criteria: Complete response: Spasm severity returns to Grade 0. Marked response: Spasm severity reduces to Grade II or lower. Partial response: Spasm severity decreases from Grade IV to Grade III. Non-response: No change in spasm grade.

Adverse reactions: The number of cases presenting adverse reactions such as eyelid edema, oral commissure deviation, facial muscle weakness, and blepharoptosis was recorded, and the incidence rates were calculated.

Neuropsychological evaluation [15]: Prior to treatment, a comprehensive neuropsychological assessment was conducted by two experienced psychiatrists. The assessment involved in-depth interviews and systematic observations. For patients exhibiting symptoms of anxiety or depression, appropriate psychological counseling was provided. Anxiety was assessed using the Hamilton Anxiety Scale (HAMA), which included 14 items. Scores <7 indicate no anxiety; scores >7 suggest possible anxiety; scores >14 imply definite anxiety; scores >21 indicate obvious anxiety; and scores >29 denote severe anxiety. Depression was evaluated using the Hamilton Depression Scale (HAMD), which includes 24 items. Scores <8 indicate no depression; scores of 8-20 suggest possible depression; scores of 20-35 indicate definite depression, and scores >35 represent severe depression.

In this study, clinical efficacy, incidence of adverse reactions, HAMA scores, and HAMD scores were the primary outcome measures. Spasm severity grading and duration of therapeutic efficacy were secondary measures.

Statistical methods

Data were collected and subsequently inputted into a computer system for statistical analysis, employing the SPSS 20 software package. Measurement data were expressed as the mean ± standard error of the mean (SEM). To evaluate differences in measurement data between the two groups, an independent samples t-test was performed. For comparing measurement data obtained from before and after treatment, a paired t-test was applied. Enumeration data were presented as frequencies (percentages), and the chi-square (χ^2) test was employed to assess differences between groups for categorical variables. The therapeutic effects among different Cohen spasticity grades were assessed using one-way analysis of variance (ANOVA). Univariate analysis was initially performed to identify potential risk factors associated with treatment efficacy. Binary Logistic regression analysis was then performed to explore the independent associations of these factors. A significance level of $P<0.05$ was considered statistically significant.

Results

Comparison of baseline data between the two patient groups

Inter-group comparisons of age, gender, smoking history, alcohol consumption history, family medical history, and Cohen grading revealed no

Table1. Comparison of baseline data between the two patient groups

Indicators	Research group (n=65)	Control group (n=55)	t/χ^2	*P*
Age (years)	53.49±7.35	55.36±10.35	1.153	0.251
Gender			0.053	0.818
Male	20 (30.77)	18 (32.73)		
Female	45 (69.23)	37 (67.27)		
Smoking history			0.094	0.760
Without	42 (64.62)	37 (67.27)		
With	23 (35.38)	18 (32.73)		
Alcoholism history			0.116	0.733
Without	37 (56.92)	33 (60.00)		
With	28 (43.08)	22 (40.00)		
Family medical history			0.839	0.360
Without	54 (83.08)	42 (76.36)		
With	11 (16.92)	13 (23.64)		
Cohen grading			0.604	0.437
I-II	22 (33.85)	15 (27.27)		
III-IV	43 (66.15)	40 (72.73)		

Table 2. Comparison of clinical effectiveness between the two patient groups

Indicators	Research group (n=65)	Control group (n=55)	χ^2	*P*
Complete response	33 (50.77)	18 (32.73)		
Marked response	20 (30.77)	11 (20.00)		
Partial response	7 (10.77)	9 (16.36)		
Non-response	5 (7.69)	17 (30.91)		
Overall response	60 (92.31)	38 (69.09)	10.725	0.001

statistically significant differences between the two groups (all *P*>0.05). Details are presented in **Table 1**.

Comparison of clinical effectiveness between the two patient groups

Following BTX-A injection therapy, patients were followed for 3 to 6 months. The overall response rates were 92.31% in the research group and 69.09% in the control group, showing significantly higher overall efficacy in the research group (P<0.05). Details are shown in **Table 2**.

Comparison of duration of efficacy between the two patient groups across various Cohen gradings

Based on the Cohen grading criteria, among the elderly HFS patients in the control group, 2 cases were classified as grade I, 13 as grade II, 17 as grade III, and 23 as grade IV after treatment. In the research group, 4 cases were at grade I, 18 at grade II, 26 at grade III, and 17 at grade IV after treatment. These findings indicate an inverse relationship between Cohen spasm grade and duration of the therapeutic effect: the higher the Cohen spasm grade, the shorter the duration of the curative effect. ANOVA revealed statistically significant differences in treatment efficacy across Cohen spasm grades (*P*<0.05). Moreover, within the same spasm grades, the research group demonstrated a longer duration of efficacy compared to the control group at grade II, grade III, and grade IV (*P*<0.05). See **Table 3** for details.

Comparison of incidence of adverse reactions between the two patient groups

In the research group, one case each of oral commissure deviation, facial-muscle weakness, and blepharoptosis was observed, yielding a cumulative incidence rate of 4.62%. In contrast, the control group presented with three cases each of eyelid edema and facial-

Table 3. Comparison of duration of efficacy between the two patient groups across various intensity gradings

Spasm intensity grade	n	Research group (n=65)	n	Control group (n=55)	t	*P*
I	4	38.75±9.54	2	40.50±9.19	1.018	0.311
II	18	36.33±12.00	13	25.85±9.36	5.262	<0.001
III	26	24.62±6.82	17	19.18±7.60	4.131	<0.001
IV	17	23.06±5.21	23	17.61±5.02	5.806	<0.001
F		11.380		9.013		
P		<0.001		<0.001		

Table 4. Comparison of incidence of adverse reactions between the two patient groups

Adverse reactions	Research group (n=65)	Control group (n=55)	χ^2	*P*
Eyelid edema	0 (0.00)	3 (5.45)		
Oral commissure deviation	1 (1.54)	2 (3.64)		
Facial-muscle weakness	1 (1.54)	3 (5.45)		
Blepharoptosis	1 (1.54)	2 (3.64)		
Total	3 (4.62)	10 (18.18)	5.676	0.017

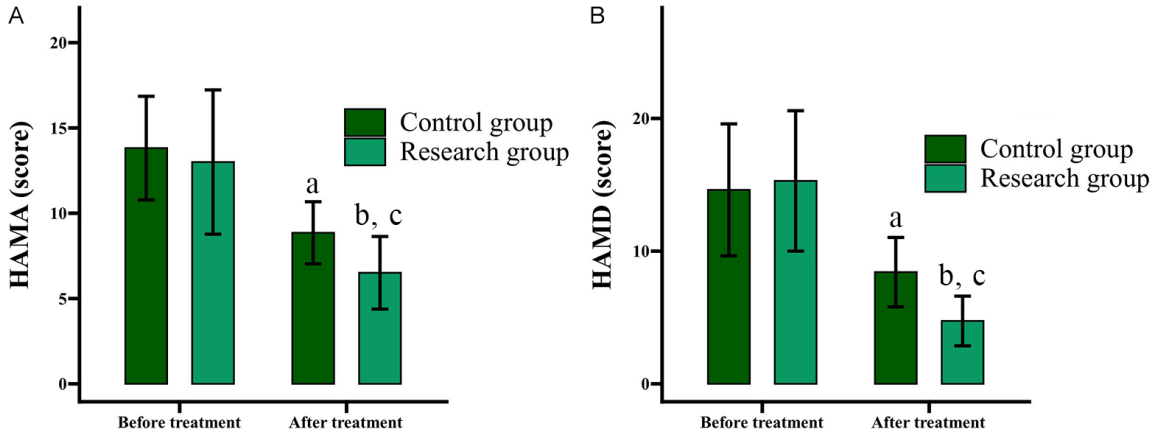

Figure 1. Comparison of HAMA and HAMD scores between the two patient groups before and after treatment. A. HAMA scores of the two groups before and after treatment. B. HAMD scores of the two groups before and after treatment. Note: HAMA, Hamilton Anxiety Scale; HAMD, Hamilton Depression Scale. [a]P<0.05, [b]P<0.05, compared to the pre-treatment score; [c]P<0.05, compared to the control group.

muscle weakness, along with two cases each of oral commissure deviation and blepharoptosis, resulting in a total incidence rate of 18.18%. The overall incidence of adverse reactions was significantly lower in the research group compared to the control group (*P*<0.05, **Table 4**).

Comparison of neuropsychological assessment between the two patient groups

Prior to treatment, no significant disparities were detected in the HAMA and HAMD scores between the two groups (*P*>0.05). After treatment, both groups demonstrated a significant reduction in scores. Notably, the research group demonstrated a significantly greater decrease in HAMA and HAMD scores compared to the control group (*P*<0.05). The results are presented in **Figure 1**.

Analysis of risk factors influencing clinical effectiveness in elderly HFS patients

The risk factors influencing clinical effectiveness in elderly patients with HFS were analyzed. Univariate analysis revealed that gender, history of alcoholism, Cohen grading, HAMA and HAMD scores, and treatment approach

Table 5. Univariate analysis of factors affecting clinical effectiveness in elderly patients with hemifacial spasm

Variable	Non-response group (n=22)	Response group (n=98)	χ^2	*P*
Age (years)			3.439	0.064
<55	8 (36.36)	57 (58.16)		
≥55	14 (63.64)	41 (41.84)		
Gender			6.516	0.011
Male	12 (54.55)	26 (26.53)		
Female	10 (45.45)	72 (73.47)		
Smoking history			3.002	0.083
Without	11 (50.00)	68 (69.39)		
With	11 (50.00)	30 (30.61)		
Alcoholism history			5.350	0.021
Without	8 (36.36)	62 (63.27)		
With	14 (63.64)	36 (36.73)		
Family medical history			0.677	0.411
Without	16 (72.73)	79 (80.61)		
With	6 (27.27)	19 (19.39)		
Cohen grading			5.971	0.015
I-II	2 (9.09)	35 (35.71)		
III-IV	20 (90.91)	63 (64.29)		
HAMA (points)			5.404	0.020
<7	3 (13.64)	39 (39.80)		
≥7	19 (86.36)	59 (60.20)		
HAMD (points)			4.310	0.038
<6	5 (22.73)	46 (46.94)		
≥6	17 (77.27)	52 (53.06)		
Treatment approach			10.725	0.001
conventional therapy	17 (77.27)	38 (38.78)		
Botulinum toxin type a treatment	5 (22.73)	60 (61.22)		

Note: HAMA, Hamilton Anxiety Scale; HAMD, Hamilton Depression Scale.

Table 6. Assignments

Indicators	Variable	Assignment
Gender	X1	Male =0, female =1
Alcoholism history	X2	No =0, yes =1
Cohen grading	X3	I-II =0, III-IV =1
HAMA (points)	X4	<7=0, ≥7=1
HAMD (points)	X5	<6=0, ≥6=1
Treatment approach	X6	BTX-A treatment =0, routine treatment =1
Therapeutic effectiveness	Y	Response =0, non-response =1

Note: HAMA, Hamilton Anxiety Scale; HAMD, Hamilton Depression Scale; BTX-A, botulinum toxin type A.

were all significantly associated with clinical effectiveness in these patients ($P<0.05$). These factors were selected as independent variables, with treatment effectiveness as the dependent variable. A multivariate analysis was then performed, and binary Logistic regression analysis indicated that Cohen grading, HAMA scores, HAMD scores, and treatment approach were independent risk factors for treatment ineffectiveness in elderly HFS patients ($P<0.05$). For detailed results, please refer to **Tables 5**-**7**.

Table 7. Multivariate analysis of risk factors affecting clinical effectiveness in elderly patients with hemifacial spasm

Indicators	β	SE	Wald	*P*	Exp (β)	95% CI
Gender	-1.139	0.618	3.398	0.065	0.320	0.095-1.075
Alcoholism history	1.128	0.612	3.400	0.065	3.090	0.931-10.249
Cohen grading	2.331	0.890	6.863	0.009	10.291	1.799-58.877
HAMA (points)	1.534	0.757	4.102	0.043	4.634	1.051-20.441
HAMD (points)	1.412	0.674	4.385	0.036	4.104	1.095-15.387
Treatment approach	2.115	0.667	10.043	0.002	8.291	2.241-30.673

Note: HAMA, Hamilton Anxiety Scale; HAMD, Hamilton Depression Scale.

Discussion

Hemifacial spasm (HFS) is characterized by involuntary, recurrent, and painless muscle contractions on one or both sides of the face. This benign condition often worsens under stress, fatigue, emotional arousal, or during voluntary movements, but typically subsides during sleep [16-18]. A significant body of research suggests that vascular pathologies are responsible for over 90% of HFS cases [19]. Despite the availability of multiple treatment options, complete resolution of HFS in elderly patients remains elusive. Therefore, further research into more effective treatment strategies is essential. This effort aims to enhance treatment efficacy, alleviate psychological distress, and improve overall clinical outcomes for elderly patients.

In this study, after 3-6 months of follow-up following BTX-A injection treatment, the research group showed an overall response rate of 92.31%, with 81.54% achieving a full response and 10.77% achieving a partial response. This rate was significantly higher than the 69.09% response rate in the control group, indicating that BTX-A injection treatment is more effective than conventional therapy for elderly HFS patients.

Furthermore, our findings revealed an inverse relationship between the Cohen spasm grade and the duration of treatment efficacy among elderly HFS patients. Specifically, the higher the Cohen spasm grade, the shorter the efficacy duration. Nevertheless, in patients with grades II, III, and IV, the research group demonstrated a significantly longer efficacy duration compared to the control group. This implies that, compared to conventional treatment, BTX-A injections can more effectively sustain therapeutic benefits for elderly HFS patients.

Additionally, we observed that BTX-A injection therapy had a lower overall incidence of adverse reactions compared to conventional treatment, suggesting that it is a safer option. In a study conducted by Ababneh OH et al. [20], BTX-A injections for blepharospasm and HFS yield long-term clinical effectiveness and high safety, which aligns with our findings. Similarly, Duarte GS et al. [21] reported that BTX-A injections for HFS patients improved symptoms while maintaining high safety, supporting the results of our study. These findings collectively affirm that BTX-A injection therapy is safer and more effective than conventional treatments for elderly HFS patients.

Moreover, when applied to elderly patients with HFS, BTX-A injection treatment significantly alleviated anxiety and depression, thereby contributing to the neuropsychological improvement of patients. In a study by Wang B et al. [22], BTX-A injections for HFS not only demonstrated remarkable efficacy and safety but also effectively relieved depression, improving patients' psychological well-being and quality of life, which supports our findings. Previous research has indicated that HFS patients often exhibit clinical manifestations such as somatization, interpersonal sensitivity, depression, anxiety, and phobia. BTX-A injection treatment can help alleviate these clinical symptoms and effectively reduce patients' psychological distress, similar to the results observed ins our study [23]. These findings demonstrate that BTX-A injection therapy is more effective than conventional treatment in alleviating negative psychological states among elderly HFS patients.

Univariate and multivariate analyses were further carried out to identify and validate the risk factors influencing clinical effectiveness in

elderly patients with HFS. High Cohen grades, elevated HAMA and HAMD scores, and the use of conventional treatment were all identified as determinants associated with treatment ineffectiveness. This underscores the need to either modify treatment strategies or implement effective psychological interventions for patients presenting with these characteristics. In a study by Wabbels B et al. [24], it was postulated that depressive symptoms could potentially impact the outcomes of BTX-A injection therapy in patients with benign essential blepharospasm, a conclusion that aligns with the results of our research. Additionally, a study by Tian S et al. [25] established comorbid hypertension as an independent risk factor for suboptimal short-term prognoses following BTX-A injections for HFS. These findings emphasize the importance of clinically monitoring factors such as high Cohen grades, elevated HAMA and HAMD scores, and the use of conventional treatment in elderly HFS patients to maximize therapeutic efficacy.

This study has several limitations. First, the relatively small sample size necessitates the need for large-scale clinical analyses in the future to enhance the generalizability of the research findings. Second, the absence of long-term follow-up analysis highlights the need for further research to evaluate the impact of BTX-A therapy on patients' long-term prognosis. Third, the underlying mechanisms linking muscle spasm grading with the duration of therapeutic efficacy remain unexplored, requiring additional foundational research to optimize the treatment's lasting effects. Future studies will address these limitations to enhance the robustness of the findings.

The results of this study suggest that local, low-dose, multi-point BTX-A injection is an effective, simple, and safe treatment for elderly patients with HFS. This approach significantly alleviates facial muscle spasms, with the therapeutic effects lasting 3 to 6 months, and repeated injections can extend the therapeutic effect. Furthermore, the neuro-psychological disorders caused by persistent and recurrent HFS symptoms are notably improved following symptom relief. In summary, BTX-A injection emerges as a safe, efficacious, and rapid treatment option for HFS. It stands as the current first-choice treatment, particularly for elderly patients, due to its proven efficacy and favorable safety profile.

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Disclosure of conflict of interest

None.

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