

Comparative Evaluation of Intralesional Injection of Botulinum Toxin Type A *versus* Triamcinolone Acetonide in Treating Post-Burn Pruritus

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ABSTRACT

Background and objectives: Pathological scars resulting from burns can impair both aesthetic and physical functions, often causing chronic pruritus. Thus, this study aimed to compare the effectiveness of intralesional botulinum toxin type A (BTX-A) and triamcinolone acetonide (TAC) in reducing pruritus and scar thickness caused by burns.

Methods: This single-blind clinical trial was conducted on 60 patients experiencing post-burn pruritus. Patients selected a scar area with the highest degree of pruritus, which was divided into two equal parts. BTX-A was injected into one half and TAC into the other. Pruritus severity was assessed using the visual analog scale (VAS), the pain was assessed using the numeric rating scale (NRS), and scar thickness and the Vancouver scar scale (VSS) scores were at four time points.

Results: The study involved 60 patients with a mean age of 35.72 years (range: 21–64 years). The results indicated that BTX-A was more effective than TAC in reducing scar thickness and pruritus. Changes in scar thickness from V1 to V4 demonstrated that BTX-A achieved more significant scar reduction than TAC ($P=0.0287$), and pruritus severity decreased significantly in the BTX-A group ($P=0.0482$).

Conclusion: Based on the results, BTX-A treatment is more effective than TAC in reducing pruritus and scar thickness in patients with chronic post-burn pruritus. Further studies with larger sample sizes and extended follow-up periods are required to confirm these findings.

Keywords: botulinum toxin type A, triamcinolone acetonide, pruritus, scar, burn.

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INTRODUCTION

Pruritus is a common medical issue, which confirms that burn patients suffer from pruritus. However, less attention has been given to identifying the most effective treatment for this condition. Various studies have reported prevalence rates of up to 87% and 100% in the lower limbs (1, 2). Pruritus can lead to psychological disturbances, sleep disorders and other detrimental effects on patients' daily activities (3, 5). Numerous treatments have been proposed, including antihistamines, gabapentin, massage therapy, silicone gel and intralesional steroid injections. Unfortunately, these treatments have not shown significant efficacy in severe pruritus cases. Despite their use, pruritus remains a persistent and severe issue for burn patients. Antihistamines are commonly employed as the standard treatment (6, 8). Additionally, gabapentin, either alone or in combination with antihistamines, has demonstrated greater effectiveness than antihistamines alone (9).

In recent years, extensive investigations into the mechanisms of pruritus have revealed that complex pathways and diverse receptors are involved in its development (10). This complexity may explain why standard treatments, such as antihistamines, are only effective in about 20% of cases (1, 9, 11).

Extensive research has examined the sensation of pruritus in burn patients, and its pathophysiology is now better understood. C-fibers in the epidermis primarily mediate the itch sensation (1, 9). Research has revealed that these fibers possess at least three distinct receptor types (1, 12, 14).

During the wound-healing process in burn injuries, the ligands that stimulate C-fibers, such as plasma histamine, substance P and neurotoxin A, are markedly increased. Simultaneously, the number of C-fibers also rises. This dual effect amplifies the stimulation and contributes to persistent pruritus.

Standard treatment for chronic pruritus associated with burn scars involves intralesional steroid injections, with triamcinolone acetonide being the most frequently used. Its anti-inflammatory properties help reduce the intensity of pruritus (13). However, despite its widespread applica-

tion, many patients fail to experience adequate relief with this therapy.

Botulinum toxin (BTX), produced by *Clostridium botulinum*, an anaerobic Gram-positive bacterium, has emerged as an alternative treatment option. This bacterium produces eight distinct neurotoxins, of which only types A and B are FDA-approved. However, type A is the primary formulation used in clinical practice (14).

Botulinum toxin consists of a 100-kDa heavy chain and a 50-kDa light chain. The heavy chain facilitates binding to presynaptic neurons, allowing the light chain to penetrate the cytoplasm. Once inside, the light chain targets and deactivates a component of the soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) complex. The SNARE complex is critical for releasing acetylcholine from presynaptic neurons and its inhibition disrupts neurotransmitter release (15-17).

Botulinum toxin products are available in various vial sizes and can be reconstituted at different concentrations. Due to these differences, there is no standardized international dosage or a dose-response equivalence across different botulinum toxin products. The diffusion area of BTX expands with increasing volume and concentration. Studies have demonstrated that the field effect among different BTX products is comparable when equal volumes and doses are utilized (15-17).

Given that previous studies' findings remain inconclusive and highlight the need for further research, this study was designed and conducted to compare the intralesional injection of BTX type A (BTX-A) with triamcinolone acetonide (TCA) for managing post-burn pruritus in Taleghani Hospital of Ahvaz, Iran. □

METHOD

This single-blind, within-subjects, controlled clinical trial involved 60 patients suffering from burn-induced pruritus treated at Taleghani Hospital in Ahvaz, Iran, in 2024. Each patient selected a scar area with the highest degree of pruritus, and that area was divided into two equal sections, with one section receiving BTX-A and the other one, TAC. This intra-patient design allowed each patient to serve as their own control. The study was approved by the Vice-Chancellor for Research and Technology and received

the ethical approval (IR.AJUMS.REC.1402.619) from the Ethics Committee in Biological Research of Jundishapur University of Medical Sciences, Ahvaz, registered with the Iranian Registry of Clinical Trials (IRCT) and assigned the registration code IRCT20240418061517N1. The single-blind study ensured that patients were unaware of the treatment applied to each section of their scars, although physicians and researchers were informed about the interventions. Randomization of the areas where BTX-A or TAC was injected was performed using computer-generated sequences via R Studio software to minimize potential bias. One of the two sections was randomly assigned for BTX-A injection for each patient, while the other received TAC. Written informed consent was obtained from all patients before their participation. Demographic data, including age, gender, burn depth, surface area and the time elapsed since the burn, were all recorded. Additional information about patients' prior treatments and the intensity of their pruritus before the intervention was also documented.

This study used BTX-A, branded as "Masport," with a concentration of 500 units. After dilution with two milliliters of saline, 25 units per 0.1 milliliters were injected. This injection was administered only once during the initial visit (V1). Triamcinolone acetonide at a concentration of 10 mg per milliliter was used for the other group, administered three times at one-month intervals (at the initial visit, one month and two months after the first visit).

Patients assessed and recorded their pruritus intensity using the visual analog scale (VAS), ranging from 0 (no pruritus) to 10 (severe pruritus). Additionally, scar pain was evaluated by the patients during each visit using the numeric rating scale (NRS), ranging from 0 to 10. Scar thickness was measured at each visit and the Vancouver scar scale (VSS) was employed to evaluate scar severity. The VSS assessment included four parameters: pigmentation, vascularity, pliability and height.

Patients were followed for six months, during which they were examined four times: at the initial visit (V1), one month (V2), three months (V3) and six months (V4) after the first visit. Pruritus intensity, pain, scar thickness and VSS score were re-evaluated during each visit.

Patients with pruritus resulting from burns and those who had not responded adequately to other conventional treatments were included in the study. The exclusion criteria comprised the lack of willingness to continue participation in the study, pregnant or breastfeeding women, patients with a history of coagulation disorders or those taking anticoagulant medications, a history of hypersensitivity to BTX, patients with neuromuscular disorders such as multiple sclerosis (MS), myasthenia gravis, or Eaton-Lambert syndrome, and a compromised immune system.

The collected data were analyzed using R Studio version 4.3.3 software. Chi-square or Fisher's exact test was used for qualitative variables, and an independent t-test or Mann-Whitney test was utilized for quantitative variables. Analysis of variance with repeated measures or generalized linear models was employed to investigate changes in quantitative variables over time. The significance level was considered 0.05 in all tests. □

RESULTS

This study was conducted on 60 patients (23 men and 37 women) with an average age of 35.72 years (range 21 to 64 years) who had been referred to the clinic due to chronic pruritus

TABLE 1. Patient profiles and scar characteristics before intervention (n=60)

Variables		Number (percent frequency)/mean±SD
Gender	Male	23 (38.33%)
	Female	37 (61.67%)
Scar site	Neck	13 (21.67%)
	Body	20 (33.33%)
	Organs	27 (45.00%)
Age (years)		14.19±35.72
Scar duration (months)		13.4±14.9
Scar size (cm ²)		56.98 ± 35.07

SD=standard deviation

TABLE 2. Clinical results in four periods of follow-up in two groups

Parameters	V1	V2	V3	V4
TAC group				
Pruritus VAS ^a	5.61 [3.31]	1.78 [2.29]***	1.50 [2.46]***	1.22 [1.77]***
Pain NRS ^b	2.83 [2.43]	1.11 [1.41]***	0.39 [0.85]***	0.28 [0.96]***
VSS score ^c	12.33 [2.43]	8.83 [2.79]***	6.72 [2.95]***	5.78 [2.71]***
Thickness (cm)	0.87 [0.47]	0.42 [0.31]***	0.35 [0.26]***	0.37 [0.30]***
BTX-A group				
Pruritus VAS ^a	5.61 [3.31]	1.12 [1.62]***	0.83 [1.47]***	0.28 [0.57]***
Pain NRS ^b	2.83 [2.43]	1.00 [1.41]***	0.39 [0.85]***	0.28 [0.96]***
VSS score ^c	12.28 [2.49]	8.72 [2.76]***	6.33 [2.74]***	5.61 [2.55]***
Thickness (cm)	0.86 [0.49]	0.42 [0.34]***	0.36 [0.32]***	0.31 [0.33]***

VAS=visual analog scale; NRS=numeric rating scale; VSS=Vancouver scar scale; BTX-A=botulinum toxin type A.

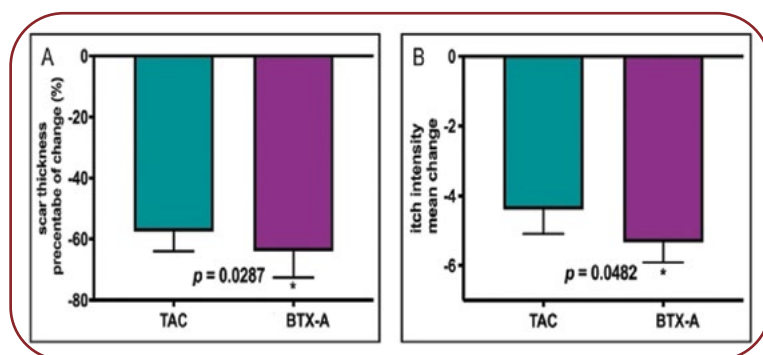


FIGURE 1. Comparison of the effects of TAC and BTX-A treatment on pruritus intensity and scar thickness from the first visit to the sixth month (TAC=triamcinolone acetonide; BTX-A=botulinum toxin type A)

TABLE 3. Clinical results at the sixth month (V4) between TAC and BTX-A groups

Parameters	TAC group	BTX-A group	P
Pruritus VAS ^a	1.22 [1.77]	0.28 [0.51]	0.04*
Pain NRS ^b	0.28 [0.96]	0.28 [0.96]	-
VSS score ^c	5.78 [2.71]	5.61 [2.55]	0.08
Thickness (cm)	0.37 [0.30]	0.31 [0.33]	0.14

TAC=triamcinolone acetonide; BTX-A=botulinum toxin type A; NRS=numeric rating scale; VAS=visual analog scale; VSS=Vancouver scar scale.

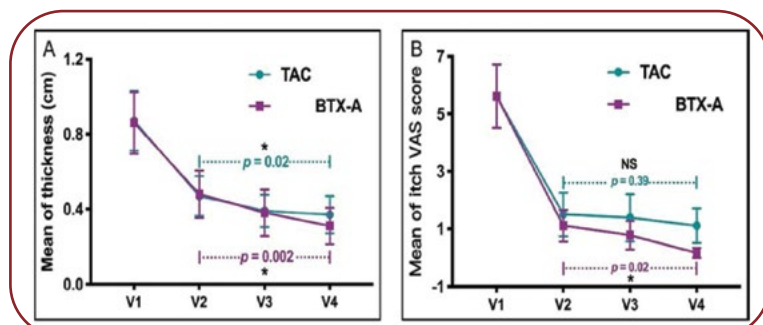


FIGURE 2. Comparison of the effect of TAC and BTX-A treatment on scar thickness and pruritus from one month after referral to the sixth month (TAC=triamcinolone acetonide; BTX-A=botulinum toxin type A)

caused by burn scars. Each patient's selected scar area was divided into two equal sections, with one section being treated with BTX-A and the other one with TAC (Table 1). Each patient was followed up for six months and the results were collected at four different times (before treatment, the first month, the third month and the sixth month). No serious adverse events were observed during the study. Mild injection site pain was reported in some patients, which resolved within a few hours. There were no cases of infection or allergic reactions.

Notable improvements in pruritus severity, pain, scar thickness and VSS scores were ob-

served in both BTX-A and TAC treatment groups during follow-up (V2, V3, and V4) compared to V1 (baseline) (Table 2). However, BTX-A was significantly more effective than TAC in reducing scar thickness and pruritus severity.

For both sections treated with BTX-A and TCA within the same patients, scar pruritus, pain, thickness and VSS scores showed remarkable improvements at V2, V3, and V4 compared to V1 (Table 2).

Changes between V1 and V4 indicated that BTX-A treatment significantly reduced scar thickness compared to TAC ($P=0.0287$). Additionally, pruritus severity decreased more significantly in the BTX-A group compared to the TAC group ($P=0.0482$). Figure 1 illustrates the scar thickness and pruritus severity changes between V1 and V2 for both treatment groups.

Figure 2 provides detailed changes in scar thickness and pruritus severity over six months of follow-up. Analysis revealed a statistically significant reduction in scar thickness from V2 to V4 in both groups (TAC: $P=0.02$; BTX-A: $P=0.002$). However, pruritus severity significantly decreased from V2 onward only in the BTX-A group ($P=0.02$), with no significant reduction observed in the TAC group ($P=0.39$) (Figure 2).

Table 3 summarizes the evaluations at V4 between the two groups, demonstrating that pruritus scores in the BTX-A group are significantly lower than the TAC group ($P=0.04$). These findings indicate that BTX-A is more effective in providing sustained pruritus relief than TAC alone (Table 3). □

DISCUSSION

Intralesional injection of BTX-A was more effective than TAC in reducing the severity of pruritus and scar thickness in patients with chronic pruritus resulting from burns. Significant clinical improvements in pruritus severity and scar thickness were observed in the BTX-A group compared to the TAC group, aligning with findings from similar studies.

Clinical data revealed that both BTX-A and TAC independently improved scar appearance and discomfort. However, the improvement in scar pruritus was significantly more sustained and pronounced in the BTX-A group by the end of the study (V4). Furthermore, no adverse effects were reported during the clinical trial. These

findings are consistent with those reported by previous studies, such as the work by Huang *et al* on a murine model. Their study demonstrated that a BTX-A regimen modulated burn-induced mechanical pruritus by reducing the expression of PGP 9.5, NGF, pSTAT3 and TRPV1 while increasing the decreasing levels of KOR (9). The results of their research further indicated that BTX-A could act as an adjunct to TAC by enhancing its efficacy and durability by inhibiting neuropeptide release and inflammation associated with neuropathic pruritus. The cutaneous nervous system also plays a role in the formation of hyperplastic scar tissue via increased nerve density and upregulation of NGF.

Additionally, previous studies indicate that BTX-A suppresses NGF release, reducing pruritus, which is associated with decreased scar thickness (9, 16, 17). The cutaneous nervous system contributes to hyperplastic scar tissue formation through increased nerve density and upregulation of NGF. Combined treatment with BTX-A and TAC significantly suppresses NGF release, limiting neurite growth and TRPV1 expression; thus, reducing pruritus correlates with diminished scar thickness (16-18).

A recent study by Rasai *et al* involving 23 patients was consistent with our findings, as it demonstrated that both TAC and BTX-A alleviated scar pain and pruritus. However, their results did not show differences in reducing the formed scar tissue (14, 15). Various mediators and receptors are associated with pruritus signaling pathways. The molecular mechanisms underlying scar pruritus remain unclear. In chronic inflammatory skin conditions such as atopic dermatitis and psoriasis, the release of neuropeptides and neurotrophic or pro-inflammatory factors contributes to pruritus. Studies on patients with atopic dermatitis have shown that IL-31- and STAT3-dependent beta-endorphin production may contribute to chronic pruritus (17-19). In pathological or burn scars, chronic pruritus, often accompanied by pain in the scar area, is likely related to pain processing. The direct activation of opioid receptors in the skin may trigger pruritus. Transient receptor potential (TRP) channels,

widely present on cell membranes, mediate cationic transport such as Ca^{2+} and play roles in various physiological processes. Among them, TRPV1 nociceptive skin channels are pivotal in producing pruritus and pain in scars (19, 20). In Huang *et al*'s findings, PGP 9.5 expression in the epidermis of pruritic post-burn lesions significantly increased compared to the sham control group across all treatment groups in mice. Furthermore, all treatment groups suppressed the upregulation of post-burn pruritus and pain mediators such as NGF, STAT3 and TRPV1 (9).

This study has several limitations. For instance, combined therapy was not included in our clinical trial. However, previous studies have indicated that combination therapy enhances symptom improvement. Further research is needed to compare clinical responses, including the administration of BTX-A in combination with triamcinolone acetonide, to elucidate the advantages, dosage, and mechanisms of TAC/BTX-A combination therapy compared to monotherapy. Another limitation is the small sample size in this study, which inherently carries a risk of bias. Future clinical trials with larger sample sizes and extended follow-up periods will provide more robust evidence of the therapeutic effects of TAC and BTX-A. □

CONCLUSION

This study demonstrates that BTX-A treatment is more effective than TAC in reducing pruritus and improving scar conditions in burn-induced scar patients. Botulinum toxin type A, as an innovative treatment for these patients, can lead to significant improvements. □

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