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Botulinum Toxin Type A and Other Non-Surgical Modalities in Hypertrophic and Keloid Scar Management: A Review of Clinical Evidence

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ABSTRACT

Hypertrophic scars and keloids are one of the most challenging scars to treat, as their high rate of relapse, functional disability, and their psychosocial effects on patients make their management a formidable task. Various treatment options are available for treating hypertrophic scars, including corticosteroid injection, silicone treatment, pressure garments, and laser therapy. However, the results obtained with these techniques have been inconsistent. None of these treatment modalities has been proven as a gold standard. Growing evidence suggests that botulinum toxin type A (BTX-A) may play an important role in both preventing and treating pathological scarring. We decided to assess the clinical and experimental data of utmost importance regarding the role of BTX-A in the management of hypertrophic and keloid scarring. According to experimental research, BTX-A reduces neurogenic inflammation, alters fibroblast function, and lessens mechanical tension in wounds by inhibiting the P-neurokinin-1 receptor system. Clinical trials spanning a range of surgical and traumatic patient populations, such as thyroidectomy, facial wounds, blepharoplasty, mastectomy, and burn scars, have all consistently demonstrated enhanced scar height, pliability, erythema/skin redness, and pain, as well as an improvement in patients' subjective assessment. Meta-analyses also show that BTX-A is statistically more effective than placebo and other treatments. Differences in dose schedules and administration timing, as well as insufficient information on long-term effects, make these results impossible to be generalizable. In general, BTX-A appears to be a safe and effective complement to the multimodal, personalized treatment of hypertrophic and keloid scars.

Keywords: Botulinum Toxin Type A; Hypertrophic Scar; Keloid; Non-Surgical Treatment; Scar Management

1. INTRODUCTION

Hypertrophic and keloid scars (HKs) are among the most problematic clinical problems. Some reasons include their chronic nature, functional limitations, and

their tendency to come back even after being properly treated before. Patients with darker skin (Fitzpatrick III–VI) have a higher chance of developing pathological scarring that responds worse to treatment than those with lighter skin (Bronte et al., 2024).These differences mean treatment needs to take into account skin type, ethnicity, and disease severity. A wide focus review on HK treatments currently available also reiterates that pathological scars are challenging to manage, despite the myriad of non-surgical modalities in clinical practice (Davies et al., 2022).This is further confounded by the absence of universally accepted guidelines and the heterogeneity of outcomes, leading some investigators to adopt a multimodal or individualised approach. The typical firm and raised nature of HK lesions is due in part to excessive fibroblast proliferation and altered remodeling of the extracellular matrix, which results in increased levels of collagen I and III, among other ECM components (Davies et al., 2022).

Unbiased analyses on the latest advances in keloid biology, a superfamily mediator that drives fibroblast activation and maintains fibrotic progression (Walsh et al., 2023). Angiogenic factors, pro-inflammatory cytokines, and dysregulated cellular apoptosis also support the self-perpetuating fibrotic loop.Although many studies have examined how pathological scars form, the exact mechanisms remain poorly understood. This lack of clarity explains why patients respond differently to current treatments and makes it difficult to develop a consistently effective therapy.

In view of this complexity, contemporary therapeutic models increasingly favour a mechanism-based approach. Updated algorithms of HK management are largely phenotypic and treatment-based stratification, guided by natural history, chronicity, anatomic site distribution, and patient-related factors, which then guide treatment combinations (Ogawa, 2022). These guidelines state that non-surgical treatments are usually more effective when used together rather than alone, because hypertrophic scar (HS) formation has many causes. However, the results of these treatments vary, and some patients—especially those with high skin tension or a family history—may experience recurrence, which limits the overall effectiveness of broader treatment strategies. The application of one treatment, Botulinum Toxin Type A (BTX-A), a neurotoxin used for many years in both neuromuscular and aesthetic medicine, has gained increasing popularity. Preliminary clinical findings and experimental investigations indicate that BTX-A may be a potential therapeutic agent for the prevention and treatment of pathologic scarring.

A detailed review of the literature on BTX-A in keloid treatment shows that it works by reducing mechanical tension at the wound edges. It does this by temporarily blocking the activity of nearby muscles, which are an important factor in the development of hypertrophic scars (Sohrabi & Goutos, 2020). By minimizing tensile forces, BTX-A may limit fibroblast overstimulation and collagen overproduction during the critical early phases of wound healing. Not only its biomechanical secretion, but also the potential direct cellular and molecular actions of BTX-A may relate to scar revision. Reviews of novel therapeutic interventions show that clinicians increasingly treat non-surgical lesions with agents that modulate fibroblast function, alter cell signaling, and reduce profibrotic cytokine activity. In the context of these etiological mechanisms, neurogenic inflammation plays a particularly important role in HK. Studies show that substance P (SP) and its receptor, NK1R, help fibroblasts move, form new blood vessels, and maintain inflammation.

Researchers have shown that this pathway plays a role in hypertrophic scar formation. Since BTX-A blocks the release of these neuropeptides, it may offer a new treatment option (Zakrzewski et al., 2025). Furthermore, this information provides a mechanistic basis for the potential application of BTX-A as a combined mechanical and neurogenic modulator in the treatment of pathologic scarring. Numerous pharmacological agents with varying degrees of efficacy further complicate the therapeutic landscape in HK. A network meta-analysis of non-surgical drugs, such as corticosteroids, 5-FU, bleomycin, and verapamil, found large differences in results between studies. The authors suggested using a consistent treatment approach based on the underlying mechanisms (Yang et al., 2021). While BTX-A is not the main focus of this review, the results underscore the heterogeneity of standard therapies and provide some indication for investigating new or co-therapies targeting multiple mechanisms to enhance repair. Other direct-prove mechanistic reviews, exclusively focusing on intralesional BTX-A, have so far confirmed its perspective as an adaptation in HK-treatment. BTX-A slows fibroblast growth, lowers collagen formation, and changes levels of microelements that promote fibrosis. This may allow it to prevent scarring, without having a direct effect on muscles (Sutedja et al., 2025).

Other studies have shown that BTX-A can improve scar quality by altering tension distribution and affecting the healing process (Jerzak et al., 2024). Together, the results suggest that BTX-A provides benefits beyond symptom relief and acts as a biologically relevant agent in managing pathological scars. The limited efficacy of available non-surgical treatments, the biological complexity of HK, and the increasingly discovered new aspects of the pharmacological mode of action of BTX-A call for a detailed review of BTX-A, comparing it with alternative scar treatment modalities.

This review aims to consolidate and summarize available mechanistic and clinical data on BTX-A, juxtapose its effectiveness with existing conservative treatment modalities, and elucidate its possible incorporation into modern, personalized therapy schemes for hypertrophic and keloid scars.

2. REVIEW METHODS

We prepared this article as a narrative review of contemporary evidence on the use of Botulinum Toxin Type A (BTX-A) in the prevention and treatment of hypertrophic and keloid scars. This review was conducted using a systematic literature search of the years 2020-2025 across the PubMed/MEDLINE, Scopus, and Web of Science databases. The queries combined the terms "botulinum toxin type A", "hypertrophic scar", "keloid", "wound healing", "scar prevention", and "non-surgical treatment". All identified studies were screened based on titles and abstracts, and subsequently on full texts. We included 22 full-text papers that directly evaluated BTX-A or similar non-surgical modalities in the treatment of hypertrophic (HTS) and keloid scars in this review (Figure 1).

The primary studies included were randomised controlled trials, clinical comparative studies, mechanistic (bench-to-bedside) experimental research, narrative review articles, and systematic reviews/meta-analyses. We included studies that examined BTX-A alone or combined with other standard therapies. We also included studies in which BTX-A was part of more complex multimodal treatments, in line with current clinical algorithms for scar management. The analysis excluded studies that did not assess BTX-A clinically or mechanistically. It also excluded studies based only on expert opinion. Studies that did not focus on hypertrophic or keloid scars were also excluded. The review then collected data from the eligible studies. Finally, it organized the data into common themes and summarized them narratively.

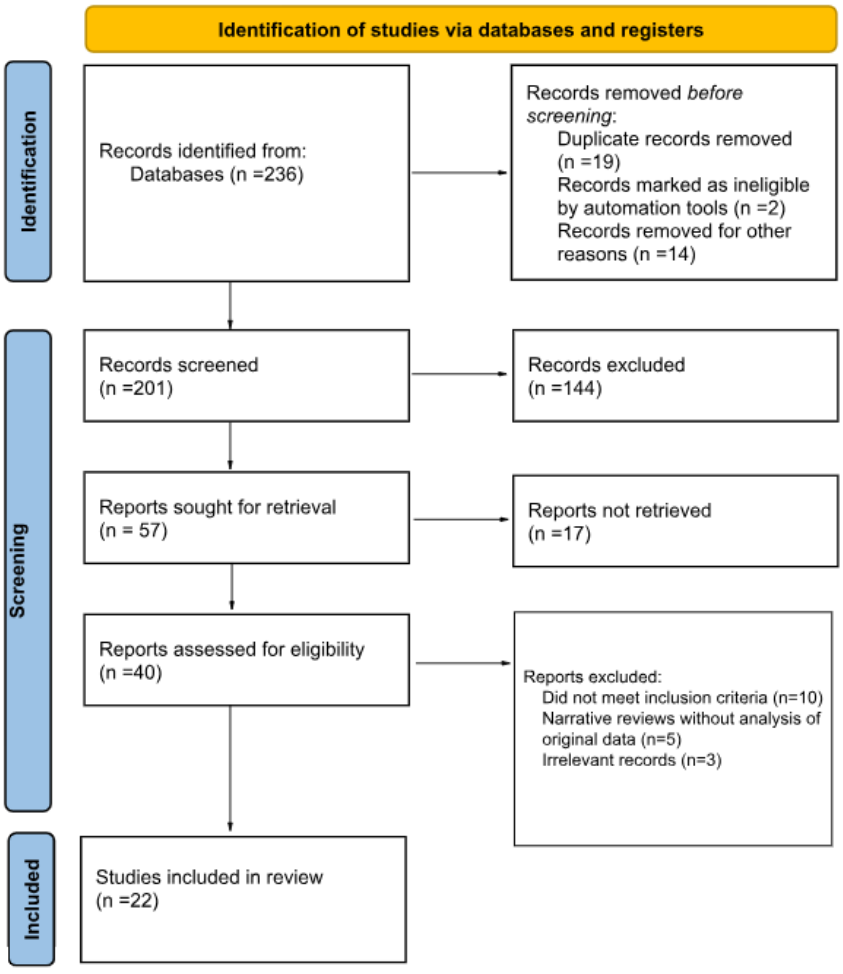

Figure 1. Flow chart

3. RESULTS AND DISCUSSION

Evidence for BTX-A Monotherapy in Surgical and Traumatic Scars

Randomized controlled trials conducted in different surgical settings consistently support the use of Botulinum Toxin Type A (BTX-A), which works well on its own to improve early scars. In a prospective, double-blind, randomized trial of patients undergoing thyroid surgery, Bae et al., (2020) found that BTX-A injected around the incision resulted in scars that were much better than those in the control group. Scars had lower scores on both the Vancouver Scar Scale (VSS) and the Patient and Observer Scar Assessment Scale (POSAS).

Previous studies have shown similar results in the periorbital area, which is sensitive and has consistent muscle movement. In a double-masked, randomized trial of patients undergoing lower blepharoplasty, Huang et al., (2021) found that BTX-A improved scar appearance. Scars were flatter, softer, and had better texture and shape than those in the control group. These benefits included higher VSS and POSAS scores and reduced postoperative pain. This shows that reducing muscle tension in the orbicularis oculi early in healing is important BTX-A also helps with traumatic wounds, not just planned surgeries. Patil et al., (2022) in a prospective randomized comparative study of post-traumatic facial lacerations. Observed a remarkable reduction in scar width and pigmentation, as well as overall contour in patients receiving BTX-A vs. those subjected to the standard treatment. Both observer and patient scales favoured against BTX-A treatment: VSS and POSAS scores were lower, and patients reported less discomfort and a better cosmetic appearance of their scars. These data have particular applicability in facial trauma, where extreme mobility and complex musculature place the area at a higher risk for visible hypertrophy.

Further support comes from gender-affirming chest surgery. In a randomized, prospective study, Winayanuwattikun et al., (2023) treated transmen who had undergone mastectomy with BTX-A injections at the incision site. The treatment led to improvements in scar elevation, contour, and overall appearance, and resulted in higher POSAS scores at the final visit compared with the control group. This is significant because mastectomy scars have a high surface area-to-volume ratio and experience great mechanical stress. In those trials, dosing regimens were not uniform but generally ranged from 2 to 5 U/cm of incision length.

Although the methods of the RCTs varied, all four RCTs yielded consistent findings that BTX-A monotherapy improved objective scar scales (VSS, POSAS) and symptoms, including tension or pain, at different high-risk surgical sites. Taken together, these results indicate that BTX-A has the potential to serve as an all-around monotherapy for early modification of surgical or traumatic SCARs, especially when such SCARs occur in regions exposed to major dynamic or static mechanical forces.

BTX-A in Burn and Post-Burn Scars

Randomized controlled trials have shown that BTX-A has significant positive effects on hypertrophic burn scar treatment, thus its use extends beyond surgical wounds. Researchers have evaluated children who have developed post-burn hypertrophic scars and observed an improvement in a number of different areas after receiving treatment with BTX-A (Tawfik & Ali, 2023). The treatment areas had less erythema, pruritus, and scar hardness, with increased pliability, compared with the control sites. These resultscould be of special relevance as children are at increased risk for developing hypertrophic scarring and have symptoms that are difficult to manage, which may make adherence to standard therapy challenging. Importantly, BTX-A was safe, and no serious side effects occurred during treatment. This makes it especially suitable for children (Tawfik & Ali, 2023).

Researchers studied the effects of BTX-A delivered through iontophoresis on scars after burns. They found that it eased symptoms faster and better than standard treatment (Alnawagy et al., 2025). Redness rapidly decreased, and the scar's texture and flexibility improved. Because iontophoresis does not require intra-lesional injections, which can cause pain or trauma (especially in scarred tissue or in children, who may be significantly more sensitive), using iontophoresis has a major practical advantage over other treatments. With a non-invasive application, iontophoresis could offer an opportunity to expand the use of BTX-A in patient practices where injection-associated discomfort reduces compliance (Alnawagy et al., 2025).

In summary, these results indicate that BTX-A is effective not only for surgical scars but also for complex, long-standing hypertrophic scars following burns. Such rapid symptom resolution in paediatric and adult patients indicates that BTX-A might act, via neurogenic or vascular pathways, on the pathophysiological process underlying scarring, as seen in burn hypertrophy. Thus, BTX-A offers a potential treatment modality for post-burn scars, especially when pruritus, erythema, or pain is excessive.

Combined and Sequential Treatments Involving BTX-A

Different studies suggest that BTX-A for hypertrophic scars is often more efficacious when combined with several treatment approaches. One of these studies was a retrospective trial showing the use of BTX-A combined with a type of specialized fractional

laser treatment and topically applied growth factors resulted in significantly better outcomes in relation to the clinical assessment of the scar's height, texture, pliability and overall cosmetic appearance, i.e. than just using BTX-A or one of the other treatment modalities by itself. Patients demonstrated a significant decrease in scar stiffness and irregularity, and an increase in elasticity and surface smoothness with treatment. The synergistic effect reported here suggests that perfusion and fecal tagging complement each other. The fractional CO_2 laser produces microthermal injuries in a controlled manner, stimulating dermal remodelling and increasing the absorption of topical treatments used after laser procedures. The use of growth factors also initiates regenerative pathways, stimulates cellular turnover, and increases the deposition of physiologic extracellular matrix.

Using Botulinum Toxin early in treatment reduces mechanical tension in scars, making it more effective than treatments without BTX-A. Its mechanism is to relax the muscle fibres right under the scarred tissue. It also lowers tension on the healing skin (Wang et al., 2024). Reducing stress may help the skin heal more effectively and respond better to laser treatment. More importantly, the results of the retrospective analysis support that in cases with complex scars, and specifically those with an increased surface area, thickness, or where fibrous tissue architecture has already developed, isolated approachesmight not be adequate. In these circumstances, combining therapies may be more effective than single therapy for treatingthe bio-, biomechanical, and structural aspects of hypertrophic scars. The study by Wang et al., (2024) provides early evidence of this possibility. This suggests that BTX-A can play a key role in these treatment plans. It prepares the tissue beforehand to help other therapies start working and makes them more effective. Although there is no strong evidence from randomized controlled trials, current data support the use of BTX-A as part of planned step-by-step treatment protocols. These combination treatments might be more effective in treating mature, resistant, or cosmetically distressing hypertrophic scars.

Systematic Evidence and Meta-Analytic Support for BTX-A

High-quality evidence from systematic reviews and meta-analyses continues to show the benefit of Botulinum Toxin Type A (BTX-A) in the treatment of hypertrophic and keloid scars. A new meta-analysis of RCTs in Cureus showed that BTX-A improves scars and lowers VSS and POSAS scores compared with placebo (Raslan et al., 2024). The investigation also revealed substantial reductions in patient-reported pain and incision-site tightness, which supported the clinical observation that chemodenervation disrupts wound healing-associated dynamic and static tension, which represents a major factor responsible for pathological scar formation. These results complement and extend the previously reported RCT data and support the notion that BTX-A effects may not be specific to particular surgical techniques but extend to a broader range of high-risk anatomic areas.

A recent scoping review and narrative compilation of BTX-A use in hypertrophic and keloid scars across various body sites and clinical indications provides additional evidence (Frątczak et al., 2025). The authors' review found that BTX-A reliably improves scar contour, softness, height, and symptoms, irrespective of aetiology (surgical, traumatic, or idiopathic keloid). The authors highlighted the fact that not just in early postoperative scars, but also in some mature scars, they observed changes, which indicate that BTX-A may interfere with both early wound remodeling and later fibrotic consolidation. The review shows that BTX-A has many roles in scar treatment (Raslan et al., 2024; Frątczak et al., 2025). Differences in scar assessment methods, injection techniques, and patient characteristics make it harder to compare results between studies. However, despite the variety of studies included, a trend is apparent throughout: that BTX-A yields both statistically and clinically significant reductions in hypertrophic scarring severity, as measured by objective assessments and subjective patient evaluations. In conclusion, systematic and meta-analyses provide clear evidence that BTX-A is an effective modality in hypertrophic scar therapy. The uniformity of the effect across different ethnic groups and scar subtypes confirms BTX-A's efficacy and suggests its incorporation into evidence-based clinical protocols.

Mechanistic and Biological Insights into the Effects of BTX-A

Increasing mechanistic evidence provides a coherent biological explanation for the clinical efficacy of Botulinum Toxin Type A (BTX-A) in modulating hypertrophic and keloid scars. A molecular review of BTX-A in scar therapy shows that it works by temporarily relaxing the muscles under the wound. This reduces tension at the wound edges, limits tissue damage, and fights fibroblast hyperactivity (Baranowska et al., 2024). Mechanical tension is known to cause hypertrophic scars, especially in rapidly moving parts of the body. BTX-A disrupts this mechanism, creating a better environment that supports proper wound remodelling with less scarring and proliferation. Aside from its biomechanical impact, BTX-A also appears to have direct cellular effects on fibroblast activity by modulating numerous signaling pathways involved in HS formation. Data collected in the molecular review presented suggest that BTX-A can influence fibroblast proliferation, inhibit myofibroblast differentiation, and reduce extracellular matrix protein production,

particularly the expression of collagen types I and III, which are overexpressed during hypertrophic remodeling. This antifibrotic effect on collagen synthesis may also be directly pertinent to the increased elevation and relative resistance of AdS scar formation.

Furthermore, BTX-Arelieved transforming growth factor-β1 (TGF-β) activity, which is a dominant profibrotic cytokine in perpetuating fibroblast activation and overproduction of extracellular matrix (Baranowska et al., 2024). Additional mechanistic understanding comes from work related to neurogenic and inflammatory mediators of hypertrophic scarring. Previous studies have shown that the substance P (SP)-neurokinin-1 receptor (NK1R) system is more active in hypertrophic scars. This increased activity attracts fibroblasts to the scar. It also raises levels of inflammatory signals. In addition, it promotes the growth of new blood vessels and makes them more leaky (Zhang et al., 2022). Overactivity of this pathway leads to ongoing inflammation, a key feature of pathological scars. Studies have shown that BTX-A reduces the release of neuropeptides at the neuromuscular junction. It likely also slows SP signaling in the skin. BTX-A helps reduce inflammation. Also, scarring after BTX-A treatment is less likely, and the development of hypertrophic scars is stopped. It has been shown that BTX-A reduces levels of pro-inflammatory mediators in many tissues (Sutedja et al., 2025; Baranowska et al., 2024). These effects help the tissue heal in a controlled way and prevent fibroblasts from becoming overactive. Taken together, our findings indicate that BTX-A is a biomechanical modulator (decreasing tension) and a neurobiological modulator (modulating neuropeptide activity and inflammatory pathways). Due to its effects on fibroblast proliferation, collagen synthesis, and cytokine production, as well as on neurogenic inflammation, it provides a multi-pathway mechanistic foundation for the clinical benefits observed in a host of randomized trials. By acting at multiple levels in the cascade of events leading up to scar formation, BTX-A favors a wound-healing environment that promotes regulated remodeling rather than pathological fibrosis, explaining not only how but also why hypertrophic and keloid scars can benefit from BTX-A treatment. To sum it up, BTX-A has many promising uses in future treatments (Table 1).

Table 1. Summary of Non-Surgical Modalities in Hypertrophic and Keloid Scar Management

Modality	Mechanism of Action	Clinical Evidence	Key Benefits
Botulinum Toxin Type A (BTX-A)	Reduces mechanical tension; modulates fibroblasts; inhibits SP-NK1R pathway; lowers TGF-β and collagen I/III.	Multiple RCTs and meta-analyses (surgical, traumatic, burn scars).	↓ Scar height, erythema, pain, pruritus; improved VSS & POSAS scores.
BTX-A in Post-Burn Scars (incl. iontophoresis)	Reduces inflammation and neurogenic signaling; improves pliability.	RCTs in pediatric and adult burn patients.	↓ Pruritus, erythema, hardness; non-invasive option via iontophoresis.
Sequential / Combined Therapy (BTX-A + Laser + Growth Factors)	Synergistic remodeling: tension reduction + dermal microthermal stimulation.	Retrospective clinical studies.	Improved elasticity, texture, scar height in complex/mature scars.
Conventional Therapies (Steroids, 5-FU, Silicone, etc.)	Anti-inflammatory, antifibrotic, pressure or occlusion-based mechanisms.	Variable efficacy; heterogeneous study outcomes.	Widely used; no clear gold standard; recurrence common.

Limitations of current treatment methods

Although the evidence in favor of the use of Botulinum Toxin Type A (BTX-A) agents for the management of hypertrophic and keloid scarring is increasing, several significant limitations persist in the literature. Systematic reviews and meta-analyses show significant heterogeneity in BTX-A treatment, including dose (commonly 2–5 U/cm), injection depth, distribution pattern, and timing relative to surgery or injury. This heterogeneity complicates the comparison of results between studies and hinders the development of universally accepted clinical guidelines. Studies check scars at different times. Some look after 1–3 months, others after 6–12 months. This makes it hard to compare results and makes long-term healing unclear. Another key limitation is that the studies do not use standard outcome measures. Most clinical trials have used objective tools such as the Vancouver Scar Scale (VSS) or the Patient and Observer Scar Assessment Scale (POSAS); other trials have used non-standardized scores, which are more subjective and therefore less reliable.

The absence of standardization, which defines both when to assess outcomes and how to define improvement, is another source of methodological inconsistency (Raslan et al., 2024; Frątczak et al., 2025). Geographical and anatomical variation also contribute to the problem. Research typically focuses on one anatomical region (e.g., neck, eyelids, trunk, or limbs) that undergoes various mechanical stresses and scarring responses. Consequently, positive outcomes seen in one area (e.g., periorbital scars) do not necessarily carry over to others (e.g., high-tension sternotomy or shoulder scars). Furthermore, most published studies are in adults, and data on pediatric conditions are scarce, as is information on darker skin phototypes, which bear a higher risk of developing pathological scarring. Finally, mechanistic reviews show that BTX-A has several effects, including relaxing tension and altering fibroblast and neuropeptide function. However, its long-term effects and the clinical results are not well studied (Baranowska et al., 2024). Available trials tend to report outcomes for the short- or medium-term, without long-term follow-up, which prevents testing whether improvements observed early in the intervention are sustained over the years.

Ultimately, these limitations highlight the importance of conducting RCTs with proper design, standardization, consistent dosing, consistent outcome measures, long-term follow-up, and representation across a variety of patient populations. Establishing this methodological consistency is essential to creating evidence-based guideline recommendations for BTX-A use in the prevention and treatment of scars.

4. CONCLUSION

Botulinum Toxin Type A (BTX-A) is emerging as a promising non-surgical modality for both prevention and treatment of hypertrophic and keloid scars. Randomized trials and reviews show that BTX-A improves scar quality. It lowers scar height and redness, and reduces symptoms such as pain and itching. Improvements can be seen across all types of scars, including surgical, traumatic, and burn scars. BTX-A reduces the tension on the scar at the wound site, regulates fibroblast activities, limits the formation of the collagen produced, and decreases the nerve-induced inflammation. These actions help prevent the formation of pathological scars. BTX-A works in several ways, unlike many standard treatments that rely on a single method. Current evidence also shows that BTX-A is effective when combined with other treatments. Differences in dose, timing, outcome measures, and follow-up make it difficult to compare studies across the various methods used in clinical practice. This also prevents the creation of standard treatment protocols. The long-term results and the best treatment plan remain unclear. Overall, BTX-A is safe and works well as an additional therapy for scars. Using it in personalized, mechanism-based plans may help patients with hypertrophic and keloid scars. However, more high-quality studies are needed to clearly define its role in everyday practice.

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Informed consent

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Ethical approval

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Conflict of interest

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Data and materials availability

All data associated with this work are present in the paper.

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