

Application of Botulinum Toxin A for Prevention of Scar Formation and Improve the Cosmetic Results in Thyroidectomy and Lateral Neck Dissection Incision Site

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Background: The aim of this study was to evaluate the effect of botulinum toxin injection on the prevention or reduction of hypertrophic scarring at the incision site following thyroid surgery.

Materials and Methods: Upon completion of thyroidectomy, half of each incision was marked, and botulinum toxin was injected 1 cm from the incision margins at a dose of 7.5 U/cm². For the control side, normal saline was injected along the remaining half of the incision. Patients were photographed at one and three months postoperatively, and scar quality was assessed using the Vancouver Scar Scale (VSS).

Results: Fourteen female patients with a mean age of 35.5 ± 7.08 years participated in the study. Eleven patients (78.6%) underwent thyroidectomy, two (14.3%) had modified radical neck dissection (MRND), and one patient underwent lateral neck dissection. The mean VSS score for the botulinum toxin-treated area was 1 at one month and 0 at three months, whereas the corresponding scores for the saline-treated area were 2 and 1, respectively (p = 0.001). In both groups, VSS scores improved significantly after three months (p < 0.001).

Conclusion: Injection of botulinum toxin at a defined dose produced satisfactory aesthetic outcomes and resulted in statistically significant improvement compared with saline control areas.

Keywords: Surgical scar, Botulinum toxin, Thyroidectomy, Lymphatic dissection

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Introduction

Facial scars hold considerable psychological and social significance. Scars resulting from facial wounds typically develop along Langer's lines, where mechanical tension on wound edges transfers to newly synthesised collagen during the healing phase. This process may result in scar widening, hypertrophy, and hyperpigmentation due to excess collagen deposition. Furthermore, elastic tension in scars aligned with Langer's lines is often inadequately resolved. In such cases, botulinum toxin (Botox) induces temporary paralysis of the surrounding muscles, thereby reducing tension on the wound edges and preventing scar widening, hypertrophy, and hyperpigmentation (1–4).

Thyroidectomy is a common surgical procedure, with recent attention directed towards improving postoperative scar appearance and exploring alternative techniques. Postoperative prognosis is important not only from a clinical perspective but also in terms of the aesthetic repair of the mid-cervical incision. Many thyroidectomies are performed for benign thyroid disorders requiring long-term follow-up, during which patient satisfaction with scar aesthetics and its effect on quality of life is emphasised. Factors such as skin thickness, body mass index (BMI), and gender influence scar formation following thyroidectomy. In various studies, the incidence of hypertrophic scarring after thyroidectomy has been reported to range between 6.55% and 16.4% (5–7).

Recent investigations have examined the therapeutic efficacy of botulinum toxin and steroid injections for hypertrophic scar management, suggesting enhanced outcomes with combination therapy (8). Laboratory and clinical research on botulinum toxin has demonstrated that it can prophylactically relax the underlying musculature, thereby reducing wound tension and potentially improving tissue perfusion. Moreover, prophylactic muscle paralysis achieved with botulinum toxin may attenuate local pain and consequently enhance perfusion (9–11).

Scar formation following thyroidectomy incisions may cause distressing symptoms and aesthetic concerns for patients. The present study aims to evaluate the prophylactic effect of botulinum toxin

injections in preventing or reducing hypertrophic scar formation at the incision site and improving aesthetic outcomes.

Materials and methods

In this clinical study, following approval of the research proposal by the Research Centre for Cardiovascular Diseases, Mazandaran University of Medical Sciences, the investigation was conducted from June to September 2020 (Registry number: IR.MAZUMS.IMAMHOSPITAL.REC.1399.029).

Patients were enrolled after providing informed consent and receiving a full explanation of the study protocol and the drug administration process. Data on age, sex, presence of diabetes, and hypersensitivity to botulinum toxin were recorded. Participants eligible for inclusion in the study on botulinum toxin A for scar prevention and cosmetic improvement following thyroidectomy or lateral neck dissection were adults aged 18–70 years scheduled for these procedures, with no pre-existing scars or keloids at the incision site, in good general health (ASA I–II), and capable of providing consent and adhering to follow-up assessments. Exclusion criteria comprised hypersensitivity to botulinum toxin A, neuromuscular disorders, active neck infections, uncontrolled systemic diseases, pregnancy, recent scar-modifying treatments, or the use of medications affecting wound healing, as well as unrealistic cosmetic expectations, a history of non-compliance, or participation in concurrent clinical trials.

The sample size for the randomised controlled trial investigating botulinum toxin A for scar prevention and cosmetic improvement following thyroidectomy and lateral neck dissection was determined through a power analysis to detect a clinically meaningful difference in a primary outcome, such as scar severity (e.g., Vancouver Scar Scale) or cosmetic satisfaction score, between the treatment and control groups. Assuming a two-sample *t*-test for continuous outcomes, the key parameters included an effect size (e.g., a 2-point difference in scar scores with a standard deviation of 3), a significance level ($\alpha = 0.05$), and a statistical power of 80% ($1 - \beta = 0.8$), with an allocation ratio of 1:1.

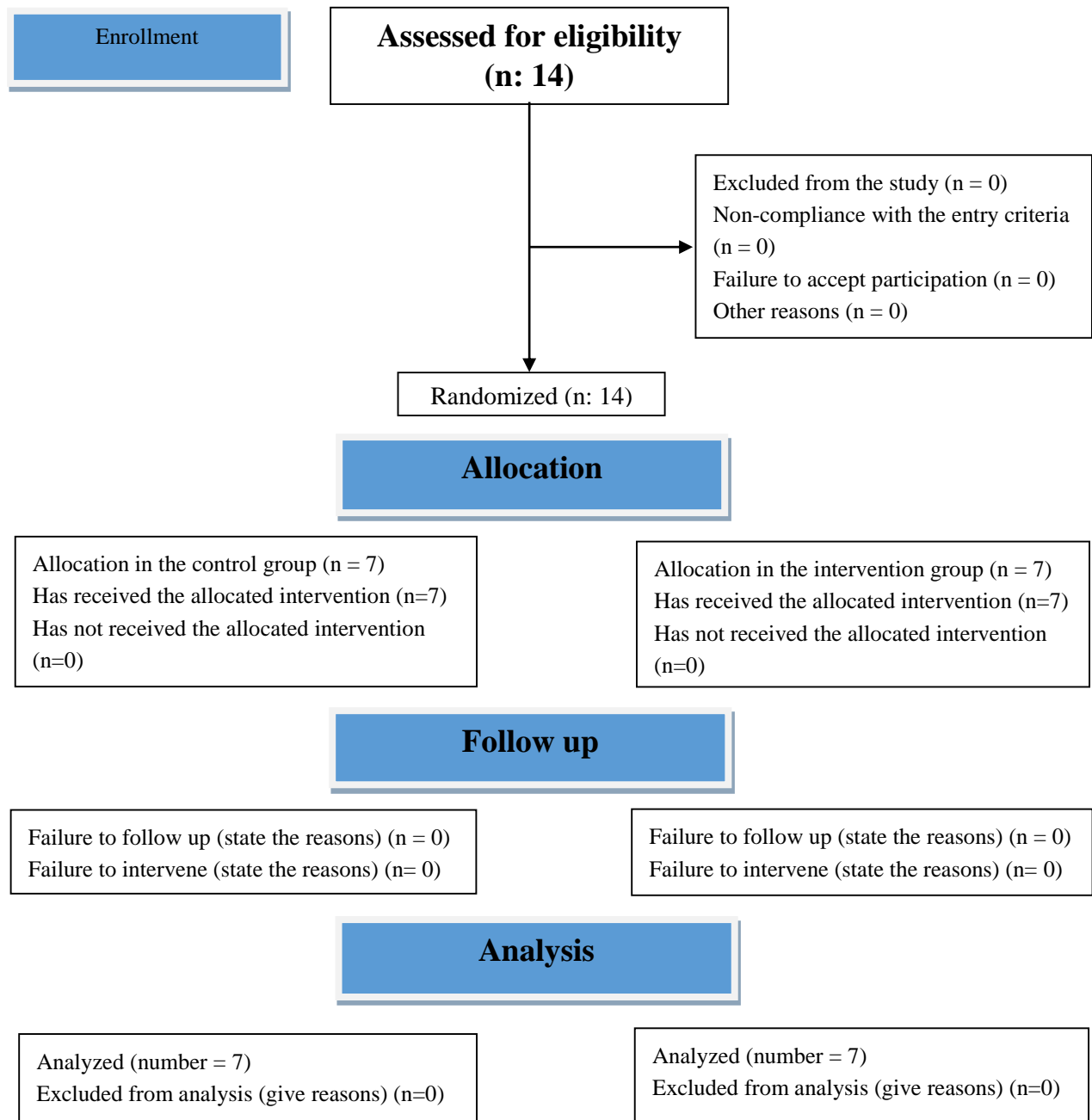


Fig. 1. Consolidated Standards of Reporting Trials Flow Diagram

Using statistical software such as G*Power or a standard calculation formula, the total required sample size was estimated to be 14 participants (Figure 1).

Based on previous studies and relevant references, half of the incision length was delineated, and botulinum toxin A was injected at a distance of 1 cm from the incision margins at a dose of 7.5 U/cm² at the

injection sites. For the remaining half of the incision, normal saline was injected as a control. All injections were administered immediately after surgery. The maximum total injection dose in the neck region was 50 units to ensure patient safety.

Masport, supplied in 500-unit vials, was prepared by dilution with 3 mL of normal saline before injection

and administered into the dermal layer parallel to and along the incision line. The injection site was photographed at 1- and 3-month intervals and evaluated using the Vancouver Scar Scale (VSS) checklist. Photographs were obtained at specified intervals by a technician blinded to the intervention. Furthermore, the images were reviewed by a dermatologist who was also blinded to the intervention, and VSS scoring was performed for the examined tissues.

In both groups, premedication was administered intravenously with Sufentanil ($1.5 \mu\text{g}\cdot\text{kg}^{-1}$) and Midazolam (2 mg). Anaesthesia induction was achieved using Thiopental Sodium ($3\text{--}5 \text{mg}\cdot\text{kg}^{-1}$), followed by muscle relaxation for intubation with Pancuronium ($0.5 \text{mg}\cdot\text{kg}^{-1}$). Anaesthesia was maintained with 1–3% Isoflurane. For thyroidectomy and lateral neck dissection, a 7 cm incision was made in the anterior neck region, 2 cm above the sternal notch (McFee incision). Upon completion of the thyroidectomy, the strap muscles and platysma were approximated with 4/0 Vicryl sutures. Skin closure was achieved with 3/0 Nylon in a running subcuticular fashion. Lateral neck dissection was performed through an apron incision. Postoperatively, patients were visited daily by a surgeon in a blinded manner until discharge and were re-evaluated on day 7 after discharge. Statistical analyses were performed using SPSS software (version 24.0), with a *p*-value of less than 0.05 considered statistically significant.

Results

In this study, 14 women participated, with a mean age of 35.5 ± 7.08 years. None of the participants had diabetes or were receiving corticosteroid therapy. According to the Fitzpatrick classification of skin

types, 10 individuals (71.4%) were categorised as type III, and the remaining 4 (28.6%) as type II. Of the total sample, 11 participants (78.6%) underwent thyroidectomy, 2 (14.3%) underwent modified radical neck dissection (MRND), and 1 underwent lateral neck dissection.

Assessment of scar thickness at the incision site showed that 8 individuals (57.1%) had normal thickness (0 mm), 4 (28.6%) had a 1 mm-thick scar, and 2 (14.3%) had a 2 mm-thick scar. With respect to scar erythema, 10 participants (71.4%) had pink scars, whereas the remainder showed no erythema. Regarding pigmentation, 4 (28.6%) had hypopigmented scars and the others exhibited normal pigmentation. In terms of scar induration (degree of firmness), 7 individuals (50%) had soft scars, 1 (7.1%) had a firm scar, and the remainder demonstrated normal induration.

Statistical analysis of the Vancouver Scar Scale (VSS) scores indicated that the mean score for the area injected with botulinum toxin A at 1-month and 3-month follow-up was 1 and 0, respectively. In contrast, the corresponding mean scores for the area injected with saline were 2 and 1, respectively, with a statistically significant difference between the two groups ($p=0.001$) (Table 1). In both the saline and botulinum toxin groups, VSS scores decreased significantly after 3 months (within-group effect, $p < 0.001$) (Figure 2).

Across the study period, VSS scores were consistently lower in the botulinum toxin group than in the saline group, and this between-group difference was statistically significant ($p=0.001$). As demonstrated, the mean VSS score decreased in both treatment areas over the 3-month period.

Table 1. Average VSS Score in Areas Treated with Botulinum Toxin and Normal Saline

	Time		Effect	
	1 month (VSS score)	3 month (VSS score)	Within group	Between group
Saline	2 (2-4.25)	1 (1-3.25)	<0.001	0.001
BTX-A	1 (1-1)	0 (0-1)	<0.001	
P value	0.001	<0.001	-----	-----

However, the score reduction was more pronounced in the area injected with botulinum toxin at both follow-up intervals, and this difference reached

statistical significance, indicating a superior aesthetic outcome following botulinum toxin injection in the neck incision sites (Figure 3).

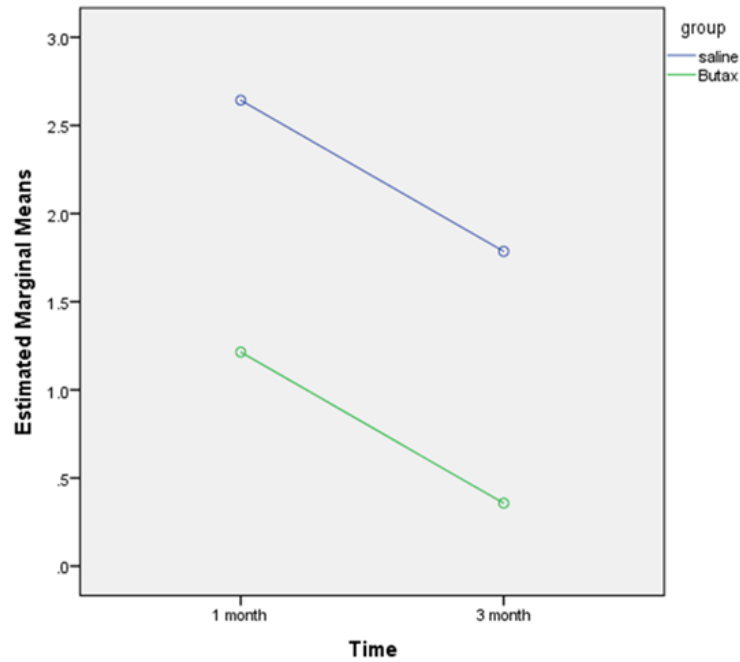


Fig. 2. Trends in the average VSS score changes in two groups: saline and botulinum toxin, at 1 and 3 months post-surgery



Fig. 3. Improved body aesthetics following injection of botulinum toxin in the thyroidectomy incision area

Discussion

In this clinical study, we investigated the effects of botulinum toxin in preventing scar formation and improving aesthetic outcomes in the incision area of thyroidectomy and lateral neck lymphadenectomy. The study design involved each participant serving as both control and experimental group, thereby eliminating certain unidentified variables influencing scar formation. Basic science research examining the effects of botulinum toxin type A on wound healing has involved multiple injections of the toxin. Xia *et al.* demonstrated in an animal model that serial injections of botulinum toxin type A reduce collagen thickness and deposition in hypertrophic scars. Although the exact mechanism of collagen reduction by botulinum toxin type A was not conclusively determined in that study, a subsequent experimental study by the same group showed that botulinum toxin type A inhibits TGF- β 1 protein expression. TGF- β 1 plays a crucial role in hypertrophic scar formation by influencing fibroblast activity. Serial injections of botulinum toxin type A may prolong the inhibitory effects on TGF- β 1 during the scarring process, potentially leading to a more profound modulation of wound healing; however, this has not been definitively proven (12).

In cosmetically sensitive areas such as the neck, wound healing is a major concern for patients. One leading motivation for the adoption of minimally invasive techniques in thyroid and parathyroid surgery, compared with conventional approaches, is the improvement of postoperative scar aesthetics, which enhances overall patient satisfaction and quality of life. Justifications for the higher cost of the specialised equipment required for these minimally invasive procedures, as well as their potential to prolong operative time, are frequently cited. Most patients who undergo standard thyroidectomy and develop symmetrical neck scars located centrally typically achieve satisfactory aesthetic results, with linear scars that gradually fade over time. However, patients predisposed to hypertrophic scarring may experience aesthetic concerns. In such cases, the risk of hypertrophic scar formation should be carefully assessed, and alternative techniques such as endoscopic or robotic thyroidectomy should be considered (13, 14).

Phillips and colleagues reported that, at six months post-surgery, scarring severity was significantly lower in areas injected with botulinum toxin than in corresponding saline-treated regions. The VSS score difference between the two sites averaged -3.0556, and patients predisposed to scarring were shown to benefit from botulinum toxin injection (15). Consistent with those results, our findings demonstrated that the mean VSS score for the botulinum toxin-injected area was significantly lower than that of the saline-injected area. Specifically, the scores at one and three months were 1 and 0, respectively, for the botulinum toxin area, compared with 2 and 1 for the saline area, with a statistically significant difference between the two groups ($p = 0.001$).

Kim and colleagues further demonstrated that the average time for hypertrophic scar formation is 3.19 months. Their study found no significant difference in age, gender ratio, tumour type, or surgery type between groups. However, multivariable analysis revealed that when a surgical incision was located within 1 cm above the sternal notch, when the sternocleidomastoid muscle was more prominent, or when the patient's BMI was high, the likelihood of hypertrophic scar formation increased. These three identified risk factors are potentially modifiable. Current findings suggest that surgeons should create thyroidectomy incisions more than 1 cm above the sternal notch and avoid incisions in areas where the sternocleidomastoid muscles are highly prominent. Moreover, weight reduction should be recommended to patients with elevated BMI before surgery. If one or more of these risk factors cannot be modified, endoscopic or robotic thyroidectomy should be considered as an alternative (16).

Previous studies have shown that informing patients about risk factors and managing expectations before thyroidectomy positively influences patient satisfaction. Identifying patients at high risk for scar formation and providing appropriate counselling can improve postoperative satisfaction. Predictive factors for hypertrophic and keloid scar formation may also guide the pre-emptive use of therapies such as intralesional corticosteroid injection, laser therapy, or radiation, thereby optimising scar outcomes (17, 18). In

our study, all participants were female and expressed satisfaction with their involvement in the trial, perhaps reflecting a heightened concern for aesthetic and reconstructive results following cancer surgery. The findings were well accepted by participants.

The mechanism by which skin thickness influences scar formation remains unclear. It is hypothesised that the distribution of collagen within the dermal layers may contribute to this effect. Type I collagen fibres are distributed throughout the entire dermis, whereas type III fibres are located predominantly within the papillary and subpapillary layers. The reticular dermis forms the bulk of the dermis and contains a higher proportion of type I collagen fibres. In patients with greater dermal thickness, a higher type I-to-type III collagen ratio is expected. Although the precise mechanism remains uncertain, the significant role of type III collagen in wound healing has been acknowledged. A higher proportion of type I relative to type III collagen may, therefore, promote hypertrophic or less pliable scars. Microscopic examination of collagen structure in patients with thick dermis may provide insights into predicting scar formation. Further research is required to confirm these observations (19, 20).

In a study by Chen and colleagues investigating the effects of BTX-A and triamcinolone, alone and in combination, on hypertrophic scar improvement in an animal model, lesion size was reduced by 10% in the control group, 17% in the triamcinolone group, 23% in the botulinum toxin group, and 30% in the combination group ($p < 0.05$). Fibroblast counts decreased correspondingly from 0.58 in the control group to 0.44 in the triamcinolone group, 0.21 in the botulinum toxin group, and 0.08 in the combination group ($p < 0.05$), indicating a marked synergistic effect when the two treatments were combined. Although the aetiology of hypertrophic scar formation remains incompletely understood, strong evidence supports the role of mechanical stress. Laboratory findings suggest that extracellular mechanical forces are transmitted into biochemical and genetic signals within cells via focal adhesion kinases triggered by extracellular matrix components (21).

Our study aimed to enhance aesthetic outcomes following thyroidectomy and lymphatic neck dissection. Over the three-month follow-up, it was clearly demonstrated that botulinum toxin injection at a specific dose produced significantly superior aesthetic results compared with normal saline injection, with statistically meaningful differences between groups.

Declarations

Ethics approval and consent to participate:

In this clinical study, following approval of the research proposal by the Research Centre for Cardiovascular Diseases, Mazandaran University of Medical Sciences, the study was initiated on 16 June 2020 (registry number: IR.MAZUMS. IMAMH-OSPITAL. REC.1399.029). Initially, the researcher obtained from a nurse a list of patients scheduled to undergo midline abdominal surgeries. In accordance with the Declaration of Helsinki and the principles of Human Ethics and Consent to Participate, the researcher explained that neither the assessment procedures nor the administration of botulinum toxin A were expected to cause any apparent adverse effects, and that participants could withdraw from the study at any time without any consequences for their care. All methods were performed in compliance with the relevant institutional guidelines and regulations.

Availability of Data and Materials:

The datasets generated and/or analysed during the current study are available from the corresponding author upon reasonable request.

Conflict of Interest:

The authors of the study entitled *Application of Botulinum Toxin A for the Prevention of Scar Formation and Improvement of Cosmetic Results in Thyroidectomy and Lateral Neck Dissection Incision Sites* declare no conflicts of interest. All financial relationships or affiliations that could potentially influence the research have been fully disclosed. No external funding affected the design, conduct, or reporting of this study.

The research was conducted in accordance with ethical standards, ensuring participant safety and unbiased presentation of findings.

Funding

This clinical study was conducted following approval of the research proposal by the Research Centre for Cardiovascular Diseases, Mazandaran University of Medical Sciences (registry number: IR.MAZUMS.IMAMHOSPITAL.REC.1399.029; approval date: 16 June 2020). No external funding was received for this research.

Limitations

Several limitations of this study should be acknowledged to contextualise the findings. First, the small sample size limits the generalisability of the results and reduces the statistical power of the analyses. In addition, the relatively short follow-up period restricts assessment of the long-term outcomes of the intervention. The inclusion of only female participants may limit the applicability of results to male patients and the broader population. Certain factors known to influence scar formation, including diabetes status, body mass index (BMI), family history, and incision orientation, were neither assessed nor controlled for. Furthermore, the absence of a comparison group receiving standard care prevented direct evaluation of the relative efficacy of botulinum toxin A. Finally, photographic documentation was suboptimal, which may affect the objectivity and reproducibility of scar assessments. Future studies should address these limitations by incorporating larger and more diverse populations, extended follow-up, comprehensive evaluation of contributing factors, comparison with established therapies, and enhanced imaging protocols.

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