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Impact of intralesional botulinum toxin type A therapy on the keloid-related quality of life

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Abstract

Background We aimed to validate the translated Arabic version of the head and neck keloid quality-of-life (QOL) questionnaire. We also aimed to evaluate the impact of intralesional botulinum toxin type A (BTA) therapy on the keloid-related quality of life.

Methods This prospective study included 140 patients with a keloid in the head and neck regions. They were divided into two groups. In Group A, the patient filled out the questionnaire four times: 1 week before the start of the treatment, the first injection (day using intralesional BTA, the second injection day, and 6 months after the first injection. In group B, the patients completed the questionnaires once before any keloid therapy (control group).

Results Cronbach's alpha between all questions was 0.921. The intra-class correlation coefficient between the first and second visits was above 0.8. In Group A, the total score in the first visit was 84.12 ± 5.86, while it was 34.87 ± 3.73 in the fourth fulfilment, with a statistically significant difference between them as the *P*-value was < 0.0001. The results of Group A differed significantly from the control group.

Conclusions The translated Arabic version of the head and neck QOL questionnaire was reliable and reproducible. It has strong internal consistency, responsiveness, and validity. According to this study, intralesional BTA injection effectively improved the QOL of patients with keloids.

Keywords Quality of life, Keloid, Head and neck, Arabic adaptation, Botulinum toxin type A

Background

Keloid is excessive skin fibrosis that extends beyond the area of injury and does not regress. Keloid scars arise from skin trauma or inflammation, may develop years after the initial insult, and rarely revert. It can be considered benign dermal fibro-proliferative nodular lesions that recur after excision [1]. Patients with keloid may present symptoms such as burning, pain, pruritus, movement limitation, and hyperesthesia [2]. Keloids tend to occur in areas with tense skin, the skin of the chest wall, and the retro-auricular areas. Also, there is an increase in the keloids in the ear lobule due to the increased piercing rate [3]. People with dark skin are more liable to keloids [4].

Disfigurement associated with keloids, especially those in exposed body areas, may cause psychological problems or even stigmatisation. This may affect the quality of life badly and may cause social isolation. Therefore, the patients usually seek medical care to eliminate this stigmatisation and return to everyday life [5].

Many treatment modalities are available to overcome this resistance lesion without a consensus on the most effective therapy. These modalities include massage therapy, silicone gel treatment, laser therapy, light therapy, radiotherapy, intralesional cryotherapy, and intralesional

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injection with 5-fluorouracil (5FU), interferon, bleomycin, and intralesional corticosteroids injection [6]. Recently, many studies used botulinum toxin type A (BTA) to manage disfiguring keloids. In most of these studies, BTA effectively improved the outcomes [7].

On the other hand, many previous tools were used to assess the impact of the keloid on the quality of life (QOL). These tools included SF-36 and SF-12 questionnaires [8, 9]. Although these tools were validated and responsive to the whole-body keloids, they were poorly responsive to the head and neck area keloids. This motivated Guy et al. to develop a head- and neck-specific questionnaire that can assess the effect of keloid on the QOL in this exposed area. The head and neck keloid QOL questionnaire comprised 15 questions (21 items) with a 126 total score. It covered many aspects, including physical symptoms, self-esteem, social functioning, and medical motivation [10].

Our study aimed for the Arabic translation and validation of the head and neck keloid QOL questionnaire to be used in 20 Arabic countries with 300 million inhabitants [11]. Also, we tried to assess the effectiveness of the intralesional BTA therapy for managing keloids and its effect on the QOL.

Methods

Ethics

The local research ethics committee approved the study (AFMG-IRB 79/202). All performed manoeuvres were according to the Declaration of Helsinki [12].

Study design

It was a prospective comparative randomised study. Before the planned injection, each patient chose a sealed opaque envelope from two offered envelopes containing one of the groups.

Settings

This study was performed at a tertiary referral university hospital between January 2021 and March 2022.

Sample size calculation

The total number of patients with one or multiple keloids in the head and neck region in the year previous to the start of our study was 210 patients. We calculated the sample size according to this number, which revealed that our analysis should include at least 137 patients with a 95% confidence level, 5% margin of error, and 50% population proportion.

Subjects

We included cases with one or multiple keloids in the head and neck region. We also excluded patients who received previous keloid treatment or still need to complete the follow-up visits. So, we excluded 30 patients (Fig. 1).

The questionnaire

The patients were asked to complete a keloid-specific quality-of-life (QOL) Likert-scale questionnaire. This questionnaire comprised 15 questions (21 items) with a 126-point score. The questionnaire covered physical symptoms (subscale 1), self-esteem (subscale 2), social functioning (subscale 3), and medical motivation (subscale 4). The first subscale consisted of eight items (the first and the second questions). The second subscale consisted of the third, the 4th, and the 9th questions. The third subscale consisted of the 5th, 6th, 7th, 8th, 12th, and 13th questions. The fourth subscale comprised the 10th, 11th, 14th, and 15th questions (Fig. 2).

The patients of Group A were asked to fill out the questionnaire 1 week before the first injection (V1), the same day of the first injection (V2), the day of the second injection, 1 month after the first visit (V3), and 6 months from the first visit (V4). In comparison, the patients of Group B (the control group) were asked to fill out the questionnaire once before receiving any intervention for keloid management.

The translation process

Two expert translators did the English into Arabic translation with a medical background. Then, the two translations were combined into one edition reviewed by two dermatology physicians and two ENT physicians with a forward (from Arabic to English) and backward translation (from English to Arabic) mechanism. Finally, we tested 25 people (not included in the study sample) to detect encounters during the questionnaire-fulfilling process to confirm its easy understanding. Then, the final version was documented to be used during our study.

Intervention

We used the botulinum toxin type A (Allergan®, Irvine, CA, USA. 100 U vacuum-dried powder in a single-use vial for reconstitution diluted in 2 mL of sterile saline) using a 30-G needle insulin syringe after applying anaesthesia and disinfection. Keloid lesions were injected until slight blanching was clinically visible. Then, the BTA dosage was adjusted to 2.5 U per cubic centimetre of the lesion, not exceeding 100 U per patient in one injection, for a maximum of 4 sessions with 1-month intervals.

Outcome measures

We evaluate the questionnaire's psychometric properties (internal consistency, test–retest reliability, reproducibility, responsiveness to change, and validity). We also

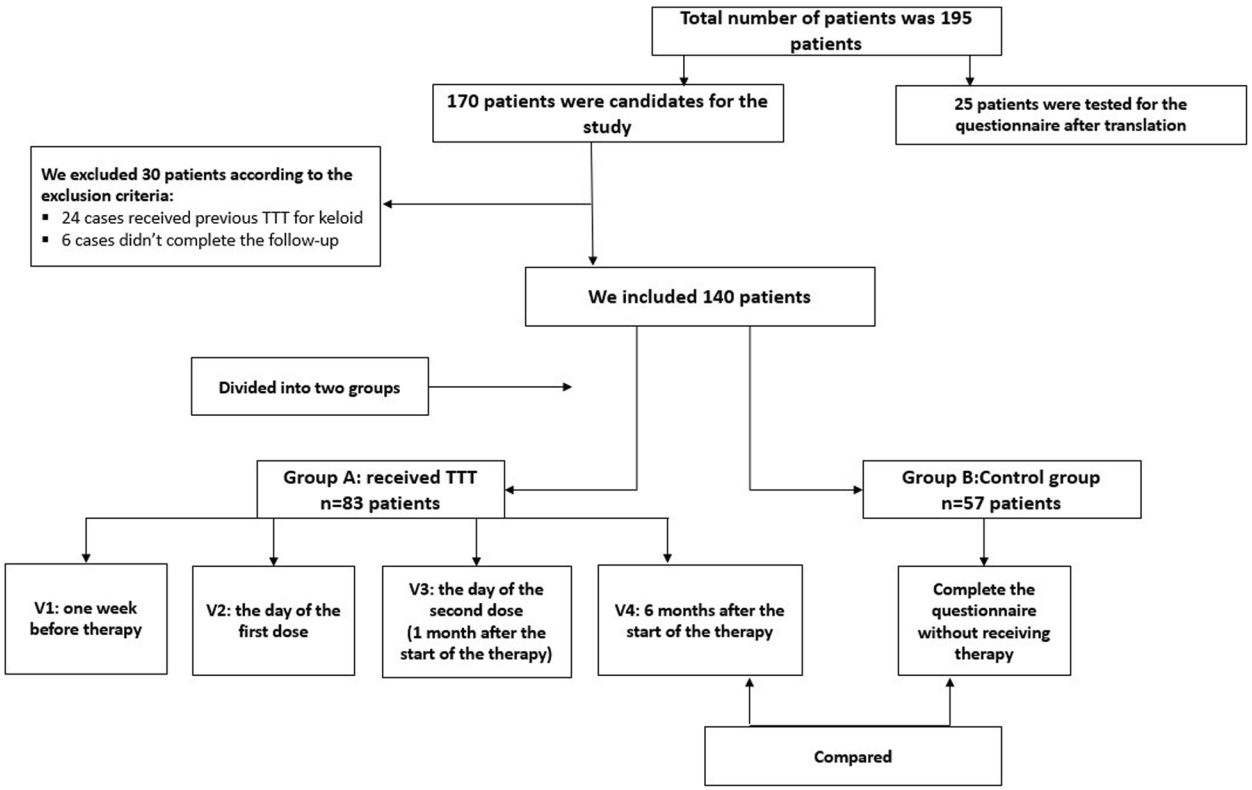

Fig. 1 A summary of the study design

assessed the impact of the BTA therapy on the quality of life by comparing the results of V1 with V4 of the first group and the results of both groups.

Statistical analysis

Statistical analysis was done using SPSS v 22 (IBM© Inc., Chicago, IL, USA). The normality of data was checked with the Shapiro-Wilks test. Numerical variables were presented as mean and standard deviation (SD). Categorical variables were presented as frequency and percentage (%). We used the Wilcoxon signed-ranks test to compare paired samples and the Mann–Whitney test to compare unpaired samples. The Pearson correlation coefficient was used to detect the relationship between V1 and V2. The interclass coefficient correlation assessed the test–retest reliability between V1 with V2 and V1 with V3. *P*-value < 0.05 was considered significant. Correlation coefficients of more than 0.7 indicated an acceptable agreement.

Results

The Shapiro–Wilk test revealed an abnormal data distribution as the *P*-value was < 0.0001 (which meant a significant difference from the normal distribution). So, nonparametric tests for statistical analysis were used in our study.

Demographic results

This study included 140 patients with a keloid in the head and neck region. They were divided into two groups: Group A included 83 patients (59%) who received therapy for the keloid, and Group B had 57 patients (41%) who did not receive any treatment for the keloid (control group). There were 69 males (49%) and 71 females (51%). At the time of enrollment, the age ranged from 18 to 69 years, with a mean of 35.61 ± 10.83 years. The keloid existence duration at the time of registration ranged from 1 to 9 years, with a mean of 3.91 ± 1.795 years. Both groups did not show statistically significant differences regarding age, sex, and the duration of keloid existence, as the *P*-values were more than 0.05 (Table 1).

Aetiology

The keloid was caused by a previous surgery in 60 cases (42.9%), a traumatic cut in 33 patients (23.9%), a prior burn in 19 cases (13.6%), acne in 21 cases (15%), piercing in 7 cases (5%), and by another cause in 4 patients (4.8%). There was not a statistically significant difference

A

Instructions: This survey asks for your views about you and your keloid(s). This information will describe how you feel about how having keloids impacts your life. Please answer every question by filling the blanks and marking one box. If you are unsure about the answer, please give the best answer you can.

These questions are about how you feel and how things have been with you during the past four weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past four weeks:

1. On a scale of 1-10 please rank the severity of the pain/itching/burning/infection of your keloid(s) (please circle). If you have more than one keloid on your head and neck, please indicate the level for each and indicate which keloid is for which number:

	None									Severe
Pain	1	2	3	4	5	6	7	8	9	10
Itching	1	2	3	4	5	6	7	8	9	10
Burning	1	2	3	4	5	6	7	8	9	10
Infection	1	2	3	4	5	6	7	8	9	10

2. Please indicate how often your keloid(s) cause you pain/itch/become infected:

	Every day	Every other Day	Multiple times per week	Weekly	Less frequent
Pain	☐	☐	☐	☐	☐
Itching	☐	☐	☐	☐	☐
Burning	☐	☐	☐	☐	☐
Infection	☐	☐	☐	☐	☐

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
3. Do you cover your facial keloid(s)?	☐	☐	☐	☐	☐	☐
4. Do you find your facial keloid(s) embarrassing?	☐	☐	☐	☐	☐	☐
5. Do you feel like your facial keloid(s) interfere with your romantic relationships?	☐	☐	☐	☐	☐	☐
6. Do you feel like your facial keloid(s) interfere with your friendships?	☐	☐	☐	☐	☐	☐

B

7. Do you feel like your facial keloid(s) interfere with your ability to get or keep a job?	☐	☐	☐	☐	☐	☐
8. Do you feel like your facial keloid(s) interfere with your schoolwork?	☐	☐	☐	☐	☐	☐
9. Do you feel like your facial keloid(s) interfere with your self-confidence?	☐	☐	☐	☐	☐	☐

10. How satisfied are you with the appearance of your head and neck keloid(s)?

Not at all	Somewhat	Moderately	Very much	Completely
0	1	2	3	4

11. How much do your head and neck keloid(s) bother you?

Not at all	Somewhat	Moderately	Very much	Completely
0	1	2	3	4

12. How much do you feel your friends and loved ones like the appearance of your head and neck keloid(s)?

Not at all	Somewhat	Moderately	Very much	Completely
0	1	2	3	4

13. Do you feel that your head and neck keloid(s) limit your social or professional activities?

Always	Usually	Sometimes	Rarely	Never
0	1	2	3	4

14. How confident are you that the appearance of your head and neck keloid(s) is the best that it can be?

Not at all	Somewhat	Moderately	Very much	Completely
0	1	2	3	4

15. Would you like to medically alter the appearance of your head and neck keloid(s)?

No	Probably not	Possibly	Most likely	Definitely
0	1	2	3	4

Fig. 2 The original English questionnaire [10]

Table 1 The demographic results, aetiology of the keloid, causes of the medical seeking, and the duration of keloid existence (group A, patients with therapy; group B, without treatment (control group); *SD*, standard deviation)

		Total $n=140$	Group A $n=83$	Group B $n=57$	*p*-value
Age (years) (mean ± SD)		35.61 ± 10.83	36.82 ± 10.6	33.86 ± 11.01	0.113
Sex	Male	69/140 (49%)	45/83 (54%)	24/57 (42%)	0.108
	Female	71/140 (51%)	38/83 (46%)	33/57 (58%)	
Aetiology	Surgical	60/140 (42.9%)	39/83 (47%)	21/57 (36.8%)	0.732
	Piercing	7/140 (5%)	3/83 (3.6%)	4/57 (7%)	
	Burn	19/140 (13.6%)	10/83 (12%)	9/57 (15.8%)	
	Cut	33/140 (23.6%)	19/83 (23%)	14/57 (24.6%)	
	Acne	21/140 (15%)	12/83 (14.5%)	9/57 (15.8%)	
Motivation for medical management	Pain	18 (12.9%)	13/83 (15.7%)	5/57 (8.8%)	0.529
	Growth	16 (11.4%)	9/83 (10.8%)	7/57 (12.3%)	
	Change of appearance	12 (8.6%)	7/83 (8.4%)	5/57 (8.8%)	
	Family urging	16 (11.4%)	6/83 (7.2%)	10/57 (17.5%)	
	Problems with social life	36 (25.7%)	21/83 (25.3%)	15/57 (26.3%)	
	Problem with work	38 (27.1%)	24/83 (28.9%)	14/57 (24.6%)	
	Others	4 (2.9%)	3/83 (3.6%)	1/57 (1.8%)	
Duration of keloid existence (years) (mean ± SD)		3.91 ± 1.76	3.71 ± 1.82	4.19 ± 1.79	0.08

between both groups regarding the keloid aetiology, as the *P*-value was 0.732 (Table 1).

Keloid location

In Group A, the keloid was present in the face in 24 (29%) patients while in other locations of the head and neck in 59 (71%) patients. However, the site did not affect the questionnaire results. Furthermore, these location categories had no statistically significant differences between the pre-treatment (*P*-value was 0.69) and the post-treatment total scores (*P*-value was 0.23).

Cause of medical seeking

The patients needed keloid management because of problems at work (27.1%), social problems (25.7%), family problems (16%), pain (12.9%), keloid growth (11.4%), change of keloid appearance (8.6%), and for other causes (2.9%). The cause of medical seeking did not show a statistically significant difference between both groups, as the *P*-value was 0.529 (Table 1).

Internal consistency

The inter-item correlation and the internal consistency were evaluated by Cronbach's alpha of 0.921 between all questions and 0.907 between the four subscales. Cronbach's alpha was 0.928 in subscale I, 0.895 in subscale II, 0.904 in subscale III, and 0.804 in subscale IV. Cronbach's alpha of more than 0.7 indicated a solid internal consistency.

Test–retest reliability

The intra-class correlation coefficient between V1 and V2 assessed the reliability and reproducibility of the questionnaire. It was above 0.8 in all questions and subscales. The reproducibility was also confirmed using Pearson's correlation coefficient between V1 and V2. It was above 0.8 in all questions and subscales with a statistically significant correlation as the *P*-values were less than 0.0001. Moreover, the intra-class correlation coefficient between V1 and V3 was above 0.7, except for the items of the first two questions and the first scale (Table 2).

Responsiveness to change

There was a statistically significant change between V1 and V4 results in all questions, subscales, and the total score, as the *P*-value was < 0.0001. The total score in V1 was 84.12 ± 5.86, while it was 34.87 ± 3.73 in V4. The ability of the questionnaire to detect a significant change (41.5%) after the treatment indicated its precise validity (Table 2) (Fig. 3). This validity was also confirmed by the highly statistically significant differences between all questions, subscales, and the total scores between groups (A and B), as the *P*-values were less than 0.0001 (Table 3) (Fig. 4).

Linear regression

The stepwise linear regression revealed that subscale I (physical symptoms) had the highest impact on the total score, followed by subscale III (social functioning), then

Table 2 The results of all questions of group A, subscales, and the total scores (*Q* question, *V1* the first questionnaire fulfilling (1 week before therapy), *V2* the second questionnaire fulfilling (the day of the first injection), *V3* the third questionnaire fulfilling (the day of the second injection one; month after the first injection), *V4* the forth questionnaire fulfilling (6 months after the first injection), *ICC* intra-class correlation coefficient, *significant *p*-value < 0.05)

		V1	V2	V1–V2			V3	V1–V3	V4	(V1–V4)	
				ICC	Correlation	*p*-value		ICC		*Z*-value	*p*-value
Q1	Item 1	5.58 ± 1.63	5.29 ± 1.72	0.928	0.93	< 0.0001*	2.89 ± 1.34	0.149	1.3 ± 0.53	7.964	< 0.0001*
	Item 2	5.81 ± 1.6	5.53 ± 1.63	0.915	0.915	< 0.0001*	2.93 ± 1.15	0.629	1.24 ± 0.48	7.957	< 0.0001*
	Item 3	5.13 ± 1.19	5.3 ± 1.35	0.832	0.839	< 0.0001*	2.59 ± 0.93	0.533	1.22 ± 0.84	8.009	< 0.0001*
	Item 4	4.86 ± 1.32	4.65 ± 1.21	0.869	0.869	< 0.0001*	2.19 ± 0.87	0.506	1.18 ± 0.44	7.976	< 0.0001*
Q2	Item 1	3.66 ± 1.19	3.52 ± 1.02	0.91	0.92	< 0.0001*	2.66 ± 1.1	0.447	1.4 ± 0.74	7.851	< 0.0001*
	Item 2	3.8 ± 1.21	3.58 ± 1.14	0.895	0.897	< 0.0001*	2.93 ± 1.06	0.602	1.3 ± 0.63	7.632	< 0.0001*
	Item 3	3.73 ± 1.39	3.6 ± 1.28	0.941	0.944	< 0.0001*	3.04 ± 0.96	0.682	1.29 ± 0.61	7.471	< 0.0001*
	Item 4	3.47 ± 1.51	3.23 ± 1.34	0.919	0.926	< 0.0001*	2.65 ± 1.02	0.622	1.22 ± 0.56	7.146	< 0.0001*
Q3		4.93 ± 1.09	4.86 ± 1.07	0.971	0.971	< 0.0001*	3.65 ± 1.15	0.89	1.83 ± 0.79	7.992	< 0.0001*
Q4		5.39 ± 0.74	5.45 ± 0.76	0.95	0.951	< 0.0001*	4.47 ± 0.9	0.783	2.71 ± 0.83	8.066	< 0.0001*
Q5		3.22 ± 1.34	3.07 ± 1.34	0.965	0.965	< 0.0001*	2.98 ± 1.23	0.879	2.05 ± 0.89	7.039	< 0.0001*
Q6		3.52 ± 1.13	3.39 ± 1.06	0.932	0.933	< 0.0001*	3.25 ± 1.06	0.757	2.19 ± 0.8	7.412	< 0.0001*
Q7		3.41 ± 1.35	3.35 ± 1.34	0.984	0.984	< 0.0001*	3.2 ± 1.29	0.924	2.07 ± 0.82	7.259	< 0.0001*
Q8		2.34 ± 1.83	2.4 ± 1.91	0.992	0.993	< 0.0001*	2.31 ± 1.85	0.964	1.52 ± 0.78	4.950	< 0.0001*
Q9		5.91 ± 3.4	5.93 ± 0.26	0.918	0.92	< 0.0001*	5.57 ± 0.56	0.843	2.95 ± 0.71	8.113	< 0.0001*
Q10		3.81 ± 0.39	3.83 ± 0.37	0.921	0.922	< 0.0001*	3.78 ± 0.41	0.78	1.67 ± 0.6	8.159	< 0.0001*
Q11		3.83 ± 0.37	3.86 ± 0.35	0.911	0.913	< 0.0001*	3.82 ± 0.38	0.792	1.83 ± 0.67	8.056	< 0.0001*
Q12		2.64 ± 0.79	2.59 ± 0.76	0.962	0.962	< 0.0001*	2.52 ± 0.75	0.828	1.31 ± 0.58	7.765	< 0.0001*
Q13		2.93 ± 0.762	2.98 ± 0.81	0.943	0.945	< 0.0001*	2.89 ± 0.81	0.834	1.08 ± 0.54	7.969	< 0.0001*
Q14		3.81 ± 0.397	3.83 ± 0.37	0.921	0.922	< 0.0001*	3.8 ± 0.406	0.811	1.73 ± 0.54	8.141	< 0.0001*
Q15		3.88 ± 0.328	3.9 ± 0.29	0.878	0.882	< 0.0001*	3.87 ± 0.34	0.728	1.76 ± 0.53	8.144	< 0.0001*
Subscale 1		36.04 ± 4.72	34.7 ± 4.78	0.931	0.931	< 0.0001*	21.88 ± 3.87	0.649	10.17 ± 2.38	7.92	< 0.0001*
Subscale 2		16.23 ± 1.58	16.22 ± 1.58	0.97	0.971	< 0.0001*	13.68 ± 1.75	0.89	7.49 ± 1.37	7.959	< 0.0001*
Subscale 3		18.05 ± 2.97	17.77 ± 2.98	0.972	0.97	< 0.0001*	17.16 ± 3.2	0.875	10.2 ± 1.62	7.93	< 0.0001*
Subscale 4		15.33 ± 0.85	15.42 ± 0.82	0.886	0.87	< 0.0001*	15.27 ± 0.89	0.868	7 ± 1.45	7.953	< 0.0001*
Total score		85.63 ± 5.8	84.12 ± 5.86	0.942	0.942	< 0.0001*	67.99 ± 5.23	0.729	34.87 ± 3.73	7.917	< 0.0001*

subscale II (self-esteem), and finally subscale IV (medical motivation).

Discussion

Guy et al. developed the first head- and neck-specific keloid questionnaire that can assess the impact of keloids in this exposed region on the quality of life [10]. They tried to evaluate this impact on the physical and psychological aspects, which are fundamental in the precise analysis of the QOL [13]. The psychometric properties of their questionnaire were proved to be acceptable. This allowed us to use this questionnaire with high confidentiality.

We decided to make an Arabic translation of this questionnaire to be used easily by Arabic dermatologists, otorhinolaryngologists, and plastic surgeons when dealing with their patients. This tool has great importance as the patient-reported outcome measures, and the impacts of medical and surgical treatment on quality of life are increasing in current medical practice [14].

The accurate translation was performed by following the proper rules of forward and backward translation [15]. As a result, our used version was clear and easily fulfilled by all the patients within a short time without needing external help.

The strength of any questionnaire is directly related to internal consistency, which depends mainly on the relation between the included items [16]. The internal consistency of our translated version was excellent, as Cronbach's alpha was 0.921 (above 0.7). This coincided with the original English version, whose Cronbach's alpha was 0.87 for the entire score. Furthermore, the physical symptoms were the most overt signs; this increased the internal consistency of subscale I. Conversely, the variable reasons for seeking medical care lowered the internal consistency of subscale IV.

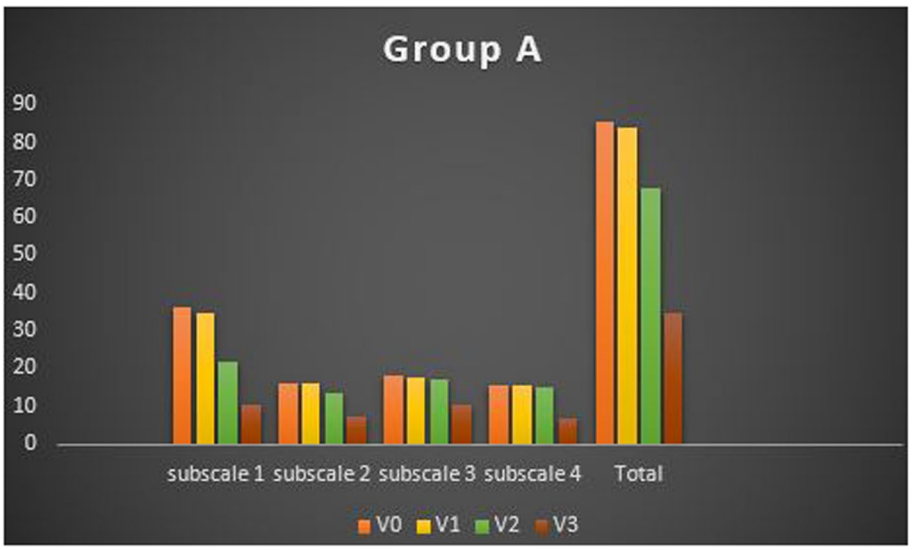

Fig. 3 Bar chart showing the comparison between the subscales' results and the total score of group A. V1, the first questionnaire fulfilling (1 week before therapy); V2, the second questionnaire fulfilling (the day of the first injection); V3, the third questionnaire fulfilling (the day of the second injection one; month after the first injection); V4, the fourth questionnaire fulfilling (6 months after the first injection)

Table 3 The results of both groups (group A, with therapy; group B, without treatment (control group); *Q*, question, *significant *p*-value < 0.05)

		Group A	Group B	*Z*-value	*p*-value
Q1	Item 1	1.3 ± 0.53	5.86 ± 1.563	10.476	< 0.0001*
	Item 2	1.24 ± 0.48	6.42 ± 1.43	10.592	< 0.0001*
	Item 3	1.22 ± 0.84	5.88 ± 1.21	10.603	< 0.0001*
	Item 4	1.18 ± 0.44	5.16 ± 1.16	10.737	< 0.0001*
Q2	Item 1	1.4 ± 0.74	4.46 ± 0.709	10.327	< 0.0001*
	Item 2	1.3 ± 0.63	4.4 ± 0.593	10.561	< 0.0001*
	Item 3	1.29 ± 0.61	4.42 ± 0.596	10.570	< 0.0001*
	Item 4	1.22 ± 0.56	4.23 ± 0.732	10.623	< 0.0001*
Q3		1.83 ± 0.79	5.18 ± 0.947	9.977	< 0.0001*
Q4		2.71 ± 0.83	5.72 ± 0.559	10.16	< 0.0001*
Q5		2.05 ± 0.89	3.58 ± 1.499	6.11	< 0.0001*
Q6		2.19 ± 0.8	3.3 ± 1.133	5.802	< 0.0001*
Q7		2.07 ± 0.82	4.21 ± 1.25	8.249	< 0.0001*
Q8		1.52 ± 0.78	2.75 ± 1.93	4.353	< 0.0001*
Q9		2.95 ± 0.71	5.79 ± 0.411	10.385	< 0.0001*
Q10		1.67 ± 0.6	3.93 ± 0.258	10.514	< 0.0001*
Q11		1.83 ± 0.67	3.95 ± 0.225	10.393	< 0.0001*
Q12		1.31 ± 0.58	3.11 ± 0.724	9.591	< 0.0001*
Q13		1.08 ± 0.54	3.39 ± 0.75	10.195	< 0.0001*
Q14		1.73 ± 0.54	3.96 ± 0.186	10.685	< 0.0001*
Q15		1.76 ± 0.53	3.95 ± 0.225	10.687	< 0.0001*
Subscale 1		10.17 ± 2.38	40.82 ± 2.752	10.126	< 0.0001*
Subscale 2		7.49 ± 1.37	16.68 ± 1.391	10.104	< 0.0001*
Subscale 3		10.2 ± 1.62	20.33 ± 2.747	10.071	< 0.0001*
Subscale 4		7 ± 1.45	15.79 ± 0.453	10.278	< 0.0001*
Total score		34.87 ± 3.73	93.63 ± 3.862	10.045	< 0.0001*

Reproducibility means the ability of the questionnaires to give the same results repeatedly if the patient's status does not change over time [17]. The intra-class correlation coefficient and Pearson's correlation coefficient of all questions, subscales, and the total score between V1 and V2 were above 0.8. This coincided with the original English version and confirmed the reproducibility of our version. On the other hand, there was an acceptable correlation between V1 and V3 except for the results of the first two questions and the first subscales. These differences indicated the ability of BTA therapy to improve the physical signs after starting BTA injections.

The responsiveness and the validity mean the ability of the questionnaire to detect health change over time with the ability to differentiate the results of medical or surgical intervention [18]. Our version could reveal a significant difference between the V1 and V4 in all questions and subscales of the first group, and the results of both groups indicated a strong validity.

Botulinum toxin type A, isolated from *Clostridium botulinum*, is a potent neurotoxin that blocks neuromuscular transmission. It has been shown to improve scar cosmoses by decreasing tension on healing wound edges, accumulating fibroblasts in GO and G1 of the cell cycle, and reducing TGF-β1 expression [19].

Zhibo et al. published the first report that described the clinical benefit of BTA injections on keloids in 2008. Twelve patients were included in this uncontrolled trial. Intralesional botulinum toxin type A was given at 3-month intervals for a maximum of 9 months. Regression from the periphery, flattening of the lesions, and a significant

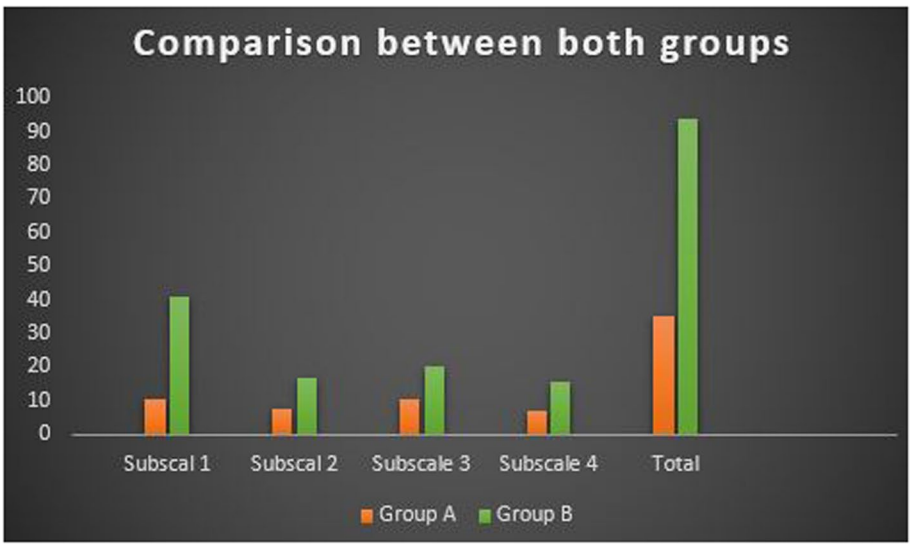

Fig. 4 Bar chart showing the comparison between the subscales' results and the total scores of both groups. V1, the first questionnaire fulfilling (1 week before therapy); V2, the second questionnaire fulfilling (the day of the first injection); V3, the third questionnaire fulfilling (the day of the second injection one; month after the first injection); V4, the fourth questionnaire fulfilling (6 months after the first injection)

decrease in size were reported in all patients. No other simultaneous therapy was reported. In the follow-up period of 1 year, no signs of the reappearance of symptoms or lesions were seen in any patients [20, 21]. Bi L. et al. did a systematic review of the use of BTA in managing keloids. They concluded that intralesional injection of botulinum toxin type A was more effective in inhibiting hypertrophic scar and keloid than an intralesional injection of corticosteroid or placebo. It was also associated with reduced pain following injection [22]. Our study found a significant improvement in the QOL after using the BTA intralesional therapy to manage head and neck keloids regardless of the aetiology without any reported side effects.

Conclusions

The translated head and neck QOL questionnaire was reliable and reproducible. It has strong internal consistency, responsiveness, and validity. Therefore, it can be easily used to assess the impact of the keloid in the head and neck on the QOL. According to this study, intralesional BTA injection effectively improved patients' quality of life with keloids in the head and neck area.

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Authors' contributions
MH, designed the work; GAO, acquired and analysed data; HE, acquired and analysed data; MB, drafted, revised, and approved the manuscript; and HHE, agreed to be accountable for all aspects of the work.

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Availability of data and materials
The data presented in this study are available on request from the corresponding author.

Declarations

Ethics approval and consent to participate
The study was approved by the Research Ethics Committee of the Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt (AFMG-IRB 79/202). All performed manoeuvres were according to the Declaration of Helsinki. We obtained the signed informed consent of all patients to use their data in our research.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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