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Efficacy and Tolerability Assessment of Deoxycholic Acid Injectable Solution for Reduction of Submental Fat Among the Iranian Population

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Abstract

Background The purpose of this study was the safety and efficacy assessment of Embella® (a deoxycholic acid injectable solution, manufactured by Espad Pharmed Daru Company), for the reduction of unwanted submental fat in Iranian patients.

Methods Twenty patients were included in this before-and-after study. One to three subcutaneous injections of maximum 2 ml of Embella® containing 20 mg of deoxycholic acid were performed monthly. Assessments included the severity of submental fat using validated Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) and diameter of submental fat, before injection, and 4 and 12 weeks after the last one. Patient satisfaction was evaluated using a visual analogue scale, and adverse events were reported.

Results At least one-grade improvement on the CR-SMFRS was seen in 79% and 62.5% at weeks 4 and 12 after the last injection. A significant decrease was observed in the median CR-SMFRS at weeks 4 and 12 (p-values<0.001 & 0.004). The median diameter of SMF decreased significantly from 1.85 cm to 1.4 and 1.45 cm at weeks 4 and 12 (p-values<0.001). The mean satisfaction scores were 7.63 and 7.43 out of 10. Adverse effects were mild to moderate and included tenderness, pain, swelling, and numbness at the injection site as well as globus sensation and cough which lasted between 2 days and 2 weeks and completely resolved at week 4.

Conclusions Embella® injectable solution was shown to be an effective way to reduce unwanted submental fat, and related adverse events were limited to mild and moderate temporary symptoms.

Level of Evidence II This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Deoxycholic acid · Submental fat · SMF

Introduction

The human skin aging phenomenon is a complex process induced by intrinsic and extrinsic factors [1] and leads to many aesthetic changes. Manifestations of the skin aging include decreased skin elasticity, increased wrinkles, irregularity of skin tissue, sagging, etc. [2]. Another important factor that plays a crucial role in aging is changes in the appearance of submental region [3].

Submental fat (SMF) is considered aesthetically unsightly and has a negative psychological impact on people [4]. It can have a substantial negative effect on a person's feelings of attractiveness and subsequently behaviors. Reduction of SMF not only improves a person's appearance, but also enhances the self-confidence [5].

Concerning the increasing demands of people for aesthetic procedures including decreasing the unwanted submental fat, evidence supports the effectiveness of noninvasive alternative procedures for liposuction and

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plastic surgery [6]. Among them, injection of deoxycholic acid (DCA) is a minimally invasive procedure [7].

Mechanism of action of DCA is through the lysis of fat cell membranes and the physical destruction of cells [8]. In 2015, the U.S. Food and Drug Administration (FDA) approved DCA, for treating fat beneath the chin [9].

According to phase I study, DCA had a favorable safety and did not impact on liver and kidney function, heart rate, or levels of cholesterol, triglycerides, free fatty acids, and pro-inflammatory cytokines [10]. Phase II studies reveal that the optimal dose for DCA was 2 mg/cm^2, administered via 0.2 ml injections, spaced 1 cm apart in the submental area with recommended injection interval of 1 month [11–13]. The results of phase III study demonstrated significant improvements in patient appearance and satisfaction, confirming the drug's safety and effectiveness [14].

Totally, DCA demonstrated significant efficacy for reducing the SMF with appropriate tolerability in clinical studies [15, 16]. To the best of our knowledge, there is no clinical trial in Iranian patients in this regard. The purpose of this study was the safety and efficacy assessment of Embella® (a deoxycholic acid injectable solution, manufactured by Espad Pharmed Daru Company), for the reduction of unwanted submental fat, in Iranian patients.

Methods

Study Design

This was a prospective single-group, before-and-after clinical study carried out at Center for Research and Training in Skin Diseases and Leprosy, Tehran University of Medical Sciences, between November 2022 and February 2023. Institutional Review Board approval was obtained (ethic code: IR.TUMS.TIPS.REC.1401.102), and written informed consent was obtained from each patient. The study has been performed in accordance with the ethical standards in the Declaration of Helsinki. The protocol was registered in the Iranian Registry of Clinical Trial Registry (IRCT) with registration number IRCT20190210042676N29.

Patients

Twenty Iranian patients between 18 and 65 years of age, with any severity of unwanted SMF, were enrolled. Exclusion criteria included previous interventions to treat SMF; anatomical features or previous trauma which is liable to interfere with SMF evaluation or result in an aesthetically unacceptable outcome after treatment; evidence of any cause of submental enlargement other than SMF; patients with a body mass index (BMI) > 30 kg m^2; undergoing or considering a weight-reduction program; patients with a history of sensitivity to any components of the study medication or topical or local anesthetics; people with a history of dysphagia; any inflammation, active infection, tissue scar, and skin lesions at injection site; using anticoagulants or NSAID or other medications which increase the risk of coagulation disorders within 7 days before injection; unrealistic expectations; pregnant or lactating woman; and those undergoing low sodium diet for disease control such as hypertension.

Intervention

Minimum one and maximum three subcutaneous injections (with at least 4-week interval) with maximum 2 ml of Embella®, which contains 20 mg of DCA, were performed. Four weeks after the first and second injections, the patients were evaluated by the investigator. If necessary, they received additional injections; otherwise, they proceeded with post-injection follow-up.

The product was a 2-ml sterile, transparent, and colorless vial containing 20 mg of DCA. Additional ingredients included hyaluronic acid, water for injection, sodium chloride, sodium hydroxide, hydrochloric acid, and disodium phosphate anhydrous.

Ice or cold packs and topical or injectable local anesthetics (e.g., lidocaine) were used to enhance patient comfort.

Efficacy and Safety Assessments

At least one-grade improvement in standard Clinician-Reported Submental Fat Rating Scale (CR-SMFRS) (Fig. 1) [17] evaluated at 4 and 12 weeks after the last injection was the primary outcome of the study. Grading was performed by the independent investigator.

Scores of CR-SMFRS scale are as follows: 0: no submental convexity—no localized fat, 1: mild submental convexity—minimal localized SMF, 2: moderate submental convexity—prominent localized SMF, 3: severe submental convexity—marked localized SMF, and 4: extreme submental convexity.

Secondary outcomes included change in median of CR-SMFRS based on digital AP and lateral global standard photography of the patient's neck, measurement of SMF diameter using caliper, and patient's satisfaction assessed by a 11-point visual analogue scale (VAS) at 4 and 12 weeks after the last injection. Also, procedural pain evaluated by VAS and adverse events during the study course were examined.

Statistical analysis: For descriptive analysis, we used mean (standard deviation) or median (range), frequency, and percentages. The efficacy of the treatment was assessed

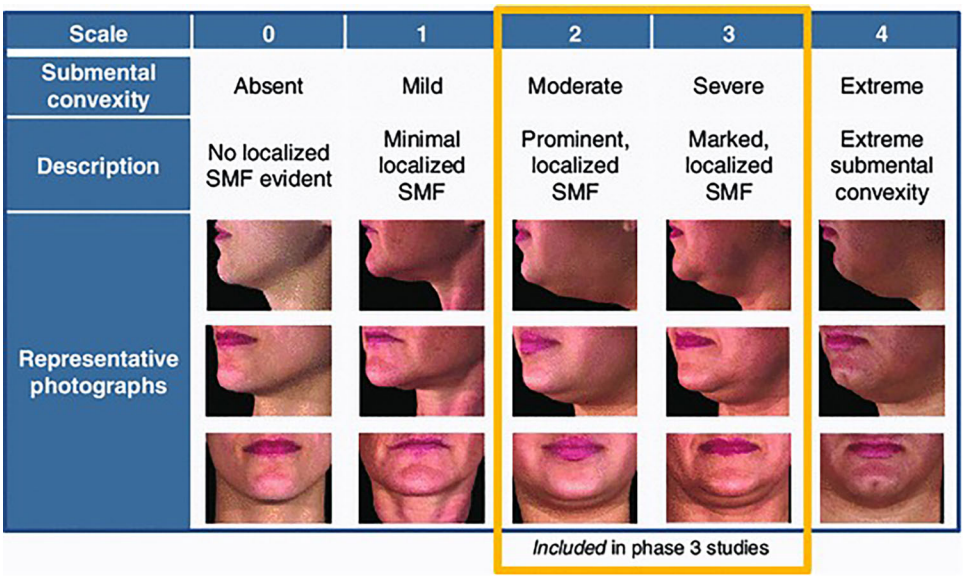

Fig. 1 Clinician-Reported Submental Fat Rating Scale (CR-SMFRS)

by comparing the mean/median values of each parameter among visits, using the paired sample t test or the non-parametric equivalent, Wilcoxon test. SPSS 24 statistical software was used for data analysis. The statistical significance level was defined as $p<0.05$.

Results

Twenty patients (17 females and 3 males) with a mean age of 44.10 years (SD: 11.35) participated in the study. According to investigator's evaluation, 14 patients received 3 treatment sessions, 1 patient received 2 treatment sessions, and 5 patients required only one treatment session.

After the first treatment session, one participant (50-year-old woman) requested to withdraw from the study due to local adverse events (numbness and tenderness at the injection site), and three more participants were lost to follow-up at week 12 after the last injection (Table 1).

At least one-grade improvement from baseline on the CR-SMFRS was seen in 79% and 62.5% of participants at weeks 4 and 12 after the last injection (Table 1).

Also, statistically significant decreases were observed in the median severity of SMF at weeks 4 [from 3 (Min: 1, Max: 4) to 2 (Min: 0, Max: 4) *P*-values <0.001] and 12 [from 3 (Min: 1, Max: 4) to 2 (Min: 1, Max: 4) *P*-values =0.004] compared with baseline. The changes in severity of SMF based on the CR-SMFRS in four patients are given in Figures 2 and 3.

Figure 2 shows baseline images of two patients, with extreme and severe SMF, who received 3 sessions of DCA injection and had two-grade improvements in SMF after 4 and 12 weeks. Figure 3 shows baseline images of two patients, with moderate SMF, who received 3 sessions of DCA injection and had no improvement in SMF after 4 and 12 weeks.

The changes in SMF diameter are shown in Table 2. As it is clear, the median diameter of SMF decreased significantly from 1.85 cm (Min: 1.6, Max: 2.7) at baseline to 1.4 cm (Min: 1.4, Max: 1.8) and 1.45 cm (Min: 1.4, Max: 1.9) at weeks 4 and 12, respectively.

Patient satisfaction was the other secondary outcome, which was recorded based on the VAS score. The mean satisfaction scores with the treatment were 7.63 (Min: 1, Max: 10, SD: 0.98) and 7.43 (Min: 1, Max: 10, SD: 2.73), out of 10 at weeks 4 and 12, respectively. The mean level of pain during injection was estimated to be 5.1, 3.9, and 3 out of 10 at first, second, and third treatment sessions, respectively (Min: 1, Max: 9).

Adverse reactions included 12 cases of mild tenderness, 7 cases of mild numbness, 1 case of moderate tenderness, 1 case of moderate skin laxity, 2 cases of mild rigidity, 4 cases of mild swelling at the injection site, and 1 case of mild globus sensation and cough, which all were temporary and self-limited. All adverse reactions lasted between 2 days and 2 weeks and completely resolved at week 4 after the last injection.

Discussion

DCA represents the first lipolytic substance approved by the FDA for fat reduction in the submental area [18]. The results of our study demonstrated that CR-SMFRS improved significantly, about 80% in 4 weeks and about 60% in 12 weeks after the last injection. The results of the objective evaluations also confirmed the subjective data since the submental fat diameter significantly decreased at

Table 1 Clinician-Reported Submental Fat Rating Scale in 20 participants

Participants	Injection visits	Total injection volume (cc)	Baseline grading	4 weeks after the last injection	12 weeks after the last injection
Case 1	3	4.70	4	2	1
Case 2	1	1.90	3	2	Lost to follow-up
Case 3	3	6.00	4	2	4
Case 4	1	2.00	3	1	Lost to follow-up
Case 5	1	2.00	3	Withdrawal	–
Case 6	3	6.00	4	2	3
Case 7	1	2.00	1	0	1
Case 8	3	4.00	3	1	Lost to follow-up
Case 9	3	5.00	2	1	1
Case 10	3	6.00	3	2	2
Case 11	3	5.80	3	2	2
Case 12	3	4.00	2	2	2
Case 13	3	5.00	2	2	2
Case 14	3	3.40	4	1	1
Case 15	3	3.70	4	3	3
Case 16	3	3.50	3	1	1
Case 17	3	3.90	4	2	3
Case 18	3	4.00	2	2	2
Case 19	2	3.00	2	2	2
Case 20	1	2.00	2	1	1
Median (range)			3 (1–4)	2 (0–4)	2 (1–4)
Percentage of at least one-grade improvement				79%	62.5%

both follow-up visits. The satisfaction rate was reported at a favorable level, and all adverse reactions were temporary and self-limited.

A 12-week double-blind, placebo-controlled study revealed that 70% of treated group showed at least one-grade improvement in SMF score. 13.4% of them demonstrated two-grade improvement, while no improvement was observed in the placebo group. These findings underscored the effectiveness of DCA in treating moderate to severe submental fat. In the MRI evaluation, the responders in the drug group (46.3%) were significantly higher compared to placebo group (5.3%) [19].

The first study assessing the outcome of treatment with DCA using high-resolution surface scans of the submental area showed the clinical effectiveness of DCA through a reduction of 4 mm in thickness of the submental fat 6 weeks after treatment [20].

During another study on 62 patients, the efficacy and safety of DCA injection in an expanded safe zone was evaluated. Authors concluded that this modality can be very useful in the reduction of submental fullness and is associated with few adverse events [21].

All the above findings are compatible with our study, indicating the effectiveness of DCA in treatment of SMF.

Regarding long-term efficacy of our studied product, we showed that the efficacy was permanent until 12 weeks because the changes in SMF measured by caliper were significant until 12 weeks. Future studies with longer follow-up period can show longer efficacy.

Our reported adverse events mostly included pain, tenderness, and transient mild to moderate numbness at the injection site, which are comparable to the similar studies. Shome et al reported tenderness and severe pain at the injection site in 80% of participants [22].

Our other reported adverse effects such as globus sensation were completely resolved within two weeks without any specific intervention. Dysphagia could be a potential side effect of DCA injection, and the drug is contraindicated for individuals with a history of dysphagia [8].

There were no reports of severe adverse events including nerve damage around the jaw, difficulty in speaking, necrosis around the treatment area, and blood vessel damage during the injection in our study. In one similar study, common side effects included pain, swelling, hematoma, and bruising at the injection site, and there were

Fig. 2 Baseline images of two patients, with extreme SMF, who received 3 sessions of treatment and had two-grade improvements in SMF after 4 and 12 weeks.

Fig. 3 Baseline images of two patients, with moderate SMF, who received 3 sessions of treatment and had no improvement in SMF after 4 and 12 weeks.

Table 2 Changes in submental fat diameter using caliper measurements at weeks 4 and 12

Thickness of submental fat (cm)			
	Baseline	4 weeks after the last injection	12 weeks after the last injection
Mean	1.96	1.48	1.53
Median	1.85	1.40	1.45
Std. Deviation	0.33	0.12	0.18
Minimum	1.60	1.40	1.40
Maximum	2.70	1.80	1.90
		p-value < 0.001	p-value < 0.001

some rare cases reported of damage to the mandibular nerve resulting in asymmetric smile which resolved without any intervention [9].

Based on a review article, local pain, edema, bruise, and numbness are the most common adverse events with DCA, which usually spontaneously subside. However, there is a possibility of complications comprising alopecia, skin necrosis, nerve injury, and vascular events, requiring complex interventions [18].

The mean satisfaction scores of the participants were about 7.5 out of 10 at both follow-up visits, which means appropriate satisfaction with the treatment process. Results of a systematic review in 2022 showed that the application of DCA has a positive effect on reducing SMF and improving patient satisfaction concerning their facial appearance [23].

There are some other treatment methods to treat SMF [24, 25], and future studies should be planned to compare different methods. A prospective study evaluating treatment of submental skin laxity by temperature-controlled monopolar radiofrequency showed that this method improved dermal laxity and was associated with submental lift. Assessments were performed by Cutometer-measured skin elasticity values [26]. Evaluating the elasticity parameters of treated skin by Cutometer device would help for laxity improvement and lift efficacy assessment [27]. Laxity improvement and skin tightening are as important as SMF diameter reduction [28].

This study is the first one that shows the safety and efficacy of DCA injectable solution for the clinical reduction of excess submental fat in Iranian patients. Moreover, it is one of the few studies that assessed the DCA efficacy by both objective (caliper) and subjective (CR-SMFRS & patient satisfaction) methods in two short-term and long-term follow-up visits. Also, pain severity and side effects were carefully evaluated, and all of them were transient and self-limited.

Our study had several limitations including small sample size and single-arm design. Although this sample size had sufficient statistical power and all changes were significant, future randomized controlled trials should be planned to assess the product's safety and efficacy with a larger sample size. Moreover, our paper evaluations included only CR-SMFRS and measurement of SMF diameter using caliper. It is recommended to use more accurate fat volume measurement such as B-ultrasound evaluation, in future studies.

Conclusion

The results of the study showed that Embella® injectable solution containing DCA is an effective way to reduce unwanted submental fat, and related adverse events are limited to mild and moderate temporary symptoms which are comparable to the similar studies.

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Declarations

Conflict of Interest Araz Sabzvari is a member of CinnaGen medical biotechnology research center, which collaborates with universities and researchers all over the world with regards to research and development of medications and health issues. Hamidreza Kafi is the head of the medical department of Orchid Pharmed Company which is in collaboration with Espad Pharmed Daru Company with respect to conducting clinical trials. The other authors declare no conflict of interest.

Ethics Approval Institutional Review Board Approval was obtained (ethic code: IR.TUMS.TIPS.REC.1401.102) and written informed consent was taken from each patient. The study has been performed in accordance with the ethical standards in the Declaration of Helsinki.

References

1. Shamsipour M, et al. Short-term effects of exposure to air pollution on biophysical parameters of skin in a panel of healthy adults. Dermatol Ther. 2020;33(6): e14536.
2. Samadi A, et al. Tolerability and efficacy assessment of an oral collagen supplement for the improvement of biophysical and

ultrasonographic parameters of skin in middle eastern consumers. J Cosmet Dermatol. 2023;22(8):2252–8.
3. Hatef DA et al. The submental fat compartment of the neck. In: Seminars in plastic surgery. Thieme Medical Publishers; 2009.
4. Rzany B, et al. Reduction of unwanted submental fat with ATX-101 (deoxycholic acid), an adipocytolytic injectable treatment: results from a phase III, randomized, placebo-controlled study. Br J Dermatol. 2014;170(2):445–53.
5. Baumann L, et al. Personal (self) perceptions of submental fat among adults in the United States. Dermatol Surg. 2019;45(1):124–30.
6. Leal Silva H, et al. Noninvasive submental fat reduction using colder cryolipolysis. J Cosmet Dermatol. 2017;16(4):460–5.
7. Ascher B, Fellmann J, Monheit G. ATX-101 (deoxycholic acid injection) for reduction of submental fat. Expert Rev Clin Pharmacol. 2016;9(9):1131–43.
8. Ava Shamban M, Somogyif C. ATX-101 (deoxycholic acid injection) for reduction of submental fat: results from a 12-month open-label study. J Drugs Dermatol. 2019;18:870–7.
9. Liu M, Chesnut C, Lask G. Overview of Kybella (deoxycholic acid injection) as a fat resorption product for submental fat. Facial Plast Surg. 2019;35(03):274–7.
10. Walker P, Lee D. A phase 1 pharmacokinetic study of ATX-101: serum lipids and adipokines following synthetic deoxycholic acid injections. J Cosmet Dermatol. 2015;14(1):33–9.
11. Dover J et al. Results from a phase IIb study evaluating the efficacy and safety of ATX-101 for reduction of submental fat using magnetic resonance imaging and investigator and subject assessment. In: 21st Annual Congress of the European Academy of Dermatology and Venereology. Prague, Czech Republic; 2012.
12. Goodman G et al. ATX-101, a pharmacological treatment, for the reduction of submental fat: results of two pooled phase IIa studies. In: 21st Annual Congress of the European Academy of Dermatology and Venereology. Prague, Czech Republic; 2012.
13. Smith K, et al. ATX-101 treatment offers long-term durability of submental fat reduction: preliminary follow-up study results of subjects from phase II studies. J Am Acad Dermatol. 2012;66(4):AB23–AB23.
14. Ascher B, et al. Efficacy, patient-reported outcomes and safety profile of ATX-101 (deoxycholic acid), an injectable drug for the reduction of unwanted submental fat: results from a phase III, randomized, placebo-controlled study. J Eur Acad Dermatol Venereol. 2014;28(12):1707–15.
15. Cunha KS, Lima F, Cardoso RM. Efficacy and safety of injectable deoxycholic acid for submental fat reduction: a systematic review and meta-analysis of randomized controlled trials. Expert Rev Clin Pharmacol. 2021;14(3):383–97.
16. Shridharani SM, Kennedy ML. Management of serious adverse events following deoxycholic acid injection for submental and jowl fat reduction: a systematic review and management recommendations. Aesthet Surg J Open Forum. 2024;6:ojae061.
17. Oh J-S, et al. The study of a validated assessment scale for a localized submental fat volume. J Clin Med. 2023;12(3):1226.
18. Farina GA, et al. Deoxycholic acid in the submental fat reduction: a review of properties, adverse effects, and complications. J Cosmet Dermatol. 2020;19(10):2497–504.
19. Jones DH, et al. REFINE-1, a multicenter, randomized, double-blind, placebo-controlled, phase 3 trial with ATX-101, an injectable drug for submental fat reduction. Dermatol Surg. 2016;42(1):38–49.
20. Chang L-Y, et al. ATX-101 (deoxycholic acid injection) in submental fat reduction: an objective outcome study. Aust J Plast Surg. 2022;5(2):23–8.
21. Khan H et al. An assessment of the reduction of submental fullness with ATX-101 (deoxycholic acid injection) in the expanded safe zone. Cureus. 2023;15(2).
22. Shome D, Khare S, Kapoor R. The use of deoxycholic acid for the clinical reduction of excess submental fat in Indian patients. JDD. 2019;18(3):266–72.
23. Vertuan M, et al. Is deoxycholic acid able to reduce submental fat and increase patient satisfaction when compared to placebo groups? A systematic review. J Plast Reconstr Aesthet Surg. 2022;75(11):4281–9.
24. Salsi B, Fusco I. Non-invasive system delivering microwaves energy for unwanted fat reduction and submental skin tightening: clinical evidence. J Cosmet Dermatol. 2022;21(11):5657–64.
25. Somji M, Solomon T. Successful treatment of submental fat using a non-focused pulsed ultrasound. J Cosmet Dermatol. 2023;22(9):2476–80.
26. Turer DM, James IB, DiBernardo BE. Temperature-controlled monopolar radiofrequency in the treatment of submental skin laxity: a prospective study. Aesthet Surg J. 2021;41(11):NP1647–56.
27. Yazdanparast T, et al. Biophysical and ultrasonographic changes in lichen planus compared with uninvolved skin. Int J Womens Dermatol. 2019;5(2):100–4.
28. Kwon HH, et al. Tightening and reduction of unwanted submental fat using triple-layer high-intensity focused ultrasound: clinical and 3-dimensional imaging analysis. Dermatol Surg. 2021;47(12):1595–600.