

Jowl Reduction With Deoxycholic Acid

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BACKGROUND The study proposes a novel protocol for targeting the jowls using deoxycholic acid (DCA) injections, with emphasis on safety and feasibility of the procedure.

METHODS This prospective study was conducted at a cosmetic practice between June 2016 and May 2017. Twelve consecutive patients seeking reduction/improvement in mild/moderate jowl fat were injected with DCA subcutaneously in a predefined circular area 1.0 cm above the mandibular border. Treatment response was assessed using physician-evaluated Global Aesthetic Improvement Scale (GAIS) and Subject GAIS.

RESULTS Twelve patients (11 women and 1 man) with mild ($n = 8$) or moderate ($n = 4$) jowls were treated. After the first treatment, GAIS responses for 24 jowls showed 5 jowls with vast improvement, 15 with moderate improvement, and 4 with no change. After the second session for 5 jowls in 3 patients, GAIS responses showed vast improvement in 4 jowls and moderate improvement in 1. Adverse events included induration ($n = 4$), bruising ($n = 6$), numbness ($n = 2$), pain ($n = 5$), redness ($n = 3$), edema ($n = 9$), and dysphagia ($n = 1$).

CONCLUSION Results of this early experience showed that DCA injections were safe and effective for non-surgical jowl reduction.

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Facial aging is a multifactorial process involving skin, soft tissue, and skeleton changes and is influenced by intrinsic (genetic) and extrinsic factors. Facial fat, for example, is categorized into superficial and deep compartments,¹ which change with age. Although the cause is unclear, the deep fat compartments (periorbital, perioral, and buccal fat) tend to atrophy with age, whereas the superficial compartments (submental, nasolabial, jowl, and lateral malar regions) are more prone to hypertrophy.^{1,2} Furthermore, the superficial fat compartments of the midface tend to deflate and descend. This, coupled with the asynchronous volumetric changes in the superficial and deep fat compartments, contributes to the loss of jawline definition (Figure 1A).³ Overall, jowls are formed

by the combination of 2 jowl fat compartments, the mandibular septum and associated submandibular fat compartments along with the overlying skin.⁴

Interest in jowl and jawline rejuvenation procedures is increasing, and according to the 2017 annual report of the American Society for Dermatologic Surgery, 73% and 63% of respondents of a consumer survey reported that they were somewhat to extremely bothered by excess fat under the chin/neck and sagging facial skin, respectively.⁵ Available treatment approaches for jowl and jawline rejuvenation include the use of botulinum toxin type A,⁶ injectable fillers,^{7,8} and liposuction.⁹

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Figure 1. Superficial facial fat compartments (A) and definition of the treatment area (B and C).

An alternative option for jowl and jawline rejuvenation is the use of minimally invasive lipolytic injectables that can help reduce accumulated subcutaneous fat.¹⁰ For example, deoxycholic acid (DCA), a naturally occurring bile acid, is available as a synthetically derived, proprietary formulation (DCA injection: ATX-101; KYBELLA, Madison, New Jersey; BELKYRA, Canada and Sweden; KYTHERA Biopharmaceuticals, Inc., Westlake Village, CA, acquired by Allergan, Inc.) that is approved by the US FDA for improvement in the appearance of moderate to severe convexity or fullness associated with submental fat.¹¹ When injected in adipose tissue, DCA acts by irreversibly disrupting the adipocyte membrane causing adipocytolysis.¹¹ The safety and efficacy of DCA injections for reducing submental fat was demonstrated in four Phase 3 randomized controlled trials (RCTs).^{12–16}

Given the subcutaneous adipocytolytic ability of DCA injections, its off-label use for reducing subcutaneous fat pockets resistant to diet and exercise located around the bra line,¹⁷ abdomen (anterior and sides), back rolls, and arms¹⁸ has been reported. A single case report also mentions DCA injections as part of a multimodal injection procedure for lower face rejuvenation.¹⁹

Here, the authors present a private-practice study demonstrating the feasibility of off-label use of DCA injections for targeting sagginess of the jowls caused by the displacement of superficial fat compartments that line the jaw. A novel protocol for targeting jowls using DCA injection is proposed, with emphasis on the safety and feasibility of the procedure.

Methods

Study Design

This prospective study was conducted at a cosmetic private office between June 2016 and May 2017. Consecutive patients seeking reduction/improvement in jowl fat were enrolled using a nonrandomized sampling technique (quota sampling). The study was conducted in accordance with the Declaration of Helsinki and the International Conference on Harmonisation Tripartite Guidelines for Good Clinical Practice. Written informed consent was obtained from each patient.

Patients

Consecutive patients of either sex who were 21 years or older and seeking reduction/improvement in jowls/jowl fat were enrolled. Patients younger than 21 years or those with a history of having undergone other cosmetic or aesthetic treatments (e.g., neurotoxins, fillers, microneedling, or Ultherapy) to the face and neck were excluded. Patients with an infection at the injection site, on anticoagulants, or who were pregnant were also excluded.

Treatment Protocol

Deoxycholic acid is available as a 10 mg/mL sterile solution for subcutaneous injection in a 2-mL, clear, colorless vial for single-patient use. Vials were stored at 20°C to 25°C (68°F–77°F), and excursions between 15°C and 30°C (59°F–86°F) were permitted.

Patients were examined in a sitting/reclining position for perceived change in anatomy associated with

sagging jowl fat along the mandibular line. To identify the treatment area, a line was marked through the lateral commissure of the lips and the inferior border of the masseteric muscle. A line was then drawn through the nasolabial crease to intersect with the other line at the lateral oral commissure (Figure 1B, C). Thereafter, to define the area of the jowls to be treated and to assess the amount of DCA to be injected, a circle was drawn of a size to fit between the 2 lines. Jowls defined by circles with approximate radii of 1.0, 1.5, and 2.0 cm were classified as mild, moderate, and severe, respectively (Figure 2). A 1.0-cm distance was kept between injection sites that were marked in the circle. All injection sites were marked 1.0 cm away from the lower end of the quadrants near the border of the mandible to avoid injury to the marginal mandibular nerve (MMN; motor branch of the facial nerve). Deoxycholic acid (approximately 0.1 mL at each injection site) was injected subcutaneously inside the jowl, focusing on the upper quadrants of the drawn circle, with a half-inch, 30-gauge needle (see **Supplemental Digital Content 1**, Video, <http://links.lww.com/DSS/A133>). Of note, care was taken to pull back on the plunger to avoid injection into the facial artery. The same physician treated all patients on both sides at the same time. Before and after treatment, ice was applied for at least 10 to 15 minutes. Patients with unsatisfactory results after the first treatment session underwent a second treatment session after 6 weeks.

Efficacy Assessments

Standard photography of each jowl was used to document treatment response before and 4 to 6 weeks after each treatment session. Two inde-

pendent physicians retrospectively reviewed the photographs of each jowl after treatment and assessed the treatment response using the Global Aesthetic Improvement Scale (GAIS; Table 1). Patients’ assessment of treatment response was evaluated using the Subject GAIS (Table 1) for both jowls simultaneously after 4 to 6 weeks of treatment.

Safety Assessments

Patients were evaluated for injection-site adverse events (AEs) and other AEs during the first week after treatment and again 4 to 6 weeks after treatment. All AEs (induration [evaluated as area of hardness], bruising, facial muscle weakness, numbness, pain, redness, edema [assessed as swelling], dysphagia [trouble swallowing], and uneven smile) were reported by patients on a scale of 1 to 10 to categorize/grade the degree of AEs ranging from very mild (1) to unimaginable (10; 1–2 was considered very mild grade, 3–4 was considered mild grade/acceptable, 5–7 was considered moderate grade/tolerable, and 8–10 was considered severe grade/intolerable).

Results

Patient Demographics and Baseline Characteristics

Twelve consecutive patients (11 women and 1 man) were enrolled and treated (Table 2). The mean (min, max) patient age was 61 (54, 74) years. Eight patients were treated bilaterally for mild jowls and 4 for moderate jowls.

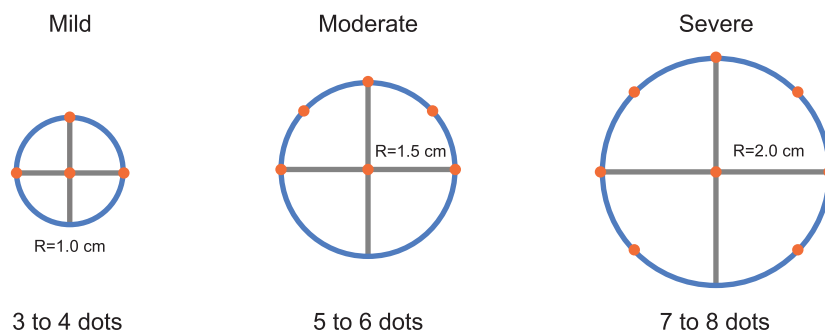


Figure 2. Demarcation of the treatment area and injection sites. Dots represent planned injection sites. R, radius.

TABLE 1. Global Aesthetic Improvement Scale and Subject Global Aesthetic Improvement Scale

| Global Aesthetic Improvement Scale | | | Subject Global Aesthetic Improvement Scale | |
|------------------------------------|-------------------------|--|--|---|
| Rating | Degree | Description | Degree | Description |
| 1 | Exceptional improvement | Excellent corrective results | Much worse | Appearance much worse than the original condition |
| 2 | Vast improvement | Appearance noticeably improved, but not completely optimal | Worse | Appearance worse than the original condition |
| 3 | Moderate improvement | Appearance somewhat improved compared with the original condition, but a touch-up is advised | No change | Appearance essentially the same as the original condition |
| 4 | Unaltered | Appearance substantially remained the same compared with the original condition | Improved | Appearance noticeably improved from the original condition |
| 5 | Worsened | Appearance worsened compared with the original condition | Much improved | Appearance substantially improved from the original condition |

Procedural Outcomes

As of September 2017, 9 patients underwent a single, bilateral treatment session, and 3 patients underwent 2 bilateral treatment sessions ($n = 29$ jowls; 1 jowl was not treated during the second session). Overall, patients were administered a mean (SD; min, max) of 0.47 (0.25; 0.2, 1.2) mL of DCA per jowl. The number of injection sites per jowl ranged from 3 to 4 for mild jowls and 4 to 6 for moderate jowls during the first treatment session. Among the 3 patients who returned for a second treatment session, the number of injection sites and DCA dose decreased from the first to second treatment session. One patient with mild jowls received 4 injections (0.5-mL DCA total) in each jowl during the first session and 3 injections (0.3 mL total) in the right jowl during the second session after 6 weeks. One patient with moderate jowls received 10 injections (right 6 [1.2 mL total]; left 4 [0.8 mL total]) during the first session and 4 injections (right 2 [0.2 mL total]; left 2 [0.2 mL total]) during the second session after 6 weeks. Another patient with moderate jowls received 10 injections (right 5 [0.5 mL]; left 5 [0.5 mL]) during the first session and 8 injections (right 4 [0.4 mL]; left 4 [0.4 mL]) during the second session after 5 weeks.

Treatment Response

According to physician evaluation of 24 jowls in 12 patients after the first treatment session, 5 jowls

vastly improved in 5 patients, 15 jowls moderately improved in 12 patients, and 4 jowls were unchanged in 4 patients (Table 2). The second treatment was for 5 jowls in 3 patients, where GAIS response showed that 4 jowls showed vast improvement and 1 showed moderate improvement. When the GAIS response was evaluated for the untreated jowl, vast improvement was observed, attributed to progressive change. Among the 8 moderate jowls in 4 patients, 1 vastly improved, 5 moderately improved, and 2 did not change after the first treatment session; however, of 4 jowls in 2 patients, 3 vastly improved and 1 moderately improved after the second session. Only 2 jowls (1 mild and 1 moderate) in 2 patients did not respond to treatment (no change in appearance on the left side).

According to patient assessments, 2, 8, and 2 jowls had no change, improvement, and much improvement, respectively, after the first treatment session. Among the 3 patients who underwent a second treatment session, 1 patient with mild jowls moved from no change to improvement after the second session, whereas 2 patients with moderate jowls reported improvement after both sessions. Examples of treatment response are shown in Figure 3 and **Supplemental Digital Content 2**, Figure, <http://links.lww.com/DSS/A134> and **Supplemental Digital Content 3**, Figure, <http://links.lww.com/DSS/A135>.

TABLE 2. Patient Demographics, Clinical Characteristics, and Treatment Description

| Pt | Sex | Age, yrs | History | Jowl Classification | | Injection Sites, n | | Injection Volume, mL | | Complication | GAIS | | |
|----|-----|----------|-------------|---------------------|------|--------------------|----|----------------------|------|--------------------------|------|----|-------|
| | | | | Rt | Lt | Rt | Lt | Rt | Lt | | Rt | Lt | SGAIS |
| 1 | F | 65 | DM HBP | Mild | Mild | 3 | 4 | 0.4 | 0.6 | None | 2 | 3 | 4 |
| 2 | F | 63 | HDL | Mild | Mild | 4 | 4 | 1.0 | 1.0 | None | 3 | 4 | 4 |
| 3 | F | 57 | None | Mild | Mild | 4 | 4 | 0.5 | 0.5 | None | 4 | 3 | 3 |
| 4 | F | 74 | HBP | Mild | Mild | 3 | 0 | 0.3 | 0 | None | 2 | 2 | 4 |
| | | | | Mod | Mod | 6 | 4 | 1.2 | 0.8 | None | 3 | 4 | 4 |
| 5 | F | 60 | HBP | Mild | Mild | 2 | 2 | 0.2 | 0.2 | None | 2 | 3 | 4 |
| | | | | Mild | Mild | 3 | 3 | 0.25 | 0.25 | None | 3 | 2 | 4 |
| 6 | M | 60 | Hypothyroid | Mild | Mild | 3 | 3 | 0.25 | 0.25 | None | 3 | 3 | 5 |
| | | | HBP | Mild | Mild | 3 | 3 | 0.25 | 0.25 | None | 3 | 3 | 5 |
| 7 | F | 54 | RA | Mod | Mod | 5 | 5 | 0.5 | 0.5 | None | 3 | 3 | 4 |
| | | | Hypothyroid | Mild | Mild | 4 | 4 | 0.4 | 0.4 | None | 2 | 2 | 4 |
| 8 | F | 65 | None | Mild | Mild | 3 | 3 | 0.3 | 0.3 | None | 3 | 2 | 4 |
| 9 | F | 65 | HBP | Mild | Mild | 4 | 4 | 0.4 | 0.4 | None | 3 | 3 | 4 |
| 10 | F | 54 | Hypothyroid | Mod | Mod | 5 | 5 | 0.5 | 0.5 | None | 3* | 2 | 5 |
| 11 | F | 60 | None | Mod | Mod | 5 | 5 | 0.5 | 0.5 | Electric shock sensation | 3 | 4 | 3 |
| 12 | F | 57 | HDL | Mild | Mild | 4 | 4 | 0.4 | 0.4 | None | 3 | 2 | 4 |

Refer to Table 1 for details of GAIS and SG AIS scoring.

*Patient had a postsurgery trauma.

DM, diabetes mellitus; GAIS, Global Aesthetic Improvement Scale; HBP, high blood pressure; HDL, high-density lipoprotein; Lt, left; Mod, moderate; Pt, patient; RA, rheumatoid arthritis; Rt, right; SG AIS, Subject Global Aesthetic Improvement Scale; yrs, years.

Safety

A total of 7 types of AEs occurred in 12 patients after the first treatment session: induration (n = 4), bruising (n = 6), numbness (n = 2), pain (n = 5), redness (n = 3), edema (n = 9), and dysphagia (n = 1; Table 3). Grade ≥5 (moderate to severe/tolerable to intolerable) AEs were induration (n = 2), bruising (n = 3), numbness (n = 1), pain (n = 2), redness (n = 1), and edema (n = 7). The time range for resolution of these AEs was 1 to 14 days for induration, 1 to 30 days for bruising, 1 to 7 days for numbness, 1 to 14 days for pain, 2 to 21 days for redness, 1 to 14 days for edema, and 2 days for the single case of Grade 2 dysphagia. No patient reported facial muscle weakness or uneven smile. Of note, 1 patient who reported Grade 7 induration for 14 days, Grade 6 numbness for 7 days, and Grade 7 swelling for 14 days was injected with a total of 0.25-mL DCA at 3 sites on each jowl, and 1 patient who reported Grade 8 bruising for 30 days, Grade 9 pain for 14 days, Grade 8 redness

for 21 days, and Grade 9 edema for 14 days was injected with a total of 0.4-mL DCA at 4 sites on each jowl. One patient experienced an electric shock sensation while being injected on the right moderate jowl.

Adverse events reported after the second treatment session were induration (n = 1; Grade 3, duration 3 days), bruising (n = 3; Grade 1–4, 3–21 days), numbness (n = 1; Grade 1, 14 days), redness (n = 2; Grade 4–5, 2 days), and swelling (n = 3; Grade 5–6, 2–5 days). All AEs resolved at the 4- to 6-week assessment.

Discussion

Results of this early experience with a novel protocol for DCA injections for treatment of mild to moderate jowl/jowl fat showed that DCA is an effective alternative, with a favorable safety profile, for jowl reduction. Overall, 11 of 12 patients reported improvement or much improvement after their



Figure 3. Patient photographs showing improvement after 4 to 6 weeks of treatment: (A) after the first treatment session and (B) after the first and second treatment sessions.

treatment sessions, indicating that a visible response was achieved early. Treatment response as evaluated by physicians was in line with that of patients; 20 of 24 jowls were considered to have vastly or moderately improved. However, 4 jowls in 4 patients did not change after the first treatment session, indicating some patients may require a second treatment session, which should occur at least 6 to 8 weeks after the first session.

Three patients returned for a second treatment session, suggesting AEs were manageable and tolerable.

However, patient satisfaction is influenced by other factors such as lack of patient enthusiasm to pursue the ideal aesthetic goal and costs, which could not be ruled out as reasons for some patients not having additional treatment sessions. Therefore, defining the ideal aesthetic goal and aggressively pursuing it in the real world may be difficult and subject to variable patient satisfaction and costs incurred. Ideal treatment outcome must be an improvement of at least 1 to 2 grades on the GAIS, with foremost consideration to the patient's impression of a favorable treatment outcome.

Nonsurgical approaches such as radiofrequency and injectables and surgical approaches such as face-lift and liposuction are the only options available for jowl reduction. Among these options, DCA is the only injectable treatment that has been extensively studied in a rigorous clinical development program where safety and efficacy was established for submental fat reduction.¹²⁻¹⁶ In this study, the jowls were defined using the lines drawn from the nasolabial crease to the lateral oral commissure. The circle drawn to fit within the area between the lines further demarcated the injection sites, which were kept 1.0 cm apart. The lower quadrants of the circle near the mandibular border were deliberately avoided to prevent MMN injury. The ideal patient for jowl reduction with DCA is a patient with mild to moderate jowl and mild laxity.

The dose of DCA per injection site (approximately 0.1 mL) used in the patients in this study was lower than the prescribed dose (0.2 mL) for submental fat reduction because of an initial apprehension of using

TABLE 3. Adverse Events After All Treatment Sessions

| | <i>Patients, n</i> | <i>Grade</i> | <i>Duration, d (min, max)</i> |
|------------|--------------------|--------------|-------------------------------|
| Induration | 4 | 1-8 | (1, 14) |
| Bruising | 6 | 1-8 | (1, 30) |
| Numbness | 2 | 1-6 | (1, 14) |
| Pain | 5 | 2-9 | (1, 14) |
| Redness | 3 | 1-8 | (2, 21) |
| Edema | 9 | 1-9 | (1, 14) |
| Dysphagia | 1 | 2 | (2, 2) |

Patients graded adverse events using a scale of 1 to 10 (1 = very mild and 10 = unimaginable; 1-2 was considered very mild, 3-4 was considered mild grade/acceptable, 5-7 was considered moderate grade/tolerable, and 8-10 was considered severe grade/intolerable).

DCA outside of the submental area. A mean total dose of 0.5-mL DCA per jowl was administered to most patients and was found to be effective and safe. The dose of total DCA required during the second treatment session was generally less than that used in the first session, possibly because of the reduction in the volume of fat after the first procedure.

The results of this study cannot be directly compared with those of the RCTs conducted for reduction of submental fat, where patients underwent up to 6 treatment sessions to achieve protocol-defined response.^{12–16} However, the observed treatment response in this study is in line with the early experience in 100 patients seeking submental fat reduction from a single-center private practice.²⁰ In that study, most (79/100) patients who underwent 1 or 2 treatment sessions had an improvement of ≥ 1 point on the clinician-reported submental fat rating scale, which was considered clinically meaningful in the pivotal RCTs.^{13,15}

The type of AEs experienced by patients in this study was consistent with those reported in RCTs of DCA treatment for submental fat reduction,^{12–16} but to a lesser degree and of shorter duration, possibly because of the smaller dose used for jowl versus submental fat reduction. In this study, the most common AEs related to DCA injection were edema (9/12 [75%] patients) and bruising (6/12 [50%] patients). Other AEs were pain, induration, redness, dysphagia, and numbness. The incidence of pain, edema, bruising, and MMN paresis in Phase 3 RCTs of submental fat reduction was 70%, 87%, 72%, and 2% to 4%, respectively.^{11–16} No case of MMN paresis occurred in this study; however, 1 patient experienced an electric shock sensation while DCA was being injected into the right moderate jowl during the first treatment session, and another patient reported Grade 2 dysphagia lasting for 2 days after the first treatment session. As in the RCTs of DCA treatment for submental fat reduction, most AEs in this study resolved within days, and all patients experienced complete resolution before the next follow-up appointment (within 4–6 weeks). In addition, the duration of most injection-site AEs was similar to that reported in the REFINE 2 study (median duration ranging from 3.0 to 15.5 days).²¹

Limitations of this study include small patient numbers from a single-center private practice, lack of a control group, targeting the superficial fat compartment only with possible aesthetic influence from changes in the deep fat compartment, and possible mismatch between patient and physician expectations. Furthermore, patients with severe jowls did not approach the clinic for treatment.

Conclusion

Results of this study provide evidence from early experience with off-label use of DCA injections for jowl reduction. The treatment was effective and well tolerated in patients seeking reduction of their mild to moderate jowls. Findings indicate that patients are likely to observe improvement after 1 treatment session but may require more than 1 session to achieve the physician-desired aesthetic goals. The dose of DCA and number of treatment sessions are likely to be low for jowls, being dictated by the amount of subcutaneous jowl fat. The information gained from this study can be used to generate hypotheses that can be tested in more rigorously designed studies, which are required to support the effectiveness and safety of DCA use for jowl reduction.

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