New Frontiers in Body Contouring for the Benefit of Our Patients

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The field of aesthetics has evolved significantly over the past decade to prominently feature exciting, new body contouring modalities in response to patient desires for low downtime, minimally or non-invasive procedures for minimizing fat in targeted areas. Increasingly, the data shows that our patients are requesting body contouring procedures and this segment of aesthetic treatment is the fastest growing portion of the aesthetic market. By partnering with industry, we, as dermatologists, plastic surgeons, and facial plastic surgeons, have become fat conquering heroes. We can now remove fat by freezing, heating, or injecting the desired areas. Our fat treatment modalities include using cryolipolysis, diode laser, radiofrequency, high frequency ultrasound, and deoxycholic acid.

It is to the benefit of our patients that these various modalities can be used alone or in combination for augmented effects to help patients achieve their desired outcomes and look. It is fantastic that body contouring treatment approaches have been widely adopted by our patients and aesthetic practitioners. One of the most exciting aspects is that physicians, together with industry, continue to advance the field of body contouring. Our partnership with industry allows for us to develop and test new treatment modalities and target new anatomical areas for body contouring to best help patients achieve their body contouring goals.

In this special body contouring segment, we are excited to prominently feature the most cutting edge body contouring manuscripts. Herein, we recruited global aesthetic body contouring expert clinician-researchers to share the newest body contouring data. These manuscripts highlight new frontiers and paradigms in body contouring, and provide practical concepts that may benefit our approach to body contouring to tremendously benefit our patients.

Future Applications of Deoxycholic Acid in Body Contouring

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ABSTRACT

Deoxycholic acid (Kybella™, Allergan Pharmaceuticals, Irvine, CA) is a novel injectable treatment used for the cosmetic reduction of redundant submental fat. By inducing adipose cell lysis, the soft tissue alteration induces subsequent contour change and sharpening of the cervicomental angle. The safety and efficacy have been well established in several prospective clinical trials and subsequent FDA approval for this purpose. This has provided an effective and less invasive alternative to surgical liposuction with virtually no recovery time and less overall discomfort. Given its success for use in this context, a logical step would be to extrapolate to other regions of the body where cosmetic deformity is caused by excessive adipose tissue. In the current article, the authors propose potential options for further use in various targeted areas where subcutaneous fat may be amenable to reduction with deoxycholic acid injection, understanding that such uses would be off-label and require an understanding of the regional anatomy and possible complications.

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INTRODUCTION

Deoxycholic acid, called Kybella™ in the United States and Belkyra™ in Canada (Allergan Pharmaceuticals, Irvine, California), is the first aesthetic injectable treatment approved for improvement in the appearance of moderate to severe convexity or fullness associated with submental fat (SMF).[1] The drug was FDA approved in April 2015 and has been used as an injectable product to reduce submental fat in the US since that time. The addition of Kybella for this purpose has given patients who are averse to surgery a minimally invasive treatment option that can be performed during an office visit.

During the pivotal studies leading up to FDA approval, physicians have learned a great deal about deoxycholic acid and its interaction with submental fat and soft tissue. This has included the treatment efficacy and the side effects and safety profile of the drug.[2-4] Understanding the expected treatment effect after injection and the potential complications from the injection are part of the physician's learning curve for any cosmetic injectable substance. This understanding allows the practitioner to develop new and innovative applications for any drug. Such is the case with neurotoxins and injectable fillers, each of which are used in many variant ways in addition to the applications indicated by their initial FDA approval.

The goal of deoxycholic acid injection is to change the contour of the anterior neck, creating a more acute cervicomental angle. The soft tissue contour difference created by Kybella

injections and the ensuing fibrosis could be applied to other areas within the face and body. In order to effectively and safely use this product in other non-FDA approved areas, the practitioner should understand the product, the local anatomy, and the potential problems that could be produced from the injections. This paper identifies potential uses of deoxycholic acid in others regions not suggested (or tested) by the original FDA process. As with most off-label indications, the practitioner and patient should be open to new applications, but skeptical of the fact that complete evidence of efficacy and safety is non-existent.

Mechanism of Action of Deoxycholic Acid

When injected subcutaneously into fat, deoxycholic acid causes adipocytolysis, and stimulates a local tissue response consisting of macrophage infiltration (to remove cellular debris and liberated lipids), fibroblast recruitment, and collagen production (neocollagenesis).[5,6] The desired affect is to improve the submental contour and decrease submental fullness. The treatment process is performed as a 20-minute procedure in an office setting and usually requires 2-4 treatments to achieve maximal improvement in neck contour. This technique has minimal downtime and can often replace submental liposution.

Injection of Kybella into the submental region can be performed with or without injection of local anesthetic and is marketed with a treatment grid to assure evenly spaced (1 cm apart) injections of the product into the submental space. The side effects of the treatment include expected swelling, regional numbness, and bruising in the area.[1,2,7] It is clear that the product is temporarily neurotoxic, causing demyelinization of affected nerves and hypoaesthesia/anesthesia to sensory nerves and weakness to affected motor nerves. A few patients in the pivotal study had transient weakness of muscles supplied by the marginal mandibular branch of the facial nerve due to the proximity of this nerve to the submental region.[1,2] Other uncommon side effects included difficulty swallowing, which occurs secondary to a direct effect on the musculature involved in deglutition.

Off-Label Applications of Drugs

The positive affect on submental fat reduction by Kybella has been well documented.[1-4] The resultant improvement in neck contour from injection of this substance comes from direct fat reduction and fibrosis from the interaction of the drug with the surrounding soft tissues. The procedure provides a minimally invasive method to reduce submental fat and is a possible replacement or adjunct to surgical liposuction in the patients averse to surgery.

As with many new drugs and technologies, FDA approval is an arduous process and the on label indications are often limited by the cost and rigorousness of the process. The usual algorithm is for a company to decide on an application that has utility and is both safe and effective. The company then proceeds along the path to gain FDA approval for this specific application. The approval process includes clinical trials which prove the efficacy and safety of the product to be used in that body region or for that application. Clinicians then use the product in the FDA approved body area and with the prescribed and FDA approved technique. If during the process of use of the drug or technology in the FDA approved manner clinicians find another area or method of use for the product or drug, they often will use it in this manner without FDA approval. The use of FDA approved drugs in non-FDA approved areas, or with techniques that were not part of the original clinical trials is commonplace.[8-12]

An example of the off-label use of a commonly used aesthetic drug is Botox (botulinum toxin, Allergan, Irvine, CA). This injectable drug has widespread use for both cosmetic and functional applications. Aesthetically, the drug was first FDA approved in 2002 for use in the glabella for hyperdynamic muscles causing wrinkles, folds, and a scowling appearance. However, the efficacy and utility of botulinum toxin was rapidly noticed by practitioners and widespread use for hyperdynamic frontalis musculature, for lateral canthal lines, and in the depressor lower facial musculature such as the depressor anguli oris and platysma muscles soon became commonplace.[13] Another example of off-label use of injectable materials can be noted with poly-L-lactic acid (Sculptra, Galderma, Dallas, Texas). The pivotal studies for this injectable collagen stimulator involved reconstitution with 5 mls of sterile water 2 hours before injection of the substance into the face. As practitioners prepared and injected Sculptra, it became clear that reconstituting Sculptra with 9-10 mls of diluent, rather than the 5 ml reconstitution on the label proved safer (creating fewer lumps and bumps) and made the product easier to inject. The larger reconstitution volume is now commonly used.[14]

The off-label use of drugs such as botulinum toxin and poly-L-lactic acid occurs as practitioners consider the best practice guidelines for use of a given drug or technology. Often, industry does not perform additional studies for added applications as the cost, both in time and money, is not financially prudent. Rather, companies may perform Phase IV investigator driven trials only if a new application or method of use is in question.

Future Uses of Deoxycholic Acid (Kybella)

The injection of deoxycholic acid has been proven to be lipolytic and to reduce excess fat and improve cutaneous bulges that result from the fat excess. It is clear that patients desire body improvement beyond that provided by diet and exercise. There is also an increasing trend toward in-office, non-surgical, and minimally invasive methods to achieve aesthetic improvement. The potential uses of deoxycholic acid in regions of the body other than the submentum is great. In order to consider these

possible areas, the negative aspects and potential side effects of Kybella should be realized.

The possible obstacles to use of Kybella in the body include drug cost and side effects/complications from injection of the drug. The most notable side effect of the drug is that it is neurotoxic. Injection of Kybella into the submental region gives all patients hypoesthesia or anesthesia in the injected area. This sensory nerve side effect is universal and occurs in virtually every patient. If injected into the wrong regions, Kybella can also cause direct motor nerve toxicity. This was seen in the pivotal studies as 4.3% experienced transient neuropraxia of the marginal mandibular nerve.[2] Weakness of the nerve post injection was a direct toxic effect to the nerve from injections that were in close proximity to the nerve. After understanding this side effect, the injection patterns were modified and this complication was rarely observed. In order to avoid neurotoxic side effects with injections of deoxycholic acid into body fat, an understanding of the neurotoxicity caused by the injections is essential.

Another consideration for Kybella injections for body fat reduction is the cost of the drug and the number of treatments needed to produce a satisfactory clinical outcome. The submental region is small, and the amount of drug necessary to produce a clinical change in submental contour is relatively small. The cost to practitioner per submental fat treatment is approximately $450-600, with the average number of treatments being 2-4. The total cost of drug is therefore $900-2400, with practitioners typically charging patients approximately twice the cost of the drug. The areas treated in the body are generally larger, necessitating a larger amount of drug and a larger cost to the patient. This must be considered as every patient measures the value of the procedure against the total cost to them.

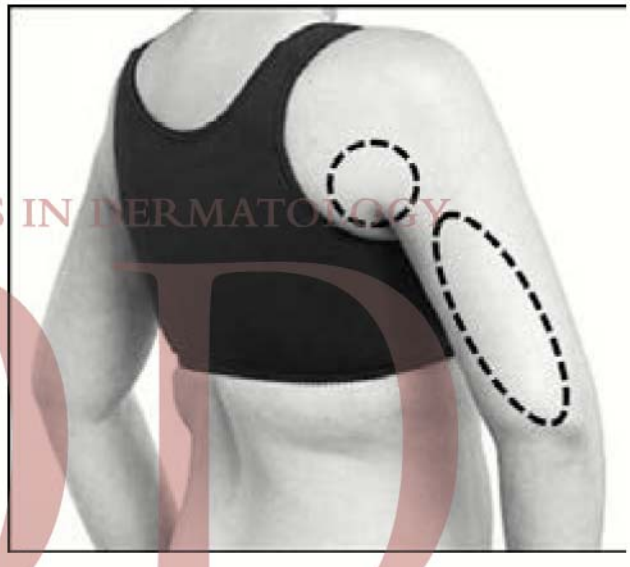
Anterior and Posterior Axillary Fat

The fat which is located near the anterior and posterior axillary fold is well suited to be treated with deoxycholic acid (Figure 1). The fat is superficial, easily accessible with a short to medium length needle, and has few important adjacent structures that can be injured with the lipolytic agent. The nerve branches from the brachial plexus are located deep within the axilla and are relatively protected from the superficial injection that would be used to treat the fat associated with the axillary folds.

Upper Arm Fat

Many patients are plagued with excess fat and soft tissue in their upper arms (Figure 1). These patients will often alter their wardrobe and not wear short sleeve garments. Surgery to correct redundant upper arm tissue (brachioplasty) can leave unsightly scars which may negate the positive outcome from removing the soft tissue excess. Use of deoxycholic acid may improve the contour of redundant upper arm soft tissues. Because a large portion of the excess tissue may be skin and soft tissue excess not related to fat, a clinical trial would be needed to determine if the drug would give the desired effect when injected into this region.

FIGURE 1. Regions of axillary and posterior arm adipose tissue.



Medial and Lateral Knee Fat

Treatment of unwanted fullness secondary to fat deposits in the knees is difficult. Liposuction in this area often does not produce desired results, and the scars, although small, can heal in a less than ideal fashion (hypertrophy, hyperpigmentation). Injection of deoxycholic acid in these areas could be clinically effective without any cutaneous scars (Figure 2). Because the volume of drug likely needed to produce clinical effect would be small, the procedure would be cost effective for patients.

Subcutaneous Abdominal Fat

The options for improving abdominal contour have included surgery (liposuction or abdominoplasty in patients with redundant abdominal wall skin) or non-invasive tightening procedures such as radiofrequency contouring. Injection of deoxycholic acid (Kybella) could diminish superficial abdominal fat in a safe method. Pinching the abdominal soft tissues away from the underlying abdominal fascia and use of a short needle could diminish the chance of any intraabdominal injection of the drug. Possible modifications of the present drug may include diluting the concentration of the drug and use of a canula into the subcutaneous space tangentially to improve an even distribution of the higher injection volumes

The rate limiting factor in using this medication into the subcutaneous plane adjacent to the abdominal wall is cost. Because the total surface area is large (Figure 2), the amount

FIGURE 2. Regions of abdominal and medial/lateral knee adipose tissue.

of drug needed to produce a clinical effect would be significantly greater than the amount needed to produce an effect in the submental space. Unless the product cost was reduced, the amount needed would likely make treatment into the subcutaneous abdominal space cost prohibitive for many patients.

DISCUSSION

Deoxycholic acid has produced an improvement in submental contour as proved by clinical studies. As with any drug introduced for a specific usage, additional possibilities for use of the drug for other applications exist. Specifically, indications in relative small volume areas that are less amenable to liposuction, such as the knees or the axillary fold fat, would be possible applications. Additionally, the drug concentration could be altered to facilitate injection into larger surface spaces.

In order to determine if further applications of deoxycholic acid are warranted, clinical trials are necessary to determine efficacy and safety. These studies could dictate that the effective treatment of fat seen in the submental region could occur in other body areas.

DISCLOSURES

Dr. Sykes is a speaker/trainer for Allergan. Dr. Allak and Dr. Klink have no conflict of interests to declare.

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