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AN EVIDENCE-BASED ASSESSMENT OF TREATMENTS FOR CELLULITE

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Abstract
Cellulite, a skin surface change that is nearly ubiquitous in women, is a condition that remains elusive to treatment. In fact, no treatment is completely successful as none are more than mildly and temporarily effective. Despite the lack of evidence to support efficacy, treatment options continue to proliferate. This article will briefly review the currently available data about cellulite treatments including noninvasive devices such as massage, radiofrequency, and laser and light-based treatments; invasive modalities including liposuction, mesotherapy, and subcision; and other treatments including topical creams and carboxy therapy.

Introduction

Cellulite is the characteristic, nonpathologic appearance of dimpled, "cottage cheese-like" skin surface change typically seen in women on the thighs and buttocks. It is also commonly seen on the abdomen, breasts, and arms. Given that the occurrence of cellulite is nearly universal in postpubertal females, it is thought of as a female secondary sex characteristic.[1] Nevertheless, it can be a distressing condition and patients spend billions of dollars on treatments that are largely ineffective.[2] Treatment offerings for cellulite are bountiful, indicating a lack of any definitive treatment.

Cellulite has variably been attributed to structural, circulatory, hormonal, and inflammatory factors, but the path of development is unsettled.[1,3-8] Although there are several purported explanations for the appearance of cellulite, the best evidence supports structural variations in the subcutaneous fat architecture in the setting of hormonal differences between men and women. Given that cellulite is present in the majority of postpubertal women and is rare in men except in cases of androgen deficiency, it is highly likely that hormones play an essential role in the pathogenesis. Moreover, compared with men, women have subcutaneous fat that is less reinforced by connective tissue septa and more prone to herniation, yielding the undulating skin surface that is clinically seen as cellulite. In addition, the dermis in women is thinner than men, allowing these herniations to be more easily visualized.

Surgical options, noninvasive devices, injectables, and topical creams have all been used in the treatment of cellulite, and the majority of these treatments lack evidence and proof of efficacy. In fact, there is little data evaluating most cellulite treatments. This article will review the current literature and data on such cellulite treatments as noninvasive devices, invasive modalities, and other offerings including creams and carboxy therapy (Table 1).

Table 1. Noninvasive skin treatment devices.

Device	Mechanism	FDA Approval
Endermologie	Handheld device that kneads the skin	FDA approved for cellulite
Intense pulsed light	Broadband light	FDA approved
VelaSmooth	Bipolar radiofrequency, infrared light, and massage	FDA approved for cellulite
Alma Accent RF System	Unipolar and bipolar radiofrequency	FDA approved for rhytides and wrinkles
ThermaCool	Unipolar radiofrequency	FDA approved for rhytides and wrinkles
Triactive	Low fluence 810-nm diode laser and vacuum massage	FDA approved for cellulite
Synergie Aesthetic Massage System	Vacuum massage ±660-880-nm probe or 880-nm light pad	FDA approved for cellulite
SmoothShapes 100	Suction and mechanical massage with 650-nm light and 915-nm laser	FDA approved for cellulite

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Noninvasive Devices

Noninvasive devices incorporate a variety of modalities including laser and light, radiofrequency, ultrasound, and massage. The greatest body of research has been published about the VelaSmooth™ (Syneron Medical Ltd, Israel) treatment; however, in general, research in peer-reviewed journals is limited. The majority of studies are small, and many do not test for statistical significance or use objective criteria to evaluate the effects of the treatments.

Massage

Based on the unproven theory that vascular and lymphatic alterations promote cellulite, a number of devices are designed to integrate massage into treatment.[9] Endermologie® (LPG, France) is an FDA-approved, hand-held device that employs massage and skin kneading to affected areas. The skin is pulled and kneaded between 2 rollers in an effort to promote lymphatic drainage and alter skin architecture.[1] One study found a 1.86-mm decrease in skin thickness after 12 treatments.[10,11] Another study reported only marginal results, with the investigator noting improvement in only 2 of 17 patients treated with Endermologie alone.[12] In a pig model, 12 Yucatan pigs underwent deep mechanical massage resulting in increased subcutaneous collagen accumulation most pronounced in the deep subcutaneous tissue and statistically significant in pigs that underwent 10 or 20 treatment sessions. Contour differences, however, were not noted in the comparison of the treated and untreated areas.[13]

Light Sources and Laser

Intense pulsed light (IPL) has been investigated in the treatment of cellulite. The rationale for the use of IPL is based on the idea that it builds collagen, creating a thicker dermis, which is more typical of the male population.[14] Fink studied the use of IPL with and without a retinyl based cream.[15] The Quadra Q4® IPL system (DermaMed, Lenni, PA) was used at fluences between 8 and 14 J/cm^2. The light emitted by this system ranges between 510 and 1200 nm, peaking at 585 nm. Of the 20 patients studied, 8 received IPL alone, while 12 received IPL and retinyl cream. Five patients discontinued the study. The majority of the patients who reported improvement greater than 50% were in the IPL and cream group. These effects diminished in some patients over time. This study was not blinded, and no control group was evaluated; thus the validity is limited.

Several devices combine massage with low-fluence light or laser with the aim that these light sources will thicken the dermis and influence circulation and lymphatic drainage. The FDA-approved Synergie Aesthetic Massage System™ (Dynatronics, Salt Lake City, UT) employs massage with or without a 660- to 880-nm probe or 880-nm light pad. Triactive™ (Cynosure, Westford, MA) is an FDA-approved low-fluence 810-nm diode laser with suction massage. SmoothShapes® 100 (SmoothShapes, Merrimack, NH) is an FDA-approved 650-nm light source combined with a 915-nm laser. Of these treatments, only the Triactive has been studied with data published in peer-reviewed journals. Boyce studied 16 female patients who had underwent 12 treatments with the Triactive and found a 21% improvement of cellulite that was not present at 1 month after the last treatment.[16] There were, however, important limitations to this study: the investigators didn't use a control group and significance was not tested.

Anderson reported that the 1210-nm and 1720-nm laser wavelengths are able to selectively heat adipose tissue; however, no devices associated with these wavelengths are commercially available. In addition, at the time of this article, no studies of these devices in the treatment of cellulite have been published.[17] However, selective laser irradiation of fat at these wavelengths may represent an important breakthrough in the treatment of cellulite.

Radiofrequency

Radiofrequency (RF) devices have been developed to reduce the appearance of cellulite. The purpose of integrating RF into cellulite treatments is to affect the connective tissue septa and fat, which contribute to cellulite. Of the available devices with RF, only the VelaSmooth is approved by the FDA specifically for this indication.

The VelaSmooth combines infrared light (700-2000 nm), bipolar RF and suction, and mechanical massage. In the largest study of the VelaSmooth, Sadick evaluated 35 patients who completed either 8 or 16 treatments with VelaSmooth.[18] A blinded dermatologist evaluated the photographs and found a 40% improvement on average. Statistical significance was not tested, and histological assessment failed to reveal any difference between the treated and untreated sites. Furthermore, the duration of improvement was not studied.

Another blinded study of 20 patients found a 50% improvement in cellulite with the Velasmooth.[19] Two of the 20 patients didn't show an improvement, and clinical effect seemed to diminish slightly over time. A study of 16 patients who received 8 treatments found a greater than 50% improvement that diminished somewhat over 6 months. The validity of this study is compromised by the absence of a control group and because the investigators did not test for significance.[20]

A more recent study of the VelaSmooth found a statistically significant decrease in thigh circumference at 4 weeks, but no immediate decrease or a decrease at 8 weeks.[21] Visual improvements of less than 50% were noted in the majority of subjects. Histologic changes were not seen. A large proportion of patients (31%) experienced bruising.

Nootheti compared the efficacy of the VelaSmooth and TriActive in 20 female patients who were treated twice a week for 6 weeks.[22] Patients were treated with the TriActive to 1 leg and VelaSmooth to the other leg. The average improvement of surface irregularities was 7% and 25% for the VelaSmooth and Triactive, respectively. These differences were not found to be statistically significant. Bruising was more commonly seen after the VelaSmooth treatments.

Like the VelaSmooth, the Alma Accent® RF System (Alma Lasers, Israel) and the ThermaCool® (Thermage, Hayward, CA) utilize radiofrequency and may be useful in the treatment of cellulite. Both the Accent and the ThermaCool are

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FDA approved for the treatment of wrinkles and rhytides. The ThermaCool is a unipolar RF, while the Accent system is a unipolar and bipolar RF device. Of the 2 devices, only the Accent system has been evaluated for the treatment of cellulite. In 1 study, 26 females were treated 2 times with the Accent system in the unipolar mode.[23] The authors evaluated the change in distance from the dermis to muscle and the dermis to Camper's fascia in the thigh and in the buttock by ultrasound. In the results, 64% to 72% of patients showed a 15% to 28% decrease in these measures. The findings were not uniformly significant. The authors noted a qualitative increase of fibrous tissue (53% of patients) and change in morphology of the fibrous tissue with a straightening of the fibrous bands (50% of patients). These qualitative observations were not tested for statistical significance. There was no control group. Treatments were complicated by blisters in 2 patients and bruising in 3 patients.

Ultrasound

It is too early to determine whether noninvasive ultrasound may have a cellulite application. The UltraShape® (UltraShape Ltd, San Ramon, CA) is a non-FDA-approved device that has been recently shown to reduce fat. In a study of 30 patients (who maintained constant weight during the treatment period), results showed a mean decrease of 2.3 cm in local deposits of fat after 3 treatments.[24] This finding was statistically significant; however, further study of this device is needed. Whether the UltraShape treatment is effective in changing the architectural component of cellulite remains to be fully proven.

Invasive Approaches

Liposuction

Liposuction, including superficial liposuction, has been employed to treat cellulite.[25] While this modality can diminish fat deposits deep in the subcutaneous fat, its effect on the superficial components of fat seen in cellulite is often disappointing.[26,27] Ultrasonic liposculpturing has not been definitively shown to improve cellulite any more than conventional liposuction, and skin necrosis from devascularization after extensive undermining has been reported.[28-30] Excisional lifts, such as a thigh lift, and liposuction in combination with fat grafting have been proposed to address the limitation of liposuction in the treatment of cellulite.[31,32]

Subcision

Originally described by Orentreich, subcision is a technique used to remove the fibrous bands that some believe contribute to cellulite.[33] Subcision describes a process whereby after injection of local anesthesia, an 18-gauge needle is inserted into the subcutaneous tissue, 10 to 20 mm below the depression, and moved parallel to the epidermis to release the fibrous bands. Hexsel reported a series of 232 patients treated with subcision.[27] Only patients with depressions visible at rest were treated. Seventy-nine percent of patients were satisfied with the improvement while 2 patients (0.86%) were dissatisfied (20% had "partially successful" results). Ninety percent of patients experienced bruises that caused some pain for up to 4 months, and 100% of patients experienced hyperpigmentation. Persistent erythema was observed in 3% of patients. The value of this study is limited as all photographs were evaluated qualitatively and significance was not tested.

Mesotherapy

Mesotherapy describes intracutaneous or subcutaneous injections of compounds or mixtures of compounds. Neither the compounds themselves nor the ratios of these compounds are well defined. Mesotherapy has been used for a variety of conditions, including cellulite; however, the role of mesotherapy in the treatment of cellulite is unsubstantiated.[34,35] Phosphatidylcholine injection, and specifically the sodium deoxycholate component of the formulation, offers a potential treatment. A number of studies have confirmed the efficacy of phosphatidylcholine for the removal of adipose tissue.[35-39] Whether or not this compound will be effective in the treatment of cellulite requires further evaluation.

Topical Treatments

The role of topical treatments in cellulite therapy is highly questionable. Topical treatments for cellulite continue to proliferate despite the dearth of any data substantiating efficacy. A variety of creams are thought to stimulate lipolysis. Strictly speaking, lipolysis is defined as fat cell shrinkage as opposed to fat cell loss. Topical creams are proposed to function through lipolysis of fat by changing the structure of the dermis and connective tissue or improving circulation. Of the topical compounds used, methylxanthines and retinoids have been studied the most.

In vitro, methylxanthines (eg, caffeine, aminophylline, and theophylline) have been shown to stimulate lipolysis.[7,10] Aminophylline is thought to temporarily stimulate lipolysis by blocking phosphodiesterase and increasing cyclic adenosine monophosphate (cAMP) concentrations, and it has been reported to decrease thigh circumference in randomized, double-blind, placebo-controlled, crossover studies; however, the degree of improvement may be minimal.[12,40-42] One study showed an increased level of free fatty acids after the application of methylxanthines.[43] Another study of a cream containing caffeine and a variety of botanicals showed a decrease in subcutaneous fat thickness that was not sustainable after discontinuation of the cream.[10,44] A double-blind, randomized trial of an anticellulite cream containing caffeine found improvement in cellulite in 68% of subjects after photographic evaluation by blinded dermatologists. (The contralateral leg served as the control). Of 40 patients enrolled, 34 completed the study. Thigh circumference was decreased by 1.93 cm in legs treated with the active product and 1.27 cm in legs treated with placebo. Significance was not tested.[45] Yohimbe is another compound thought to stimulate fat metabolism.[44] The clinical relevance of these findings in the treatment of cellulite or the reduction of fat has not been established.

Like aminophylline, the effect of retinoids has been evaluated in some detail. The basis for treatment with retinoids involves the impact of these compounds on dermal thickness.

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Kligman performed a double-blind, randomized, placebo-controlled trial of 66 women treated with a topical retinol and found that dermatologists (63%) and subjects (68%) found the retinol-treated side more improved in comparison to the control side.[46] This finding was statistically significant. The authors also found a significant difference in blood flow on the retinol-treated side and a 0.16 mm increase in dermal thickness on the retinol-treated side. Significance did not appear to be tested for dermal thickness.

In another study, a topical retinol was compared to a placebo in a randomized, controlled trial of 15 women.[47] After 6 months of treatment, skin elasticity was increased from baseline by 10.7%. While this difference is a significant change from baseline, the standard deviation of the final result included the baseline value, raising questions about the true validity of these results. Mean dermal thickness was unaffected. The authors also noted a 2- to 5-fold increase in the number of XIIIa$^+$ dendrocytes after treatment with retinol. Again, it is unclear whether there was any clinical relevance to these findings.

Based on their *in vitro* effects, Sillicium and *Centella asiatic* are 2 other compounds that are used in the treatment of cellulite and are purported to influence the connective tissue structure of cellulite. *Centella asiatic* has also been reported to increase lower limb perfusion in patients with chronic venous insufficiency and to decrease adipocyte size in a double-blind study of 35 patients.[7] The clinical relevance of these findings with regard to cellulite has not been established.

Compounds that affect circulation have been proposed for use in the treatment of cellulite, although there is minimal support for this theory conceptually and experimentally. Bladderwrack (*Fuccus vesciculosus*), Butcher's Broom (*Ruscus aculeatus*), Ginkgo biloba, common and ground ivy, sweet clover (*Melilotus officinalis*), horse chestnut (*Aesculus hippocastanum*), Papaya (*Carica papaya*), pineapple (*Annas sativus*), and artichoke (*Cynara scolymus*) may have an effect on circulation.[44] One herbal product, Cellasene, which contains a variety of the aforementioned botanicals failed to produce a significant change in cellulite in a study of 24 women, and furthermore, subjects complained of weight gain in the first few weeks of therapy.[48] The ability of these compounds to improve cellulite is questionable, and moreover, the safety of these creams is also an issue. In a study of 32 products, 263 chemical substances were found, of which 25% are known allergens.[49]

Carboxy Therapy

Carboxy therapy is a treatment in which carbon dioxide is injected into the subcutaneous tissue. This treatment purports to affect fat cells and circulation.[50,51]

Conclusion

The best of the currently available treatments have, at most, shown mild improvements in the appearance of cellulite, most of which are not maintained over time. Studies about cellulite treatments are often limited by small patient groups, a lack of a control group, inadequate blinding of investigators, and a failure to test for statistical significance. Thus, the promise of cellulite reduction with any treatment should be regarded as speculation. Certainly, there are interesting treatments on the horizon including phosphatidylcholine injections as well as ultrasound and laser-based therapies; however, these treatments are untested and whether or not they will address cellulite with any greater efficacy remains to be seen.

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