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An Overview with Noninvasive Body Countering in The Management of Cellulite

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ABSTRACT
Nowadays cellulite, or gynoid lipodystrophy (GLD) is the most concerning and displeasing skin problem. It is a condition in which the skin appears dimpled, bumpy and "orange peel-like." It's caused by changes in the structure of the connective tissues and fat cells that lie underneath the skin's surface [1]. This article aimed at reviewing the classification, pathophysiology and treatment in general, as well as the management of cellulite with non-invasive body countering.
Keywords: Cellulite, Adipocyte, connective tissue septae, noninvasive devices.

INTRODUCTION

Cellulite is a topographic and localized skin condition that is most commonly found on the posterolateral thighs, buttocks, and abdomen. It is often identified by a dimpled or orange-peel appearance of the skin's surface.

In 1978, Nürnberger and Muller [2] first described cellulite as a result of sex-related differences in the structure of skin and subcutaneous tissue. Cellulite affects all races, and it is estimated that 85% of women older than 20 years have some degree of cellulite. Despite its high prevalence (80%–90%) in postpubertal female patients of all races, little epidemiological data on its exact prevalence, incidence, and associating factors have been published [3].

Several therapies have been designed, marketed, and/or purported to improve cellulite, including topical therapy, injectable (e.g., chemical septolysis with collagenase), lymphatic or vacuum-assisted massage, acoustic wave therapy, light therapy, external noninvasive lasers, and radiofrequency (RF) devices [4].

METHODOLOGY

This review was conducted using online research by reviewing all articles which were published between1976 to 2017. Different terms as following were used to obtain the articles related to the current subject: "cellulite", "body counting", "noninvasive devices", "fat reduction ".

The study was done after approval of ethical board of King Abdulaziz university.

RESULTS

The management of cellulite by using noninvasive body countering devices play a role in reduction of cellulite. Studies have shown effectiveness of fat reduction in the improvement of cellulite. Further studies are needed to be done on this subject.

Classification of cellulite

Nürnberger and Müller [2] described four stages of cellulite:

- **Stage O:**
  Skin on thighs and buttocks is smooth surface with patient standing or lying. Pinch test throws the skin into folds and furrows.
- **Stage I (or one plus):**
  Skin surface is smooth while patient stands or lies. Pinch test clearly positive for mattress phenomenon.
- **Stage II (or two plus):**
  Skin surface is smooth while lying down. Mattress phenomenon (dermo-panniculosis deformans) when standing.
- **Stage III (or plus three):**
  Mattress phenomenon (dermo-panniculosis deformans) positive in both lying and standing positions.

Physiology of cellulite

"The four leading hypotheses that purport to explain the physiology of cellulite include sexually dimorphic skin architecture, altered connective tissue septae, vascular changes and inflammatory factors"[5].

Sexually dimorphic skin architecture

The 'anatomic' hypothesis of cellulite is based on gender-related differences in the structural characteristics of subcutaneous fat lobules and the connective tissue septa that divide them. According to this theory, originally detailed by **Nürnberger and Müller** [2] , the appearance of cellulite, i.e. 'pits' and 'dells', or dimpled skin, is caused by herniations of fat, termed 'papillae adipose', that protrude from the subcutis through the inferior surface of a weakened dermis at the dermo-hypodermal interface. These herniations of fat into the dermis are a characteristic of female anatomy, and their presence has been confirmed by

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ultrasound imaging as low-density regions among denser dermal tissue [6].

Altered connective tissue septae

Although the Nürnberger and Müller[2], hypothesis maintains that the presence of cellulite is determined by fatty protrusions through the dermal-hypodermal interface. Piérard and co-workers[7] found no correlation in their study between the extent of these protrusions and clinical evidence of cellulite, thereby questioning their relevance in the physiology of the condition. In a study using autopsy specimens from the thighs of 24 previously healthy 28–39- year-old women with cellulite and a control group consisting of 11 men and four women without cellulite, the authors revealed important distinguishing characteristics within the micro-architecture of the subcutaneous connective tissue strands, well below the level of the dermal-hypodermal interface [7]. "Thirteen of the women in the study group demonstrated overt dimpling without pinching, or 'full-blown cellulite,' whereas the remaining 11 women exhibited cellulite only with the application of pressure, a phenomenon termed 'incipient cellulite' or 'cellulite-prone'. The authors concluded that persistent skin dimpling results from continuous and progressive vertically oriented stretch within these hypodermal collagen fibrous strands, a process that weakens the connective tissue buttress and allows for fat herniation"[5].

Vascular changes

Based on descriptions by Curri[8] and others, the authors detail the metabolic and structural events that lead to cellulite formation (referred to as gynoid lipodystrophy). According to their theory, the process originates with the deterioration of the dermal vasculature, particularly in response to alterations of the pre-capillary arteriolar sphincter in affected areas coupled with deposition of hyper polymerized glycosaminoglycans (GAGs) in the dermal capillary walls and within the ground substance between collagen and elastin networks. Increased capillary pressure leads to increased capillo-venular permeability and the retention of excess fluid within the dermis, inter-adipocyte and interlobular septae. GAGs, which have hydrophilic properties, raise the interstitial pressure and additionally attract water. Edema causes cellular changes that ultimately result in vascular compression, vessel ectasia, decreased venous return and tissue hypoxia. Hypoxia, coupled with the increased proteoglycan deposition in dermal collagen and elastic fibers, triggers fibroplasia, collagenesis and capillary neoformation. Focal capillary rupture and microhemorrhage are noted histologically at this stage. Increased lipogenesis, presumably triggered by estrogen, prolactin, and diets rich in carbohydrates, in concert with increased lipolytic resistance caused by hypoxia, leads to adipocyte hypertrophy [2]. "Enlarged adipocytes, together with hypertrophy and hyperplasia of the peri-adipocyte reticular fibres, leads to the formation of micronodules or enlarged, grouped adipocytes surrounded by clumps of protein fibres. In time, continued edema, vascular congestion, and hypoxia lead to thickening and sclerosis of the fibrous septae in the superficial adipose tissue and deep dermis, causing a padded appearance" [5]. Although Lotti and others [2,7], supported the finding of increased edema and abundant GAG deposition at the lower dermal/subcutaneous junction in affected patients with cellulite [2, 7], this observation has not been replicated by additional studies.

Inflammatory factors

In perspective on cellulite, Kligman [9], has reported the diffuse appearance of chronic inflammatory cells, including macrophages and lymphocytes, in the fibrous septae from biopsies of cellulite. According to Kligman, the septae are the source for a low-grade inflammation that results in adipolysis and dermal atrophy. Others, however, find no evidence of inflammation or adipolysis in patients with cellulite [2, 7].

Treatment of cellulite

There are many different techniques which may help in the improvement of cellulite such as surgical options (eg. liposuction and Subcision), injectable (eg.Phosphatidylcholine and Mesotherapy), topical agents (eg. Methylxanthines, Retinoids, Lactic Acid and Herbals)[5]. Recently, the popularity of body contouring and non-invasive approaches have been increasing dramatically. This is due to shorter recovery periods, fewer side effects and less discomfort and pain, compared to the surgical methods, which carry higher risk of complications and have longer recovery period.

Non- invasive body countering in the management of cellulite

- **High-Intensity Focused Ultrasound**

By using an external transducer, HIFU energy cuts off targeted adipose tissue. However, it has no effects on surrounding tissues. Due to the high convergence of ultrasound energy at high frequencies, tissue damage is limited to a small focal point. Ultrasound energy makes molecular vibrations at the zone, that leads to increasing temperature at targeted tissue above 56°C and coagulative necrosis of fat cells [10].

There are various types of HIFU devices in the market such as LipoSonix (Medicis Technologies Corporation, Bothell, Washington), which are approved by the food and drug administration (FDA), yet there are also other ultrasound devices developed for noninvasive body contouring not yet approved by the FDA such as Proslimelt (medical care consulting, Murten, Switzerland), Medcontour (general project, Florence, Italy), Ultracontour (Medixsysteme, Nimes, France), Novashape (UltraMed,Milton,ON, Canada), Accent Ultra (Alma, Buffalo Grove, IL, USA and Vaser-Shape (sound surgical technologies, Louisville, CO, USA) [11].

In a randomized, single-blind, sham-controlled study in 2012, 180 males and females (18 - 65 years) participated with BMI of $\leq$ 30 kg/m^2 and Subcutaneous adipose tissue (SAT) thickness of $\geq$ 2.5 cm in the treatment region (anterior abdomen and flanks). During the study, participants continued their usual diet and physical activity. Patients were divided into three groups and received HIFU treatment at one of the three total doses of energy: 177 J/cm^2 (three passes at 59 J/cm^2), 141 J/cm^2 (three passes at 47 J/cm^2), or 0 J/cm^2 (three passes at 0 J/cm^2; sham group) for nearly one minute for each targeted zone and 15 minutes for the total treatment session. No abnormalities in blood lipids or inflammatory markers were reported. The most adverse effects of treatment were pain, ecchymosis, and swelling. Post-treatment follow-up at 12 and 24 weeks revealed no significant changes in cholesterol, triglycerides, free fatty acids, markers of inflammation and liver or renal function [12]. Moreover, **Jewell *et al.*** confirmed HIFU as a useful method for reducing waist circumference. After 12 weeks, a significant reduction in waist circumference in the two studied groups was reported. The mean decrease in waist circumference was more than 2 cm. However, no changes in weight or BMI were reported [13].

- **Radiofrequency**

Radiofrequency is an electromagnetic wave that was initially used for treating periorbital wrinkles, rhytids and skin laxity [14].

Radiofrequency is commonly used for increasing deeper skin temperature without any epidermal or dermal ablation. It is not only used as an efficient method for contracting or inducing skin tightening but also as an effective method for reducing fat in repetition [15]. However, there is no standard protocol for treatment time with RF, and the range of therapeutic sessions was widespread between 1 and 24 weeks [14]. However, higher temperature at the shorter time could be lethal for adipose tissue, but it is not necessarily comfortable for patients; longer time, for example, eight to ten minutes, with lower temperature, leads to intended adipose cells damage [16]. Former researchers insisted that different parameters in addition to time are related to the success of RF, such as power and the frequency of treatment sessions, yet the exact protocols in this area are unavailable [14].

Radiofrequency generates heat in different tissues by transforming energy through three basic mechanisms from the electromagnetic field [16].These mechanisms include (i) orientation of electric dipoles that already exists in the atoms and molecules in the tissue; (ii) polarization of atoms and molecules to produce dipole moments; and (iii) displacement of conduction electrons and ions in the tissue. The frequency of an RF device ranges between 3 kHz and 24 GHz, and the monopolar and the bipolar configuration are used commonly in medicine [15].

Vela Smooth was the first RF device, which was used widely for body contouring. Now, there are various types of RF devices in the market such as Thermage (SoltaMedical, Hayward, CA, USA), Accent (Alma Lasers), TriPollar (Pollogen, TelAviv, Israel), Freeze (Venus Concepts, Karmiel, Israel) and most recently TiteFX (Invasix). A variety of studies demonstrated smoothening of the cellulite exposure using RF and reduction of subcutaneous tissue, which leads to circumference reduction[17].

- **Cryolipolysis**

Cryolipolysis is one of the newest procedures for non-invasive fat reduction, which was introduced as a body contouring technique in 2007 [18].The principle of cryolipolysis is based on the higher sensitivity of adipocytes to cold in comparison with other water-rich cells [19].

In 2010, cryolipolysis received FDA clearance for love handles (Zeltiq). In 2012 and 2014, FDA clearance was obtained for fat removal by cryolipolysis at abdomen and thighs, respectively [20].

Shek *et al.* [17] reported that increasing the number of treatment sessions to two, improved the positive results. In this study, the fat layer reduction in the abdomen region rose by 7.2%, two months after the last treatment, and 4.3% improvement was found in the flank. This was statistically significant for abdominal fat . **Zelickson *et al.*** [19], demonstrated a 0.9-cm reduction in inner thigh fat bulges at a 16-week fallow up, and 93% of the participants were satisfied .

- **Low-Level Laser Therapy**

Low-level laser therapy is another noninvasive method for reducing adipose tissue and received

FDA clearance in 2010. Before that, LLLT was widely used for treating other problems such as neurologic, ophthalmic, dental and dermatologic diseases [21].

Although there are some evidence, which show the effects of LLLT on reducing fat in combination with liposuction, the evidences for the effects of this method as a stand-alone procedure, are not sufficient. Applying LLLT for fat removal has no observable consequence on surrounding tissues and does not increase tissue temperature. Moreover, it takes time to show its effect on the treated zone [21].

The type of device available in the market works at a wave-length of 635 nm and has four adjustable arms. One treatment session with LLLT lasts up to half an hour, and six to eight sessionsare required to obtain optimum results. Also, manufacturers encourage consumers to use some supplements such as vitamin B5 and L-carnitine, Ginkgo biloba or green tea to reinforce circulatory and lymphatic systems [21].

Using LLLT for fat reduction and body contouring is based on experiences, which showed that applying 635-nm laser leads to deflation of tiny temporary openings within the membrane of adipose cells and releasing fats into the interstitial space. The result of these changes is a reduction of unwanted fat. However, the openings have no destructive effect on body cells but let lipids enter the interstitial space and excrete from the body. It seems that the mechanism mentioned above is the consequence of photo excitation process of cytochrome c oxidase in mitochondria's respiratory chain [21].

Jackson *et al.*[22] reported that applying LLLT to reducing body fat could be effective on the overall circumference. They assessed 67 overweight participants (BMI 25 to 30 kg/m^2), which underwent LLLT (635-nm light with 2.5 mW power) for two weeks (three treatment sessions in each week). After treatment by LLLT (Zeronalipo laser was the first device that received FDA clearance), a total of 891-mm fat reduction was observed across waist, hips, and thighs.

Extracorporeal Shockwave Therapy

Extracorporeal shockwave therapy has been a method for treating kidney stones since 1980 [36]. Also, the procedure has been used for curing lesions and wounds. Nowadays, the device is being used for body contouring and treating cellulite [20]. The energy created in this process is limited to target zones by affecting acoustical interfaces, and no significant changes in surrounding tissue were observed [20].

The commonly used form of ESWT in treating soft tissue is defocused, low-energy shockwaves, which comes in contrast with focused, high-energy ESWT and is commonly applied to delay-union or non-union fractures [20]. It seems that applying extracorporeal shockwave could be an effective method for treating cellulite due to skin collagen remodelling [20]. **Angehrn *et al.*[20]** assessed the shockwave effects on cellulite of 21 women. The participants received 12 sessions of low-energy defocused ESWT (96000 shots for each person) during six weeks in the lateral thigh. After the last session, high-resolution ultrasound measurements and personal questionnaire showed some degrees of improvement in their skin elasticity.

CONCLUSION

Most females suffer from cellulite. Pregnant women have a high risk of developing cellulite due to the hormonal disturbance during pregnancy.

There was no definite cause for developing of the cellulite. Although there are many methods of treatment, there is still no perfect way to eliminate the cellulite. Increasing understanding of the complicated pathophysiology of cellulite will likely enhance current treatment options and lead to the development of more targeted therapies shortly. Non- invasive body countering techniques are effective in the management of cellulite. Most studies which concerned with cellulite containing a low number of populations and it also lacks post-treatment follow-up .Therefore, further studies on higher population are recommended.

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