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Physiology extracorporeal shock waves

Extracorporeal shockwave: mechanisms of action and physiological aspects for cellulite, body shaping and localized fat – systematic review.

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Abstract: Extracorporeal Shockwave Therapy – ESWT has had a wide use in rehabilitation, and has presented positive effects in the treatment of unaesthetic affections. The objective of the present study was to search, in the literature, the mechanisms of action and the physiological aspects of shockwaves acting on the biological tissue to improve the condition of cellulite and localized fat. A systematic review of the literature was carried out in the period from September 2016 to February 2017 based on the bibliographic databases Lilacs, MedLine, PubMed and Scielo. Fifteen articles were identified in that systematic review, three of which were excluded because they did not make the complete access to the article available or the theme investigated did not encompass the objective of the study. The revision demonstrated that extracorporeal shockwaves present relevant effects on the biological tissue, which

leads to the restructuring of skin properties and subcutaneous tissue, clinically improving the aspects of cellulite and localized fat.

Keywords: cellulite, acoustic wave therapy, extracorporeal shockwaves, shockwaves cellulite, shockwaves subcutaneous fat.

Introduction

Growing technological advances in technology have promoted the development of new electromedical devices that can stimulate new therapeutic modalities. The Extracorporeal Shock Wave Therapy - ESWT is an example of technological evolution that opens the possibility for a non-invasive therapeutic modality, validated for use in the healthcare sector, indicated for the treatment of musculoskeletal disorders and which has recently been explored in the scope of aesthetic affections. Even with the growing use of this technology, its mechanisms of action have not yet been clearly established (1,2).

The use of ESWT had its beginnings in the early 70s in Extracorporeal Lithotripsy, then becoming a golden standard for the treatment of gallstone, renal calculi, ureteral calculi and vesical calculi [3,4]. During Lithotripsy treatment for lower ureteral calculi, physicians observed that some patients presented increase in bone density in the pelvic region. Based on this observation, they began to use equipment designed for Lithotripsy for the treatment of orthopedic dysfunctions, originating a new technology that allowed the grading of depth and intensity with which shockwaves penetrate biological tissues (4,5).

In 1997 in Vienna, Austria, the European Society for Musculoskeletal Shockwave (ESMST) was founded, with the objective of promoting the research and development of therapy in Europe. In Brazil, the use of shockwaves as an orthopedic

therapy started in 1998. In 2001, ESWT was approved by the Federal Drug Administration (FDA), for the treatment of chronic plantar fasciitis in the United States (EUA) (5,6).

The possibility of the use of ESWT in aesthetic treatments emerged from the observations of surgical results, when women suffering from muscle disorders, after receiving hip prosthesis, reported an enhancement in mobility and pain, an improvement in the aspect of the skin and body contour, suggesting that there was a decrease in the body circumference in the treated area (4,7,8).

The ESWT technology appeared during World War II when submarines were attacked by bombs and remained intact, and the sailors on board presented serious trauma with visceral and pulmonary lesions without external lesions. These lesions were attributed to the shockwaves, which went through the submarine walls and propagated amongst the sailors. In everyday life, shockwaves can be perceived when there is thunder, which occurs due to the intense heating and the rapid expansion of the air surrounding the lightning (4,9).

ESWT is characterized by a high pressure pulse (80 MPa) in a time interval of extremely short duration (in the order of nanoseconds), which produces mechanical pressure waves that promote cavitation in liquid medium (gas bubbles in fluid medium) and increase in local temperature. These shockwaves propagate in the target tissue, generating essential mechanisms of action such as the mechanical impact in the tissues and formation of microbubbles, which favors the achievement of the therapeutic objective (4).

For therapeutic purposes, there are four types of shockwave generators: The electro-hydraulic system, the piezoelectric system, the electromagnetic system and the pneumatic system, the latter two being the most frequently used in rehabilitation and

aesthetics (6,10). The electromagnetic generator presents two coils inside that generate a magnetic field when run through by electricity – the action of the field causes the projectile, situated inside the applicator, to move quickly and collide with the tip of the applicator. In the collision of the bullet, there is the transfer of energy from the projectile to the tip of the applicator, which then transfers the energy received in the form of mechanical waves to the treatment area. In the pneumatic generator, differently, the projectile is displaced towards the tip by the pressure exerted by the compressed air (5,6,10) (Figure 1).

ESWT equipment can be built in such a manner that it emits two types of waves, classified as focal waves (more intense and profound), directed at the target tissue, or radial waves (less intense and more superficial) diverge over the treatment area (5,11). There is equipment which offer the two types of wave and other that use only one which is adequate to the therapeutic objective. The ESWT energy can also be classified as low, medium and high, and that favors the field of action because each energy reaches structures like muscles, tendon and bones in different depths and forms (7,8,12).

Considering that this technology is relatively new in the aesthetic area, there are few studies that discuss the interaction between ESWT and the biological tissues for this purpose, which makes decision-making about the use of this technology difficult based on evidence. Therefore, the objective of this study was to present a revision of the literature about the technical aspects, mechanisms of action and physiological effects that involve the use of extracorporeal shockwave therapy in aesthetic alterations.

Material and Methods

This is a revision of the literature carried out from September 2016 to February based on bibliographic databases Lilacs, MedLine, PubMed and Scielo. As the theme is relatively recent, there is difference in the indexing processes in the bibliographic databases; therefore, the search for free themes, without the use of the controlled vocabulary (descriptors) was the option chosen. Using this strategy, there was an upturn of a greater number of references, guaranteeing the detection of most of the published studies within pre-established criteria. Terms such as cellulite, acoustic wave therapy, extracorporeal shockwaves, shockwaves cellulite, shockwaves subcutaneous fat were combined. The selected studies included the extracorporeal shockwave theme and the discussion of the mechanisms of action and physiological effects in the treatment of aesthetic alterations.

All of the original articles indexed about the action of ESWT on cellulite and localized fat written in English published between 2005 and 2017 with experimental (clinical trials, randomized or not) or observational (case studies, case-control, cross-sectional studies and before-and-after treatment studies) approaches carried out in humans were included. Experimental studies were excluded.

After checking titles, authors and abstracts, with the objective of avoiding the repetition of publications, the availability of complete access and the theme were investigated, and an evaluation of articles by peers, specialists in the investigated area, was carried out.

After the inclusion of the articles, an analytical reading of each study was performed, as well as a record of concept, method used for evaluation, classification of ESWT use in the pre-established area, in the mechanisms of action, the physiological

effects and last but not least, a comparative analysis between the findings and the theoretical discussion.

Results

In the systematic review, 15 papers were identified, three of them were excluded because not providing complete access availability, or they were animal studies or the theme investigated did not encompass the objective of the study. The selected papers are presented according to Table 1.

Discussion

The objective of the present study was to search for literary evidence about the physiological effects of ESWT in biological tissues in aesthetic disorders. ESWT has continuously been indicated for the treatment of cellulite, also known as Gynoid Lipodystrophy (12-14). Cellulite is an aesthetic alteration which attacks the thighs, gluteus, abdomen and upper region of the arms. It is a multifactor disorder with increase of adipose tissue that causes cellular dystrophy, dysfunctions of the hydraulic metabolism with blood congestion, tissue fibrosis and proliferation of fibroblasts around the adipose cells (1,12,14). Cellulite is more common in women, because they present about 21 to 22 billion adipose cells, whereas men present about 17 to 18 million. This difference in the quantity of adipocytes causes men to have a smaller ability to store fat in relation to the female sex. Besides, the subcutaneous conjunctive tissue of women presents some particularities such as the fine fibrous septum, directed vertically in the cutaneous surface, causing the adipose cells to present a regular form and the projection of these structures become superficial reaching the dermis, giving the skin the "orange peel" appearance (9,15-17).

Several treatments for cellulite have been developed in the last decades, with the objective of promoting the improvement of blood and lymphatic circulation using physical treatments, pharmacotherapy and treatments in association with electromedical equipment. However, there is not any one treatment that is completely effective (16–20).

The first ESWT study for the treatment of cellulite was carried out in 2005, in a clinical study with 26 women with average age of 45 years, which compared the independent application of ESWT and in combination with decongestive therapy for two weeks. Six sessions of ESWT were performed with 1.000 shots in only one thigh and the decongestive therapy was performed in both thighs. The authors concluded that one single application of ESWT can significantly decrease the levels of Plasma Malondialdehyde (MDA), a biomarker of the level of oxidative stress, which would cause improvement of the biomechanical properties of the skin (19). Oxidative stress is generated when there is imbalance in the production and tamponade of free radicals, biochemical physiological alterations during metabolic processes or due to external factors such as poor nutrition, exhausting exercise, psychological stress, and tobacco use, among others. As we suffer the influence of these factors, the cell walls and their molecules are attacked, causing a continuous and aggressive imbalance, which unleashes a cascade of events that induce the cellular aging. When the oxidative stress reaches high levels in the body it causes inflammation and cytotoxicity and it plays an important part in fibrotic degeneration, which can contribute to the formation of cellulite (7,19-21).

According to Wang (2003), the use of ESWT promotes a cascade of physiological events, which have not yet been entirely elucidated. What is known is that after the application there is improvement in the metabolism with subsequent stimulus

of microcirculation by the liberation of nitrous acid and improvement in cell permeability, which favors the exchange of substances and the reorganization of the cellular matrix. This leads to the rebalance of the production and tamponade of free radicals. This data was reaffirmed by the findings of Siems et al. (2005), where there was improvement of the aspect of the skin after six sessions of ESWT (9,19,21–23).

Angehrn et al. (2007) evaluated the effects of ESWT in the treatment of cellulite in 21 women aged between 20 and 60 years. 40 thousand shots were applied in the lateral area of the thigh, twice a week, during six weeks of treatment. The authors used diagnostic ultrasound as evaluation method (Collagenoson®), which evaluated the distribution of the epidermis, dermis and subcutaneous tissue. The results showed that ESWT was effective for the treatment of cellulite, because it promoted the remodeling of the collagen by realigning the dermal fibers and the improvement in the aspect of the skin, which remained latent after six months (8).

Corroborating the findings of Angehrn et al. (2007), in 2008 two studies evaluated the effects of ESWT in cellulite and body contour. First Kuhn et al. (2008) presented a case study with a 60-year-old woman with cellulite degree three in the gluteus and thighs, where four sessions of ESWT were applied only in the left thigh; after the end of the application the patient underwent orthopedic surgery in the region of the hip in which a sample of tissue of the treated and of the non-treated regions were removed. The authors concluded that there was histological improvement of the dermis with increase of the thickness of the extracellular matrix of the dermis, by means of induction of neocollagen and neo-elastin (8,24).

The second study was developed by Christ et al. (2008), who evaluated 59 women with cellulite, subdivided in two groups in which: the first received six sessions of ESWT for three weeks and the seconds eight sessions in four weeks of treatment.

The results presented were considered excellent, because there was an increase in the elasticity and firmness of the skin in both groups after three and six months of therapy of 95 to 105%, respectively (15).

Angehrn et al. (2007); Kuhn et al. and Christ et al. (2008) found in their studies similar results which involve induction of formation of collagen, neo-elastin, improvement of the aspect and elasticity of skin and remodeling of collagen (8,15,24).

Collagen is a protein synthesized by the fibroblast, fundamental in the constitution of the extracellular matrix and of the conjunctive tissue, and its main objective is to structure and protect the properties of the skin. In cellulite, there are structural alterations in the intracellular and extracellular matrix, degradation of collagen and of fibroblasts. One of the objectives to be achieved is to stimulate the fibroblasts to induce the synthesis of new collagen fibers (neocollagen) and elastin (neo-elastin) with subsequent restructuring of the properties of the tissue, which we call collagen remodeling (14-16,25,26). The cells in our body recognize mechanical stimuli, due to this the fibroblasts are activated and start a cascade of formation of neocollagen and neo-elastin and the restructuring of the tissue. This mechanism is called mechanotransduction of signal, when the cell responds to a mechanical stimulus with biochemical reactions in cascade and act on the cellular level transmitting the energy to the extracellular matrix (27).

The first stimulus of ESWT is mechanical, characterized by the peak of pressure, short duration, with high density of energy and low frequency; when in contact with the treatment area this mechanical energy leads to the activation of mechanotransduction of signal and the extracellular matrix mobilizes the cells. These cells, respond to the indirect effect of shock wave cavitation, bringing forth alterations beneficial for the treatment of cellulite such as the increase of local circulation and

stimulus to the production of collagen, leading to the restructuring of the dermis and epidermis, thus restoring the elasticity of the conjunctive tissue and improving skin texture (2,28).

Adatto et al. (2010) and Adatto et al. (2011) evaluated the effects of ESWT in cellulite and the improvement of body contour, and in their last study the objective was to evaluate ESWT in localized fat (29,30).

For the treatment of cellulite, 25 women who received 3000 shots in an area of 10x15cm² in the lateral region of the thigh were evaluated and six sessions twice a week were performed. The results demonstrated reduction of the appearance of cellulitis after three months of the last treatment. The authors concluded that the shockwave therapy can stimulate lymphatic drainage and microcirculation. In the study about improvement of the body contour, 14 women were evaluated after eight sessions in the lateral region of the thigh, with the application of 4500 shots. There was temporary improvement in the texture and elasticity of skin, and a reduction? of the adipose tissue (29,30).

Besides the mechanical effects, ESWT has the effects of unstable cavitation, which is the formation of gas microbubbles in the biological liquids, which implode causing physiological effects (3-6). According to Steinbach et al. (1993) and Kuhn et al. (2008), the effects caused by cavitation are related with the dose of energy used to achieve the therapeutic objective. When high doses of energy are used, the damages are the increase of cellular diffusion with improvement in the permeability of the cellular membrane, lesions in the endoplasmic reticulum in the cytoskeleton that gives form to the cell and in the cellular junctions. All these factors may lead to apoptosis. There is still the liberation of endothelial growth factor, synthesis of eNOS enzyme, which induces the production of endothelial nitric oxide (NO) (24,31). For smaller doses of

energy, the principle of action of ESWT is the stimulus to the self-regeneration of the tissue; therefore, smaller doses are indicated for the treatment of different types of musculoskeletal diseases. However, both doses stimulate the local blood circulation and the metabolism (31).

During the bibliographic revision carried out in the present study, out of the 12 articles evaluated, most of them used high doses between 3 and 4 bar for devices with pneumatic shockwave energy generators. Therefore, we can suggest that, by the findings in this study, that high energy is efficient in the treatment of localized fat, because the effects of ESWT can lead to cellular apoptosis (28,32,33).

Another Ferraro et al. (2012) study, also demonstrated decrease in thickness of the layer of localized fat and of the circumference of the treated area and improvement in the aspect of the skin after 12 months of the end of treatment. However, the study protocol evaluated the combination of ESWT with cryolipolysis sliding mode, using the device that presents both these therapies, but it was not possible to evaluate if the results could be attributed solely to the use of ESWT, because cryolipolysis also presents significant results for the reduction of localized fat. It is worth mentioning that the technique of cryolipolysis sliding mode differs from conventional cryolipolysis usually mentioned in literature [33].

Knobloch et al. (2013) compared two groups, application of ESWT (0,25mJ/mm²) in gluteus and thighs, followed by thigh strengthening training and the second control group with application of ESWT (0,01mJ/mm²) in gluteus and thigh, followed by thigh and gluteus strengthening training. In both groups, six sessions were applied for two weeks. The objective was to evaluate if the muscle strength training would lead to additional effects to the ESWT therapy in the improvement of cellulite. The results obtained demonstrated that the combination of therapies presented superior

results in relation to the control group, with significant alterations of 24% in the improvement of the aspect of cellulite. The authors suggest that this improvement occurred through the mechanical energy of ESWT, which acts on the fibrous septum and induces their reorganization, making the skin smoother (34).

Proving the previous results, Russe-Wilflingseder et al. (2013) evaluated, in their double blind randomized clinical trial, the effects of ESWT in the treatment of cellulite. A placebo group was evaluated, where the transfer of energy was blocked and for a second group that effectively received intervention were performed weekly sessions for seven weeks. The treated group presented improvement in the aspect of skin, in the appearance of cellulitis with decrease of undulations and depth and reduction in the circumference of thighs after three months of treatment; however, the researchers suggested that these results can be temporary (28).

The findings corroborate the effects of ESWT in the remodeling of collagen, formation of neocollagen and neo-elastin, acting in the improvement of tissue firmness and preventing that the irregularities present in the subcutaneous tissue project onto the dermis, decreasing the aspect of "orange peel" skin (8,15,30,35).

In 2014, Schlaudraff and collaborators evaluated the individual clinical result of the treatment of cellulitis with ESWT in 14 women who received 7500 shots in unilateral thigh and gluteus in two sessions per week in four weeks, totalizing eight treatments. The authors concluded that there was improvement and decrease in the degrees of cellulite, but that this result cannot be correlated with individual variables such as body mass index (BMI), weight, height or age (28).

Nassar et al. (2015) evaluated the efficacy of lipolysis induced by ESWT, in 15 individuals; eight sessions during four weeks were carried out, and 4000 shots were applied. The authors concluded that ESWT was efficient in the improvement of body

contour, with reduction of the circumference and the fat layer and improvement of the appearance of cellulite after three months of the end of the treatment (36).

The most recent study published, Hexsel et al. (2016), is in accordance with the previous findings. This study evaluated the efficiency of ESWT in the treatment of cellulite and body contour with 5000 shots in the region of gluteus and posterior region of thigh for 12 sessions. The authors concluded that there was decrease in the circumference of the treated area, measured in the magnetic resonance exam, with improvement of the severity of the degrees of cellulite (37).

The systematic review carried out in the present study shows that the use of ESWT in the treatment of cellulite and localized fat seems to be a tool with efficient results, provided that the parameters used are observed. The main effects reported in these studies are related with the activation of the mechanisms of action and the physiological effects as a result of the stimulus by mechanical shockwaves and effects of cavitation promoted by the shockwave therapy.

The main effects observed in the biological tissue are: damage to the extracellular matrix which promotes a cascade of physiological reactions that favor the reorganization of the extracellular medium, increase of blood and lymphatic circulation, alterations in the permeability of the cellular membrane, liberation of nitric oxide, balance of free radicals, drainage of molecular proteins, stimulus for fibroblast activation by mechanotransduction, formation of neocollagen, neo-elastin and remodeling of collagen. Other results of the action of ESWT in the biological tissues were described by Kuhn et al., (2008) and Nassar et al., (2015), the authors suggest that ESWT can induce lipolysis and/or apoptosis of the adipose cell (8,24,36).

The few studies about ESWT in aesthetic affections show that the mechanisms of action and physiological effects of this technique are beneficial and

promising for the treatment of cellulite, body contour and localized fat, particularly because they represent a safe and non-invasive therapeutic mode. There are no reports of adverse reactions of ESWT in the treatment; only the discomfort reported by the therapist due to the noise emitted by the shock of the projectile colliding with the tip of the applicator; to minimize this discomfort, the use of an auricular protector is suggested.

Conclusion

The results presented in this study show the efficacy of the ESWT technique as a safe and non-invasive method. Its mode of action in the biological tissue benefits the treatment of cellulite, body contour and localized fat. Because it is a relatively new therapy in the aesthetic area, ESWT is a promising field for studies and application, but it still requires investigation as to the mechanisms of action and their interaction with the adipose tissue, which demands further experimental studies with ESWT in aesthetic affections.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Table 1. Published studies about the action of ESWT on cellulite, body contour and localized fat.

Author	Year	Protocol	Treatment Area	Conclusion
Siems et al.	2005	ESWT + Decongestive therapy	Thigh	Decrease of oxidative stress and improvement of skin properties.
Angehrn et al.	2007	ESWT	Lateral region of thigh	Remodeling of collagen and improvement of the aspect of skin.
Kuhn et al.	2008	ESWT	Thigh and gluteus	Histological improvement of epidermis and of the extracellular matrix of the dermis.
Christ et al.	2008	ESWT	Thigh and gluteus	Improvement of elasticity and tightness of skin.
Adatto et al.	2010 2011	ESWT	Lateral region of the thigh	Improvement in skin texture and elasticity, number of depression and decrease of thickness of the subcutaneous tissue.
Ferraro et al.	2012	ESWT+ Cryolipolysis	Abdomen, arms, gluteus and thigh.	Decrease of the thickness of the adipose tissue, circumference of the treated area and improvement of the aspect of the skin.
Knoblock et al.	2013	ESWT+ Muscle strengthening.	Thigh and gluteus	Improvement of the aspect of cellulite.
Russe-wilflingseder et al.	2013	ESWT	Thigh	Temporary improvement of the aspect of the skin and reduction in the circumference of the thigh.
Schlaudraff et al.	2014	ESWT	Thigh and gluteus	Decrease in the degree of cellulitis.
Nassar et al.	2015	ESWT	Thigh	Reduction of the circumference of the treated area, thickness of the fat layer and appearance of cellulite.
Hexsel et al.	2016	ESWT	Thigh and gluteus	Decrease of the circumference of the treated area and severity of the degrees of cellulite.

Figure 1. Electromagnetic System (a): (A) coils, (B) projectile, (C) tip of the applicator. Pneumatic System (b): (B) projectile; (C) tip of the applicator, (D) compressed air inlet.