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Study on the Reduction of the Localized Panniculus Adiposus (Adipocyte Lysis) Through the Use of a Controlled Cooling System

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Abstract— Introduction*: Cryoadipolysis is a non-invasive technique for fat reduction based on the sensitivity of fatty tissue to cold, which results in adipocyte lysis with despicable damage of surrounding tissues. The main objective of this study is to evaluate efficacy and safety in the removal of localised fatty tissue in abdominal and flank areas using a controlled cooling system.* ***Materials and methods****: A study was carried out on 15 patients with localised fat in abdominal and flank areas. One session per area was completed using the Cooltech system, applying -8ºC for 70 minutes with 235 mbar suction. Efficacy was evaluated through plicometry, iconography and measurements of abdominal perimeter in 3 different areas. Side effects were also evaluated.* ***Results****: Patient's weight did not show significant changes. However, abdominal skin fold and infraumbilical perimeters displayed a notable reduction ((19.6±8.50) % and (2.33±3.13) cm, respectively). The most common side effects were pain at the beginning (73.43%) and at the end of the treatment (66.67%), besides temporal disorder in sensations (100%), which resolved in a maximum of 21 days.* ***Conclusions****: The Cooltech cryolipolysis is a safe, effective and tolerable system for reducing localised fat while respecting the surrounding tissues. It causes few reversible side effects.*

Keywords— *Adipocyte lysis through cold, localised fat, magnet therapy, cryolipolysis, non-invasive fat reduction, apoptosis.*

I. INTRODUCTION

An important and highly demanding topic within aesthetic medicine is body contouring. Since its introduction in the 1960s, liposuction has proven to be the most effective method for body fat reduction and contour remodelling (1). The technique has evolved over the years (laser-assisted liposuction (2)) in terms of time and in terms of results, however, it is not free from adverse side effects, such as the inherent risks of anaesthesia, infections, scars or long recovery time. Nowadays, patients demand less invasive techniques with little to no adverse side effects and no time off work required. The most widely used techniques, include devices using electroporation, mesotherapy, deoxycholate infiltration, cold compresses, carboxytherapy, ultrasound, cavitation, radiofrequency and low-power lasers among others. (3)

The elimination of the adipocytes through controlled cooling (Cryoadipolysis) was introduced in 2007. First device was approved by the FDA in 2010 (K080521). (4) It has shown positive results as a non-invasive method of reducing fat tissue. Recent studies have shown that the sensitivity of fat tissue to cold specifically triggers lysis of fat cells with almost despicable and temporal damaging of surrounding tissues. (3,5) It has also been observed that the use of suction is significantly more effective to create a cryogenic effect in fatty tissue. (6)

The objective of the procedure is to execute controlled cooling of the subcutaneous tissue reaching temperatures of damage of the adipose cells (<10^{o}C), while also respecting the surrounding tissues, (5) thereby producing an inflammatory reaction that starts approximately 2 days post-exposure, peaks at between 2 and 4 weeks, and persists until 90th-day after treatment. Histologically, a perivascular infiltration of histiocytes, neutrophils and lymphocytes occurs (7,8); this inflammation triggers apoptosis of adipocytes which are then digested by macrophages and eliminated over the course of a period of months with no effect on blood lipid levels or liver function. (8-10)

The aim of this study is to evaluate the efficacy and safety of the treatment for the removal of localised fatty tissue in the abdominal area using a controlled cooling system, and also to establish the most common side effects caused by this method.

II. MATERIALS AND METHODS

A. Materials

This prospective study is based on the analysis performed in a medical centre in Barcelona, where the treatment of localised fat in the abdomen was performed using a system involving tissue suction followed by cooling of the suctioned area.

The study involved 15 patients of both genders (11 women and 4 men) with localised fatty deposits. 12 patients had fatty deposits in the upper abdomen area and 3 patients had the deposits in the lower abdomen and flanks. None of the patients were significantly overweight, their skin phototypes ranged from II to IV and their ages from 27 to 66 years, with an

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average of 42 years (SD±15). All patients signed the informed consent for the execution of the procedure.

The exclusion criteria were: under 18 years of age, pregnancy, severe kidney failure, severe liver failure, diabetes, cancer, febrile states, Raynaud's disease (cryoglobulinemia) and systemic conditions with cutaneous involvement and cold urticaria. A patient with an old scar on his/her abdomen was included, along with another with a record of severe thrombocytopenia.

The device used was the Cooltech®, with Straight HP applicator from the Cocoon Medical brand. The applicator for the abdominal and flank areas produces a suction of the tissue in the treated area through positive pressure of 235 mbar, before cooling the area to -8oC for 70 minutes. In some cases, a coupler was fitted to the applicator to reduce the treated area (Figure 1).

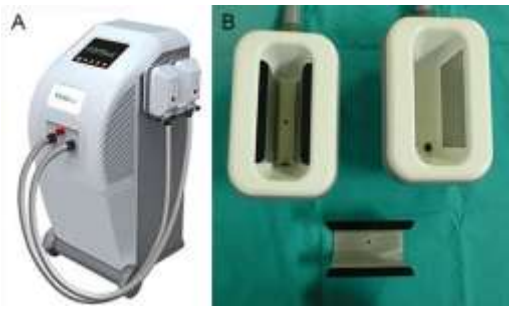

Figure 1. A. Cooltech® device with Straight HP applicator. B. Suction and cooling applicators (with and without coupler – in the lower part of the Figure).

The following were also used:

- A Cool Gel Pad® cellulose membrane impregnated with glycerine and water, which acts as an anti-freeze agent protecting the skin from freezing.
- Pulsating Magnetic Fields (Ronefor model) as a complementary treatment immediately after the procedure, with anti-inflammatory and anti-oedematous effects.

The results were assessed through:

- Iconography, which was recorded using the Lumix DMC-LX2 camera.
- Measurements taken with a tape measure in the umbilical, infraumbilical and waist areas.
- Measurements of the cutaneous fold using a plicometer.

B. Method

Once the measurements and iconography were taken, and with the patient in a semi-seated position, a cellulose membrane impregnated with glycerine and water (which acted as an anti-freeze barrier for the skin) was positioned. The parameters were then programmed, the applicator was positioned on the membrane and the suction was activated. Once the programmed suction was achieved, the temperature began to lower until it reached -8oC (Figure 2). In some cases, a coupler was added to the applicator, when a smaller area was being treated (Table 1).

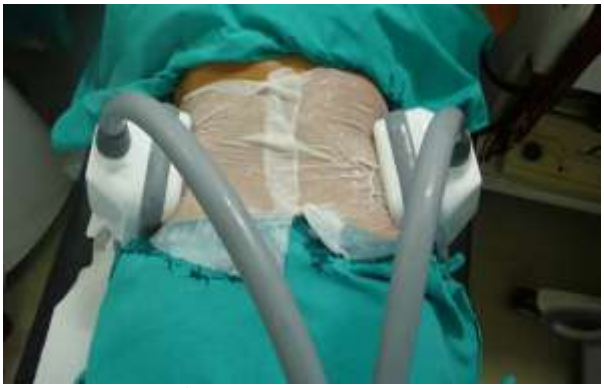

Figure 2. Positioning of the device on the abdominal area (two applicators simultaneously).

Table 1. Number of patients treated with coupler and treatment area.

Variable		N_15 (ration in %)
Coupler		
	Yes	3 (20)
	No	12 (80)
Treated area		
	Lower abdominal	7 (46.6)
	Upper abdominal + flanks	3 (20)
	Lower abdominal + flanks	5 (33.3)

The treatment was performed on all patients, based on fixed and variable parameters: the fixed parameters were suction at 235 mbar, temperature at -8ºC and 70 minutes of treatment duration (Figure 3). The variable parameters were: the thickness of the fatty tissue (abdominal fold) measured in mm (millimetres).

Figure 3. Instrument panel with the data being applied.

After removing the applicators, a manual massage was immediately performed (Figure 4). Topical corticosteroid and a 30-minute magnet therapy session were then applied on all patients.

Figure 4. A fat lump is observed immediately after removing the applicator (A), which is later massaged (B).

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The treatment consisted of 1 session per area. Four areas were treated: supraumbilical abdomen, infraumbilical abdomen, right flank and left flank (Table 1). The Cooltech® device allows the use of two Straight HP applicators simultaneously, enabling to treat two areas at the same time.

Magnetic fields were used immediately after treatment to reduce primary oedema and inflammation.

The results were analysed between 30- and 100-days post-treatment, which also included an iconographic control.

Patients were recommended to supplement the treatment with physical exercise from the second day onwards, and also to avoid sun exposure on the treated area for one week.

C. Evaluation Criteria

Variables recorded were: gender, age, weight, skin fold in the treated area using a plicometer and the abdominal perimeter using a tape in the umbilical area and 4 cm above and below it. These results were analysed before and after the treatment (weeks 6 and 12).

The following side effects were also analysed:

- Pain (immediate, during and post-treatment) using the VAS scale (Visual Analogue Scale), with the pain being classified as pain-free (VAS equal to 0), mild pain (VAS between 1 and 3), moderate pain (VAS between 4 and 7) and intense pain (VAS between 8 and 10).
- Other adverse effects such as erythema, hematoma, paresthesia and dysesthesia were classified as: without adverse effect or with adverse effect (mild, moderate or intense). The duration of side effects was classified in three groups of 1 to 7 days, 8 to 14 days, and 15 to 21 days; this information was gathered immediately after the treatment and at the control visit.

D. Statistical analysis

The results were expressed as the mean ± SD. Wilcoxon score tests were used to compare the means between groups. Statistical analyses were performed using the SPSS 20. A P value < 0.05 was considered to indicate statistical significance.

III. RESULTS

A total of 15 patients (11 women and 4 men) with an average age of (42.8±8.1) years were treated (Table 1).

Table 2 shows the average of the measurements obtained before and after the treatment. The initial average weight was (68.83±16.31) kg and the final average weight was (68.79±15.77) kg, resulting in an average reduction of (0.05±1.49) kg or (0.07±1.95) %; P = 0.875. The average measurement of the initial skin fold was (33.67±6.45) mm, the post-treatment average was (27.07±5.19) mm, and the average reduction was (6.60±3.34) mm, or (19.6±8.5) %. The largest reduction was 12 mm 34.29 %; P = 0.001. In just one case, a skin fold reduction was not achieved. In terms of the abdominal perimeter, the average value of the supraumbilical perimeter at the beginning of the treatment was (84±10.09) cm and post-treatment was (83.13±9.23) cm, with an average reduction of (0.87±2.23) cm; P = 0.152. The largest reduction was 4 cm. Regarding umbilical perimeter, the average pre-treatment was (93.33±9.25) cm and post-treatment was (91.93±7.91) cm, with an average reduction of (1.4±2.69) cm; P = 0.058. The largest reduction was 7 cm. Finally, for infra-umbilical perimeter, at the beginning of the treatment the average was (97.07±8.96) cm, post-treatment was (94.73±8.08) cm, with an average reduction of (2.33±3.13) cm; P = 0.013. The largest reduction was 8 cm.

Table 2. Average of the measurements obtained before and after treatment: weight, skin fold, supraumbilical perimeter, umbilical perimeter, infra-umbilical perimeter.

Variable	Pre-Treatment Mean ± SD N=15	Post-Treatment mean ± SD N=15	Difference ΔD=Post-Pre ± SD (%) N=15	P-Value*
Weight (kg)	68.83±16.31	68.79±15.7	-0.05±1.49 (0.07)	0.875
Skin fold (mm)	33.67±6.45	27.7±5.19	-6.60±3.34 (19.45)	0.001
Supra. Per. (cm)	84.00±10.09	83.13±9.23	-0.87±2.60 (-0.91)	0.152
Umb. Per. (cm)	933.33±9.25	91.93±7.91	-1.40±2.89 (-1.36)	0.058
Infra. Per. (cm)	97.07±8.96	94.73±8.08	-2.33±3.11 (-2.31)	0.013

*p values were calculated using the Wilcoxon test.
SD: Standard deviation; Supra. Per: Supraumbilical Perimeter; Umb. Per: Umbilical Perimeter; Infra. Per: Infra-umbilical Perimeter; Pre: Pre-Treatment Post: Post-Treatment;

Figures 5, 6 and 7 show iconographies of some of the patients before and after treatment.

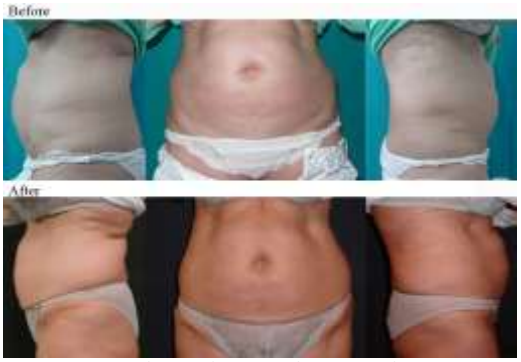

Figure 5. Iconography of the before and after results for patient nº 1 and the extent of the reduction of the abdominal perimeters. Follow-up at 73 days Supraumbilical Perimeter: -1 cm; Umbilical Perimeter: -2 cm and Infra-umbilical Perimeter: -3 cm

Figure 6. Iconography of the before and after results for patient nº 7 and the extent of the reduction of the abdominal perimeters. Follow-up at 81 days Supraumbilical Perimeter: -2 cm; Umbilical Perimeter: -7 cm and Infra-umbilical Perimeter: -8 cm

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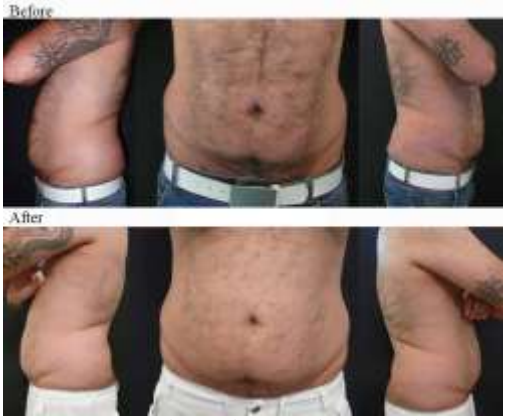
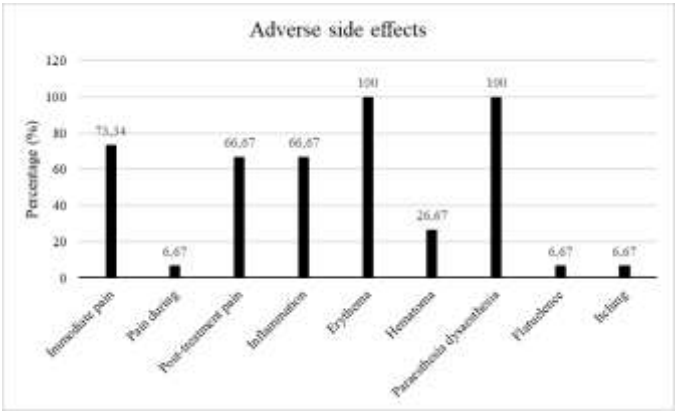
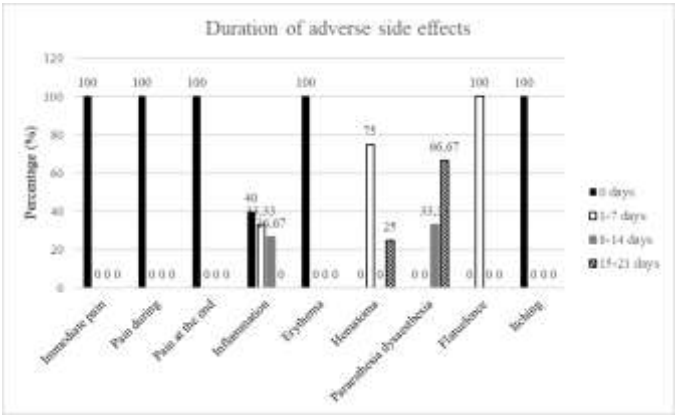


Figure 7. Iconography of the before and after results for patient nº 14 and the extent of the reduction of the abdominal perimeters. Supraumbilical Perimeter: -4 cm; Umbilical Perimeter: -4 cm and Infra-umbilical Perimeter: -7 cm

The adverse side effects encountered in the study are reflected in Graphics 1 to 5.

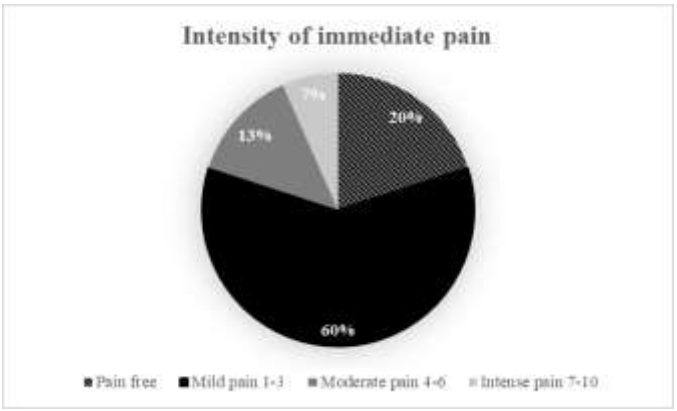


Graphic 1. Adverse side effects in percentage of patients

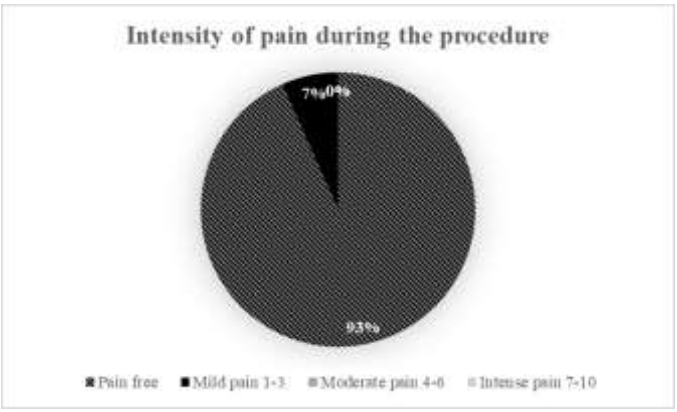


Graphic 2. Duration of adverse side effects in terms of the percentage of patients.

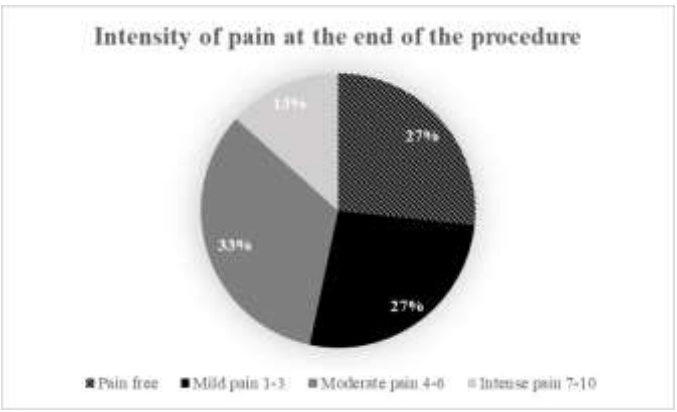
Pain was found to occur at the beginning of the treatment (73.34% of patients) with an average duration of 30 seconds, and at the end of the treatment (66.67% of patients) with an average duration of 60 seconds. The degree of pain at the beginning of the treatment was mild in 80% of the patients. During the treatment pain was mild (6.67% of patients). At the end of the treatment, it was moderate in 93.3% of cases. (Graphics 1-5)



Graphic 3. Assessment of immediate pain.



Graphic 4. Assessment of pain during the treatment.



Graphic 5. Assessment of post-treatment pain.

Erythema was present in 100% of cases with a maximum duration of 24 hours. (Graphics 1-2)

Sensations of paraesthesia and dysesthesia were present in 100% of cases with a maximum duration of 21 days in 66.67% of cases. (Graphics 1-2)

Inflammation or oedema occurred in 66.67% of cases, with a duration of less than 24 hours in 40% of cases, between 1 to 7 days in 33.33% of cases, and between 8 and 14 days in 26.67% of cases. (Graphics 1-2)

In the case of the patient with thrombocytopenia, more

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severe ecchymosis occurred at the borders of the treated area, and in the case of the patient with the scar, an almost violet erythema was produced on the scar. (Graphics 1-2)

Other adverse side effects included pruritus and flatulence which both occurred in 1 patient.

IV. Discussion

Weight was not determinant for the results as there was no significant variance pre- and post-treatment (0.07% (SD 1.95%)). Similar results have been reported, where fat reduction was observed despite fluctuation in body weight. (11, 12) This suggests that weight is not a variable to be considered in this method, since it is in fact applied to localized fat that represents a low a small percentage of mass as compared with the total mass of the body.

The abdominal skin fold displayed a notable reduction of 19.6% (SD 8.50%). In similar studies, in which the abdominal area was treated, a reduction of 21.0% was obtained with a post-treatment massage (6). In other studies, there was a reduction of 22.4% after 4 months (13). Of note, measurements of the cutaneous fold using a plicometer may be affected by the force applied by each evaluator.

The abdominal perimeters also presented an obvious reduction in most patients, especially for the infra-umbilical measurement, so these measurements can also serve as guidance to demonstrate the efficacy of the treatment, but may also be subjected to variations depending on the evaluator.

The fact that the occurrence of side effects is much lower when compared to much more invasive techniques like liposuction, should also be noted (14). Pain and inflammation were the most commonly observed adverse side effects, but they did not require any therapy or systemic medication in order to be resolved and were tolerated well by the patients.

The most pain is caused post-treatment when a massage is performed on the treated area following the removal of the applicator, however, a greater decrease of the panniculus adiposus has been reported when this is performed. (6)

Another side effect, erythema, did not last for more than one day in all patients. Inflammation decreased completely in 14 days. There are other publications stating that there is inflammation after treatment. The death of adipocytes induced by cold is a gradual process that is not completely clarified. It is suggested that it may be due to internal mechanisms of adipocytes, such as mitochondrial signaling, by specific enzymatic processes or inflammatory processes in response to cell damage (for review see: (15)). However, it is important to remark that a 30- minutes magnet therapy and corticosteroid treatment were then applied on all patients.

The side effects that persisted for the longest period, between 8 and 14 days, were the reduction in sensation. This may be due a temporal disorder of the peripheral nervous system that includes loss of motor and sensory function due to blockage of nerve conduction (Neuropraxia). This effect is also commonly associated with process of dysesthesias and paresthesias in the treated area as a transient reduction in sensation. However, they were also resolved without any complications, and as stated by Coleman et al., they are completely reversible. (16)

In other studies, only mild, non-durable, and reversible side effects have been reported (17-22), while obtaining remarkable results of fat reduction. Of note, most patients have no complaints about these side effects and feel that the treatment presents no disruption to their daily doings.

It is important to remark that results of only one session have been evaluated in this study. However, the manufacturer's recommendation must be considered to increase fat reduction, i.e. to conduct 1-3 sessions at 6-8-week intervals, depending on the patient's characteristics.

V. Conclusion

The cryoadypolysis technique, and specifically the Cooltech® system, is an effective, safe and highly tolerated treatment technique for the reduction of localised fat in the abdominal and flank areas, with a minimum and reversible side effects on the surrounding tissues. However, further studies should be conducted, with more patients, a longer follow-up time and a higher number of sessions. Furthermore, it would be interesting to identify those areas that better respond to treatment and see if, based on sex, adipose tissue reacts differently when exposed to low temperatures.

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