

Evaluation of the Efficacy of Injection Lipolysis using Phosphatidylcholine/Deoxycholate Versus Deoxycholate Alone in Treatment of Localized Fat Deposits

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Abstract

The practice of injection lipolysis, using drugs generally based on phosphatidylcholine and deoxycholate (PCDC), evolved from the initial intravenous use of those drug formulations to treat blood disorders. Formulations containing phosphatidylcholine and bile salts (phosphatidylcholine bile salt formulations, PBF) are increasingly being utilized to treat localized fat accumulation. Several open label clinical studies have reported promising results using injections of PBFs for the treatment of localized fat accumulation, including lower eyelid fat herniation and "buffalo hump" lipodystrophy.

Bile salts have been used to improve the aqueous solubility of phosphatidylcholine. Highly purified phosphatidylcholine can be combined with the secondary bile salt sodium deoxycholate, an anti-microbial, benzyl alcohol, and water to form a stable, mixed micelle preparation that can be rapidly sterilized and used for intravenous administration. Pharmaceutical preparations of this mixture are marketed in other countries for treatment of liver disease and hyperlipidemia, respectively.

Deoxycholate is used to solubilize phosphatidylcholine by forming mixed micelles composed of phosphatidylcholine and deoxycholate. It is common practice to combine intravenous medications with bile salts to improve their water solubility.

These findings suggest that sodium deoxycholate is the primary active ingredient in the phosphatidylcholine preparations. These findings have been translated clinically. The effects of deoxycholate and the phosphatidylcholine formulation with deoxycholate are nonspecific, such that injection into tissue besides fat may cause necrosis.

Introduction

Obesity is a serious medical problem resulting in significant morbidity and mortality. Many people spend hours exercising and trying all kinds of diet regimens, but the obesity remains in some areas. Surgical and non-surgical procedures for improving appearance have increased in prevalence as the population grows and gain weight especially in the last few years [1].

For patients requiring substantial fat reduction, surgical lipoplasty remains a popular method for body sculpting in the United States. However, the number of lipoplasty procedures performed annually has decreased dramatically as patients look for less invasive methods of body sculpting.

Lipoplasty is associated with the highest potential for significant complications, morbidity, and mortality. Mortality is most often caused by embolism complications of anesthesia, necrotizing fasciitis, and hypovolemic shock. Ultrasound-assisted liposuction has reduced but not eliminated the risk of complications. Laser-assisted liposuction demonstrates only a minor incremental benefit over conventional lipoplasty and exposes the patient to the risk of burns and thermal injury to deeper tissue.

Noninvasive alternatives to liposuction include cryolipolysis, radiofrequency ablation, laser therapies, injection lipolysis, and low-intensity nonthermal (mechanical) focused ultrasound [2].

Injection lipolysis is a controversial cosmetic procedure which aims for reduction of localized fat accumulations by intralesional injection of chemical substances that induce destruction of adipocytes.

Formulations containing phosphatidylcholine and bile salts are increasingly being utilized in injection lipolysis [3].

Currently, there is no standardization of dosage and no protocol or treatment algorithm to enable prediction of how much tissue or fat will be "dissolved" with a specific solution in a defined quantity, and injected at a specified subcutaneous tissue depth [4].

Formula and Additives

This practice, using drugs generally based on phosphatidylcholine and deoxycholate (PCDC), evolved from the initial intravenous use of those drug formulations to treat blood lipid disorders [4].

Formulations containing phosphatidylcholine and bile salts (phosphatidylcholine bile salt formulations, PBF) are increasingly being utilized to treat localized fat accumulation.

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Received May 02, 2012; **Accepted** June 07, 2012; **Published** June 13, 2012

Citation: El Kamshoushy A, Abel Maksoud R, El Mahdy N (2012) Evaluation of the Efficacy of Injection Lipolysis using Phosphatidylcholine/Deoxycholate Versus Deoxycholate Alone in Treatment of Localized Fat Deposits. J Clin Exp Dermatol Res 3:146. doi:10.4172/2155-9554.1000146

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Bile salts have been used to improve the aqueous solubility of phosphatidylcholine.

Compounded phosphatidylcholine preparations are marketed as minimally invasive (although less dramatic) alternatives to liposuction, or as postliposuction “touch-up” procedures [5].

Phosphatidylcholine

It is a glycerophospholipid extracted from soy bean lecithin. Chemically, it has three carbon atoms. Fatty acids have attached themselves to the first two and phosphoric choline has attached itself to the third carbon atom [6].

Physiological functions of PC in the body: Phosphatidylcholine is the most important membrane lipid. It plays an important role in the biosynthesis of prostaglandins, leukotrienes, and thromboxanes, it is the major delivery form of choline which is a precursor in the synthesis of acetylcholine, it increases cholesterol solubility and inhibit plaque aggregation and also it plays a role in hepatic export of VLDL [7-9].

Mechanisms of action of PC in the subcutaneous tissue: The exact mechanism of action is not well understood yet. Several theories were mentioned in literature such as acting as an emulsifying/tenso active agent making lipids water soluble, [10] it may stimulate fat splitting lipases activity and release so that triglycerides are hydrolyzed into fatty acids and glycerol [11]. Also, PC may act to stimulate β -receptors or inhibit α 2-receptors, thus increasing lipolysis activity and accelerates fat elimination through the gastrointestinal and urinary System [12].

Sodium deoxycholate

It is a bile salt that is also used as a laboratory detergent and is used to solubilize phosphatidylcholine by forming mixed micelles composed of phosphatidylcholine and deoxycholate [13].

Mechanism of action of DC: Deoxycholate seems to induce fat cell destruction in a non specific fashion due to its detergent action [14]. Human fat injected with a compounded phosphatidylcholine formulations (PC/DC) results acutely in vacuolization of adipocytes and in acute and chronic inflammation within the septae and lobules of the subcutaneous fat, the recruited inflammatory cells directly disrupt or indirectly destroy the adipocyte cell membranes via cytokine or lytic enzyme release resulting in fat necrosis eventually, the inflammatory response may abate with ingrowth of fibrocytes and collagen production [15,16].

Moreover, combinations of lipolytic stimulators such as melilotus, aminophylline, yohimbine, and isoproterenol seem to produce greater stimulation of lipolysis than each of the individual components alone. It must be noted though that lidocaine and other topical anesthetics inhibit lipolysis. It is thus believed that local anesthetics such as lidocaine and its class derivatives should not be used in combination with mesotherapy solutions designed to cause local fat reduction or to reduce the appearance of cellulite [17].

Indications of injection lipolysis

Indications of injection lipolysis are becoming plenty. Among these are the small, well-localized deposit of subcutaneous fat where a volume of 100 to 500 ml is considered ideal especially if soft, spongy fat [18]. Other indications include lipoma or multiple lipomas, [19] and post liposuction deformities. Fat grafting if there is an area with too much “take” of the injected fat, or where the injected fat “take” unevenly is another indication for this procedure.

Injection lipolysis with collagenase could be used for treating depressed scars as post cesarean section scars that are bounded by areas of protruding fat.

Also, skin contour irregularity due to traumatic fat necrosis is another condition candidate for injection lipolysis.

Contraindications

Absolute Contraindications [18,20] are so many including age younger than 18 years, pregnancy, breast feeding, fully anticoagulated patient receiving Coumadin or heparin, current serious illness or active infection, known allergy to soy products or any ingredients of the injection compound, for breast reduction, insulin-dependent diabetics with unstable diabetic control or impaired circulation, severe generalized obesity ,previous significant adverse reaction to this treatment, severe needle phobia and immunocompromised patients of transplant recipients and those undergoing chemotherapy.

Relative Contraindications

Unrealistic expectations with regard to outcome, microangiopathy or vascular insufficiency of distal extremities, autoimmune conditions such as scleroderma, Sjogren’s syndrome, lupus, and other autoimmune diseases, Diabetes type 2,unstable hypertensive or cardiac patients, patients with HIV, although the HIV “buffalo hump” responds well to injection lipolysis, patients receiving aspirin or non steroidal anti-inflammatory agents, patients receiving high doses of steroids, patients with liver or renal failure, an open sore or localized skin conditions in or near the treatment area, active eczema or psoriasis in or near the treatment area and inability or refusal to follow a diet and exercise maintenance program steps are among the relative contraindications to injection lipolysis [18].

Localized side effects

Subcutaneous injection of phosphatidylcholine formulations are associated with localized burning sensation, erythema & oedema, transient urticaria, ecchymoses & hematomas, [21] infectious granulomatous reaction that spontaneously resolve within one month, skin ulceration that could be either due to injections placed too superficially or to compression of blood vessels in the area by severe oedema. Also, inadvertent injection into muscles causes immediate pain. Panniculitis with aggregation of neutrophils and fat necrosis could also occur [22]. Angiogenesis which can improve the appearance of aged and lax skin but in relatively ischemic areas, this reaction can be observed as persistent telangiectasias or prominent veins. Also, skin irregularities due to skip area could occur, but no persistent unwanted clinical side effects [23].

Systemic side effects

Rare to occur and include: nausea, diarrhea, abdominal pain, menstrual irregularities and syncope and are associated with high doses (1200 mg or more) [24].

Areas of injection lipolysis

The abdomen and the back regions in non obese patients are excellent sites to treat. The submental neck and submandibular jaw line could be done when the correct technique is used. Also, upper arms, thighs, and knees all get mixed reviews. While area distal to the patella, forearms, breast, face above the jaw line, lower eyelid fat pad, epigastrium and the central neck region all should be avoided when performing injection lipolysis to avoid skin laxity or ulceration and also haematomas [25-28].

Aim of the Work

The aim of the work was to compare the efficacy of injection lipolysis using PC/DC mixture versus DC alone in the treatment of localized fat deposits.

Patients and Method

This study was carried out on twenty female patients complaining of localized fat accumulation in the lower abdominal region.

Inclusion criteria

The age range of the patients was from 20 to 55 years old. Patients included in the study complained of localized fat in the abdominal region. They were not subjected to previous treatment with injection lipolysis for at least 6 months. They had no cutaneous disease in the treatment area, no systemic diseases, and no known allergies. They were neither pregnant nor lactating [20].

Exclusion criteria

Failure to follow the study protocol, concomitant disease during the study (hepatic, cardiac, renal, autoimmune diseases, DM, and bleeding disorders or any skin disease at the site of injection), important adverse events (such as panniculitis or allergic reaction) and weight gain or weight loss of more than 2 kg during the study were the exclusion criteria employed in this study [20].

All cases were subjected to the following

Signing a written consent, history taking, general and local examination, circumferential measurement at a specific location (just above the iliac crest from the sides to the largest diameter below the umbilicus), photographing: Frontal and side view and monitoring of side effects occurrence and duration.

This was done following each session with assessment of the duration of each side effect and it included monitoring of pain, sensitivity to touch, bruises, erythema, oedema, itching, subcutaneous nodules, induration, burning sensation, hyperpigmentation, hematoma and diarrhea or steatorrhea.

Monitoring of patients satisfaction

All patients were asked about their degree of satisfaction about the results of their treatment and whether they were very satisfied, satisfied, fairly satisfied or not satisfied.

NB: Both circumferential measurement and photographing were done at every step of the study and 2 weeks after the last treatment session for a final judgment.

The study group was divided into two subgroups:

Group A: Ten patients received subcutaneous injection of PC/DC mixture.

Group B: Ten patients received subcutaneous injection of DC only.

Medications used in the injection of group A: Phosphatidyl choline / Sodium deoxycholate (dermastabilon) manufactured by Aesthetic Dermal Spain and distributed in Egypt by Bio-Egypt pharmaceuticals. The PC/DC preparation has a composition of 50/20 mg per ml in 5 ml vials which means 250/100 mg per vial with a PC concentration=5% and DC conc.=2% .

Medications used for injection of group B: Sodium deoxycholate

(deoxylase) manufactured by Aesthetic Dermal Spain and distributed in Egypt by Bio-Egypt pharmaceuticals. The preparation has a composition of 25 mg per ml in 5 ml vials (125 mg per vial) with a DC concentration=2.5%.

To have a comparable deoxycholate values, the dosing of the treatment was set to 500/200 mg for the PC/DC compound (two 5 ml vials) and 200mg (8 ml) for the DC formulation [22].

Technique of Injection

Injection was done to all patients manually at a depth of 13 mm. Injection spacing was 2 cm.

The amount injected at each prick was 0.4 cc. Injection was perpendicular to skin with the bevel of the needle directed upwards at regular intervals. Sessions were done every two weeks with a total number of six sessions for each patient.

Punch Biopsy

Five patients were randomly selected from each group and were subjected to a 6 mm punch biopsy before the start of treatment and two weeks after the last treatment session. Specimens were stained by H&E and examined under light microscope.

Aim of punch biopsy

It aimed to compare the condition of fat cells in normal subcutaneous tissue before treatment and after injection lipolysis with PC/DC and with DC only, to detect if any disruption of fat cells occurred after both treatments and to detect signs of inflammation in the subcutaneous fat tissue and its type in both groups, also to detect any dermal changes following injection lipolysis.

Technique of punch biopsy

First, the direction of the skin tension lines at the biopsy site was determined.

Local anesthetic was injected at the site, and a 6 mm punch was used with some stretching of the skin slightly perpendicular to the normal skin tension lines to produce an oval rather than a round wound, facilitating closure. The punch was placed perpendicular to the skin and a firm and constant downward pressure with a circular motion was applied in a clockwise direction. When the punch reached the subcutaneous fat, there was a definite "give" indicating that a full-thickness cut had been made.

The punch was then removed, and a downward finger pressure at the sides of the wound to pop up the core was applied. The core was completely elevated with the gentle use of forceps, and was excised at its base with small tissue scissors. Pressure was applied to the wound with gauze in preparation for closure. Two sutures were done to produce a better cosmetic result.

Processing the biopsy sample

The specimens were placed in a 10% buffered formalin solution provided by pathology; each specimen was placed into a separate bottle and identified.

Histological evaluation

Histological evaluation was done using light microscopy examination of the paraffin embedded specimens after staining with H&E stain.

Statistical analysis

Statistical assessment was carried out with the SPSS 17.0 for Windows statistical software. Quantitative variables were tested for normality using Kolmogorov-Smirnov test and were thus described accordingly. For abnormally distributed variables the Mann-Whitney test was used for comparing two groups. Mixed-design ANOVA was used to compare the circumferential measurement in the two groups at sessions of treatment. In cases where Mauchly's test indicated that the assumption of sphericity had been violated, the degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity. Significant mixed design ANOVA was followed by adjusted post-hoc pair-wise comparisons. Categorical variables were described using frequencies and percentages. The chi-square, Fisher exact and Monte Carlo tests were used for testing associations. To indicate statistical significance, the threshold for p values was taken at 5% level. All tests used in this study were two-sided.

Results

A total of 20 patients (all females) with a mean age of 38.4 ± 8.5 years (range 23–53 years) were enrolled in this study. Group A: The PC/DC group (n = 10) had a mean age of 38.9 ± 8.4 years (range 29–53 years). Group B: The DC group (n = 10) had a mean age of 36.9 ± 8.9 years (range 23–53 years).

There was a significant main effect of the treatment session on circumferential measurement, $F = 58.003$, $p < 0.001$. But there was no significant main effect of group (whether PC/DC or DC) on circumferential measurement improvement, $F = 0.334$, $p = 0.571$. All patients in both groups improved in circumferential measurement at the end of sessions and the decline was almost parallel in the two

groups. There was no significant interaction effect between the session of measurement and group, $F=0.362$, $p=0.699$. This means that the group of cases whether PC/DC or DC did not have different effects on circumferential measurement at different sessions (Table 1, Figure 1).

The incidence of pain was significantly higher in the DC group (100%) than in PC/DC group (50%), FET, $p=0.03$. The occurrence of subcutaneous nodules was significantly higher in the DC group (70%) than in the PC/DC group (10%). FET, $P=0.020$ (Table 2). The occurrence of other localized side effects namely; bruising, erythema, induration, itching, and hyperpigmentation was not significantly different between the two groups, $p>0.05$. All cases in both groups suffered from burning, swelling and sensitivity to touch while none of the patients in either group experienced hematoma. Systemic side effects were infrequent clinically in both groups. Only 20% of all cases in the study developed diarrhea / steatorrhea and the difference between both groups was not statistically significant. FET, $p=1.00$

All cases included in this study (of both groups) improved by circumferential measurement yet, not all of them were equally satisfied, one case was not satisfied, four cases were fairly satisfied, twelve cases were satisfied and three cases were very satisfied (Table 3).

Of the 20 cases included in the study, only 1 case showed no improvement by photographing and that was the only case who was not satisfied. Three cases reported being very satisfied two of which showed moderate improvement by photographing and 1 showed marked improvement. The other patients who showed moderate improvement (7 other patients) reported being "satisfied". Of the 9 patients who showed mild improvement by photographing, 4 reported being "fairly satisfied" and 5 reported being "satisfied".

Circumferential measurement (Mean ± SD)	Session 1	Session 2	Session 3	Session 4	Session 5	Session 6	Session 7	Sig. for repeated measures comparison
PC/DC group	106.1 ± 10.9	102.7 ± 8.8	101.8 ± 8.3	100.8 ± 8.1	99.1 ± 8.4	98.5 ± 8.4	97.4 ± 8.5	$F = 58.003$, $p < .001$
DC group	107.6 ± 7.0	105.7 ± 7.0	103.9 ± 7.8	102.6 ± 7.4	101.3 ± 7.9	100.5 ± 7.9	99.4 ± 8.1	$F = 58.003$, $p < .001$
Sig. for between group comparison	$F = .334$, $p = .571$							Sig. for interaction effect $F = .362$, $p = .699$

Table 1: Repeated circumferential measurements of both groups. There was no significant interaction effect between the session of measurement and group, $F=.362$, $p=.699$. This means that the group of cases whether PC/DC or DC did not have different effects on circumferential measurement at different sessions.

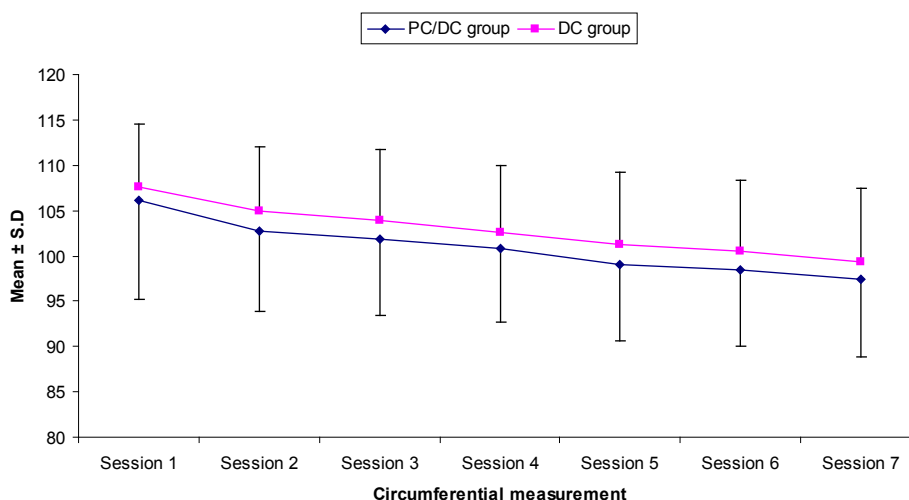


Figure 1: Circumferential measurements of both groups at repeated sessions. There was a significant difference between the first session and all other sessions and a significant difference between the last session and all the previous sessions in both patient groups).

There was a significant association between the level of patient satisfaction and the degree of improvement as detected by photography, $\chi^2=32.222$, $p=.002$ (Table 3).

Patients with stria before treatment showed a significantly lower decrease in circumferential measurement at the end of the six sessions of treatment (median= 6 cm) than patients without stria (median= 8 cm), $Z= 3.528$, $p<.001$ (Figure 3).

Clinical photography of two patients treated with PC/DC are demonstrated before (Figures 3.a and 4.a) and after 6 sessions of injection (Figures 3.b and 4.b).

Total (n=20)		DC (n=10)		PC/DC (n=10)		Side Effects	
No.	%	No.	%	No.	%		
Pain							
75		15	100	10	50	5	Yes
25		5	0	0	50	5	No
FET, p=0.03							
Subcutaneous nodules							
40		8	70	7	10	1	Yes
60		12	30	3	90	9	No
FET, p=0.020							

The occurrence of subcutaneous nodules was significantly higher in the DC group (70%) than in the PC/DC group (10%), FET, $P=.020$

Table 2: The occurrence of pain and subcutaneous nodules in both groups. The incidence of pain was significantly higher in the DC group (100%) than in PC/DC group (50%), FET, $p=.03$.

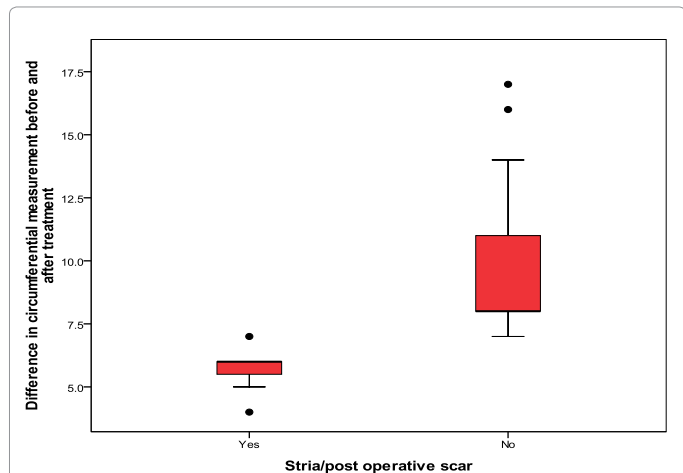


Figure 2: The degree of circumferential measurement improvement in the presence and absence of stria.



Figure 3a: Before PC/DC injection.



Figure 3b: Two weeks after 6th session of PC/DC injection.



Figure 4a: Before PC/DC injection.



Figure 4b: Two weeks after 6th session of PC/DC injection.



Figure 5a: Before DC injection.

Clinical photography of two patients treated with DC are demonstrated before (Figures 5.a and 6.a) and after 6 sessions of injection (Figures 5.b and 6.b).

Histologic photomicrographs are demonstrated in Figures 7 to 12 respectively.

Figure 7 demonstrates normal histology of the subcutaneous fat;



Figure 5b: Two weeks after 6th session of DC injection.



Figure 6a: Before DC injection.



Figure 6b: Two weeks after 6th session of DC.

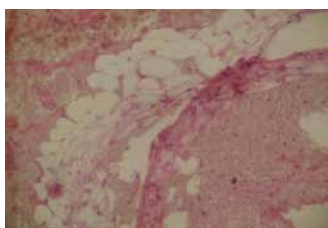


Figure 7: Histology of normal subcutaneous fat before injection lipolysis.

Figures 8 and 9 demonstrate histopathologic changes after PC/DC injection while Figures 10, 11 and 12 demonstrate histopathologic changes after DC injections.

Discussion

Fat dissolution with injectable phosphatidylcholine /deoxycholate formulations has become a popular technique for the treatment of localized fat accumulation. Several clinical trials have shown a positive effect in reduction of localized fat [29].

Several authors have assumed that phosphatidylcholine is the active component of the subcutaneous injection compounded preparations [30]. Some reports showed through a series of laboratory

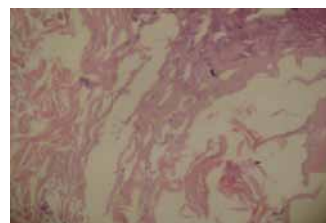


Figure 8: Dilated vacuolated empty spaces in the subcutaneous tissue due to fat necrosis with increased fibrosis two weeks following PC/DC injection.

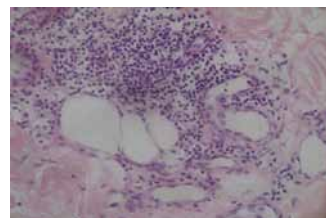


Figure 9: High resolution of inflammatory cells around fat cells two weeks after PC/DC injection.

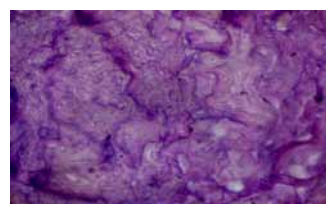


Figure 10: Marked necrobiosis of the lower dermis two weeks after DC injection.

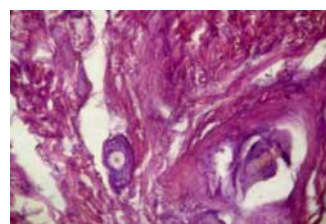


Figure 11: Loss of fat cells around hair follicles with marked fibrosis and atrophy of skin appendages.

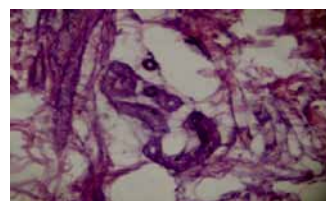


Figure 12: Atrophy and collapsing of sweat glands with thickening of blood vessels walls and dilated vacuolated spaces with increased fibrosis two weeks following injection lipolysis.

Patient satisfaction	Not satisfied (n=1)		Fairly satisfied (n=4)		Satisfied (n=12)		Very satisfied (n=3)		Total (n=20)	
	no.	%	no.	%	no.	%	no.	%	no.	%
Circumferential measurement										
Improved	1	100	4	100	12	100	3	100	20	100
Did not improve	0	0	0	0	0	0	0	0	0	0
Photographing										
No improvement	1	100	0	0	0	0	0	0	1	5
Mild improvement	0	0	4	100	5	41.67	0	0	9	45
Moderate improvement	0	0	0	0	7	58.33	2	66.67	9	45
Marked improvement	0	0	0	0	0	0	1	33.33	1	5
$\chi^2=32.222, p=.002$										

Table 3: Distribution of patient satisfaction among patients in both groups according to improvement by circumferential measurement and photographing. All cases included in this study (of both groups) improved by circumferential measurement yet, not all of them were equally satisfied, one case was not satisfied, four cases were fairly satisfied, twelve cases were satisfied and three cases were very satisfied. There was a significant association between the level of patient satisfaction and the degree of improvement as detected by photography, $\chi^2=32.222, p=.002$.

experiments that sodium deoxycholate, the bile salt component of the formula used to dissolve the phosphatidylcholine, was as effective as the presumed “active” component and fully accounted for the action commonly ascribed to phosphatidylcholine. In view of these latter results, the PC/DC formula may work primarily by the detergent action of deoxycholate causing nonspecific lysis of cell membranes [31].

In the present study there was no significant effect of group (whether PC/DC or DC) on circumferential measurement improvement. All cases of both groups showed circumferential improvement after treatment. The decrease was almost parallel in the two groups. On comparing the decline in circumferential measurement throughout the sessions in the PC/DC group versus the DC group, there was no significant difference between the two groups too. This means that both substances moderately reduced fat and can be considered equivalent in terms of efficacy and thus supporting the theory originally postulated by Routanda et al. that deoxycholate has lipolytic activity of its own and could be the active ingredient in the PC/DC formula [19,31].

Results were similar to those of Salti et al. in a double blind randomized study on 40 female patients where each patient received bilateral subcutaneous injections in the gluteotrocanteric region with PC/DC on one side and DC on the contralateral side, each patient being herself the control. Four sessions were done once every 8 weeks, where an overall moderate reduction of circumferential measurement occurred in both injected sides without statistically significant differences between the treated sides in 34 patients [20].

An interesting finding in the present study was that pairwise comparison of repeated sessions showed no significant difference in circumferential measurement between successive sessions (2 and 3), (3 and 4) and (session 5 and 6) in both groups, while all other sessions were significantly different, meaning that after the first session there was improvement of the circumferential measurement then there was a quite stationary phase where although there was a reduction yet, it wasn't significant. This occurred from the second to the fourth session. Then good improvement occurred at the fifth session. Although not explained scientifically, but it gave us an idea that for good results to be obtained from injection lipolysis, patients should receive multiple sessions and that results are cumulative with the best results obtained at the end of treatment not in between sessions. So, for best results it is recommended to have a complete course of sessions.

Regarding the occurrence of side effects, the incidence of pain in this study was significantly higher (100%) in the DC group than in the PC/DC group (50%) suggesting that the treatment was quite painful at

the site of injection especially for those who received DC, which is quite similar to the results of Salti et al. [20] where pain during injection occurred in 100% at the DC side and in 78.4% at the PC/DC side.

The incidence of occurrence and the duration of persistence of subcutaneous nodules were significantly different between the two groups. They occurred in 70% of cases of the DC group and were palpable clinically on examination, whereas in the PC/DC group they were clinically palpable in one case only (10%).

Subcutaneous nodules are supposed to be the evolution of the acute inflammatory phase and are consistent with the hypothesis of a real adipocito necrosis, followed by an inflammatory reaction causing a final fibrosis with microscopic scarring [20,32].

In the PC/DC group, the subcutaneous nodules were observed clinically in one patient and resolved within less than one month. Whereas, in the DC group the nodules were clinically more palpable, larger and more tender on examination and lasted for about two months. While in the study of Salti et al. they found that subcutaneous nodules occurred in all patients on the side treated with PC/DC and the side treated with DC. These nodules lasted for about one month in the PC/DC side and for two months in the DC side. They found that nodules were larger and more painful in the DC side [20].

Common immediate effects were edema, erythema, and stinging/tenderness, all of which resolved within hours. Other effects that resolved within days or weeks were edema, tenderness, ecchymoses, and paresthesia. Long-term effects persisting for several weeks included nodularity. The same immediate and long term side effects occurred in the present study and were typical to any inflammatory reaction with no statistically significant differences between both groups and all confirm the side effect profile of subcutaneous compounded phosphatidylcholine preparations noted in previous clinical uses on fat [6,20,33,34].

The only systemic side effects noted in this study were diarrhea and steatorrhea. These were detected in 20% of patients in both groups with no differences between the two groups. The condition could be due to fat excretion in the GIT although no tests were done to prove the exact cause. The lack of systemic side effects in this study could partially be due to the small dose of injectables given to the cases.

Palmer et al. found that systemic adverse effects are rare and are usually “very mild” or “mild” including nausea, diarrhea, dizziness, light headache and inter-menstrual bleeding [35].

Although most of cases of both groups were satisfied at the end of the study period and asked for more sessions yet, the degree of patient satisfaction differed from one case to another. Only one patient was not satisfied (5%), four patients were fairly satisfied (20%), twelve patients were satisfied (60%) and three patients were very satisfied (15%).

Palmer et al. found that patient satisfaction with treatment was found to be high, with 41.6% of patients reporting to their doctors that they were “very satisfied” with the results of treatment. 31.5% of patients were reported to be “satisfied”, 16.1% “fairly satisfied” and only 10.5% “dissatisfied” [35].

The presence of stria or post operative scars at the treated site significantly affected the degree of patient improvement by circumferential measurement. Patients who had appendectomy scar or striae significantly improved less than patients with no striae or scars with a median improvement of 6 cm in cases with stria and 8 cm in cases with no stria. This finding suggests that fibrous tissue at the site of injection could prevent the spread of the injected materials whether PC/DC or DC causing bad treatment outcome. This explains why these patients could benefit from the use of other substances in injection lipolysis cocktail such as collagenase which cause dissolution of fibrous bands and septa that interfere with the spreading of the materials in the subcutaneous tissue.

Histopathological findings in specimens from patients of the PC/DC group were consistent with fat cell lysis with large vacuolated spaces replacing fat cells and increased fibrosis with inflammatory infiltrate in some areas consisting mainly of lymphocytes (sterile lobular panniculitis). There was a mild degree of atrophy of sweat glands. Blood vessel showed dilatation and thickening of its wall.

While Duncan et al. found in the PC/DC specimens two weeks following injection that all four elements of fat necrosis were present: inflammation, neovascularization, fat cell lysis, and macrophage infiltration, as well as thickening of fibrous septa [36]. In the study conducted by Rose et al. they found that two weeks following PC/DC, lymphocytes and histiocytes predominated. The histiocytes consisted of conventional epithelioid forms, lipid-laden foam cells, and multinucleated lipid-containing giant cells. In addition, evidence of fat necrosis including adipocyte microcyst formation and serous atrophy were seen also [15].

Schuller-Petrovec et al. found that the subcutaneous tissue of a human volunteer treated several times with PC/DC showed clear histological signs of panniculitis, fat cell necrosis, and vascular injury [37].

In the present study, thickening of blood vessels wall was noted in both groups suggesting that both PC/DC and DC injection causes inflammatory reaction and fibrosis that affected also the blood vessels at the site of injection. On the other hand, the histopathological study conducted by Rose et al. noted that following injection lipolysis there was damage to blood vessels with signs of vascular necrosis and thrombosis. The authors considered that vascular necrosis might partly explain the occurrence of bruises. Bruising is a frequent side effect observed after injection lipolysis treatment while it might be just due to mechanical trauma of using multiple injections technique.

In the present study, the inflammatory infiltration in the PC/DC group was focal; not affecting all areas of subcutaneous fat. Fibrosis was noted in this group by histopathologic examination, but was not clinically evident in most patients of the PC/DC group. Those patients who developed subcutaneous nodules were a minority (10%). The nodules were transient with no evidence of permanent scarring.

This was consistent with the findings in the study done by Beshara et al. in which the authors studied the fat tissue after lipolysis of lipoma. Their histological examination revealed that only focal, spot like areas of fat tissue were affected by the inflammatory process. This may explain why, despite the frequent and widespread use of PC/DC, no corresponding observations of scarring were described in the literature. The limited inflammatory reaction might not be extensive enough to result in clinically visible complications [14].

The DC specimens in the current study showed large moth eaten vacuolated spaces. There was also marked fibrosis which corresponds to subcutaneous nodules that occurred clinically in most cases of the DC group (70%).

These findings support the findings of Duncan et al. who did serial biopsies at 1 hr, 1day, 1 week, 2 weeks, 3weeks and 4 weeks following injection with PC/DC and with DC. The authors found that DC specimens after 2weeks showed large regions of “moth-eaten” fat, where no cells were present. At 1 month, they found that the PC/DC specimens still showed a fractionated response, while the deoxycholate specimens showed a dramatic and extensive eradication of adipose cells with severe fibrotic scarring in the subcutaneous layer [37].

Histopathological findings in the present study support the previous evidences that deoxycholate is lipolytic in its own and is the active component of PC/DC formulations that were previously postulated by Routanda et al and by Schuller-Petrovec et al [19,31,38].

Conclusion

Both PC/DC and DC alone are effective in reducing localized subcutaneous fat accumulations to the same degree. Results are cumulative during the course of treatment and sessions should be repeated to obtain best results at the end. The PC/DC mixture is more tolerated by patients than the DC due to less pain during injection and less side effect occurrence and duration. The presence of stria or post operative scars in the treatment area reduces the effect of injection lipolysis. Lipolysis is not a replacement for liposuction but is an effective therapy to reduce smaller fat areas in face and body.

Recommendations

Only well trained doctors with experience in injection lipolysis should do the sessions and should respect proper injection techniques and be aware of side effects associated with high doses. Detailed medical history and drug history should be taken for any case before performing injection lipolysis. Also full clinical examination before treatment is a must to avoid dangerous side effects or drug interactions. Injection lipolysis should not be used when treating patients who have large volumes of fat (BMI >30), or patients who have unrealistic expectations and this depends on good selection of cases by the doctor. As with any other medication, injection lipolysis needs wide investigation protocols for new indications and long-term studies, so that the recommended dose and safe application technique can be standardized. Further histopathological studies should be done for more understanding of the mechanism of action of both materials.

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