Preliminary Report

A Pilot Study on the Use of Injection Lipolysis in Visceral Adipose Tissues

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Abstract

Background: Intraperitoneal fat, also known as visceral adipose tissue (VAT), poses significant metabolic risks. Reduction of this fat is functionally and aesthetically desirable. Since surgical reduction has serious risks, a noninvasive method for reduction of this fat would have important clinical benefits. Objectives: The authors evaluate the reduction in VAT in an animal model using injection lipolysis. Methods: Phosphatidylcholine was injected in half of the omentum of 16 dogs (weight 30-40 kg) by surgical laparotomy. The dogs' vital signs were followed postoperatively. A second laparotomy was performed at 2 weeks (n = 10), 4 weeks (n = 4), or 6 weeks (n = 2). Reduction of fat in the injected side was assessed by comparing with the control side. Specimens of the injected and the control sides were examined microscopically. Intraperitoneal cultures were also obtained. Results: There was a major reduction in the amount of fat in all 16 dogs. No intraperitoneal abscesses, collections, or adhesions developed, and there was no injury to any intra-abdominal organs. Microscopic examination showed significant fat loss and lysis of fat cells with cellular infiltrate formed of predominantly macrophages, with fibrosis developing in the 6-week specimens. No bacterial or fungal growth was observed on the cultures. The dogs' vital signs showed no significant variation from the preoperative baseline. Conclusions: Injection lipolysis is effective and safe in reducing VAT in dogs. Further studies are needed to prove its efficacy and safety in humans and refine its indications and method of injection.

Keywords

phosphatidylcholine, omentum, bariatric surgery, diabetes, abdominoplasty

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The intraperitoneal fat present in the omentum and mesentery, also known as visceral adipose tissue (VAT), has significant and peculiar functional and aesthetic consequences. Increased VAT is considered to have a more detrimental effect on blood glucose, lipid profile, and insulin resistance than corresponding increases in subcutaneous fat. Although the exact pathogenesis of this phenomenon is not well defined,1-3 reduction of VAT has beneficial metabolic effects that are not produced by subcutaneous fat reduction.4-6 However, reduction procedures for VAT are currently unpopular due to the tissue’s relation to nearby important structures and the hazards of surgical access. Furthermore, patients are often denied an aesthetic abdominoplasty if a major portion of the deformity is caused by excess VAT.7-10 If a minimally invasive method, such as injection lipolysis (IL), proves effective and safe in reduction of VAT, it could have tremendous clinical potential. Phosphatidylcholine (PPC) is the material often used for IL and has been studied extensively in the subcutaneous fat but, to our knowledge, has not been tested in the VAT.11-20 The aim of this pilot study is to examine the feasibility and effect of injecting PPC into visceral fat and to document the occurrence of complications in the peritoneal cavity in a limited number of animals.

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METHODS

Sixteen Egyptian Baladi dogs, 10 males and 6 females ranging in weight from 30 to 40 kg and in age from 2 to 3 years old, were used in this study. Study approval and protocols for animal use and euthanasia were approved by the institutional ethical committees at Cairo University Hospitals.

General anesthesia was induced using ketamine hydrochloride (5 mg/kg intravenous [IV]) and lidocaine (1 mg/kg IV) through the femoral vein. The specimen was placed in a supine position, and a midline laparotomy was performed. The peritoneal cavity was examined for any anomalies or pathologies. The omentum was identified, spread on a laparotomy sponge, and examined to detect any irregularities, deficiencies, or signs of previous pathology. A blue marker was used to draw a vertical line separating the omentum into 2 equal halves. The right and left sides alternated between the injection side and the control. The injection side was marked with 2 Prolene sutures (Ethicon, Inc, Somerville, New Jersey). Prior to injection, multiple biopsies were obtained from both sides of the omentum for pathological examination, and a bacterial swab was obtained from the peritoneum and sent for aerobic, anaerobic, and fungal culture. The injection consisted of 5 mL Lipostabil (Natterman Aventis, Köln, Germany), containing 50 mg phosphatidylcholine and 25 mg deoxycholate/mL mixed with 2.5 mL vitamin B complex (vitamins B₂, B₃, B₅—1%) mixed with 2.5 mL 0.9% saline. The solution was injected with a 27-gauge needle into multiple points in the omentum, spaced 1.5 to 2 cm apart.

Postoperatively, the dogs received intramuscular analgesics and antibiotics. Their pulse and temperature were recorded daily for the first 10 days. The dogs were divided into 3 groups according to the timing of a second laparotomy, which occurred at 2 weeks in group 1 (n = 10), 4 weeks in group 2 (n = 4), and 6 weeks in group 3 (n = 2). The animals were sacrificed at that time. During the second laparotomy, the peritoneum was examined for signs of inflammation, collections of fluid, fibrosis, or other complications. The injected side was identified by the Prolene suture and compared grossly with the control side to evaluate the reduction in omental fat, if any. Multiple biopsies were obtained from both sides of the omentum and bacterial and fungal cultures were obtained from the peritoneum. Pre- and postinjection pathological samples were stained with hematoxylin and eosin as well as trichrome stains and examined microscopically.

RESULTS

The initial laparotomies did not show evidence of any previous or current pathology, and thus all dogs were included in the study. All dogs survived and showed no signs of toxicity or other complications. Comparison of pulse rate and temperature showed insignificant variations in the first 10 days (P < .05) in all dogs.

The second laparotomy did not show evidence of adhesions, fibrosis, or infection. The omentum showed significant diffuse loss of fat in the injected side in all 16 specimens (Figure 1). There was minimal or no change in the size of the control side, especially further away from the injected side.

In the dogs in groups 1 and 2, the omentum could be stretched to its preinjection dimensions (despite the reduction in volume). However, in the group 3 dogs, the omentum was rolled on itself and significantly contracted, so it could not be stretched to match the control side. The bacterial cultures were negative in all 16 dogs, both in the initial and the second laparotomies.

Microscopic analysis showed disruption of the normal lobular architecture of fat, reduction in the size of fat cells with variation in their form and size, and lysis of the fat cell membrane (Figure 2). Vasculitis was observed, with an inflammatory infiltrate that was predominantly formed of neutrophilic granulocytes and erythrocytes in the group 1 (2-week) specimens (Figure 3), with an increase in lymphocytes and macrophages in the group 1 (6-week) specimens (Figure 4). Fibrosis was seen in the group 2 (4-week) specimens and was more evident in the group 3 (6-week) specimens (Figure 5).

DISCUSSION

Although increasing volumes of total body fat correlate with significant cardiovascular and metabolic risks, the location of this adiposity is equally important. Visceral adipose tissue, the intraperitoneal fat present in the omentum and the mesentery, is metabolically and histologically distinct from the subcutaneous fat. Visceral adipose tissue poses a higher risk of metabolic derangements. It has been linked to insulin resistance, glucose intolerance, dyslipidemia, and increased cardiovascular risk. Several animal studies have proven the beneficial metabolic effects of reduction of this fat. In addition, increased VAT causes an aesthetic...
deformity that is difficult to treat. Males in particular tend to have excess VAT, and most surgeons would be cautious in advising an abdominoplasty in this population.

Unfortunately, surgical reduction of the VAT is an invasive procedure associated with significant morbidity, risk of surgical complications, and increased time and cost.\textsuperscript{5,6} To our knowledge, noninvasive or minimally invasive procedures have not been attempted for reduction of this VAT. This study examined the effect of injection lipolysis on VAT. If substantiated, this model could have significant clinical potential by offering a minimally invasive method with considerable aesthetic and functional benefits.

Injection lipolysis has been used for more than a decade, mostly in Europe. It was initially met with suspicion and cynicism, especially since the US Food and Drug Administration (FDA) had not yet approved its use for subcutaneous injection.\textsuperscript{15-17,19} However, there is a growing sum of evidence that with the proper training and the correct indications, it deserves a place in the surgeon’s armamentarium.\textsuperscript{11-14,18-20} Many surgeons are reluctant to try it for subcutaneous fat reduction, especially in light of the proven track record for liposuction, direct excision, and the newer, competing technologies such as laser lipolysis. However, these methods are not applicable for VAT reduction. On the

Figure 2. The control microscopic picture is shown before injection lipolysis, demonstrating mature adipocytes containing a large vacuole stretching the cytoplasm and displacing the cell nucleus to the periphery of the cell (arrow), producing the “signet ring” appearance. The cells are arranged in a regular lobular pattern.

Figure 3. Microscopy is shown at 2 weeks after injection lipolysis, demonstrating an inflammatory cell infiltrate (arrow), disrupted fat cells, and angiogenesis.

Figure 4. High-magnification hematoxylin and eosin stain is shown 2 weeks after injection lipolysis, demonstrating disrupted fat lobules and a mononuclear inflammatory infiltrate predominantly composed of macrophages (arrow).

Figure 5. Marked fibrosis is shown at 6 weeks after injection lipolysis. The trichrome stain shows the amount of fibrosis (green) compared with the fatty tissue (brown).
contrast, VAT may actually be a better indication for injection lipolysis than is subcutaneous fat, as the common complications of subcutaneous injection lipolysis—namely, skin irregularities, unpredictable response, pigmentation, induration, and interruption of skin circulation—do not hold true for VAT lipolysis.

This study proves that the omentum in dogs responds favorably to injection lipolysis using PPC mixed with vitamin B complex. Dogs were chosen due to their gene homology with humans and their similar fat distribution.21,22 During the study period, we did not find evidence of infection, unusual adhesion, inflammation, injury to surrounding organs, or other intraperitoneal complications. All dogs survived without evidence of local or general complications. There were no adhesions between the omentum and the surrounding organs. However, in the group 3 animals examined at 6 weeks postinjection, the omentum had curled upon itself, possibly due to the significant fibrosis that was also evident on the histological sections. Absence of adhesions to surrounding organs is a positive sign. However, all animals were sacrificed at a maximum of 6 weeks, and it would be interesting to study the effect of injection lipolysis several months later to evaluate whether adhesions do eventually develop between the omentum and the surrounding structures.

Although several randomized, controlled trials examined the effect of removing the VAT at the time of bariatric surgery in humans, it is difficult to reach a consensus due to the different methodology and significant variation in the results between studies.4,6 Surgical omentectomy is an invasive procedure associated with increased operative time and serious complications.5 A minimally invasive method such as injection lipolysis for VAT may prove valuable in many situations, either in conjunction with another surgery (eg, bariatric surgery or abdominoplasty) or as an isolated procedure in diabetics and patients with unfavorable lipid profiles that are refractory to medical treatment.

The results of this study should be placed in the context of several drawbacks to the study design; we are planning to address these in future projects. First, this is a pilot study to assess whether injection lipolysis is a possible option for reduction of intraperitoneal fat. Although these preliminary results are encouraging, as they showed significant reduction in the size of the omentum with no adverse events at different time frames, a larger study with strict randomization and injection of a control (eg, saline) would be helpful. Future studies will include a more objective assessment of the decrease in the size of the omentum by volume and weight measurement, surgical division of the omentum into 2 halves, use of saline injections as a control, and comparing different concentrations of the injectate. We also did not examine the effect of VAT injection lipolysis on glucose levels, lipid profiles, and other metabolic markers. These measures have been documented before in several animal studies in which a direct surgical excision was performed, and it would be interesting to directly compare injection lipolysis with surgery. Finally, no comparison was made between the effects of injection lipolysis on intraperitoneal versus subcutaneous fat in this animal model.

The questions yet to be answered include how to administer injection lipolysis to the VAT and for which clinical indications. The main advantage of injection lipolysis is the fact that it is minimally invasive. Obviously, our experiment did not involve a minimally invasive method, as we actually performed a formal laparotomy. This was done to confirm an accurate location of the injection. Should further studies confirm that injection lipolysis actually reduces the amount and deleterious effects of VAT in humans, the ultimate goal would be to define the indications and the method of injection. This could possibly be done laparoscopically, especially in conjunction with bariatric or other procedures.

CONCLUSIONS

As with many pilot studies, ours introduces a new concept and raises many questions. In our canine subjects, injection lipolysis was a safe and effective method for reducing the size of the omentum. Its safety in humans must be investigated, and we must further refine its indications, dosage, injection method, and side effects.

Disclosures

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