The Effect of Injection of PhosphatidylIcholine On Visceral Fat: Experimental Study

Thesis

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By

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Acknowledgment

*First of all, I would like to thank "**GOD**", for his grace and mercy and for giving me the effort to complete this work.*

It is hoped that this study will stimulate further debate in the application of this therapy in the non surgical management of visceral adiposity in humans and funding of appropriate scientific and clinical studies to confirm the mode of action, clinical safety and outcome of the use of PPC in visceral lipolysis.

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I dedicate this work to my beloved wife and son who helped me out in this thesis and give me the light and shine to keep on.

Finally, I dedicate this work to my parents who have done and still doing a lot to me without waiting for anything in return and hope I can pay even a small part of my debt to them.

Abstract

This study is to evaluate the effect of phosphatidylcholine injection on visceral fat in dogs. The experiments were carried out in ten dogs using the PPC formula of the network lipolysis .The injections delivered to the omentum of dogs through minilaparotomy. After 7 -10 days; omental biopsies from the site of injection were taken and examined by light microscope after processing and staining. Follow up postoperatively was done by daily pulse and temperature for all dogs. A control half of the omentum and a control omental biopsies before injection were used for comparison. Complications excluded by peritoneal swabs before injection and on relaparotomy.Histopathological results show significant lipolysis of visceral fat .while peritoneal swabs show no peritonitis and vital signs follow up show no significant changes.

Key words

Visleral fat
Phosphatidylcholine
experimental

CONTENTS

Introduction

Anybody with a belly has visceral fat, and the more he has the worse off he is. It is not clear why visceral fat is riskier; it may be more active metabolically and produces more toxic substances. Also, its secretions go straight to the liver and may interfere with its functions, removal of visceral fat helping to regulate blood glucose and cholesterol ***(Nelson et al., 1997).***

Not all visceral fat can be removed safely because of where it is situated. The omentum is a pad of fat weighing two to four pounds that hangs like a curtain in the abdomen, it is more than one-third of the visceral fat ***(Jeffrey-Popp, 2004).***

In the average person, about 10 percent of total body fat is visceral while 90 percent is subcutaneous. In a very obese person, that ratio changes to about 25:75 ***(Jeffrey-Popp, 2004).***

There is a correlation between visceral fat and various metabolic diseases (like diabetes) that put persons at risk for cardiovascular disease and in this respect visceral fat is more dangerous than subcutaneous fat ***(Nelson et al., 1997).***

When looking at visceral fat cells out of the body, they appear to be more active than subcutaneous fat cells. Studying visceral fat cells inside the body is difficult because this would necessitate access to the portal vein, which drains visceral fat and that would mean inserting a catheter into it ***(Hasengschwantdtner et al., 2004).***

Lipodissolve injections should not be regarded as a new miracle drug for weight reduction, but rather a method to control small fat

deposits that cannot be removed by diet or exercise ***(Hasengschwantdtner, 2004).***

Lipodissolve injections are effective by helping the natural metabolic process during which the fat cell wall dissolves to release the fat in an emulsified form to be transported to the liver for elimination, Hence it is important that the liver is in good condition ***(Hasengschwantdtner, 2004).***

The active substance used in these injections, phosphatidylcholine (referred to as PPC), is a natural compound produced from the soya bean, the body uses the same substance in a number of chemical pathways, including fat metabolism ***(Hasengschwantdtner, 2004).***

Phosphatidylcholine was initially used in emergencies and in the treatment of atheromatous plaques in cardiac diseases. Recently, it has also been used in the treatment of localized fat deposits, the use of 250 mg/ml phosphatidylcholine injections in the treatment of subcutaneous fat deposits, laboratory tests were performed during the period of the drug use, clinical results reflect that phosphatidylcholine was efficacious in reducing the fatty pads in the treated areas, with few side effects,use of phosphatidylcholine in the treatment of fatty pads and small areas of localized fat is safe,has a low cost, and is effective ***(Doris Hexsel et al., 2003).***

Aim of the work:

Is to Study the effect of injection of phosphatidylcholine (ppc) on the visceral fat and to assess the complications of injection on animal.

Central Obesity (Visceral Adiposity)

Central obesity

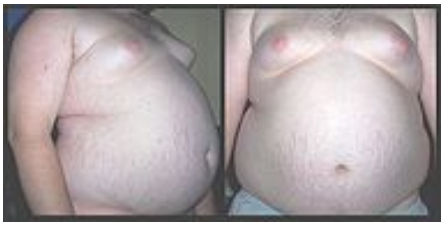

Fig.1: An obese male Weight 146 kg/322 lbs, height 177 cm/5 ft 10 in The body mass index is 46 ***(Janssen et al., 2004).***

Central obesity, the "apple-shaped" obesity commonly referred to as **belly fat**, is the accumulation of visceral fat (fat deposited between the internal organs in the torso) resulting in an increase in waist size. There is a strong correlation between central obesity and cardiovascular disease ***(Yusuf et al., 2004).***

VISCERAL FAT

Visceral fat, also known as organ fat or intra-abdominal fat, is located inside the peritoneal cavity, packed in between internal organs, as opposed to subcutaneous fat which is found underneath the skin, and intramuscular fat which is found interspersed in skeletal muscle. Visceral fat is composed of several adipose depots including mesenteric and perirenal depots ***(Yusuf et al., 2004).***

An excess of visceral fat is known as **central obesity**, the "pot belly" or "beer belly" effect, in which the abdomen protrudes excessively. This

body type is also known as "apple" shaped, as opposed to "pear" shape, in which fat is deposited on the hips and buttocks ***(Yusuf et al., 2004).***

DIAGNOSIS

While central obesity can be obvious just by looking at the naked body (see fig.1); the severity of central obesity is determined by taking waist and hip measurements. The absolute waist circumference (>102 centimeters (40 in) in men and >88 centimeters (35 in) in women) and the waist-hip ratio (>0.9 for men and >0.85 for women), are both used as measures of central obesity. In the cohort of 15,000 people participating in the National Health and Nutrition Examination Survey (NHANES III), waist circumference explained obesity-related health risk better than the body mass index **(**BMI = weight (kg) /Heigt² (meters)**)** when metabolic syndrome was taken as an outcome measure and this difference was statistically significant. A differential diagnosis includes distinguishing central obesity from ascites and intestinal bloating ***(Janssen et al., 2004).***

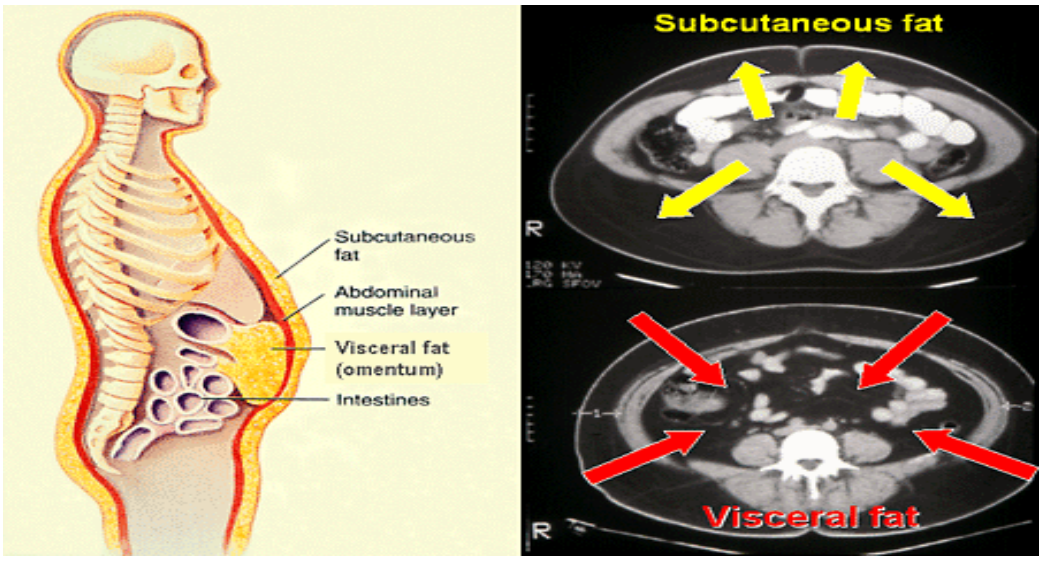

Fig.2:the difference between s.c. and visceral fat *(Janssen et al., 2004).*

HEALTH RISKS

Central obesity is associated with a statistically higher risk of heart disease, hypertension, insulin resistance, and diabetes mellitus type 2 (see below). Belly fat is a symptom of metabolic syndrome, and is an indicator used in the diagnosis of that disorder ***(Grundy et al., 2004).***

Central obesity can be a feature of lipodystrophies, a group of diseases which is either inherited, or due to other causes (often protease inhibitors, a group of medications against AIDS). Central obesity is a symptom of Cushing's syndrome and is also common in patients with polycystic ovary syndrome (PCOS). Central obesity is associated with glucose intolerance and dyslipidemia ***(Bujalska et al., 1997).***

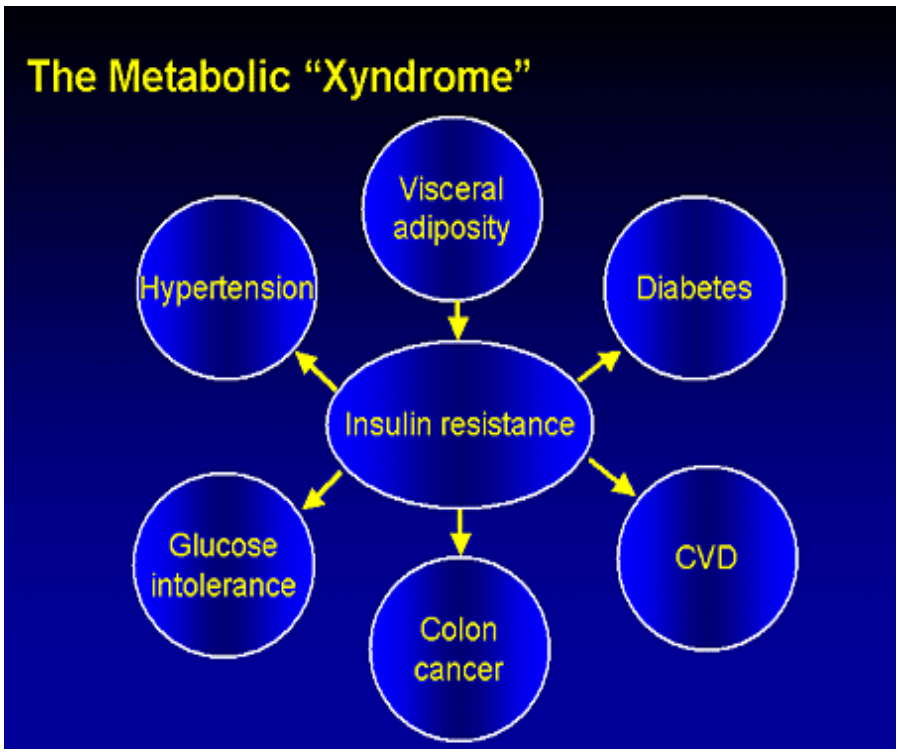

Fig.3 :metabolic syndrome *(Grundy et al., 2004).*

RELATIONSHIP WITH DIABETES

There are numerous theories as to the exact cause and mechanism in type 2 diabetes. Central obesity is known to predispose individuals for insulin resistance. Abdominal fat is especially active hormonally, secreting a group of hormones called adipokines that may possibly affect tolerance. Insulin resistance is a major feature of diabetes mellitus type 2 (T2DM), and central obesity is correlated with both insulin resistance and T2DM itself ***(Asensio et al., 2004).***

Increased adiposity (obesity) raises serum resistin levels, which in turn directly correlate to insulin resistance. Studies have also confirmed a direct correlation between resistin levels and T2DM. And it is waistline adipose tissue (central obesity) which seems to be the foremost type of fat deposits contributing to rising levels of serum resistin. Conversely, serum resistin levels have been found to *decline* with decreased adiposity following medical treatment ***(Lee et al., 2005).***

CAUSES

The main causes of central obesity are overeating and a sedentary lifestyle. Hypercortisolism, such as in Cushings syndrome also leads to central obesity. Many prescription drugs(eg.cotisone) can also have side effects resulting in obesity ***(Bujalska et al., 1997).***

PREVENTION AND TREATMENTS

Performing adequate aerobic exercise and eating a healthy diet prevent central obesity, and losing weight via these methods is the main way to reverse the condition. Adjunctive therapies which may be prescribed by a physician are orlistat or sibutramine. In the presence of diabetes mellitus type 2, the physician might instead prescribe metformin and thiazolidinediones (rosiglitazone or pioglitazone) as anti-diabetic drugs rather than sulfonylurea derivatives. Thiazolidinediones may cause slight weight gain but decrease "pathologic" abdominal fat, and therefore may be prescribed for diabetics with central obesity ***(Fonseca et al., 2003).***

SIT-UPS MYTH

There is a common misconception that spot exercise (that is, exercising a specific muscle or location of the body) most effectively burns fat at the desired location, but this is not the case. Spot exercise is beneficial for building specific muscles, but it has little effect on fat in that area of the body, or on the body's distribution of body fat. The same thing applies to sit-ups and belly fat. Sit-ups and other abdominal exercises are useful in building the abdominal muscles, but they have little effect on the adipose tissue located there. In order to burn fat, one must take part in aerobic exercises ***(Janssen et al., 2004).***

SLANG TERMS

Several terms used to refer to central obesity, and to people who have it, refer to beer drinking. However, there is little scientific evidence that beer drinkers are more prone to abdominal obesity, despite it being known colloquially as "beer belly", "beer gut", or "beer pot". One of the few studies conducted on the subject did not find that beer drinkers are more prone to abdominal obesity than nondrinkers or drinkers of wine or spirits. "Love handles" is a colloquial term for a layer of fat that is deposited around a person's midsection, especially visible on the sides over the muscle." Muffin" is a pejorative term used for a person whose midsection spills over the waistline of his or her trousers in a manner that resembles the top of a muffin spilling over its baking pan ***(Bobak et al., 2003).***

Adipocyte Biology

Adipose tissue; fat, is the largest endocrine organ in mammals and exerts a profound influence on whole body homeostasis. It comes in two colours. White adipose tissue (WAT) stores energy when food intake exceeds energy expenditure and brown adipose tissue expresses the uncoupling protein 1 (UCP-l), which has the ability to dissipate energy through adaptive thermogenesis ***(Adipocyte Differentiation http://www.sdu.dk).***

Adipose tissue is a major source of numerous signalling molecules affecting most if not all tissues in the body, and consequently plays an important regulatory role, extending far beyond energy homeostasis. De novo adipocyte differentiation can be initiated during the entire lifespan of mammals by recruiting fibroblastic precursors. This process is dependent on an intricate molecular symphony, activating key regulatory transcription factors of which Peroxisome Proliferator-Activated Receptor g (PPARg) is the *"Musical Director"*. Subsequently, the committed precursor cells synthesize specific lipid metabolites that bind to PPARg and promote terminal differentiation ***(Adipocyte Differentiation http://www.sdu.dk).***

Massive accumulation of WAT; obesity, is becoming an increasing problem globally in developed and developing countries. Obesity is a prime condition predisposing to the development of the metabolic syndrome, and to a number of serious and common diseases such as type II diabetes, cardiovascular diseases, and certain cancers ***(Adipocyte Differentiation http://www.sdu.dk).***

Early Stages of Adipogenesis:

A novel regulatory pathway has been described which is involved in the early stages of adipogenesis. Lipid-metabolising enzymes are involved in the production of PPARg agonists, and a retinoblastoma protein (pRB) appears to function as a molecular switch determining whether an adipocyte precursor cell differentiates towards a white or a brown adipocyte ***(Adipocyte Differentiation http://www.sdu.dk).***

Although the process of differentiation of the preadipocyte has been thoroughly investigated, little is known about the early process of determination of mesenchymal stem cells to the preadipocytic cell lineage. Furthermore, as differentiation of brown and white preadipocytes into mature adipocytes apparently involves the same set of regulatory factors, brown versus white lineage determination still remains an enigma ***(Adipocyte Differentiation http://www.sdu.dk).***

The Mature Adipocyte:

The mature adipocyte contains a large vacuole which stretches the cytoplasm and displaces the cell nucleus to the periphery of the cell producing the so-called signet ring appearance. From a metabolic perspective, fat cells have two poles, one lipogenic, where fatty acids are taken up from the circulation, and a lipolytic, where accumulated triglycerides are released back into the circulation as free fatty acids ***(http://www.geodata.soton.ac.uk).***

Obesity is an excess of body fat that frequently results in a significant impairment of health, and is a function of hypertrophy followed by hyperplasia. One pound of body fat represents about 3,500 calories ***(http://www.geodata.soton.ac.uk).***