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ORIGINAL ARTICLE

Comparison of exenatide and acarbose on intra-abdominal fat content in patients with obesity and type-2 diabetes: A randomized controlled trial

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KEYWORDS
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Summary
Objective: To investigate exenatide, a GLP-1 analogue, compared with acarbose, for intra-abdominal fat reduction in patients with obesity and type-2 diabetes.
Methods: This randomized controlled trial included 36 patients with obesity and type-2 diabetes, who were metformin-unresponsive, receiving metformin/

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exenatide (GLP-1 group) or metformin/acarbose (control group) for 3 months. Primary end-point: intra-abdominal fat content from baseline to 3 months; Secondary end-points: changes in fasting blood glucose, glycated haemoglobin (HbAlc), fasting insulin, blood lipids, weight, body mass index, and inflammatory cytokines from baseline to 3 months.

Results: Intra-abdominal fat content decreased in the GLP-1 group from baseline to 3 months ($17,947 \pm 5804$; $13,717 \pm 3628\ mm^2$, $P = 0.001$, respectively), but was not significantly reduced in the control group ($P = 0.197$) and at 3 months post-treatment, it was significantly lower in the GLP-1 group than control group ($P = 0.043$). Glucose control, measured by HbA1c (GLP-1: 9.72 ± 1.38; $7.09 \pm 0.60\%$, $P < 0.001$, 9.46 ± 1.25; $7.42 \pm 0.84\%$, $P < 0.001$, respectively) and insulin resistance index LN(HOMA-IR) (GLP-1: 1.58 ± 0.40; 1.01 ± 0.33, $P < 0.001$, Control: 1.53 ± 0.57; 1.10 ± 0.33, $P = 0.003$, respectively) significantly improved in both groups with no significant difference between them. TNF-α, IL-6, and leptin were lower and adiponectin levels higher in the GLP-1 group at 3 months compared with baseline (all $P < 0.05$), but not significantly changed in the control group. TNF-α, IL-6 and leptin levels were similar between groups. Adiponectin level was higher in the GLP-1 group than the control group at 3 months ($P = 0.025$).

Conclusion: Combined exenatide/metformin reduced intra-abdominal fat content, and enhanced insulin resistance and inflammatory status in patients with obesity and type-2 diabetes, representing a novel treatment regimen.

Introduction

The prevalence of obesity and therefore type-2 diabetes continues to increase significantly, with approximately 6.71 hundred million people with obesity globally [1]. Insulin resistance is the predominant feature and primary cause of obesity-related metabolic disorders. Increased intra-abdominal fat content is the main reason for insulin resistance and subsequent development into type-2 diabetes in patients with abdominal obesity [2]. Although the mechanism for increased visceral fat-induced insulin resistance is unclear, studies indicate that the intra-abdominal fat cells in people with obesity are greater in size, meaning they have more resistance to insulin and conduct lipolysis more easily to release more free fatty acids (FFAs) [3]. Low-dose spiral computed tomography (CT) can be used to determine the nature of adipose organisation, and can accurately calculate intra-abdominal fat-binding using specialized software and is therefore considered the gold standard for measurement of intra-abdominal fat [4].

Obesity is associated with chronic subclinical inflammation, therefore much research is presently focused on the relationship between cell factors secreted by intra-abdominal fat and insulin resistance [5,6]. Inflammatory cytokines can interfere with the signal transduction pathway of insulin receptor substrate (IRS)/phosphatidylcholine-3-kinase, inducing defects in signal transduction after insulin receptor-activation on target cells to cause insulin resistance.

Glucagon-like peptide-1 (GLP-1) is a hormone that acts on pancreatic β cells in a glucose-dependent manner, promoting insulin gene transcription, increasing insulin biosynthesis and secretion, and inhibiting glucagon secretion to control blood sugar. However, because GLP-1 is rapidly degraded by dieptidyl peptidase-4 (DPP-4) in human blood, resulting in a very short in vivo half-life [7] it is difficult to obtain for clinical application. Exenatide is an artificially synthesized polypeptide analogue of natural GLP-1 and can therefore combine with the GLP-1 receptor for its activation [8]. However, exenatide cannot be degraded by DPP-4, therefore its plasma half-life is significantly longer than that of GLP-1 [9].

Treatment of patients with obesity and type-2 diabetes is difficult and poses a significant clinical problem. In many cases, patients find it difficult to achieve both sugar level reduction and weight loss. For many of these patients, metformin treatment alone cannot safely control blood sugar level

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