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Brief Communication

Mechanisms of bariatric surgery in control of type 2 diabetes and Alzheimer's diseases: GLP-1 is the key factor-Maybe

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Introduction

Obesity is the primary cause of hyperinsulinemia, which potentiates insulin resistance that may trigger type 2 diabetes (T2D) and increases the risk for dementia (1-3).

Globally, the number of people with diabetes mellitus has quadrupled in the past three decades, and diabetes mellitus is the ninth major cause of death. About 1 in 11 adults worldwide now have diabetes mellitus, 90% of whom have type 2 diabetes mellitus (T2DM). Asia is a major area of the rapidly emerging T2DM global epidemic, with China and India the top two epicenters (4).

The prevalence and incidence of dementia increase exponentially from the age of 65 onwards. As a consequence of the progressive aging of the population and the increase in life expectancy, the number of cases of dementia will increase in the coming decades. Recent studies point to a slight drop in the accumulated risk of dementia adjusted by age groups and sex over the last few decades in some countries (5). Obesity associated with a higher risk for dementia (6).

Bariatric surgery may help to diminish Alzheimer's disease risk, while offering other health benefits to patients with severe obesity. Similarly, metabolic surgery in diabetic non-obese patients might delay the onset of Alzheimer's disease in addition to providing glycemic control (7).

Surgery is an effective treatment of type 2 diabetes mellitus in obese patients. The most optimal surgical procedure for the treatment of obese patients with type 2 diabetes mellitus is still to be established. More research is needed to explore the mechanisms of glycemic control after bariatric surgery (8).

We reviewed the effect of molecular pathway of bariatric surgery on T2DM and Alzheimer remission that is likely to be related to increased production of the incretin hormone, GLP-1. So that it is important to increase GLP-1 receptor agonists (GLP-1RAs) as a complementary pathway for bariatric surgery.

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Methods

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Results

Obesity continues to be a worldwide health problem in the twenty-first century. Bariatric surgery is a safe and effective long-term treatment for severe obesity that results in long-term weight loss, improvement and remission of obesity-related comorbid conditions (particularly T2DM and Alzheimer disease), improvement in quality of life and prolonged survival. New minimally invasive procedures, endoscopic devices and lower BMI indications will probably increase the adoption of the surgical treatments for patients with obesity.(9)

Studies show bariatric surgery as an effective treatment of type 2 diabetes mellitus in obese patients. The most optimal surgical procedure for the treatment of obese patients with type 2 diabetes mellitus is still to be established. More research is needed to explore the mechanisms of glycemic control after bariatric surgery (8, 9). Also Bariatric surgery may reduce the risk of Alzheimer's diseases (7).

Glucagon-like peptide-1 (GLP-1) is an incretin hormone that binds to GLP-1 receptors mainly expressed on pancreatic beta-cells and the gastrointestinal system, which are G-protein coupled receptors (10). Largely from preclinical models, but data from patients as well, support a role of the postprandial rise in GLP- 1 as driving the increased insulin and decreased glucose response to a meal. Less, clear is the extent to which GLP-1 changes are responsible for T2DM resolution.(11)

A systematic review e on the management of postoperative GLP-1 analogue usage after metabolic surgery revealed that GLP-1 analogues may have beneficial effects on additional weight loss and T2D remission postoperatively (12).

GLP-1 receptors are also found in the brain (13). GLP-1 in the brain, similar to insulin, is principally a growth factor that increases cell growth, proliferation, and repair and inhibits apoptosis (14). GLP-1 protects against excitotoxic cell death and induces neurite outgrowth and oxidative injury in cultured neuronal cells (15).

So that bariatric surgery may reduce the risk of Alzheimer's diseases through GLP-1 mediated neuroprotective effects (7). Svane et al showed that food intake increased with combined blockade of GLP-1 and peptide YY (PYY) actions after RYGB. This study support that these hormones have a role in decreased food intake postoperatively.(16). Guida et al (2018) investigated changes in pancreatic PYY in diabetes and following RYGB. RYGB strongly increased islet PYY content, but did not lead to full restoration of pancreatic GLP-1 levels. Proteolytic enzyme dipeptidyl peptidase IV (DPP-IV) Modulate islet PYY. DPP-IV inhibition or RYGB caused Local regulation of pancreatic PYY that can directly modulate the insulin secretory response to glucose and indicate a novel role of pancreatic PYY in diabetes and weight-loss surgery (17).

The effect of bariatric surgery upon weight loss is less clear. It is possible that the acute calorie restriction which occurs immediately post surgery, coupled with a beneficial hormonal milieu promotes weight loss which, unusually, can be maintained over the long-term. This may, at least in part, be related to sustained increases in satiety-promoting peptides (GLP-1, glucose-dependent insulinotropic hormone , PYY3-36, oxyntomodulin, gastrin) and reductions in hunger-promoting factors (ghrelin) (18)

GLP-1RAs are approved for treating T2DM (19, 20). As a drug class, GLP-1RAs have proven efficacy for lowering glycated haemoglobin (HbA1c) and decreasing weight in T2DM, with a reduced risk of hypoglycaemia compared with insulin (Table 1) (20).

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Table 1. Some drug as GLP-1 receptor agonists and Percentage amino acid sequence similarity to native GLP-1

	Exenatide twice daily	Exenatide once weekly	Liraglutide once daily	Albiglutide once weekly	Dulaglutide once weekly	Taspoglutide once weekly
Properties of the drug	Resistant to DPP-4 cleavage, largely due to the substitution of alanine in position 2 by glycine (22)	Encapsulated in biodegradable polymer microspheres (23)	C-16 fatty acid confers albumin binding and heptamer formation (24)	GLP-1 dimer fused to albumin(25)	The GLP-1 portion of the molecule is fused to an IgG4 molecule, limiting renal clearance and prolonging activity (26)	Modifications designed to hinder cleavage by DPP-4 and by serine proteases and also allows greater receptor binding (27)
Percentage amino acid sequence similarity to native GLP-1	53%(28)	53%(28)	97%(24)	95%(25)	90% (26)	93%(27)

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