Obesity, Insulin Resistance, Diabetes, and Related Cardio Metabolic Complications: Immune and Inflammatory Processes

Monica Gaetano*

Department of Diabetes, University of Galway, Ireland

Corresponding Author*

Monica Gaetano,

Department of Diabetes, University of Galway, Ireland

Phone: 3538922016734

E-mail: gaetano.monica@ucd.ie

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Abstract

Diabetes and obesity are becoming more commonplace worldwide. Obese people have significant rates of vitamin deficiencies while overindulging in food. Diabetes may occur in the obese population as a result of deficiencies in certain vitamins and minerals that are crucial for insulin signalling pathways and glucose metabolism. This essay evaluates the available data that backs up this claim.

A significant health challenge is the high prevalence of obesity and diabetes in both developed and developing countries. One of the main causes of type 2 diabetes and insulin resistance is obesity. The primary cause of type 1 diabetes is insulin insufficiency brought on by the autoimmune-mediated death of pancreatic beta cells. This is typically followed by changes in lipid metabolism, increased inflammation and oxidative stress caused by hyperglycemia, endothelial cell failure, and apoptosis. Similar to type-1 diabetes, type-2 diabetes is characterised by increased inflammation, glucotoxicity, lipotoxicity, and apoptosis, which result in the progressive death of beta cells and, in the later stages of the disease, insulin insufficiency. Therefore, inflammation in diabetes may be brought on by immunological response or hyperglycemia. Elevated inflammatory events, however, may impact insulin responsiveness in target tissues, leading to insulin resistance, as well as insulin production in type-2 and type-1 diabetes. Although type-2 diabetes has historically been linked to insulin resistance, growing evidence suggests that type-1 diabetes is now seeing an increase in insulin resistance. Deciphering the role of inflammation in insulin resistance in type-1 and type-2 diabetes, therefore, requires fresh mechanistic techniques. The pathophysiological causes of insulin resistance are numerous. Although the precise nature of these components is not well understood, a strong majority of experts agree that oxidative stress, inflammation, and genetic, dietary, environmental, and epigenetic factors are involved.

Keywords: Cardio-metabolic disorderα-1 antitrypsin; Immunology; Inflammatory response; Type 1 diabetes; Effero-metabolism; Resolution Pharmacology

Introduction

As the most economically significant modifiable risk factor for public health and illness, obesity is expected to overtake tobacco use in both the United States and the rest of the world. The rising trend in obesity is a result of numerous genetic, environmental, and behavioural variables. Over the past 40 years, there has been a significant increase in the supply of low-priced, high-calorie, and nutrient-poor foods, which is a major factor in the global rise in obesity. The amount of micronutrients in popular foods has decreased somewhat as a result of modern agricultural and food processing methods. Despite eating more calories than necessary, vitamin shortages are relatively common in fat people. A lack of some micronutrients may contribute to the onset of type 2 diabetes due to their significance as cofactors in the insulin signalling cascade, pancreatic beta-cell function, and the metabolism of glucose [1].

Patients who are obese have a 4-fold greater chance of developing type 2 diabetes. Obesity and diabetes are related to one another in a complex way. Obese people are more likely to acquire diabetes because of increased incretin hormone resistance, oxidative stress, pancreatic beta-cell malfunction, hereditary, and behavioural variables. Obese people's specific micronutrient deficiencies may also affect how type 2 diabetes develops. Obese people and diabetics have been found to have high rates of vitamin D inadequacy and outright deficiency. 80–90% of obese people have vitamin D deficiency, which is indicated by a blood level of less than 30 mg/dL. While there is some debate regarding the best course of treatment for people with mild vitamin D deficiency, particularly in light of vitamin D supplementation's alleged extra skeletal effects, a substantial body of research indicates that vitamin D supplementation may have some positive effects on glucose metabolism and insulin signalling in people with type 2 diabetes or impaired glucose tolerance [2].

The existence of vitamin D receptors in human pancreatic -cells, the observation of 1-hydroxylase activity, and the responsiveness of insulin gene transcription to vitamin D in pancreatic -cells provide preclinical evidence for the role of vitamin D in insulin secretion and function. Animals without enough vitamin D exhibits pancreatic -cell malfunction, which can be corrected with vitamin D administration. Numerous epidemiological researches show a negative correlation between the amount of 25-hydroxyvitamin D and the prevalence of type 2 diabetes. Variations in vitamin D levels may also contribute to seasonal variations in the glycemic control of type 2 diabetics, while behavioural differences may also account for these results [3].

The development of type 2 diabetes in high-risk patients may be influenced by vitamin D administration, according to recent reviews and metaanalyses of clinical studies. In people with insulin resistance or impaired fasting glucose, three of five randomised trials show improvements in insulin sensitivity with vitamin D treatment. In one study, supplementing 71 obese males with 120,000 increased their ability to tolerate oral glucose and their insulin sensitivity. A second trial that gave 81 vitamin D deficient participants with baseline insulin resistance 4,000 i.e. cholecalciferol daily or a placebo demonstrated improvement in insulin sensitivity and lowered fasting insulin levels after 6 weeks of follow-up. After three years of daily supplementation with 700 i.e. of cholecalciferol, patients in the third study who had impaired fasting glucose levels demonstrated stability in those levels as opposed to an increase in the placebo group's fasting glucose levels. The effects of vitamin D supplementation were not demonstrated in two trials. Over 89% of the participants in one of these did not reach normal levels of vitamin D by the end of the experiment because it only employed low doses of vitamin D (400 i.e. daily), which may not have been sufficient. According to the findings of these five trials, vitamin D supplementation may be advantageous for people who are at risk of developing type 2 diabetes [4].

Research has also been done on the usage of vitamin D in people who have type 2 diabetes already. Two of the four recently released randomised trials show advancements in glycemic control. In one study, 92 people with early type 2 diabetes—defined as having a glycosylated haemoglobin level below

5.8% and a 2-hour postprandial glucose level below 140 mg/dL—were randomised to receive 2,000 IU of cholecalciferol or a placebo once a day for four weeks. The therapy group showed a discernible improvement in the assessed glucose disposition index. In another study, 90 type 2 diabetic patients who received 1,000 IU of cholecalciferol or a placebo once a day for 12 weeks showed increased insulin sensitivity, lowered fasting glucose by 13 mg/dL, decreased glycosylated haemoglobin by 0.4%, and 1-2 kg of weight reduction in the treatment group [5].

Patients who received a single dose of 300,000 international units (i.e.) of cholecalciferol found no change in fasting glucose, fructosamine, or insulin sensitivity despite normalisation of plasma 25-hydroxyvitamin D levels in one of the studies that showed minimal effect of vitamin D supplementation in type 2 diabetics. However, in this trial, appropriate serum 25-hydroxyvitamin D levels were not attained. At the end of the follow-up period, the average 25-hydroxyvitamin D level was 16 ng/dL [6].

The second unfavourable study involved 32 diabetic patients who received 40,000 units (i.e.) of cholecalciferol or a placebo every two weeks. There was no difference in the amount of glycosylated haemoglobin, fasting blood glucose, or insulin sensitivity. In this experiment, subjects in both treatment arms had rather high baseline levels of 25-hydroxyvitamin D (24 ng/dL), which may have influenced the unfavourable outcomes.

It is still debatable whether vitamin D supplementation should be used especially to increase insulin sensitivity. Ten on-going clinical trials that examine the utilisation of vitamin D supplements in people with type 2 diabetes and people with impaired glucose tolerance may offer more insight on this subject. Clinicians may think about vitamin D supplementation in this population given the high incidence of vitamin D insufficiency in the obese community and the advantages seen [7].

Methods and Materials

The Health Research Ethics Committee at AM University approved the study, which was carried out in compliance with the guidelines of the Helsinki Declaration. Each participant provided written informed permission after being told of the study's purpose. In a cross-sectional study, patients with T1DM and T2DM who had not previously received an osteoporosis diagnosis totalled 98 (female: 57/male: 41) and 137 (female: 85/male: 52), respectively. Patients who participated in the survey ranged in age from 40 to 70 (55.8 0.7 for T1DM and 58.4 0.9 for T2DM). With a mean HbA1c of 57 0.2 for T1DM and 58 0.4% for T2DM, respectively, the average duration of diabetes was 16.6 0.6 for T1DM and 8.1 0.7 for T2DM; 42% and 88% of patients with DM had neuropathy and retinopathy, respectively [8].

Patients with acute complications of diabetes, hepatic dysfunction, renal dysfunction, and diabetic nephropathy of the 4-5 stages in the anamnesis were excluded, as were patients who have received treatment with steroids, glitazones, and type 2 sodium-glucose transporter (SGLT-2) inhibitors, who have received treatment for osteoporosis, or who have a history of fracture. The control group included 82 patients (age: 55.9 0.9; females: 48; males: 34). As controls, normoglycemic subjects who appeared healthy were chosen. The BMI of the control group was 28.7 0.4 kg/m^2.

Standardized methods were used to measure both height and weight. BMI was calculated as weight per square of height (kg/m2). Before 10 a.m., blood samples were taken centrifuged in heparin, frozen at 70°C, and then quickly thawed before serum biomarker and hormone analysis. An automatic electrochemiluminescence analyzer was used to measure the biochemistry panel, which included HbA1c, sodium, potassium, magnesium (Mg2+), total calcium (tCa), ionised calcium (Ca2+), phosphate (P+), creatinine, albumin, alkaline phosphatase (ALP), amino terminal propeptide of procollagen type I (PINP), and C-terminal telopeptide of type I collagen (be (COBAS C, Roche Diagnostics GmbH Mannheim, Germany) [9]. The CKD-EPI equation was used to compute glomerular filtration rate (GFR) as follows: (=141 min (SCr (smg/dl)/k, 1)a max (SCr/k, 1)1,209 0.993 age (x1.018 if female) (in ml/min/1.73 m2). According to the manufacturer's instructions, commercially available ELISA tests of insulin, parathyroid hormone (PTH), calcitonin (CT), and vitamin D (25(OH) D) were run. The homeostasis model assessment of insulin resistance (HOMA-IR) used the following equation to calculate insulin sensitivity: (fasting insulin (mIU/ml) fasting glucose (mmol/L))/22.5.

On a densitometer (DXA HOLOGIC, Discovery QDR 4500A, and USA), all individuals had DXA for the lumbar spine, proximal, and femoral neck regions. The World Health Organization uses BMD (T-score 2.5 SD), osteopenia (T-score between 1 and 2.5 SD), and normal (T-score > 1) as the criteria for diagnosing osteoporosis. The STATISTICA 10 tool was used to conduct the statistical analysis. Unless otherwise stated, data were reported as mean (M) and confidence interval (95% CI). The Mann-Whitney U test was used to examine unpaired parametric data included in the statistical analysis. To evaluate the strength of the relationship between the parameters, Spearman's rank correlation was determined [10].

Discussion

Numerous variables, including diabetes, raise the risk of diseases of bone turnover. As a result, we studied biochemical markers of bone metabolism in patients of the same age who were both healthy and diabetic. Only patients with well-controlled diabetes and no late-stage complications made up the institutionalised group. The association between the Ca2+ and 25(OH)D level for T1DM (R = 0.507); for T2DM (R = 0.277;) indicates that there was some variation in the serum concentration of vitamin D between the three patient groups. Vitamin D acts by promoting intestinal absorption of calcium and phosphorus. As a result, vitamin D controls the equilibrium of calcium and phosphorus.

The ability of the kidneys to eliminate these signals, which clears the circulation and lowers GFR, is related to the connection between bone remodelling markers and renal function. For instance, a lower GFR will result in less CTX being excreted through the urine, which will raise serum levels. According to studies, there is a strong relationship between GFR and vitamin D (R = 0.346), as well as PTH and GFR in T2DM (R = 0.213). Phosphate retention, which results from a decline in renal function, aids in the development of secondary hyperparathyroidism by a number of interrelated processes [11].

In line with previously published data, the mean values of the bone resorption marker b-CTx in both DM groups were higher than those in the control group but within reference intervals, indicating enhanced bone resorption. Additionally, the analysis's findings showed that people with low serum b-CTx had higher BMIs, as has been shown in a number of other researches. HbA1c and P1NP were found to be significantly inversely related in both T1DM and T2DM (R = 0.252 and 0.254, respectively). The adverse connection suggested that elevated blood glucose levels may impact bones by disrupting the process of bone production; as a result, those with diabetes are more likely to sustain fragility fractures.

Patients with both DMs exhibited a higher incidence of bone fractures in the lumbar spine T-score (64% for T1DM and 44% for T2DM; 26% for controls) and femoral neck area (41% for T1DM and 36% for T2DM; 22% for controls) according to an analysis of bone density. The probability of a bone fracture in the proximal femur region was also reduced (36% for T1DM and 31% for T2DM compared to 20% for controls). These results are in line with those of other studies, too. Patients under the age of 50, particularly men, showed the greatest severity of the lowered bone mineral content, which varied depending on the length of diabetes.

Our study has a number of advantages. First off, patients with T1DM and T2DM show an inverse relationship between serum electrolytes, hormone levels, and BMD in this study. The cross sectional design that was adopted in this investigation only allowed for the measurement of the investigated parameters at a single time point, placing restrictions on the study's scope. The small sample size may limit the importance of our findings, and some of the results described may be erroneous due to inadequate data access. As a result, several important statistics could not be quantified further, which could have an impact on the choice of controls. BMD was only measured once at each anatomical site after we obtained all of the participants' serum samples; this could be why some factors varied (bone remodelling marker levels and BMD values) [12].

Conclusion

The findings of this investigation demonstrate that, regardless of age or length of disease, patients with T2DM exhibited lower b-CTx values and significantly greater levels of P1NP, implying less dramatic changes in bone metabolism than patients with T1DM. According to research, osteoporosis was found

more commonly in T1DM patients (50%) than in T2DM patients (13%). Bone density and biochemical indicators can be used to identify skeletal metabolism problems. However, in some circumstances, such as in the early phases of T2DM, when the BMD measurement does not accurately reflect the actual tendency, bone remodelling markers may be helpful to enhance the assessment of the condition of bone tissue. When assessing the condition of bone tissue in the early stages of diabetes, bone remodelling markers can be helpful because changes in bone microarchitecture may not always be picked up by tests of bone mineral density.

Conflict of Interest

None

Acknowledgement

None

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