GDM susceptibility in pregnant women is most commonly associated with SNPs in the tcf7l2 gene, the product of which is an effector of the canonical Wnt signaling pathway. It has also been reported that certain actions of steroid hormones are mediated by Wnt signaling. Moreover, we found that tcf7l2 and other components of this pathway (β-catenin, lrp5) were up-regulated following treatments with E2 (3.8±0.2 fold, p<0.001 in GWAT; 5.3±0.2 fold, p<0.001 in soleus) and P2 (2.1±0.2 fold, p<0.05 in GWAT; 2.9±0.3 fold, p<0.001 in soleus). We therefore hypothesized that the metabolic actions of these steroids may be mediated by Wnt signaling. To test this hypothesis, we conducted experiments in which OVX rats treated with steroids as described above, were additionally treated with niclosamide (NIC), a Wnt pathway inhibitor. NIC in conjunction with E2 increased GWAT accumulation and lipogenesis, thereby reversing the action of E2. NIC treatment in OVX rats did not change these parameters, indicating that this effect is specific to the inhibition of Wnt signaling modulated by E2. Additionally, NIC inhibited the E2-modulated increase in insulin sensitivity in GWAT and soleus. Taken together, the results suggest that the actions of E2 on insulin sensitivity and lipogenesis are mediated by the Wnt signaling pathway. No such observation was made with respect to the effect of P2 on lipogenesis. Understanding the mechanistic actions of these steroids may play an important role in devising methods to prevent conditions like GDM before its onset.

Adipose Tissue, Appetite, and Obesity

OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

The Efficacy and Safety of Sodium-Glucose Transport Protein 2 (SGLT-2) Inhibitors for Weight Loss Among Individuals Without Diabetes: A Systematic Review and Meta-Analysis

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Background

With the growing prevalence of obesity and its associated metabolic consequences, new strategies for safe and effective weight loss are called for. SGLT2i is a class oral antidiabetic agents that lowers glucose levels through renal glucose loss, with weight reduction as a consequence. Hence, its role in diabetes and obesity is well-recognized. However, its use among individuals without diabetes for safe and durable weight loss has not yet been sufficiently evaluated, although initial studies are promising.

Objective

To determine the efficacy and safety of SGLT2i compared to placebo among subjects without diabetes mellitus in terms of weight loss and adverse effects.

Methods

A meta-analysis was conducted on randomized controlled trials (RCTs) comparing different SGLT2i and placebo among patients without diabetes mellitus using RevMan 5.3 software.

Results

Five trials involving 779 patients met the eligibility criteria. SGLT2i used in these studies include Canagliflozin, Dapagliflozin, Sergliflozin and Remogliflozin with treatment duration ranging from 2 to 26 weeks.

Pooled data of these 5 trials showed a significant difference in weight loss among subjects given SGLT2i (MD -1.34 kg [95% CI -1.51, -1.17]; p < 0.00001, I² = 0%) as compared to placebo. Four studies reported change in BMI as an outcome measure, likewise showing a significant difference favoring the use of SGLT2i (MD -0.50 [95% CI -0.56, -0.44]; p < 0.0001, I² = 0%). Two RCTs reported the percentage of weight loss. There was a significantly higher proportion of subjects achieving >5% weight loss among those given SGLT2i (RR 1.61 [95% CI 1.09, 2.38]; p = 0.02, I² = 0%). There was no significant difference in the proportion of subjects who achieved >10% weight loss (RR 1.42 [95% CI 0.60, 3.33]; p = 0.42, I² = 12%). Urogenital infections were more common in the SGLT2i group (RR 2.62 [95% CI 1.76, 3.91], p < 0.00001, I² = 0%) as reported in 4 studies. Only one study reported occurrence of hypoglycemia which did not differ significantly between both groups.

Conclusion

Although this meta-analysis shows a statistically significant decrease in weight (-1.34 kg, [95% CI -1.51, -1.17]) with the use of SGLT2i among subjects without diabetes, this might not be clinically relevant. With the increased risk of urogenital infections with its use, there is insufficient evidence to recommend its routine use as monotherapy for weight loss outside the population of individuals with diabetes.

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Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS II

Acute Abdominal Pain and the Pheochromocytoma

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MON-915

Background:
Pheochromocytomas are neuroendocrine tumors that release large amounts of metanephrines and catecholamines, resulting in a wide array of symptoms including hypertension, diaphoresis, and headaches. If left unrecognized they can lead to serious morbidity including ischemic or hemorrhagic CVA, encephalopathy, MI, Aortic Dissection, and renal injury.

Clinical Case:
A 62-year-old male began having difficulties with his blood pressure over the past year. He was first hospitalized for an acute ischemic CVA with hypertensive urgency. His blood pressure was generally controlled throughout the admission but he continued to have intermittent elevations. After transferring to an inpatient rehabilitation unit he had an episode of acute nausea, severe lower abdominal pain, and emesis following dinner. He was tachycardic and
Hypertensive saline stimulated copeptin measurements have recently been described for the diagnosis of central DI. A copeptin cut-off of >4.9 pmol/L has a diagnostic accuracy of 96.5% for distinguishing primary polydipsia from central DI (3). A copeptin assay has recently been established in our laboratory. Validation of hypertonic saline-stimulated copeptin concentrations in our local population is needed before this test can be used with confidence in patients presenting to our institution with polyuria-polydipsia syndrome. The aim of this study was to develop a local reference range for hypertonic saline-stimulated copeptin in healthy volunteers.

Twenty healthy volunteers (10 male and 10 female) were recruited. Subjects underwent a hypertonic saline test, as previously described (3). Hypertonic saline (3%) was administered as an initial 250 mL bolus followed by 0.15 mL/kg/minute until a target serum sodium of ≥150 mmol/L was reached. At this time, blood was drawn for copeptin.

Twelve healthy volunteers (7 females; 5 males) have undergone the study to date. Median age was 28 years (range 26-50); median body weight 75.7 kg (range 57.9 -94.5); median baseline plasma sodium 138 mmol/L (range 136 - 140) and median serum osmolality 289.5 (range 281-297). Median peak sodium was 152 mmol/L (range 150-154) with osmolality 314.5 mmol/kg (range 306-320). Median volume of hypertonic saline infused was 1583 mL (1230-2177) and median hypertonic saline stimulated copeptin was 29.2 pmol/L (9.6-167.4). Overall symptom burden was 5/10 (range 3/10-9/10). There were no serious adverse events.

Development of a local reference range for hypertonic saline-stimulated copeptin measurements will assist in interpretation of the test in our local population of patients presenting with polyuria-polydipsia syndrome.

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