Diabetes Mellitus and Glucose Metabolism

DIABETES DIAGNOSIS, TREATMENT AND COMPLICATIONS

Is the Stepping-Down Approach a Better Option Than Multiple Daily Injections in Patients With Chronic Poorly-Controlled Diabetes on Advanced Insulin Therapy?

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In the traditional step-up approach, patients with poorly-controlled T2DM are eventually advanced to multiple daily insulin injections (MDI). However, some on advanced insulin therapy (AIT) continue to have poor control due to poor compliance with MDI and fear of insulin-induced weight gain. The recent guidelines recommend the use of anti-hyperglycemic agents with weight loss benefits, such as SGLT2i or GLP1 RA, with basal insulin before the patients are advanced to MDI. Objective: To determine if de-escalating from AIT to the combined use of metformin, SGLT2i, GLP1 RA and basal insulin by using the stepping-down approach is a better option than MDI in obese patients with poorly- controlled T2DM on AIT. Research Design: This pilot, prospective, randomized, open-label, controlled, parallel-group trial enrolled 22 obese patients with T2DM on AIT, who had BMI ≥30 kg/m2, A1c >8% and eGFR >45. Patients were randomized to either intervention (Step-Down) or control (MDI) group. In the control group, the patient was advised to remain on MDI. In the intervention group, all prandial insulin injections were discontinued; but the patient remained on the basal insulin and metformin to which SGLT2i, Empagliflozin, and GLP1 RA, Dulaglutide, were added. They were followed up for 16 weeks. The primary outcome was A1c change and secondary outcomes were the change in fasting BG, weight, BP, HR, fasting lipids, serum Na and K, serum Cr, liver enzymes, CBC and Diabetes Medications Satisfaction (DM-SAT) scores at 16 weeks. Results: There was no difference in A1c between 2 groups (10.36% vs 9.69%;p=0.171) at baseline. However, A1c was significantly lower at 4 weeks (9.54% vs 7.31%; p=0.0088) and 16 weeks (9.7% vs 8.25%; p<0.001) in intervention group (n=10). Compared to baseline, in the control group (n=8), there was no significant change at secondary outcome variables except slightly higher SBP at 16 weeks. In intervention group, compared to baseline, there was a significant decrease in weight (-16.38 Lbs; p=0.003), BMI (-3.06; p<0.001), LDL cholesterol (-15.7 mg/d; p=0.0378), total cholesterol (-18.5 mg/dL; p=0.0386), total daily insulin dose (-57.3 units; p<0.001) and a significant improvement in DM-SAT patient satisfaction 0-100 scores - total score (+45.3; p <0.001) and subscale scores (Convenience +35.28, p =0.019; Lifestyle +35.8, p=0.0052; Medical control +51.3, p<0.001; Wellbeing +47.2,p=0.0091) at 16 weeks. Conclusions: De-escalating from AIT to the combined use of metformin, SGLT2i, GLP1 RA and basal insulin in obese patients with poorly-controlled T2DM by using the stepping-down approach results in the significant improvement in glycemic control, weight loss, and significantly higher patient satisfaction. This noble stepping-down approach may be a better option than continuing MDI in such patients. This pilot study result needs to be confirmed with a larger trial. ClinicalTrials ID: NCT02846233

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CLINICAL AND TRANSLATIONAL STUDIES IN DIABETES

Differences in Metabolic Control, Treatment and Associated Complications in Patients Living With Type 1 Diabetes Receiving Private or Public Health Care in Mexico.

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Differences in metabolic control, treatment and associated complications in patients living with Type 1 Diabetes receiving private or public health care in Mexico. **Background.** Type 1 Diabetes (T1D) is the most common chronic endocrinological disease diagnosed during childhood. It requires continuous education, monitoring and treatment. An analysis was developed to learn if there were discrepancies in the level of metabolic control and complications between private and public healthcare in Mexico, based on the data obtained in the National Registry of patients with Type 1 Diabetes (RENACED DT1). **Objective:** Describe the sociodemographic characteristics, metabolic control, treatment and complications in patients receiving private or public health care registered in RENACED DT1.**Methodology**: Sociodemographic and anthropometric variables,

metabolic control, diabetes education, type of insulin and delivery method used for treatment, glucose monitoring and acute and chronic complications were compared between patients receiving private vs public health care. **Results** Of the 1458 patients registered, significant differences between HbA1c levels were seen (7.8% private health care vs 8.7% public healthcare, p<0.001), achievement of glycemic goal HbA1c <7% (30.1% private healthcare vs 19.6% public healthcare, p<0.001). In private institutions, 47.1% of patients use an insulin pump and 44.7% a basal bolus regimen with insulin analogues (MDI) (p<0.001). Meanwhile in public institutions, 2.6% use an insulin pump and 84.8% use MDI (p<0.001). 30.4% of patients in private institutions check their blood glucose levels 6 to 10 times a day vs 14.3% of patients from public institutions (p<0.001). Continuous glucose monitoring is used in 46.4% of patients from private healthcare vs 5% from public healthcare (p<0.001). A larger number of patients from private healthcare use insulin to carbohydrate ratios to calculate meal insulin compared with patients from public healthcare (89.1% vs 31.3%, p<0.001). No significant differences were found related to the incidence of mild to moderate hypoglycemia, but there was a higher incidence of severe hypoglycemia in the public sector compared to the private one (57 vs 43%, p<0.001). Also, a higher prevalence of diabetic nephropathy was found in patients from public vs private healthcare (82.9 vs 17.1%, p=0.034). **Conclusions:** Significant differences were found in glucose monitoring, carbohydrate counting and insulin delivery methods, between patients from public and private healthcare, which could explain the differences observed in metabolic control and diabetes associated complications. It is imperative that better public policies are implemented in public health, to reduce this health disparity.

Reproductive Endocrinology
REPRODUCTIVE ENDOCRINOLOGY: REPRODUCTIVE FUNCTION AND DYSFUNCTION ON DEVELOPMENT

A Preconception Lifestyle Intervention Maintained Throughout Pregnancy Improves Some Gestational and Neonatal Outcomes in Women With Obesity and Infertility

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Background: Obesity in women of childbearing age is associated with infertility and increases significantly the risks of many pregnancy and neonatal complications. Adopting a healthy lifestyle prior conception and maintaining it during pregnancy may reduce these complications. Our aim was therefore to determine whether a lifestyle program targeting women with obesity and infertility and maintained during pregnancy improves gestational and neonatal outcomes.
Methods: We report on 46 women who became pregnant and had available outcome data during pregnancy and at birth, among 127 women with infertility and obesity (body mass index, BMI ≥30 kg/m²), or overweight with PCOS (BMI ≥27 kg/m²), who were enrolled in a lifestyle randomized-controlled trial. Participants were randomized to the control group (CG, n=20), who received standard of care, or the lifestyle group (LSG, n=26), who followed a lifestyle program alone for 6 months, and then in combination with usual fertility care for 18 months or until the end of pregnancy. Pregnancy and neonatal outcomes were retrospectively retrieved from mothers' and newborns' medical records.
Results: At enrollment, both groups were similar for age (29.3 vs 31.0 years), BMI (38.7 vs 38.4 kg/m^2) and waist circumference (113.7 vs 112.7 cm). Preconception weight loss was significantly higher in the LSG compared to the CG (4.86 kg vs 1.21 kg, p=0.013), but gestational weight gains were similar (+10.83 vs +10.52 kg, p=0.987). During pregnancy, groups did not differ for the rates of preeclampsia, gestational diabetes or other clinical outcomes, but significantly less women in the LSG required insulin for treatment of their gestational diabetes (12.5% vs 42.1%, p=0.027) as well as urgent cesarean section due to failure of vaginal delivery (0.0% vs 21.1%, p=0.021). Regarding neonatal outcomes, there was no significant difference between groups for gestational age, weight at birth and head circumference, as well as rates of prematurity, LGA, SGA, birth defects or other clinical outcomes, but babies from the LSG displayed significantly lower tricipital skinfolds (4.73 mm vs 5.72 mm, p=0.031) and trends for lower sum of four skinfolds (16.61 mm vs 19.06 mm, p=0.056) and increased length at birth (50.82 cm vs 49.63 cm, p=0,053).
Conclusion: In women with obesity and infertility, our lifestyle program initiated prior to fertility treatments and maintained throughout pregnancy improved their preconception weight and lifestyle, but not their gestational weight gain. Such intervention was nonetheless effective to reduce significantly some clinically relevant pregnancy and neonatal complications. If these results are replicated in a larger sample, it would strongly suggest that women with obesity should be supported to adopt a healthy lifestyle prior conception in order to increase their likelihood of giving birth to a healthy baby.

Diabetes Mellitus and Glucose Metabolism
DIABETES COMPLICATIONS II

Diagnosis and Management of Euglycemic DKA in the Setting of SGLT2 Inhibitor Use and Prostate Abscess

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Introduction: SGLT2i has been associated with euglycemic DKA by increasing lipid oxidation and glucagon synthesis. In the event of an underlying infection, increased ketogenesis could lead to the presentation of DKA. **Clinical case:** A 35 year old male patient who was