Effects of Evogliptin as Add on in Type 2 Diabetes (T2DM) Subjects Inadequately Controlled With Metformin and Glimepiride Combination

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Objective: To achieve targeted glycemic control people with diabetes required multiple drug therapy. We retrospectively studied effect of adding newly approved DPP4i evogliptin in T2DM subjects having high HbA1c value despite being on tolerable stable doses of Metformin and Glimepiride. **Methods:** We retrospectively analysed the effects of evogliptin 5 mg OD over 6 month preriod when added to patients who were initially having HbA1c ≥ 7.5% on on stable fixed dose combination of Metformin (1000 -2000 mg/day) and glimiperide (2 - 4 mg/day) at least from 3 months prior. Any patients who were other OHA drugs or in Insulin of have been up or down titrated of the studied drug were excluded. We compared HbA1c, fasting (FPG), postprandrial (PPG) plasma glucose, total cholesterol (TC), triglyceride (TG), HDL, LDL at baseline and after 6months of evogliptin initiation. Self-monitored blood glucose (SMBG) was performed using the patients' own BG meter. Physicians gave all patients training to ensure they could perform SMBG correctly and accurately. **Results:** Data of 185 subjects [85(46%) females, Mean age 52.3±2.8 years, mean duration of diabetes 8.2±1.9], who met the inclusion criteria were extracted for analysis from the hospital and clinics records. A drop in HbA1c from 8.8±1.1 to 7.8±0.5% ($p<0.05$) were resulted after addition of evogliptin. FPG decreased from 159.2±13.5 to 128.3±11.2 and PPG from 238.2±28.7 to 188.1±22.6 respectively ($p<0.05$). Total cholesterol (TC), triglyceride (TG) were significantly improved after addition of evogliptin, whereas little effect on LDL and HDL. There was no incidence of severe hypoglycemia, though 7 (3.8%) cases of suspected hypoglycemia were managed at home. **Conclusion:** Evogliptin is a suitable add-on option for those with high HbA1c values as it offer low risk of hypoglycemia despite significant improvement in glycemic parameters.

Diabetes Mellitus and Glucose Metabolism

TYPE 2 DIABETES

Effects of Roux-en-Y Gastric Bypass on Type 2 Diabetes Mellitus

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Abstract: Bariatric surgery is the most effective treatment for classes II and III obesity patients. This surgically induced weight loss is associated with better glycemic control and higher type 2 diabetes mellitus (T2DM) remission rate compared to conventional medical therapy. Roux-en-Y gastric bypass (RYGB) is the most commonly technique performed, and its risks and benefits are well known. We sought to assess the effects of one-year post-RYGB on glycemic control and T2DM remission in a tertiary care teaching public hospital in Porto Alegre, Southern Brazil. This retrospective cohort study included all patients submitted to RYGB between 2010 and 2019 at Hospital de Clínicas de Porto Alegre. Type 2 diabetes mellitus remission was defined as the absence of oral antidiabetic medication and insulin use in association with a glycosylated hemoglobin (HbA1c) <6.5% one-year post-RYGB. This study was approved by the local Ethics Committee (2018-0088). A total of 549 RYGB procedures were performed from 2010 to 2019 among patients aged 42.2 ± 10.7 years, mostly women (84.7%), white (88%), and with a body mass index (BMI) of 49.4 ± 8.5 kg/m². The preoperative prevalence of T2DM was 31.2% (n=171), of which 93.6% used oral antidiabetic medication and 15.6% used insulin. Among T2DM patients, 39% used at least two oral antidiabetic drugs in association, most of them being metformin (91%) and sulfonylureas (19.3%). Preoperative fasting plasma glucose and HbA1c were 143 ± 48.1 mg/dL and 7.3 ± 1.6%, respectively, reducing to 93.6 ± 21.3 mg/dL ($p<0.001$) and 5.4 ± 0.7% ($p=0.002$), respectively, one year after RYGB. Excess weight loss one-year post-RYGB was 68.7 ± 17.1%, similar between patients with and without T2DM ($p=0.48$). At 12 months, 77.4% of T2DM patients discontinued their oral antidiabetic drugs or insulin, and the disease remission rate was 71.3%. Bariatric surgery was effective for T2DM remission among classes II and III obesity patients, which is in accordance with the current literature.
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Diabetes Mellitus and Glucose Metabolism

TYPE 2 DIABETES

Efficacy and Safety of a Sodium-Glucose Co-Transporter-2 Inhibitor Versus Placebo as an Add-on Therapy for People With Type 2 Diabetes Inadequately Treated With Metformin: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Metformin monotherapy is often insufficient to achieve or sustain glycemic targets in people with type 2 diabetes. Therefore, we performed a systematic review and meta-analysis to assess the efficacy, safety and tolerability of sodium-glucose co-transporter-2 inhibitors versus placebo as add-on therapy after metformin in type 2 diabetes. The systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A search was performed in the PubMed, www.clinicaltrials.gov and Cochrane Central Register of Controlled Trials databases for relevant randomized controlled trials up until 30th October 2020 that compared sodium-glucose co-transporter-2 inhibitors versus placebo as add-on therapy to metformin. A random-effects model was used. Thirteen randomized controlled trials (4270 participants) met the inclusion criteria.

Compared with placebo, sodium-glucose co-transporter-2 inhibitor treatment, as add-on therapy to metformin, was associated with a significant reduction in HbA1c level (mean difference [MD]: -0.6%, 95% CI: -0.7, -0.5; p<0.01), fasting plasma glucose level (MD: -1.4mmol/l; 95% CI; -1.5, -1.3; p<0.01), weight (MD: -2.0kg; 95% CI: -2.2, -1.8; p<0.01), systolic blood pressure (MD: -4.7mmHg; 95% Cl: -5.4, -3.9; p<0.01) and diastolic blood pressure (MD: -2.0mmHg; 95% Cl: -2.5, -1.5; p<0.01). Significantly more participants achieved HbA1c <7% (odds ratio [OR]: 3.1; 95% CI: 2.6, 3.6; p<0.01) in the sodium-glucose co-transporter-2 inhibitor group. Genital mycotic infections (OR: 2.6; 95% CI: 1.4, 4.6; p<0.01) were more common with sodium-glucose co-transporter-2 inhibitors, but there was no significant statistical difference in urinary tract infections (OR: 1.4; 95% CI: 1.0, 2.0; p=0.06), in hypoglycemia (OR: 1.5; 95% CI: 1.0, 2.4; p=0.07), or in discontinuation rates due to adverse events (OR: 0.9; 95% CI: 0.6, 1.5; p=0.68) between the two groups. In summary, in comparison with placebo, add-on therapy with a sodium-glucose co-transporter-2 inhibitor is significantly more efficacious in lowering HbA1c, fasting plasma glucose, weight and blood pressure in people with type 2 diabetes following inadequate glycemic control with metformin. The rate of discontinuation due to adverse events was similar despite higher risk of genital mycotic infections.

Diabetes Mellitus and Glucose Metabolism

TYPE 2 DIABETES

HbA1c Is Not Potent Glucose Control Assessment Tool in Type 2 Diabetes Patients Treated With Insulin

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Glycated haemoglobin (HbA1c) is used for defining of glucose control in diabetic patients nevertheless its insufficiency to present overall control in some specific cases. Continuous Glucose Monitoring (CGM) is usually used for adjustment of insulin doses but the derived data are helpful for exact glucose control. We assess the potency of HbAc for defining of real glucose control in subgroup of type 2 diabetes patients treated with different insulin regimens. We studied 54 diabetic patients (33 men, 21 women; age 60.23±5.99 years, disease duration 12.64±5.02 years) - 33 with type 2 diabetes on pre-mixed insulin, 21 with type 2 on multiple insulin injection (MII). Patients performed multiple daily blood glucose measurements of fasting and prandial blood glucose for three months period. HbA1c was measured and CGM by using iPro^{TM} for seven days was performed at the end of this period. In pre-mixed insulin treated group and in intensified regimen group, moderate positive correlation was found between HbA1c and mean blood glucose derived from CGM (7.64±1.40% and 7.69±1.23%, respectively 7.64±1.48mmol/l and 7.60±1.30mmol/l), with r1=0.642 (p<0.01) and r2=0.570 (p<0.05). Even lower was correlation between HbA1c and time-in-range (r1=0.431 and r2 =0.401). There were no correlations between HbA1c and percentage of time spent below the target and number of hypoglycemic episodes in each group. Same trend of correlations was found comparing HbA1c and mean BG level in eight-point profile. Based on HbA1c assessment 36.36% of patients on premixed insulin, 19.05% of type 2 patients on MII were with good control. After estimation of results from SMBG these percentage were respectively 28.14% and 12.11%. CGM defined 27.27% of patients on premixed insulin, 13.80% of type 2 patients on MII as well controlled. We conclude that in insulin treated type 2 patients HbA1c gives relative information about overall control with no precise presenting of glucose fluctuations and out-of-range values of blood glucose with no information about hypoglycemic episodes. Nevertheless, short observed period CGM data could give much information that is comparable to three months blood glucose measurement and could replace the use of HbA1c for assessment of overall control. **Reference:** (1) Chehregosha H, et al. Diabetes Ther. 2019; 10, 853–863 (2) Beyond A1c Writing Group. Diab Care. 2018; 41: e92-e94 (3) Hirsch I et al. Diabetes Tech Ther 2017, 19 (3): S38-S48

Diabetes Mellitus and Glucose Metabolism

TYPE 2 DIABETES

In Obese Patients Without Diabetes, 12 Weeks of Time-Restricted Eating (TRE) Does Not Alter β-Cell Function: A Randomized Pilot Study

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Impairment of β-cell function is a precursor to impaired glucose tolerance, which is a pathophysiological basis for the development of Type 2 Diabetes Mellitus (T2DM). Previous literature has reported varying effects of TRE on metabolic measures in different populations, yet the effect of TRE on β-cell function has not been well-characterized. We hypothesized that in obese patients without diabetes, 12 weeks of TRE (8-hour eating window) would improve β-cell function relative to baseline and the unrestricted eating group (non-TRE). Participants (17 women and 3 men; (mean ± SD); 45.5±12.1 years; BMI 34.1±7.5 kg/m2) with a prolonged eating window (15.4±0.9 hours) were randomized to either TRE (n=11) or non-TRE (n=9) for 12 weeks. Weight and 2-hour oral glucose tolerance (OGTT) were measured during at baseline and end-intervention. B-cell function was assessed by multiple OGTT-based measures, including Glucose AUC, Insulin AUC, insulinogenic index, disposition index, QUICKI index, Matsuda index, Stumvoll index, and Avignon index. At baseline, these measures are within normal range across both groups. We found that TRE did not significantly alter these measures relative to baseline or the non-TRE group. In addition, the degree of eating window restriction did not correlate with any observed changes in β-cell function. We concluded that in obese patients without diabetes, TRE did not significantly alter β cell function; whether TRE may be beneficial in patients with dysglycemia warrants further investigation.