Abstract #1328

IN T2D PATIENTS WITH BASELINE A1C <8.0%, LIRAGLUTIDE ACHIEVES A1C TARGETS MORE OFTEN THAN SITAGLIPTIN OR EXENATIDE

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Objective: Limited data are available to clinicians on the efficacy of incretin therapies in type 2 diabetes (T2D) patients who are within 1% of glycemic target (≤7.0%). Methods: Our post-hoc analysis compared the efficacy of liraglutide 1.8 mg once-daily (OD) to exenatide 10 μg twice daily (BID) (LEAD-6) and sitagliptin 100 mg OD (LIRA-DPP-4) after 26 weeks’ treatment; only patients treated as true add-on to metformin with a baseline A1c <8% were included. Patient baseline data were similar in each study (mean A1c 7.3-7.6%) except a shorter mean disease duration in LEAD-6 for exenatide vs. liraglutide (3.9 vs. 6.9 years). Change in A1c and body weight were analyzed using an analysis of covariance (ANCOVA) model based on the intention to treat (ITT) population, last observation carried forward (LOCF). Logistic regression analysis was performed on ITT population, LOCF to compare the proportion of patients achieving glycaemic targets (≤6.5% and ≤7.0%).

Results: In LEAD-6, liraglutide produced a numerically greater mean A1c reduction vs. exenatide (-0.86% vs. -0.61%; estimated treatment difference (ETD) -0.27%, p=0.05), reflected in a higher proportion of patients achieving A1c ≤7.0% (84% vs. 73%; p=NS) and around twice as many reaching A1c ≤6.5% (61% vs. 37%; p=0.05). In LIRA-DPP-4, liraglutide produced a significantly greater reduction in A1c (-1.00% vs. -0.49%; ETD -0.53%, p<0.0001) and higher proportion of patients achieving both A1c ≤7.0% and A1c ≤6.5% vs. sitagliptin (82% vs. 46%; p<0.0001 and 51% vs. 20%; p<0.005). Weight loss with liraglutide was greater vs. exenatide (-3.67 kg vs. -2.63 kg; ETD -1.06 kg) but did not reach statistical significance, whereas the difference was significant vs. sitagliptin (-3.39 kg vs. -0.58 kg; ETD -2.96 kg, p<0.0001). Few patients (8-10%) experienced minor hypoglycemia with all therapies.

Discussion: In patients already close to target A1c, liraglutide 1.8 mg brings more patients to target with more weight loss than exenatide or sitagliptin.

Conclusion: In contrast to liraglutide, sitagliptin and exenatide are unlikely to reduce A1c by approximately 1% in this baseline A1c range and this should be considered when choosing an add-on to metformin in patients close to target.

Abstract #1329

A RARE CAUSE OF FRACTURES: CARBONIC ANHYDRASE II ENZYME DEFICIENCY

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Objective: To report a rare cause of recurrent fractures. Case Presentation: A 22 year-old pregnant lady presented with lower extremity pain and weakness. She was diagnosed with Osteopetrosis and Renal Tubular Acidosis (RTA type-1) at the age of 2 years in Puerto Rico after she presented with a fracture. She was later found to have Carbonic Anhydrase II (CA II) deficiency as the cause of her RTA. She now reported progressively worsening leg pains and weakness ongoing for months since she stopped taking her Bicarbonate pills. Examination revealed a short stunted female with multiple bone deformities and mild mental retardation. Her labs revealed -K 1.7mmol/L, Bicarbonate 16mmol/L, serum anion Gap 9mmol/L, positive urine anion gap (U.Na 87, K 27, Cl 89). Other labs were, Cl 116mmol/L, Ca 8.6mg/dl, albumin 3.2gm/dl, Phosphate 3.9 mg/dl, ALP - 52 IU/L, 25-OH Vit D 11ng/ml, 1,25-OH Vitamin D 109pg/ml, PTH 48pg/ml, Serum osm 278mosm/kg, Urine studies -pH 7. These labs confirmed Severe Hypokalemia with Non Anion gap Metabolic Acidosis secondary to RTA type-1. She was treated with IV sodium bicarbonate and IV potassium and her acidosis and symptoms improved dramatically. She was discharged on potassium chloride, PO Bicarbonate and ergocalciferol.

Discussion: CA II deficiency is a rare Autosomal Recessive disorder leading to development of Osteopetrosis, RTA and mental retardation. This enzyme is found in bone, kidney, and erythrocytes. CA2 is involved in proximal tubular bicarbonate reabsorption and distal tubular acidification; hence deficiency causes Proximal and/or Distal RTA. CA II deficiency impairs osteoclast function which inhibits bone resorption. As the balance between osteoclast and osteoblast activity is disrupted, the excessive accumulation of brittle bone leads to Osteopetrosis and increased fractures risk. These patients have normal levels of calcium and phosphorus and diagnosis is established by quantifying carbonic anhydrase activity in erythrocytes. Early institution of alkali supplementation is the key in the management of RTA as chronic RTA causes growth retardation and metabolic bone disease.

Conclusion: Our patient had the triad of symptoms of CA2 deficiency. Her noncompliance with treatment resulted in severe bone disease with recurrent limb fractures with poor healing. CA II deficiency should be considered in evaluation of young adults with osteopetrosis associated with metabolic acidosis.