OBJECTIVES: Dipeptidyl peptidase-4 inhibitors (DPP4I) include sitagliptin, saxagliptin, vildagliptin and linagliptin. Except for linagliptin, dosage adjustments based on renal function are recommended to avoid adverse events (e.g., hypoglycemia). However, data on the effect of DPP4I on hemoglobin A1c (HbA1c) in patients with renal impairment is sparse. This meta-analysis seeks to determine the effect of DPP4-I on HbA1c in patients with chronic kidney disease (CKD).

METHODS: Multiple databases using the generic name of each DPP4I plus the following search terms: “renal impairment”, “hypoglycemia” and “SBP” were searched. Excluded were studies involving patients with T1D, those with a duration of diabetes <24 months, those with anemia, those with AKI and those with a creatinine clearance of <20 ml/min/1.73 m². The analysis was performed in patients with moderate-severe renal impairment. Studies were excluded for multiple AHAs with one-fifth of patients discontinuing use of other AHAs after treatment with CANA 300 mg. The proportion of patients with A1C <7.0% baseline, the proportion of patients with A1C ≥7.0% at baseline that decreased from baseline to <7.0% at 26 weeks (n=4017), 43% were female and average age was 56 years; 826 had baseline and follow-up A1C available. Approximately 30% of patients used CANA concomitantly with ≥3 other AHAs, the remaining 20% used CANA alone. The most common baseline regimens comprised oral agents only (43%), and 25% contained insulin. Of patients using CANA in combination with either AHAs or insulin, discontinuous use of at least 1 AHA during follow-up. CANA index dose was 100mg for 65% of the population and 300mg for the remainder; 30% of patients initially observed on CANA 100mg titrated to 300mg. Among patients with A1C ≥7.0% at baseline, the proportion of patients with A1C ≥7.0% at baseline that decreased from baseline to <7.0% at 26 weeks (n=4017) was 21% (follow-up), and those with A1C ≥9.0% decreased from 33% (baseline) to 61% (follow-up). CONCLUSIONS: CANA was often prescribed as add-on therapy to triple AHAs with one-fifth of patients discontinuing use of other AHAs after CANA was added to their treatment regimen. In patients with uncontrolled A1C, their A1Cs improved following treatment with CANA.

PDB17

TIME UNIL INSULIN INITIATION FOR CANAGLIFLOZIN (CANA) VERSUS DAPA GLIFLOZIN (DAPA) IN DUAL AND TRIPLE THERAPY FOR TYPE 2 DIABETES MELLITUS (T2DM) IN IRELAND

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OBJECTIVES: The purpose of this study was to examine the effect of CANA versus DAPA in T2DM, treatment is often characterised by gradual intensification, ultimately requiring multiple daily insulin injections. CANA and DAPA are agents with activity on SGLT2 that may delay the need for insulin. Network meta-analyses (NMA) have found that CANA 300 mg lower HbA1c more than DAPA in dual and triple therapy. Mechanistic differences support these results. Specifically, CANA 300 mg has been shown to reduce the renal threshold for glucose excretion more than DAPA 10 mg, resulting in 25% greater 24-hour urinary glucose excretion. In addition, unlike DAPA, CANA 300 mg may transiently block intestinal SGLT1, delaying glucose absorption and reducing postprandial glucose. This study evaluates differences in time in insulin initiation using CANA versus DAPA in patients with T2DM and triple therapy. A network meta-analysis (NMA) of 20 trials was conducted using CANA index dose of 300 mg. Confirmation of hypoglycemia was significantly lower with CANA versus DAPA (MD: 1.0) than all other agents in the comparison group, with a higher risk for UTI or GTI vs. placebo. Study results were compared with current clinical guidelines to determine the potential clinical impact of CANA versus DAPA.

PDB18

EFFICACY AND SAFETY OF INSULIN ANALOGUES COMPARED TO HUMAN INSULIN IN PATIENTS WITH DIABETES TYPE 1 (DM1): SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES: The use of insulin analogues for the treatment of diabetics is often a difficult clinical decision that requires the integration of multiple factors. The main objective of this study is to compare the safety and efficacy of human insulin with its analogues in patients with diabetes type 1 (DM1).

METHODS: Multiple databases were searched (March 2010 – March 2013) using the keywords (insulin analogues OR insulin analog OR insulin aspart OR insulin lispro OR insulin glargine OR human insulin) and the inclusion criteria were studies with human insulin and their analogues in patients with DM1. The search was performed in PubMed, Embase, and CINAHL. The meta-analysis was performed according to the guidelines of the Cochrane Collaboration and the PRISMA statement.

RESULTS: A total of 36,673 publications were searched, 35 studies were included: 14 studies compared glargine with NPH, 02 (Glargine vs. Detemir), 08 (NPH vs. Detemir), 04 (regular insulin vs Aspart), 06 (regular insulin vs Lispro) and 01 (Regular Insulin vs. Glulisine). The insulin analogues showed no differences (p<0.05) compared to human insulin preparations in relation to HbA1C (except Aspart vs regular insulin: favor Aspart) and occurrence of hypoglycemic episodes (except Detemir vs. NPH: favored Detemir). Glargine, Detemir and Lispro compared to human insulin preparations showed slightly improved fasting or post-prandial blood glucose concentrations, however this outcome had no influence to the overall glycemic control measured by HbA1C. Most studies showed poor methodological quality and conflicts of interests.

CONCLUSIONS: There is poor evidence for the recommendation of first-line therapy using analogues instead of human insulin preparations, which efficaciy and long-term security is better known. The analogues for the treatment of DM1 should be better assessed on randomized clinical trials with good methodological quality, as we can use this information to improve treatment for our patients.