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Canagliflozin or acarbose versus placebo to ameliorate post-bariatric hypoglycaemia – the glycaemic variability findings of the HypoBar I randomized clinical trial

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Introduction: Post bariatric hypoglycaemia (PBH) is a late complication of bariatric surgery, that can be impairing and limit quality of life. It is triggered by fast meal absorption followed by pronounced insulin secretion. PBH treatment options are limited and empirical. Acarbose slows down carbohydrates digestion and thus absorption. It is popular for PBH treatment, but it is often associated with gastrointestinal side-effects that limit patient compliance with the treatment. Canagliflozin reduces sodium-dependent glucose absorption in the kidney but also in the gut, and has been shown to change entero-pancreatic hormone dynamics and reduce glycaemic excursions after a meal, so it could potentially be useful for PBH treatment. We aimed at validating acarbose and canagliflozin for the treatment of PBH.
Methods: Eleven people with PBH previously submitted to gastric bypass joined the study and underwent 4-week treatment interventions with acarbose 50 mg thrice daily, canagliflozin 300 mg twice daily and placebo in a cross-over design. Over the last 2 weeks of each intervention, they underwent 10-days continuous glucose monitoring (CGM) and a mixed-meal tolerance test. CGM data was analysed for time under hypoglycaemia (glucose < 3.9 mmol/L; primary endpoint), time in range (3.9-7.8 mmol/L), percentiles and glycaemic variability metrics targeted at the rate of glucose

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changes (mean absolute glucose change [MAG change] and continuous overlapping net glycaemic action [CONGA1]) and variability across days of monitoring (mean of daily differences [MODD]). Each day was parted in day- and night-time for analysis (1-6 a.m.).

Results: Following intention-to-treat analysis, neither of the treatments reduced time under hypoglycaemia significantly ($p > 0.05$), despite there was a tendency for hypoglycaemia amelioration with acarbose. Acarbose increased time in range and reduced the postprandial glucose excursions in test settings. Both treatments lowered the maximum and P90 glucose, slowed glucose postprandial excursions (MAG change and CONGA1) and increased glycaemic stability across the monitored days (MODD) during daytime.

Conclusion: Acarbose has a mild non-significant effect on hypoglycaemia. Canagliflozin has a neutral glycaemic effect. Yet, both treatments reduced the magnitude and speed of glucose fluctuations and increased glycaemic stability during the periods of meal ingestion (daytime). EudraCT 2022-000157-87.

Conflict of Interest: NBJ reports having taken a position with Novo Nordisk A/S, Søborg, Denmark. Other authors have nothing to declare in relation to the current trial.

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