**Title:****Dynamic Contrast Enhanced MRI to Assess Add-on Empagliflozin Effect on Kidney Function in People with Type 2 Diabetes**

**Aims**

Empagliflozin is renoprotective in Type 2 diabetes, although its mechanism of action on the kidneys is not fully understood. We aimed to assess the effects of empagliflozin on MRI-derived GFR, renal plasma flow (RPF), renal blood flow (RBF) and mean transit time (MTT) of injected contrast obtained from dynamic contrast enhanced MRI (DCE-MRI), compared to sitagliptin.

**Materials and methods**

Prospective randomised open-label crossover clinical trial of adult people with Type 2 diabetes (T2DM) with eGFR≥45 ml/min/1.73m2. Subjects received a 12-week course of empagliflozin or sitagliptin in random order with intervening washout with DCE-MRI performed pre- and post- each drug using a 3T MRI and 5ml injected gadoterate with a 6-minute acquisition. Brochner-Mortensen corrected GFR (MRI-BM-GFR), and single kidney cortical and medullary RPF, RBF and MTT of unfiltered contrast were estimated from DCE-MRI images using dedicated software. Changes in metrics following drug intervention were assessed with mixed effect linear regression.

**Results**

12 T2DM people (8 male, median age 64y, median eGFR 94ml/min/1.73m2) completed cross-over with both drug courses. Significant decreases in MRI-BM-GFR, RPF and RBF were observed with empagliflozin compared to sitagliptin treatment (Table 1). Increases in MTT-A (slower vascular transit) were observed for both medications. There were no differences in MTT-K or eGFR with either medication intervention.

**Conclusion**

Empaglifozin decreased MRI-BM-GFR, cortical and medullary RPF and RBF, with elevated MTT-A. These changes may reflect afferent arteriole vasoconstriction and proposed empagliflozin restoration of glomerular-tubular feedback. DCE-MRI has potential to non-invasively depict treatment-related changes at the individual kidney level with a less than 10-minute scan.

**Table 1.** Mixed effect linear regression analysis of effect of empagliflozin and sitagliptin on MRI metrics and eGFR with 95% confidence intervals listed in parentheses. Significant differences between medications adjusted for order of administration are presented in the final column.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Empagliflozin** | **p** | **Sitagliptin** | **p** | **Adjusted for order** |
| **MRI\_BM\_GFR (ml/min/1.73m2)** | **-3.03**  **(-4.88, -1.19)** | **0.001** | 2.77  (-0.35, 5.90) | 0.08 | **0.003** |
| **RPF\_cortex**  **(ml/min)** | **-23.5**  **(-31.57, -15.43)** | **<0.001** | 7.72  (-0.26, 15.71) | 0.06 | **<0.001** |
| **RPF\_medulla**  **(ml/min)** | **-4.73**  **(-7.29, -2.18)** | **<0.001** | 2.18  (-0.79, 5.14) | 0.15 | **0.002** |
| **RBF**  **(ml/min)** | **-41.24**  **(-58.35, -24.12)** | **<0.001** | 13.50  (-4.19, 31.18) | 0.14 | **<0.001** |
| **MTT (s)** | **1.57**  **(1.01, 2.12)** | **<0.001** | **0.89**  **(0.42, 1.35)** | **<0.001** | 0.08 |