Supplementary Table 1. Study termination times and reasons. Unwell defined as nausea, headache or vomiting.

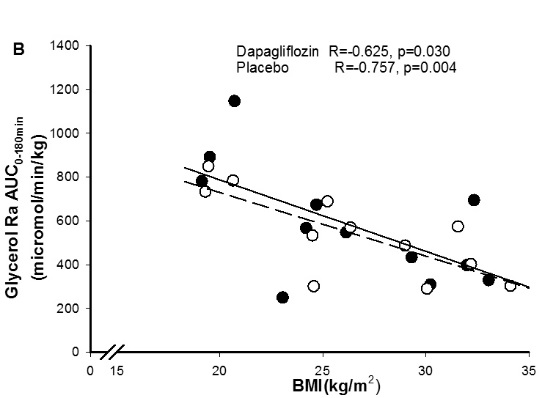
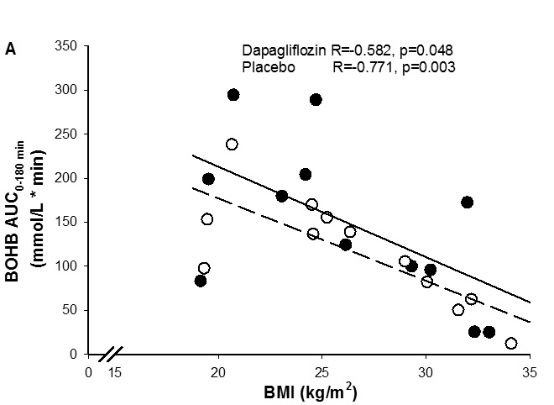
|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Participant | Dapagliflozin visit duration minutes | Reason for termination | Placebo visit duration minutes | Reason for termination |
| 1 | 540 | Midnight | 480 | Patient’s choice |
| 2 | 190 | Decreased pH | 300 | Unwell |
| 3 | 210 | Unwell | 180 | Unwell |
| 4 | 540 | Patient’s choice | 480 | Increased glucose |
| 5 | 480 | Patient’s choice | 540 | Patient’s choice |
| 6 | 360 | Unwell | 480 | Unwell |
| 7 | 480 | Decreased pH | 270 | Increased glucose |
| 8 | 540 | Increased BOHB | 540 | Unwell |
| 9 | 360 | Decreased pH | 600 | End |
| 10 | 180 | Decreased pH | 600 | End |
| 11 | 540 | Unwell | 480 | Unwell |
| 12 | 600 | END | 420 | Unwell |

Supplemental Table 2- Patient characteristics with BMI grouping.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Dapagliflozin BMI <27 kg/m2 | Dapagliflozin BMI >27 kg/m2 | Placebo BMI <27 kg/m2 | placebo BMI >27 kg/m2 | BMI <27 Dapa vs Placebo P Value | BMI >27 Dapa vs Placebo P Value |
| Age (y) | 34.4±1.9 | 49.4±1.5\* | 34.6±1.9 | 49.4±1.5\* |  |  |
| BMI (kg/m2) | 22.5±0.4 | 31.4±0.3\*\* | 22.9±0.4 | 31.4±0.4\*\* |  |  |
| HbA1c (mmol/mol) | 61±1.2 | 59±1.6 | 61±1.2 | 59±1.6 |  |  |
| Duration of diabetes | 18.7±5.4 | 29.8±5.6 | 18.7±5.4 | 29.8±5.6 |  |  |
| C peptide concentration (nmol/L) | 0.08±0.01 | 0.12±0.02 | 0.08±0.01 | 0.12±0.03 | 0.628 | 0.268 |
| NEFA concentration (mmol/L) at arrival (-120 min) | 0.61±0.05 | 0.28±0.04 | 0.45±0.03 | 0.26±0.03 | 0.328 | 0.693 |
| NEFA Concentration (mmol/L) at baseline (0 min) | 0.77±0.04 | 0.39±0.04\* | 0.60±0.04 | 0.29±0.02\* | 0.116 | 0.282 |
| Insulin infusion rate at baseline (mU/kg/min) | 0.92±0.07 | 1.58±0.17 | 1.05±0.04 | 1.52±0.11 | 0.520 | 0.838 |
| Insulin concentration (pmol/L) at arrival (-120 min) | 165±16 | 311±27 | 175±13 | 390±38\* | 0.941 | 0.198 |
| Insulin concentration (pmol/L) at baseline (0 min) | 154±22 | 298±25 | 159±11 | 341±39\* | 0.924 | 0.316 |
| AUC0-120 insulin concentration (pmol/L\*min) | 12985±1572 | 26117±2585 | 13436±914 | 29215±3727\* | 0.941 | 0.344 |
| Glucagon concentration (ng/L) at arrival (-120 min) | 37.5±1.1 | 48.5±3.4 | 27.8±0.4 | 45.5±3.3\* | **0.007** | 0.398 |
| Glucagon concentration (ng/L) at baseline (0 min) | 35.3±1.1 | 36.5±2.3 | 25.5±0.5 | 39.3±3.5 | **0.010** | 0.490 |
| AUC0-120 glucagon concentration (ng/L\*min) | 4561±151 | 4686±273 | 3401±47 | 4876±426 | **0.018** | 0.791 |
| Glucagon to insulin ratio at arrival (-120 min) | 0.31±0.03 | 0.17±0.01 | 0.23±0.03 | 0.13±0.01 | 0.344 | 0.569 |
| Glucagon to insulin ratio at baseline (0 min) | 0.37±0.03 | 0.14±0.01† | 0.19±0.01 | 0.12±0.01 | **0.009** | 0.856 |

Significance between BMI groups, P value \* <0.05; †<0.01, \*\*<0.001

Supplementary figures



Supplement Figure 1. Inverse correlation between BMI and BOHB AUC and Glycerol Ra AUC. Dapagliflozin closed symbols and placebo open symbols.

Supplement Figure 2. Glucagon/insulin ratio. All subjects completed 180 minutes of each metabolic study (n=12). By 480 min n=5. Dapagliflozin closed symbols and placebo open symbols.

Supplement Figure 3. Correlation between BOHB and NEFA concentration at baseline and BOHB AUC and NEFA AUC. Dapagliflozin closed symbols and placebo open symbols.

Supplement Figure 4. Spot urine ketones (n=12) and urine glucose excretion rate (n=6) (micromol/kg/min). Dapagliflozin closed symbols and placebo open symbols.