Additional file 1

**The Effect of Insulin Administration on C-Peptide in Critically Ill Patients with Type 2 Diabetes**

**Table S1**. Details of insulin administration and use of oral hypoglycemic agents.

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| --- | --- | --- | --- | --- |
| **Variable** | **All patients**  **(n = 45)** | **Non-insulin group**  **(n = 25)** | **Insulin**  **group**  **(n = 20)** | **P\*** |
| Intravenous insulin therapy |  |  |  |  |
| Before Day 1 | 12 (27) | 3 (12) | 9 (45) | 0.02 |
| Between Day 1 and Day 2 | 14 (31) | 0 | 14 (70) | <0.001 |
| Subcutaneous insulin therapy |  |  |  |  |
| Before Day 1 | 3 (7) | 1 (4) | 2 (10) | 0.56 |
| Between Day 1 and Day 2 | 7 (16) | 0 | 7 (35) | 0.002 |
| Biguanides |  |  |  |  |
| Before Day 1 | 5 (11) | 4 (16) | 1 (5) | 0.36 |
| Between Day 1 and Day 2 | 1 (2) | 1 (4) | 0 | 1.0 |
| Sulfonylureas |  |  |  |  |
| Before Day 1 | 1 (2) | 0 | 1 (5) | 0.44 |
| Between Day 1 and Day 2 | 4 (9) | 0 | 4 (20) | 0.03 |
| Dipeptidyl Peptidase-4 Inhibitors |  |  |  |  |
| Before Day 1 | 2 (4) | 1 (4) | 1 (5) | 1.0 |
| Between Day 1 and Day 2 | 4 (9) | 2 (8) | 2 (10) | 1.0 |
| Any oral hypoglycemic agent, n (%) |  |  |  |  |
| Before Day 1 | 7 (15.6) | 4 (16.0) | 3 (15.0) | 1.0 |
| Between Day 1 and Day 2 | 8 (17.8) | 3 (12.0) | 5 (25.0) | 0.44 |
| Values are n (%)  \*Fisher's exact test | | | | |

**Table S2**. Biochemical variables and insulin therapy in patients who did and did not receive secretagogues in the 24 hours before ICU admission and/or during the first 24 hours in ICU.

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| **Variable** | **No Secretagogue group**  **(n = 37)** | **Secretagogue group**  **(n = 8)** | **P** |
| Blood Glucose Level, mmol/l |  |  |  |
| Day 1 | 9.4 (7.0, 11.0) | 10.0 (7.6, 11.0) | 0.67 |
| Day 2 | 11.0 (8.6, 12.0) | 8.9 (6.8, 14.0) | 0.56 |
| Plasma C-peptide Level, nmol/l |  |  |  |
| Day 1 | 1.3 (0.6, 2.7) | 1.5 (0.9, 3.0) | 0.81 |
| Day 2 | 1.6 (0.9, 4.4) | 1.9 (1.2, 3.1) | 0.66 |
| Creatinine Level, µmol/l |  |  |  |
| Day 1 | 120 (72, 212) | 138 (94, 177) | 0.77 |
| Day 2 | 109 (72, 216) | 123 (90, 215) | 0.70 |
| Ketonemia, n (%)a |  |  |  |
| Day 1 | 10/28 (36) | 2/6 (33) | 1.0 |
| Day 2 | 11/29 (38) | 0 | 0.08 |
| Ketonuria, n (%)b |  |  |  |
| Day 1 | 1/28 (4) | 2/6 (33) | 0.07 |
| Day 2 | 2/29 (7) | 1/7 (14) | 0.49 |
| Insulin therapy, n (%) |  |  |  |
| Before Day 1 | 10 (27) | 3 (38) | 0.67 |
| Between Day 1 and Day 2 | 14 (38) | 6 (75) | 0.11 |
| Values are median (IQR) or n (%)  aBlood ketone level ≥0.6 mmol/l  bUrine ketone level ≥1 mmol/l | | | |

**Table S3**. Multivariable linear regression analysis of the association with c-peptide change (%) from ICU to the next day value.

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| --- | --- | --- | --- | --- |
|  | **Univariable analysis** | | **Multivariable analysis** | |
| **Variable** | **Crude Estimate**  **(95% CI)** |  | **Adjusted Estimate**  **(95% CI)** | **P-value** |
| Insulin administration, per unita | 0.6 (-0.5 to 1.5) | 0.29 | 0.9 (0.04 to 1.8) | 0.04 |
| Insulin-requiring diabetes |  |  |  |  |
| No |  |  | Reference |  |
| Yes | 7.0 (-55.7 to 69.8) | 0.82 | -72.2 (-127.7 to -16.8) | 0.01 |
| Blood glucose change, per % | 1.2 (0.7 to 1.6) | <0.001 | 1.4 (0.9 to 1.9) | <0.001 |
| aTotal intravenous and subcutaneous insulin dose administered between ICU day 1 and ICU day 2. | | | | |