P535

Personalisation of treatment with metformin by age, weight and sex: a MASTERMIND study

ME Lonergan[1], B Shields[2], OF Agbaje[3], J Dennis[2], M Weeden[2],L Rodgers[2], RR Holman[3], A Hattersley[2] and EW Pearson[1]

[1]School of Medicine, University of Dundee, Dundee, UK, [2]Medical School, University of Exeter, Exeter, UK, [3]Diabetes Trials Unit, University of Oxford, Oxford, UK

Aims: The same maximum dose of metformin is currently recommended for all patients with normal kidney function. However, metformin pharmokinetics (PK) are known to vary with age and body size. We investigated these parameters' effects on responses to metformin.

Methods: Age, creatinine, dose, sex and measures of body size were included in linear and non-linear regression models based upon knowledge of metformin PK. The dependent variable wasHbA1c reduction over 12 months, adjusted for baseline HbA1c. The data described 1,014 participants in the GoDARTS study and 6,622 in the CPRD dataset.

Results: The best fitting model was a linear regression containing all terms, with body mass index (BMI) rather than lean body-weight, plus a creatinine–dose interaction. A 10 year increase in age was associated with 1.6 mmol/mol [95% confidence interval(CI) 0.8–2.4, $p<0.001$] greater HbA1c reduction in GoDARTS;1.3 mmol/mol (95% CI 1–1.6, $p<0.001$) in CPRD. A 10 unit BMI increase was associated with 2.4 mmol/mol (95% CI 1.1–0.38, $p<0.001$) smaller HbA1c reduction in GoDARTS;1.7 mmol/mol (95% CI 1.2–2.3, $p<0.001$) in CPRD. Female responses were 2.8 mmol/mol (95% CI 1.1–4.4, $p<0.001$) greater than males in GoDARTS; 2.4 mmol/mol (95% CI 1.8–3.1,$p<0.001$) in CPRD. These PK derived models suggest that a male aged 50 with BMI 35 and creatinine 80 mmol/l requires 3 gof metformin to achieve the effect 2 g produces in a woman aged70 with BMI 25 and similar creatinine.

Conclusions: Higher doses should be considered for younger, larger and male patients, as they appear to respond less well to metformin.