Patient characteristics are associated with treatment response to second line glucose lowering therapy: a MASTERMIND study
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Background and aims: The most common second-line glucose-lowering agent in type 2 diabetes is a sulfonylurea (SU). Draft NICE (UK) guidelines, currently out for consultation, propose using a thiazolidinedione (TZD), pioglitazone, as second-line. There is no guidance regarding which treatment is most effective in which patients. We assessed whether patient clinical characteristics could be used to predict response and aid treatment decisions.

Materials and methods: 12-month glycaemic response (HbA1c change from baseline) was calculated for patients in the CPRD (UK primary care) dataset treated with SUs (n=8748) or TZDs (n=8876). Relationships between clinical phenotype and glycaemic response were assessed using linear regression, with adjustment for baseline HbA1c. This analysis was repeated for the ADOPT randomised controlled trial (SUs n=1441; TZDs n=1456).

Results: In CPRD, patients diagnosed younger had a smaller glycaemic response to both SUs and TZDs (~2mmol/mol greater response per 10-year increase in age at diagnosis, p<0.0001). Female patients responded better to TZDs (1.9mmol/mol greater HbA1c reduction compared with males, p<0.0001), but worse to SUs (2.4mmol/mol smaller response, p<0.0001). Obese patients (BMI≥30kg/m2) responded better to TZDs (2.1mmol/mol greater HbA1c reduction compared with non-obese patients, p<0.0001), but non-obese patients responded better to SUs (1.9mmol/mol greater HbA1c response, p<0.0001).
Combining categories led to greater differences (obese females: 4.4mmol/mol greater response to TZDs; non-obese males: 3.3mmol/mol greater response to SUs). Effect sizes were similar in ADOPT.

Conclusion: Clinical phenotype helps determine likely initial response to second-line glucose lowering therapies, and could influence therapeutic choices. Obese females have the greatest HbA1c reduction with TZDs, and non-obese males with SUs.

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