Patient stratification using gender and BMI can predict side-effect risk in patients initiating thiazolidinediones but not sulphonylureas: a MASTERMIND study

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Background/Aim: We have shown that the initial glycaemic response for non-obese (BMI<30) males is greater when treated with sulphonylureas (SUs), whereas obese (BMI>=30) females respond better to thiazolidinediones (TZDs). We investigated whether these patient subgroups were also at increased risk of weight gain, oedema and hypoglycaemia.

Methods: We analysed obese females (N786) and non-obese males (N768) randomised to either TZD (Rosiglitazone) or SU (Glyburide) therapy in the ADOPT trial. Cox regression models compared time to 5kg weight gain, first oedema and first hypoglycaemic episode over 48m post-therapy start. Patients were censored if they withdrew or reached the primary study outcome (2XFPG 180g/dl).

Results: Obese females initiating Rosiglitazone rather than Glyburide were at 2.25 times greater risk of 5kg weight gain (HR=2.25, 95%CI 1.69-3.01), and were also at increased risk compared to non-obese males starting Rosiglitazone (HR=2.15, 95%CI 1.76-2.62). On Glyburide, weight gain risk was similar in obese females and non-obese males (HR=0.95, 95%CI 0.80-1.18). Obese females had a greater oedema risk than non-obese males (HR=4.93, 95%CI 3.18-7.64) on both drugs. On Glyburide, non-obese males were not at increased risk of hypoglycaemia compared to obese females (HR=0.99, 95%CI 0.80-1.20).

Conclusion: Obese females are more likely to experience clinically significant weight gain on TZDs compared to SUs, and on both therapies are more likely to develop oedema than non-obese males. On SUs hypoglycaemia risk does not differ in non-obese males and obese females, nor does weight gain. The results suggest that on TZD but not SU therapy patients likeliest to respond well are at greatest risk of side-effects.