Personalizing Therapy in Type 2 Diabetes: The Effect of BMI and Gender on Response and Side Effects to Sulfonylureas and Thiazolidinediones

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Disclosures


Sulfonylureas (SU) and thiazolidinediones (TZD) are second-line therapy options in type 2 diabetes, but there is no guidance as to which drug is best for which patients. We studied whether clinical characteristics could predict glycemic response and side effects. Associations between clinical features and 1 year baseline-adjusted HbA1c fall were assessed in patients treated with SU (n=8748) and TZD (n=8876) in UK primary care data (CPRD). In the ADOPT trial (TZD n=1393; SU n=1337), mean HbA1c change/year and risk of 5% weight gain, oedema, fracture and hypoglycaemia over 5 years were compared in predefined subgroups showing the greatest differential response in CPRD.

In CPRD, obese (BMI \( \geq 30 \)) female patients had 4.4mmol/mol better 1 year glycemic response to TZD than SU (p<0.001), whilst non-obese males had a 3.3mmol/mol better response to SU than TZD (p<0.001). These findings were replicated in ADOPT: obese females mean HbA1c 4.8mmol/mol lower per year on TZD; non-obese males 2mmol/mol lower per year on SU. Obese males and non-obese females both had better glycemic response with TZD (mean HbA1c 2.4 & 2.6mmol/mol lower per year). Risk of 5% weight gain on TZD compared with SU was greater in obese females (Hazard ratio (HR) 1.9, 95% CI (1.5-2.2)) but similar in other subgroups (HR 0.98, (0.9-1.1)). Risks of oedema and fracture were greater on TZD compared with SU in females (HR 1.5, (1.1-2.1); fracture HR 2.5, (1.4-4.2)) but not males (HR 0.98-2.1); fracture HR 1.1, (0.65-1.85)). Hypoglycemia risk was lower with TZD and similar in all subgroups (HR range 0.18-0.23, all p<0.001). BMI and gender should be considered when choosing between a TZD or SU. Non-obese males have the best glycemic response to SU and are not at increased risk of side effects. Females have the best glycemic response to TZD, but are at higher risk of side effects. Obese males have the best glycemic response on TZD and may not have an increased side effect risk.