Unique Interaction of Saroglitazar with Insulin

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Sir,

The recent launch of the dual PPAR-α and PPAR-γ agonist Saroglitazar has added a new weapon to the armament of dyslipidemic drugs. While much attention has been focused on its anti-triglyceridemic efficacy, courtesy its predominant PPAR-α action, its anti-glycemic effect has largely been relegated to the sidelines. This is in spite of it being marketed as a drug for diabetic dyslipidemia. We would like to present a case which underlines its effect on the glycemic status, in addition to its lipidemic activity.

A 51 year old lady, weighing 62 kg (BMI 26.4) who was on multiple daily subcutaneous insulin injections Aspart insulin 12 units thrice a day before each meal and Glargine 24 units at bedtime with an HbA1c of 5.7% and FBS between 94-110 mg/dl and post meal sugars between 140-170 mg/dl, presented to the outpatient department, with an LDL level of 112 mg/dl and serum triglyceride level of 336 mg/dl. She was already on treatment with Atorvastatin 40 mg per day. To control hypertriglyceridemia, she was initiated on Saroglitazar 4 mg. Saroglitazar was selected because it offers the additional advantage of lowering LDL over fenofibrate.

Two weeks later, she presented to the OP with recurrent hypoglycemic episodes, and her insulin dose was reduced. Eventually, over the next one month, her insulin doses were constantly down-titrated till she reached a dose of Aspart 6 units thrice a day before each meal and Glargine 18 units at bedtime. At present her FBS is 98 mg/dl and post meal blood sugar is 138 mg/dl. We had ruled out other reasons which may be responsible for decrease in Insulin doses. She was consistently on 1200 kcal diet and as such there is no change routine activity and lifestyle. Her renal, hepatic and thyroid functions were also normal. She was on Ramipril 5 mg daily for blood pressure control and there was no other medication that causes hypoglycemia. On further follow up after 2 months LDL reduced to 90 mg/dl and triglyceride level was 143 mg/dl.

This case brings into sharp focus, the nexus between blood glucose and triglycerides. It is a very well known fact that high blood glucose levels are accompanied by hypertriglyceridemia, and treatment of blood glucose lowers triglyceride levels and, in a majority of cases, vice versa.¹ This can be partly explained by lipotoxicity due to high triglyceride levels, and also more importantly, the glucose–fatty acid (Randle) cycle, wherein, excess fatty acids (produced from triglycerides) and their oxidation, and reduce the utilisation of glucose.²,³ Usually, the lipid lowering drugs (especially statins) cause some hyperglycemia, though coleselvam does lower blood glucose marginally. On the contrary, Saroglitazar, in addition to its anti-triglyceride effects, has also been associated with a not insignificant reduction in fasting blood glucose and HbA1C, when compared either to pioglitazone⁴ or placebo.⁵ Whether this effect is mediated by its PPAR-γ agonist action or by its triglyceride lowering action which reduces lipotoxicity and insulin resistance, courtesy the Randle Cycle, is debatable. However, saroglitazar, in spite of being used as an anti-lipidemic drug, also can cause lowering of blood glucose, and this attribute of the drug needs to be factored in while prescribing it to well controlled subjects.

References