chotics. Data from pharmacovigilance studies suggest that a significant proportion of recent-onset cases of diabetes can be reversed. Recent Belgian guidelines for screening and monitoring patients treated with antipsychotics propose a switch to an antipsychotic with a safer metabolic profile, but this strategy has not been evaluated systematically (3).

We have recently reported on five patients with treatment-emergent diabetes who were successfully switched to a more suitable antipsychotic, which resulted in the reversal of diabetes (to risperidone in one patient [4] and amisulpride in four patients [5]). Since aripiprazole, a second-generation antipsychotic agent described as having a good metabolic profile (6–8), became available on the Belgian market, all consecutive patients with recently detected diabetes were switched to this agent.

Over the last year, a switch to aripiprazole was initiated in seven consecutive patients (mean age [±SD] 37 ± 14 years) after diabetes was detected and confirmed during their previous antipsychotic treatment. All patients underwent an extensive metabolic evaluation, including an oral glucose tolerance test (OGTT) at baseline and 6 weeks and 3 months of follow-up. All but two were treated with antipsychotic medication for >1 year. One patient was switched from a first-generation antipsychotic, one from clozapine, one from olanzapine, two from quetiapine, and two from risperidone.

All cases of diabetes met criteria at 120 min in the OGTT. Two patients also met criteria for diabetes while fasting, and all others had impaired fasting glucose (fasting glucose between 100 and 125 mg/dl).

All cases of recent-onset diabetes were reversed at 3 months of follow-up. Six patients had normal glucose values both in the fasting state and at 120 min in the OGTT. One patient had impaired glucose tolerance (glucose at 120 min between 140 and 200 mg/dl) at end point. There was a significant reduction in all glucose values in the OGTT, fasting insulin, in the homeostasis model assessment of insulin resistance, and in HbA_{1c} glycated hemoglobin, weight, waist circumference, and BMI (online appendix [available at http://care.diabetesjournals.org]).

Whether this reversibility was due to stopping the prior antipsychotic alone could not be evaluated. Although patients were included prospectively, the number of patients remains limited. The duration of the study was only 3 months, so the observed favorable evolution on metabolic parameters should be confirmed over a longer period of time. Future research should address these issues more specifically in large, multisite samples.

To our knowledge, this is the first prospective case series addressing the metabolic safety of aripiprazole using an extensive metabolic evaluation in patients with recently detected antipsychotic treatment–emergent diabetes. If during treatment with an antipsychotic severe metabolic abnormalities emerge, a switch to a safer metabolic agent should be considered as the first treatment option if acceptable for the patient.

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Additional information for this article can be found in an online appendix at http://care.diabetesjournals.org.

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Ovarian Stockpiling in Polycystic Ovary Syndrome, Infertility, and the Combined Use of Rosiglitazone and Metformin

We read with interest the recent report by Vaughan and Bell (1), in which the addition of rosiglitazone to metformin to control glycemia in their 46-year-old patient of Euroasian decent resulted in an unplanned and unexpected, yet successful, pregnancy. This case is another anecdote for the potential usefulness of the glitazone class of drugs in treating the infertility of women with polycystic ovary syndrome (PCOS).

We recently encountered a similar situation in a woman in her 40s with a long-standing history of primary infertility due to PCOS. Her PCOS has been extensively, but ineffectively, managed since her early 20s, to the extent that she gave up hope of having children when she reached her mid-30s. She developed type 2 diabetes when she was 37 years of age, and after the addition of rosiglitazone to metformin to improve glycemia, she had an unexpected, successful pregnancy, giving birth to viable healthy twin males.

This case adds to the recent accumulating scientific usefulness of the combination of metformin and the glitazone class of drugs for improving the metabolic

milieu and correcting the metabolic defects in women with PCOS (2–4). Vaughan and Bell's case and ours suggest that the combined use of metformin and a glitazone agent may prove to be an attractive combination to tackle the infertility of women with PCOS; however, this will need to be tested by randomized controlled trials.

Though Vaughan and Bell have rightly pointed out the need to exercise caution in the use of this combination therapy and to fully counsel such women for the possibility of unexpected conception, we feel that only a randomized controlled trial will prove such safety.

Finally, such a combination may also provide some help to tackle other metabolic abnormalities of PCOS, like hirsutism and glucose intolerance (5,6).

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COMMENTS AND RESPONSES

Triple Therapy in Type 2 Diabetes: Insulin Glargine or Rosiglitazone Added to Combination Therapy of Sulfonylurea Plus Metformin in Insulin-Naïve Patients

Response to Rosenstock et al.

Rosenstock et al. (1) reported on the safety and efficacy of add-on insulin glargine versus rosiglitazone for patients with type 2 diabetes not adequately controlled on dual oral therapy with sulfonylurea plus metformin. The main finding of the study was similar glycemic control in both groups. About 50% of participants in both groups achieved an HbA_{1c} of <7%. However, the authors comment on two positive aspects that favor the use of glargine over rosiglitazone therapy.

First, an improved lipid profile was reported with the glargine therapy. There was an increase in total cholesterol from 196 to 215 mg/dl in the rosiglitazone group versus a decrease from 196 to 186 mg/dl in the glargine group (+10.1 vs. −4.4%, respectively; $P = 0.0001$) as well as an increase in LDL levels from 106 to 120 mg/dl vs. 117 to 115 mg/dl (+13.1 vs. −1.4%, respectively; $P = 0.0004$). A similar difference was found with triglyceride levels, which increased from 241 to 252 mg/dl in the rosiglitazone group and decreased from 217 to 176 mg/dl in the glargine group (+4.6 vs. −19%, respectively; $P = 0.0011$). We question whether this degree of cholesterol and triglyceride reduction translates into better clinical outcomes and would like the authors to comment about any ongoing outcome studies. It should be noted that the increase in LDL levels with rosiglitazone may not be clinically detrimental, as it may reflect an increase in larger, less atherogenic LDL particles previously reported with thiazolidinediones (2–4).

The other finding of the study that favors glargine therapy, according to the authors, was a better cost profile, which is an important consideration. However, the estimated cost of glargine was $216 for 24 weeks, yet the average monthly cost of a vial is $70 (5). This results in a total cost of glargine therapy of $420 for 24 weeks. We would like the authors to comment on how they accounted for the cost of glargine.

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