A more recent RCT evaluated 357 patients (pramipexole 178, placebo 179) for 12 weeks of treatment. At 12 weeks, the adjusted mean change from baseline was significantly greater for pramipexole vs placebo for IRLS score (−13 vs −9.6; P<.01) and MOS sleep disturbance score (−25 vs −17; P=.0008).

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Can metformin be safely used in a patient with elevated creatinine concentration?

Evidence-Based Answer

Metformin use in patients with diabetes who have a creatinine concentration between 1.5 and 2.5 mg/dL has not clearly been shown to worsen renal function or increase the risk of lactic acidosis. (SOR: B, based on a small RCT and cohort studies.) Still, clinical caution is advised, as rare serious adverse outcomes are hard to study.

Metformin is a first-line treatment for patients with type 2 diabetes mellitus and has been shown to reduce total mortality in this population. However, metformin is thought to increase the risk of lactic acidosis and is considered contraindicated in patients with renal insufficiency.

A 2010 Cochrane review studied prospective and retrospective cohort trials assessing the risk of lactic acidosis and metformin use in patients with type 2 diabetes. In this review, a total 96,295 participants were followed for 125,941 patient-years. The incidence of metformin-associated lactic acidosis was 4.3 per 100,000 patient-years, compared with 5.4 per 100,000 patient-years in the non-metformin group. However, only 53% of the studies reviewed allowed the inclusion of patients with renal insufficiency (defined as having a serum creatinine concentration >1.5 mg/dL), which involved 37,360 patient-years of metformin use. Therefore, most patients in the review did not have an elevated creatinine level and an assessment for the worsening of renal function or association of renal failure and lactic acidosis could not be made.

A 2002 randomized trial followed patients with elevated serum creatinine and continued metformin use. This study randomly assigned 393 metformin-treated patients with diabetes who developed the contraindication of an elevated creatinine concentration (1.49–2.49 mg/dL) to either continue metformin (198 patients) or discontinue metformin (195 patients). The average creatinine at baseline was 2.14 mg/dL in the metformin group and 2.11 mg/dL in the discontinuation group. The serum creatinine increased to 2.34 mg/dL (16%) in the discontinuation group and to 2.35 mg/dL (10%) in the metformin group (difference not significant). The plasma lactate concentration level increased from 1.5 mmol/L in both groups to 1.61 mmol/L in the metformin group and 1.63 mmol/L in the discontinuation group (difference not significant) over a 4-year period. In this study, there were no cases of lactic acidosis.

In 2001, a retrospective cohort study of 1,847 adult patients with type 2 diabetes evaluated the use of metformin after the development of contraindications—including renal insufficiency. During the 30-month study, 88 patients developed renal insufficiency and 66 of those patients (75%) were either continued or started on metformin. Out of the total study population, there was only 1 episode of lactic acidosis in 4,600 patient-years, and that 1 episode was attributed to a myocardial infarction. No patients with renal impairment developed lactic acidosis.2

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References