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Metformin for Prediabetes

The oral biguanide metformin (Glucophage, and others) is generally the drug of choice for initial treatment of type 2 diabetes. It has also been used to prevent or at least delay the onset of diabetes in patients considered to be at high risk for the disease. Recent guidelines recommend considering use of metformin in patients with prediabetes (fasting plasma glucose 100-125 mg/dL, 2-hr post-load glucose 140-199 mg/dL, or A1C 5.7-6.4%), especially in those who are <60 years old, have a BMI ≥35 kg/m², or have a history of gestational diabetes. Metformin has not been approved for such use by the FDA.

CLINICAL STUDIES – In the Diabetes Prevention Program (DPP) trial, 3234 nondiabetic adults with a BMI ≥24 kg/m² (≥22 kg/m² in Asian patients) and elevated fasting and post-load plasma glucose concentrations were randomized to receive intensive lifestyle intervention focusing on weight loss and exercise, metformin 850 mg twice daily, or placebo. After a mean follow-up of 2.8 years, the incidence of diabetes was reduced, compared to placebo, by 58% with intensive lifestyle intervention and by 31% with metformin. Metformin was as effective as lifestyle intervention among patients <60 years old or with a BMI ≥35 kg/m².

When the 3-year DPP trial ended, the intensive lifestyle intervention group was offered semi-annual counseling and the metformin group could continue to take the drug. During a follow-up of 15 years, the average annual incidence of diabetes, compared to placebo, was 27% lower in patients originally randomized to lifestyle intervention and 18% lower in those randomized to metformin.

ADVERSE EFFECTS – No significant safety issues have been detected with long-term use of metformin. The drug can cause adverse gastrointestinal effects such as metallic taste, nausea, diarrhea, and abdominal pain, which usually decrease over time and can often be avoided by starting with a low dose. Metformin can cause weight loss, which is usually considered to be a benefit. Hypoglycemia is rare to nonexistent with metformin monotherapy. Decreases in hemoglobin and hematocrit levels have occurred during the first year of treatment. Vitamin B12 deficiency has been reported. Lactic acidosis is a rare complication that can occur in patients with severe renal impairment or hepatic failure.

CONCLUSION – In patients with elevated fasting and post-load plasma glucose concentrations, long-term metformin monotherapy can delay or possibly prevent the onset of diabetes. Lifestyle intervention, which has been more effective than metformin in clinical trials, is preferred and should be tried first.
