

Metformin Use in Children and Adolescents with Prediabetes

Aditi Khokhar, MBBS^a, Vatcharapan Umpaichitra, MD^b,
Vivian L. Chin, MD^b, Sheila Perez-Colon, MD^{b,*}

KEYWORDS

• Metformin • Prediabetes • Obesity • Insulin resistance • Children • Adolescents

KEY POINTS

- Early recognition and treatment of prediabetes may prevent development of type 2 diabetes.
- Clinicians consider pharmacologic intervention including metformin therapy for treatment of prediabetes when lifestyle interventions are not successful.
- There are few data in children regarding metformin therapy in diabetes prevention.
- The long-term effects of metformin have not been studied in the pediatric population.

INTRODUCTION

Prediabetes is a state of higher than normal blood sugar levels that does not fall within the diabetes range. There is a strong association between prediabetes in childhood and the development of diabetes in young adulthood.¹ The prevalence of prediabetes among adolescents has increased.² It is important for physicians to identify prediabetes in obese youth for early introduction of lifestyle modifications and pharmacologic interventions when indicated. Metformin, a biguanide derivative, is the first line of pharmacologic treatment for type 2 diabetes mellitus (T2DM), in conjunction with lifestyle modifications.³ Metformin therapy improves insulin sensitivity, as shown by a reduction in fasting plasma glucose and insulin concentrations.⁴ This article focuses on

Support: No funding was sought or obtained for this review, and the authors had no conflict of interest or personal gain during its completion.

Financial Disclosure: None.

Conflicts of Interest: None.

^a Division of Pediatric Endocrinology, Department of Pediatrics, SUNY Upstate Medical University, 3229 East Genesee Street, Syracuse, NY 13214, USA; ^b Division of Pediatric Endocrinology, Department of Pediatrics, SUNY Downstate Medical Center and Kings County Hospital Center, 445 Lenox Road, Box 49, Brooklyn, NY 11203, USA

* Corresponding author.

E-mail address: sheila.perez-colon@downstate.edu

Pediatr Clin N Am ■ (2017) ■–■

<http://dx.doi.org/10.1016/j.pcl.2017.08.010>

0031-3955/17/© 2017 Elsevier Inc. All rights reserved.

pediatric.theclinics.com

the mechanism of action of metformin, including evidence supporting its clinical use, and its safety profile in obese prediabetic children and adolescents.

SCREENING FOR DIABETES

Obesity is increasing worldwide and is a major risk factor for metabolic and cardiovascular morbidities. Data suggest that 16.9% of the youth in the United States are obese.⁵ The increasing prevalence of obesity has led to an increased incidence of comorbidities like insulin resistance, hypertension, dyslipidemia, and T2DM.^{6,7} The American Diabetes Association⁸ recommends diabetes screening in asymptomatic overweight and obese (body mass index [BMI] >85th percentile for age and sex, weight for height >85th percentile, or weight >120% of ideal for height) children and adolescents, who have 2 of the following risk factors: (1) first- or second-degree relative with T2DM, (2) minority race/ethnicity, (3) signs of insulin resistance (acanthosis nigricans) or comorbidities (hypertension, dyslipidemia, polycystic ovarian syndrome), or (4) mother with diabetes or gestational diabetes during child's gestation.

PREDIABETES DEFINITION

The American Diabetes Association defines prediabetes (category for increased risk of diabetes) as impaired fasting glucose, which is a fasting plasma glucose of 100 to 125 mg/dL (5.6–6.9 mmol/L), or impaired glucose tolerance, which is a 2-hour plasma glucose after 75 g of oral glucose intake of 140 to 199 mg/dL (7.8–11.0 mmol/L), or glycated hemoglobin (HbA1c) of 5.7% to 6.4% (39–46 mmol/mol).⁹

PROGRESSION OF PREDIABETES TO DIABETES

The rate of progression of prediabetes to overt diabetes has been assessed to be 5% to 10% annually.¹⁰ Besides being a precursor for development of diabetes, prediabetes itself has been associated with the development of microvascular and macrovascular complications.^{11,12} The prevalence of microalbuminuria and polyneuropathy is slightly increased in patients with prediabetes compared with individuals with normoglycemia.^{13,14} Once detected, prediabetes is managed with lifestyle modifications and, when needed, medication to prevent or aim to slow the transition to diabetes. Prediabetic individuals have been shown to revert to normoglycemia with a reduced risk of diabetes development after lifestyle and drug-based interventions.^{15–17} Early identification of prediabetes can help to adequately direct the resources and interventions toward the patients at greatest risk for developing diabetes.

HISTORY OF BIGUANIDES

Chemically, biguanides are composed of 2 guanidine groups joined together with the loss of ammonia. There is evidence of biguanide use in medieval Europe in the form of a herb *Galega officinalis*, commonly referred as goat's-rue or French lilac.¹⁸ Guanidine, the active component of *G. officinalis*, was used to synthesize several antidiabetic compounds in the early 19th century, but was found to be toxic. Diguanydes (synthalin A and synthalin B), composed of 2 guanidines connected by an alkyl chain, were used clinically for a short time, but marked toxicity was noted quite quickly. The 2 main biguanides, metformin and phenformin, were introduced into clinical practice in 1957; however, phenformin was withdrawn from several countries 2 decades later after recognizing its association with lactic acidosis.^{19,20} Metformin continues to be used as a major oral antidiabetic medication all over the world given the impressive safety record of the drug.²¹

Download English Version:

<https://daneshyari.com/en/article/8813286>

Download Persian Version:

<https://daneshyari.com/article/8813286>

[Daneshyari.com](https://daneshyari.com)