Beneficial effect of metformin treatment in obese children and adolescents

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Introduction

Obesity (defined as BMI >95 th percentile for gender and age) in children and adolescents is a growing global health problem. Obese children and adolescents with or without insulin resistance provide the pediatric healthcare professionals management challenge. Obesity with insulin resistance, dyslipidemia and elevated blood pressure constitute the metabolic syndrome and each of these is an independent risk factor for cardiovascular disease,diabetes mellitus, non-alcoholic fatty liver disease, chronic respiratory disease.

Lifestyle modification is a primary and main milestone in treatment, but often has short or limited effect. On the other hand metformin is well established oral hypoglycemic agent in the treatment of adult and young patients with type 2 diabetes.

There are several publications on the effect of metformin on body weight, glucose level and insulin resistance in adolescents.

Objectives

In a retrospective analysis to evaluate the effect of metformin treatment in children and adolescents on the body mass index (BMI), fasting serum glucose and insulin (calculated as Homeostasis model assessment for Insulin resistance – HOMA-IR) and blood glucose at the second hour of an oral glucose tolerance test (OGTT). In addition we examined secondary health outcomes as total cholesterol, triglycerides, HDL- and LDL- cholesterol and blood pressure. All patients received strong support for lifestyle modification (dietary, behavioral and physical activity)

Methods

Investigation and follow up of 57 children and adolescents (16 boys), aged 7 years 6 months - 16 years 9 months. Patients received Metformin for an average period of 14,6 months (6-36 months) twice daily dosage of 1000–1700 mg.
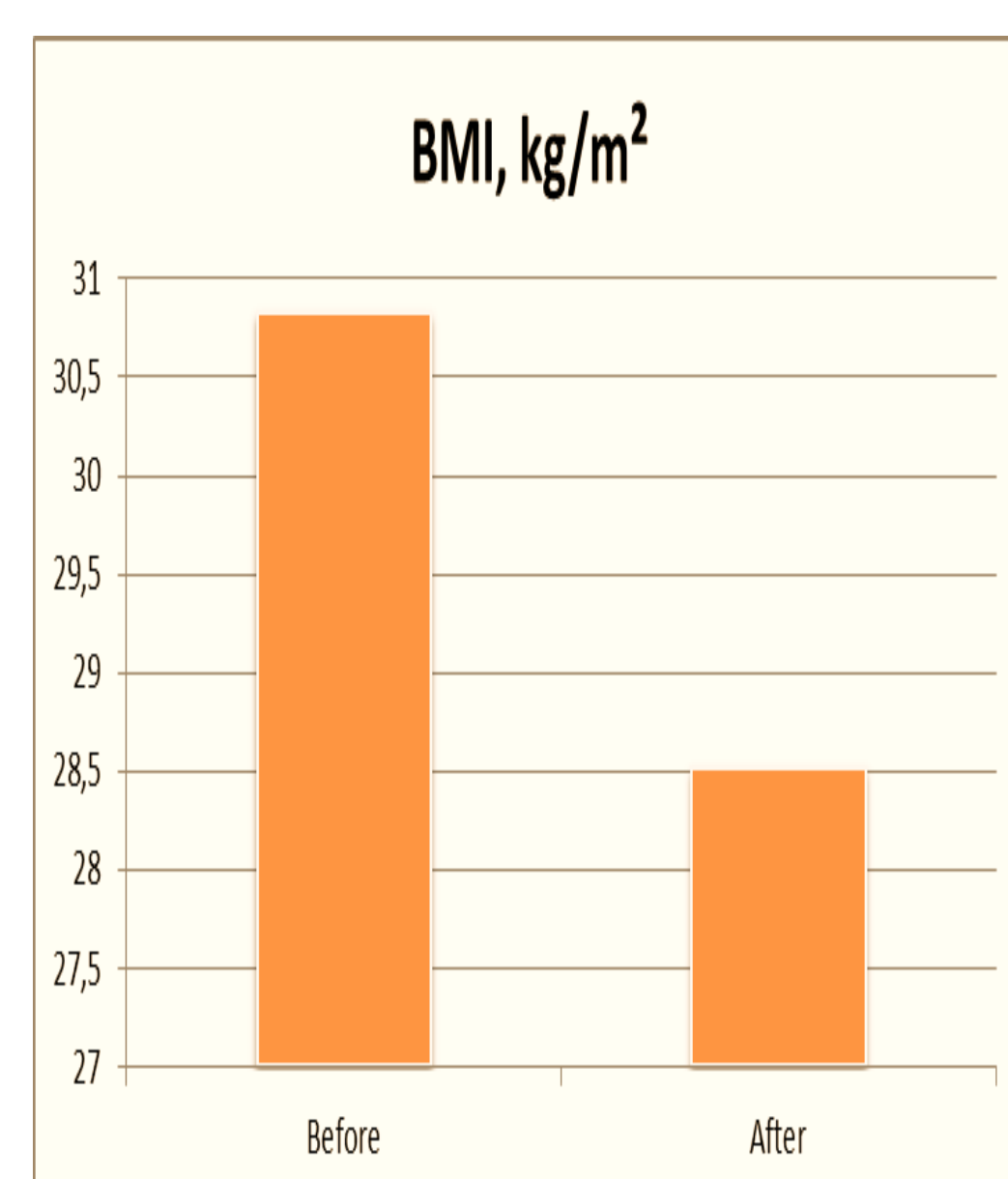
Anthropometry (height, weight, waist circumference), clinical examination with regard to presence of acanthosis nigricans (AN) and hypertension (AH)(systolic and/or diastolic blood pressure above 95 percentile for age, gender and height), serum lipid level, liver enzymes, OGTT were performed at baseline, every six months and end of treatment period.
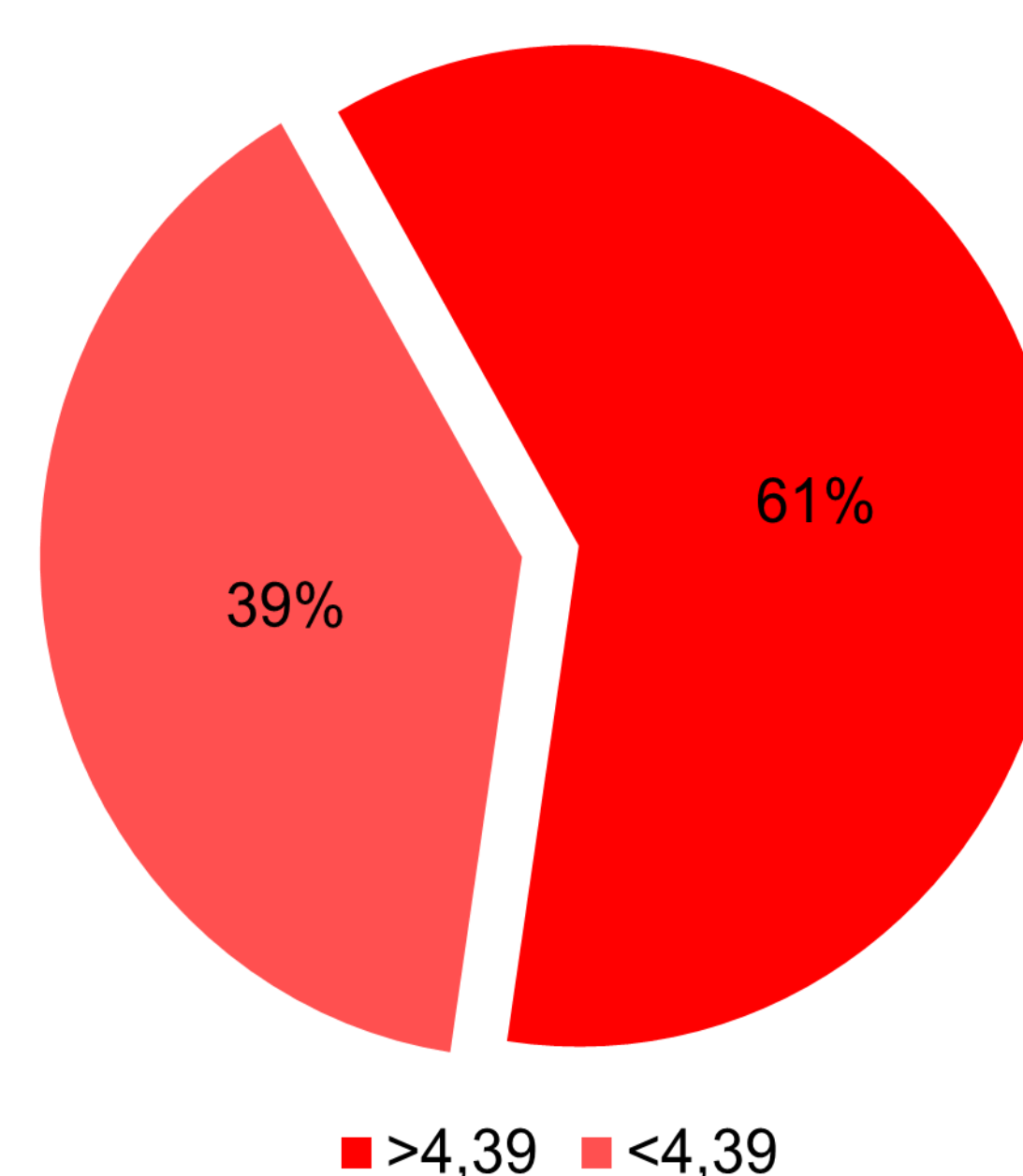
Results

Mean age of subjects at baseline was 13 years 7 months with median BMI 30,95 kg/m^2. After the treatment period BMI was reduced to 28,51 kg/m^2 (t=2.33 p<0.05).

Insulin resistance, strictly related to excessive weight gain, is the first step in the pathogenesis of T2DM. Marker of IR is the HOMA-IR index, based on the measurement of fasting insulin and glucose with higher levels representing greater degrees of IR. Based on a study of 1,802 adolescents aged 12–19 years from the 1999–2002 NHANES, a HOMA-IR 4.39 was recommended as evidence for IR. Pretreatment HOMA-IR was 5,52. Metformin therapy had beneficial effect on HOMA-IR which fall to 3,16 (t=4.4 p<0.001)Acnathosis nigricans was found in 5 1% initially and in 27 patients(47,3%) after treatment .Of all patients 21%(12) were found to have Impaired glucose tolerance before treatment and only one at the end of treatment period. Total cholesterol was average 4,34 mmol/l and fall to 4,11 mmol/l(p>0,05). Reduction of other lipid measurements was also found but also without statistical significance. AH was found in 26 patients (45,5%) at beginning and in 25,7%after treatment.
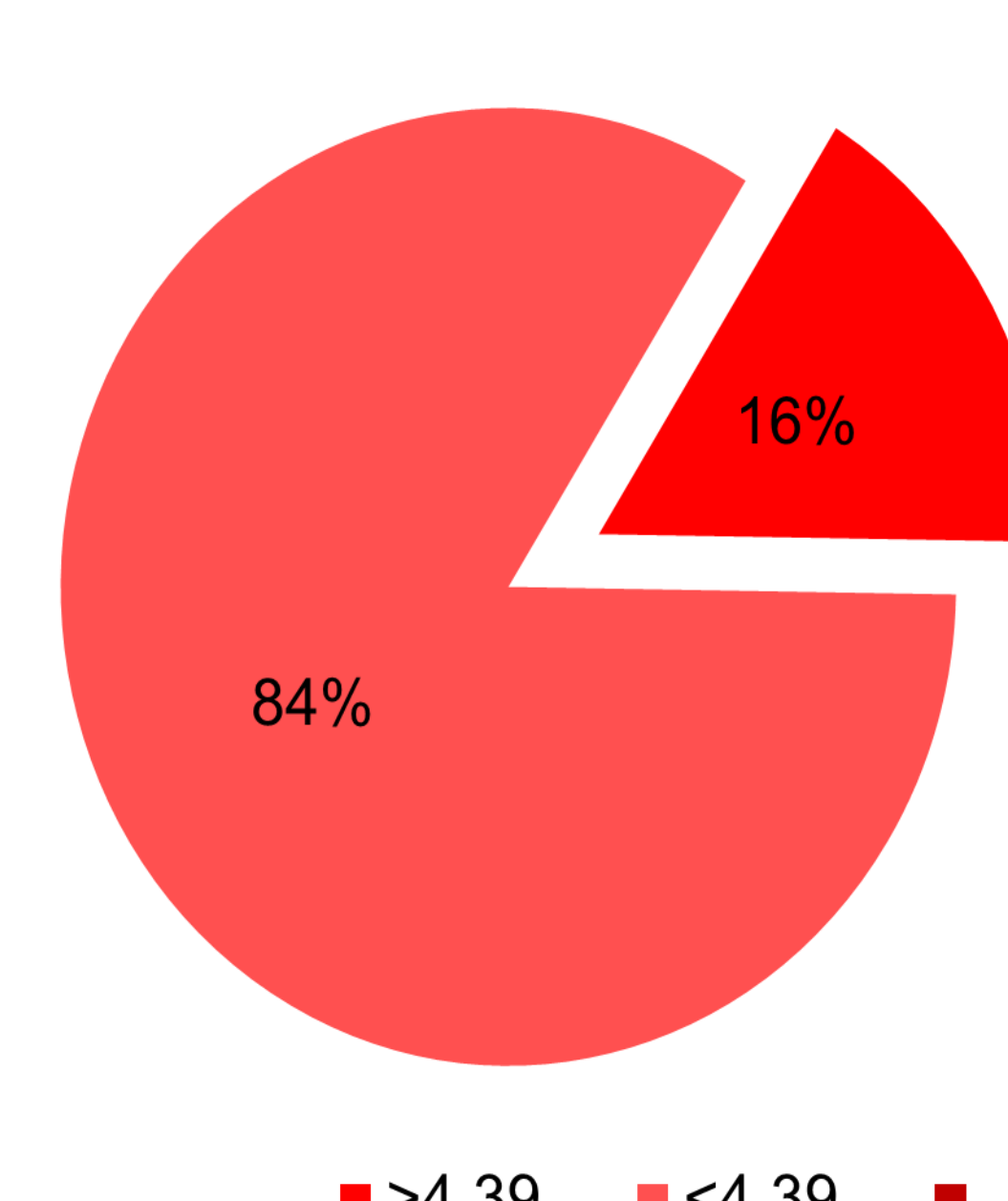
Before metformin treatment 30 % of patients have elevated total cholesterol (>4,8 mmol/l), 23 % have elevated TG (> 1,7 mmol/l) and 64 % were measured with elevated LDL –cholesterol. With reduction of body weight, lifestyle modification and treatment with metformin these numbers fall to 24%, 15 % and 47 %

BMI, kg/m^2

HOMA-IR before treatment

39% | 61%

■ >4,39 ■ <4,39

After treatment

16% | 84%

■ >4,39 ■ <4,39 ■

Conclusion

Metformin can be efficacious treatment that lead to improvement in BMI, HOMA-IR, IGT and AH in obese children and adolescents, but although it has lowering effect on serum lipids, it does not show statistical significance.

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168--P3
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