METFORMIN TREATMENT IN OBESE CHILDREN ENHANCES WEIGHT LOSS RELATED IMPROVEMENT IN IMPAIRED GLUCOSE TOLERANCE

Bartucci A[1], Martos-Moreno GÁ[1,2,3], Barrios V[1,3], Muñoz-Calvo MT[1,2,3], Pozo J[1,2,3], Argente J[1,2,3]

1. Department of Endocrinology. Hospital Infantil Universitario Niño Jesús. Instituto de Investigación Sanitaria La Princesa. Madrid. Spain. 2. Department of Pediatrics. Universidad Autónoma de Madrid. Madrid. Spain. 3. CIBER Fisiopatología de la Obesidad y Nutrición. Instituto de Salud Carlos III. Madrid. Spain.. CONTACT: Jesús Argente: argentefen@terra.com

THE AUTHORS DECLARE NO CONFLICT OF INTEREST

Introduction:

• Obesity associated impaired glucose tolerance (IGT, glucose >140 mg/dl at 120´ in oral glucose tolerance test [OGTT]) is highly influenced by the degree of BMI excess. It is frequently reversed after weight loss, although an eventual indication for metformin (first step drug for type 2 diabetes mellitus) has been postulated.

Aim of the study:

• To evaluate the benefits afforded by the addition of metformin to conservative treatment on weight loss and IGT in obese children.

Patients and methods:

• The anthropometric and biochemical features of **88 children** (mean 11.20±2.63 years; 46% females/54% males) with **obesity and IGT** were studied at baseline (B) and after 1 year follow-up (1-Y).

• The characteristics of those who were prescribed metformin (**MET,** n=41 at **B**, n=38 at **1-Y**) and their evolution were compared with those exclusively on conservative treatment (No-MET, n=47 at **B**, n=33 at 1-Y).

• IR was estimated by HOMA [glucose (mg/dl) x Insulin (μU/ml)/405], WBISI [10000/√(fasting glucose × fasting insulin) × (mean glucose in the OGTT × mean insulin in the OGTT)] and QUICKI [1/log glucose (mg/dl) + log insulin (mcU/ml)] indexes. The area under the curve (AUC) for glucose and insulin in the OGTT were calculated as: 0.25 × fasting value+ 0.5 ×value at 30´ + 0.75 × value at 60´ + 0.5 × value at 120´.

Results:

• At **B** both groups had similar BMI-SDS, ethnic, sex, and pubertal distribution, but those prescribed metformin treatment (**MET**) were significantly older and showed more severe IR as estimated by HOMA, QUICKI, WBISI indexes and by the AUC for insulin (Table).

• At **1-Y** both groups significantly decreased their BMI-SDS, but weight loss was greater in MET patients (BMI-SDS decrease 1.23 ± 0.99 *vs.* 0.78 ± 0.93 in No-MET, p< 0.05; Figure 1). Also, the number of patient classified as "great weight losers" (reduction in BMI-SDS > 1 SDS) was higher in the **MET** group (X^2 = 6.28; p< 0.05) and relative metformin dose (mg/kg) was directly correlated with the intensity of BMI-SDS decrease (Figure 2).

• At **1-Y** the **MET** group showed a more intense improvement in IR, abolishing the differences initially observed at **B** between both groups in HOMA, QUICKI, WBISIS and insulin-AUC (Table).

	MET at B n=41	NO MET at B n=47		MET at 1-Y n=38	NO MET at 1-Y n=33	
AGE (years)	12.18 ±1.79	10.35 ± 2.89	p < 0.01	13.56 ± 1.66	11.13 ± 2.96	p < 0.001
BMI-SDS	4.80 ± 1.83	4.23 ± 1.54	NS	3.71 ± 2.17	3.04 ± 1.77	NS
ETHNICITY (%) Caucasian Hispanic Black	82.9 14.6 2.4	83 17 0	NS	81.6 15.8 2.6	93.9 6.1 0	NS
SEX (%) FEMALE MALE	46.3 53.7	44.7 55.3	NS	42.1 57.9	48.5 51.5	NS
PUBERTY (%) Prepubertal Pubertal	63.4 36.6	68.1 31.9	NS	28.9 71.7	54.5 45.5	p < 0.05
GLUCOSE (mg/dl)	97.3 ± 6.3	96.0 ± 8.2	NS	93.1 ± 5.7	95.5 ± 10.5	NS
GLUCOSE 120´ (mg/dl)	154.54 ± 14.38	151.34 ± 13.31	NS	125.34 ± 20.38	130.67 ± 28.48	NS
AUC_GLUCOSE	307.42 ± 36.82	298.83 ± 35.53	NS	260.33 ± 23.37	266.08 ± 50.75	NS
INSULIN (μU/ml)	24.0 ± 22.2	15.4 ± 8.0	p < 0.01	14.1 ± 5.4	12.6 ± 7.9	NS
INSULIN 120´ (μU/ml)	190.1 ± 102.0	134.2 ± 74.5	p < 0.01	82.5 ± 68.6	92.0 ± 61.6	NS
HOMA	5.79 ± 5.52	3.67 ± 1.98	p < 0.01	3.22 ± 1.21	3.05 ± 2.06	NS
WBISI	1.94 ± 0.91	2.93 ± 1.61	p < 0.01	3.82 ± 1.56	4.16 ± 1.97	NS
QUICK	0.30 ± 0.01	0.32 ± 0.02	p < 0.01	0.32 ± 0.01	0.33 ± 0.02	NS
AUC_INSULIN	310.8 ± 198.3	219.3 ± 114.8	p < 0.05	138.1 ± 75.6	141.9 ± 78.3	NS

Table legend: Demographic, anthropometrical and biochemical features of the two subgroups of patients with obesity associated IGT studied according to their treatment modality: No-MET: Exclusively conservative treatment; MET: Conservative + metformin treatment. The significance level displayed is the result from the cross-sectional comparison between both subgroups (MET vs. No-MET) at the two time-points considered (B: baseline and 1-Y: after 1 year of treatment).
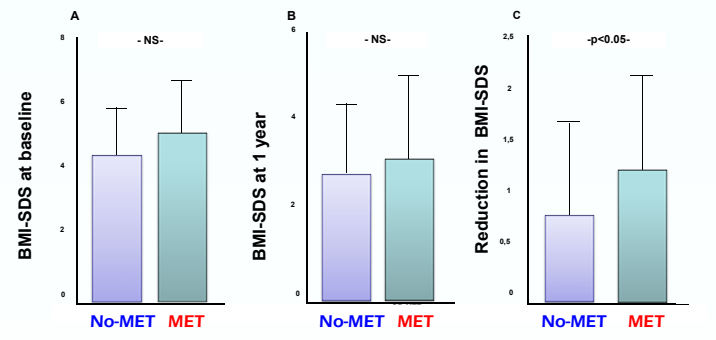

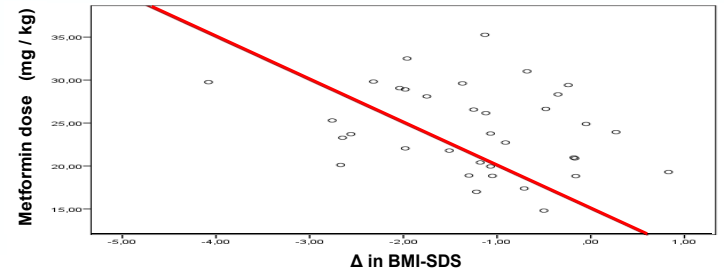Figure 1: BMI-SDS at baseline (A), at 1 year (B) and BMI-SDS reduction after follow up (C)

Figure 2: Correlation between relative metformin dose (mg/kg) and intensity of BMI-SDS reduction in MET.

Conclusion:

Weight loss is effective in resolving obesity-associated IGT and can be enhanced by the addition of metformin treatment, with further improvement of fasting and postprandial IR.