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Treatment of gestational diabetes mellitus with Myo-inositol: analyzing the cutting edge starting from a peculiar case

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Abstract. – OBJECTIVE: The robust data about myo-inositol (Myo-Ins) safety profile and effectiveness opened a new scenario for the treatment and prevention of Gestational Diabetes Mellitus (GDM). We report our experience about a case of GDM successfully treated with Myo-Ins.

PATIENTS AND METHODS: An overweight 29-year-old Caucasian pregnant woman, nulliparous, affected by GDM, according to the National Institute for Health and Care Excellence (NICE) Guideline. After diagnosis, the patient underwent regular glycemia checks: mean fasting blood glucose value was 103.63 ± 1.46 mg/dl, whereas 1-hour and 2-hours after-meal values were 122.74 ± 11.14 mg/dl and 110.74 ± 10.70 mg/dl, respectively. We decided to prescribe a low-calorie diet and oral treatment with 4 g of Myo-Ins, 3 times per day for 3 weeks.

RESULTS: After the treatment, mean fasting value was 90.74 ± 5.30 mg/dl, whereas 1-hour after and 2-hours after-meal values were 108.11 ± 6.05 mg/dl and 101.21 ± 4.78 mg/dl, respectively.

DISCUSSION: We reported a significant decrease of glycemia in a faster and steady way at fasting, 1-hour and 2-hours after-meal post oral treatment with 4 g of Myo-Ins 3 times per day, in a patient affected by GDM.

CONCLUSIONS: On the one hand, we could confirm the safety profile of the molecule also at this high dosage, free from any side effects; on the other hand, our experience highlighted the faster glucose-lowering effect due to a higher dose of Myo-Ins. This outcome may open a new scenario in the treatment of GDM.

Key Words
Gestational Diabetes Mellitus, Myo-inositol, Treatment, Inositol.

Introduction

Gestational diabetes mellitus (GDM) represents a form of glucose intolerance and insulin resistance at the onset of pregnancy or first recognized during pregnancy[1]. Although validated data estimate its prevalence between 2 and 10% of all pregnancies[2], this rate is progressively increasing probably due (at least in part) to the newly proposed criteria for the diagnosis of GDM[3]. In particular, according to the National Institute for Health and Care Excellence (NICE)[4], the 2-hour 75 g Oral Glucose Tolerance Test (OGTT) is recommended in women with risk factors for GDM: Body Mass Index (BMI) > 30 kg/m^2, previous macrosomic infant, previous GDM, family history of diabetes mellitus (first-degree relatives) and family origin in an area with high prevalence of diabetes mellitus. GDM is diagnosed if the woman has either a fasting plasma glucose level ≥ 101 mg/dl or a 2-hour plasma glucose level ≥ 140 mg/dl[4].

To date, it is widely accepted that GDM can increase the risk of adverse maternal-fetal outcomes, such as cesarean section rate, macrosomia, and neonatal hypoglycemia; also, it may play a pivotal role in promoting childhood obesity and cardiovascular diseases in the offspring, through an epigenetic imprinting[5]. GDM is also associated with increased risk of diabetes in the later life of the mother: these women have high levels of insulin resistance in puerperium and/or later in life, suggesting that GDM is a transient manifestation of longstanding metabolic impairment with a predisposition to re-appear in the future[6]. Despite consistent and continue efforts, the pathogenesis of GDM is still far from be fully understood. Nevertheless, it was already showed that pregnancy itself represents a state of insulin resistance, and GDM occurs when insulin secretion fails to counterbalance the increased insulin resistance during pregnancy[7]. Also, GDM onset and progression seem to be associated with a significant dysregulation of inflammatory pathways mirrored by an increase in circulating inflammatory molecules and overexpression of inflammation-related genes in the placenta[8]. Considering this background, several studies[9] and meta-analyses already tried to shed light

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on the possible strategies to prevent GDM: among these interventions, lifestyle modification during pregnancy can reduce the risk of GDM[10]. This evidence led to the rationale of using insulin-sensitizing molecules to ameliorate maternal insulin resistance: on the one hand, recent data suggest that metformin is an effective and safe alternative to insulin for GDM patients[11]; on the other hand, the robust data about myo-inositol (Myo-Ins) safety profile[12] and effectiveness in postmenopausal women with metabolic syndrome[13] and Polycystic Ovary Syndrome[14-16] broaden the horizon also for the treatment and prevention of GDM. Based on the already explored mechanisms, we take the opportunity to report our experience about a case of GDM successfully treated with Myo-Ins.

Case Report

A 29-year-old Caucasian woman, nulliparous, came to our observation for her first pregnancy at the Obstetrics and Gynecology Centre AGUNCO. As standard protocol, the patient was informed at the admission and signed an informed consent allowing data collection for research purposes. Also, this report was approved by an independent Institutional Review Board (IRB) and conforms the CARE (Consensus-based Clinical Case Reporting) Guideline[17], available through the EQUATOR (Enhancing the QUAlity and Transparency Of health Research) network.

Despite a family history of type 2 diabetes within first-degree relatives, patient's personal history was negative for any disease. Her pre-pregnancy BMI was 27.24 kg/m^2 (overweight), which increased to 30.44 kg/m^2 (class I obesity) during pregnancy. The pregnancy was uneventful until the 24th week when the patient underwent 75 g OGTT (fasting blood glucose value was 101 mg/dl; 1-hour and 2-hours after-meal values were 132 mg/dl and 126 mg/dl, respectively), and GDM was diagnosed according to NICE guideline[4]. After the diagnosis, the patient followed a low-calorie diet for 3 weeks and underwent regular glycemia checks: mean fasting value (± SD) was 103.63 ± 1.46 mg/dl, whereas 1-hour after and 2-hours after-meal values were 122.74 ± 11.14 mg/dl and 110.74 ± 10.70 mg/dl, respectively. In full agreement with the patient, after 3 weeks an oral treatment with 4 g of Myo-Ins 3 times per day was combined with the low-calorie diet, for further 3 weeks. The patient was monitored daily. After the treatment, mean blood glucose value at fasting was 90.74 ± 5.30 mg/dl, whereas 1-hour after and 2-hours after-meal was 108.11 ± 6.05 mg/dl and 101.21 ± 4.78 mg/dl, respectively. As summarized in Figure 1, following the treatment there was a significant decrease of fasting ($p < 0.0001$), 1-hour ($p < 0.001$) and 2-hours after-meal ($p < 0.01$) glycemia. Remarkably, lower values of glycemia were observed after the first administration of Myo-Ins and no side effects were recorded. The rest of pregnancy lacked of noteworthy events and finally patients had physiologic labor and vaginal delivery at 39 weeks of gestation, without any adverse maternal-fetal outcome. Restoration of normal glucose tolerance postpartum was recorded.

Discussion

Inositol, also known as cyclohexane-1,2,3,4,5,6-hexol, belongs to vitamin B complex. Due to epimerization, this polyol exists as nine stereoisomeric forms depending on the spatial orientation of its six-hydroxyl groups[18]. Inositol is synthesized by both prokaryotic and eukaryotic cells, while in mammals it is obtained from dietary sources (as free inositol(s), phosphatidyl-inositol or inositol-6-phosphate), and endogenous synthesis from glucose[19]. The Myo-Ins derivative inositol triphosphate (ins-1,4,5P3, insP3) acts as an intracellular second messenger, regulating the activities of several hormones such as insulin, follicle stimulating hormone (FSH), and thyroid stimulating hormone (TSH)[20,21]. Also, previous data[22] showed that Myo-Ins concentrations in amniotic fluid increase significantly in women later developing GDM, probably due to the higher urinary fetal excretion of this molecule under hyperglycemic conditions.

Considering the widely recognized insulin-sensitizing activity[23], Myo-Ins was recently used to prevent and treat GDM. It was already showed that Myo-Ins supplementation, administered since early pregnancy, reduces GDM incidence both in overweight non-obese[24] and obese[25] women. Apart from these elegant randomized controlled trials, several systematic reviews and meta-analyses[26,27] seem to confirm the key role of Myo-Ins in preventing GDM and ameliorate insulin resistance. A recent Cochrane systematic review found that Myo-Ins was associated with a reduction in the fasting and 1-hour post-prandial blood glucose concentration at the end of treatment[28]. Our case outcome is perfectly in line with this trend, even though higher dosage of Myo-Ins was used, which lowered blood glucose levels in a faster and steady way.

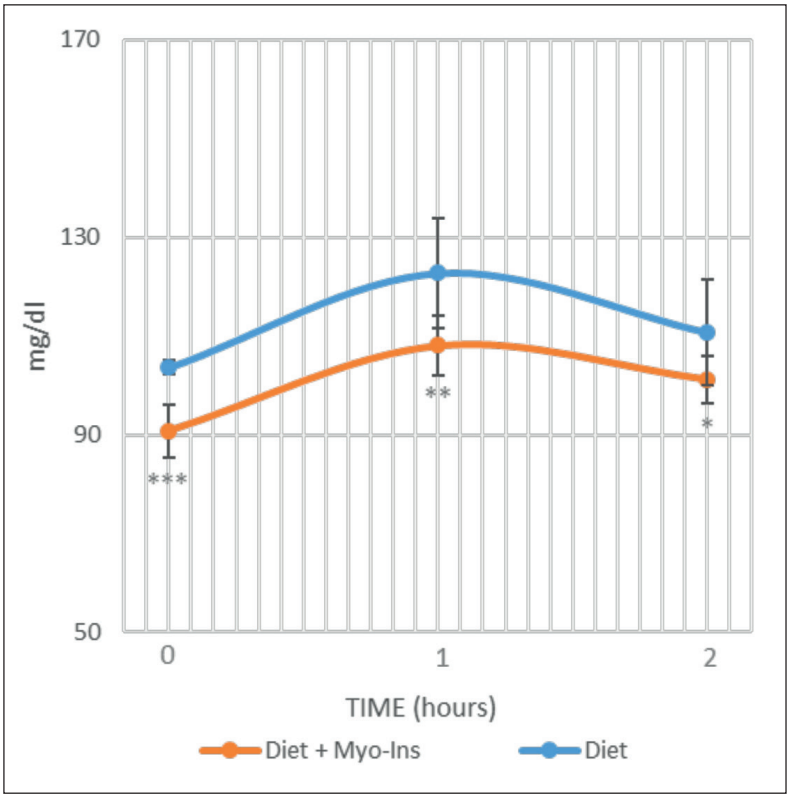

Figure 1. Mean blood glucose values at fasting, 1-hour and 2-hours after meal. Diet was followed for 3 weeks and then it was combined with 4 g of Myo-Ins, 3 times per day for further 3 weeks, during late pregnancy. Values are shown as mean ± SD. Statistical differences are calculated between means (Diet vs. Diet + Myo-Ins). *p*-value: * < 0.01; ** < 0.001; *** < 0.0001.

Conclusions

On the one hand, we could confirm the safety profile of the molecule also at this high dosage, free from any side effects; on the other hand, our experience highlighted the faster glucose-lowering effect due to a higher dose of Myo-Ins. This outcome may open a new scenario in the treatment of GDM.

Conflict of Interest

Vittorio Unfer is employee at LO.LI. Pharma, Rome, Italy. The other author declares that has no conflict of interests regarding the publication of this paper.

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