

Letter to the editor

**TOWARDS DEFINING CRITERIA FOR METFORMIN USAGE IN
MANAGEMENT OF GESTATIONAL DIABETES MELLITUS**

Hamidreza Mahboobi^{1,2}, Tahereh Khorgoei³, Aida Najafian¹

1: Reproductive Health Research Center, Hormozgan University of Medical Sciences (HUMS), Bandar Abbas, Iran

2: Payame Noor University (PNU), Iran

3: Hormozgan Cardiovascular Research Center, Hormozgan University of Medical Sciences (HUMS), Bandar Abbas, Iran

Corresponding author:

Hamidreza Mahboobi, Hormozgan University of Medical Sciences (HUMS), Bandar Abbas, Iran. Phone: + 98. 9364300250, E-mail: hamidrezamahboobi@yahoo.com

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Dear Editor,

Gestational Diabetes Mellitus (GDM) complicates about 1 to 14 percent of pregnancies (1), and pregnancy outcomes in GDM are strongly related to glucose control

(2). Without treatment, GDM is associated with fetal macrosomia and perinatal complications (3). Insulin is commonly used in patients who do not reach optimized glycemic control with medical nutritional therapy (4), because it is effective in

lowering the blood glucose as well as being safe for both mother and fetus during pregnancy (5-7). However, patients need educating with regard to insulin injection before they start using it, and there is also always a chance of hypoglycemia in these patients. Moreover, insulin resistance and decreased insulin secretion are pathophysiological mechanisms underlying the development of GDM (8). These facts have led to increasing interest for the usage of oral hypoglycemic agents in the treatment of GDM(9). Patients prefer oral hypoglycemic agents to insulin (10), and oral agents are easier to administer than insulin in clinical practice (11). However, there are concerns that oral agents can cross the placenta, and their role in fetal teratogenesis and other fetal complications, and in neonatal obesity and insulin resistance, remains unclear (7, 12).

Metformin is an attractive option for induction of ovulation in PCOS patients (13) and is associated with a reduction in gestational diabetes (14-18). The pharmacokinetics of metformin in pregnant women is similar to those in non-pregnant patients (12). Metformin was found to be readily transferable from the maternal to fetal circuits across placentas that were obtained from uncomplicated pregnancies and pregnancies with GDM (12, 19). One study showed that preeclampsia and prenatal mortality are more common in patients who were treated with metformin in comparison with those treated with insulin (20). However, other studies have contradicted these findings (21). Potential hypoglycemic agents have been shown to have no adverse outcomes on neonates (22). Metformin may have additional benefits, including reducing insulin resistance, body weight, long term risk of diabetes (23), and development of GD. Metformin was not found to be

teratogenic, and did not adversely affect birth length and weight, growth, or motor social development in the first 18 months of life (18).

Although metformin seems to be as effective as insulin in management of patients with GDM, while having many advantages over insulin, there are still concerns about its safety in neonates. Randomized controlled trials assessing metformin safety in neonates and long-term follow-up of these neonates is lacking. Insulin is still the drug of choice in management of GDM but long-term follow-up of metformin effects on neonates could change this role and may revolutionize the management of GDM. In the mean time, we should consider that specific patients such as PCOS and patients with severe insulin resistance (24) may benefit more than others from metformin. Consequently, studies should be carried out on specific patients in order to establish criteria for usage of metformin or insulin in GDM.

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