Effect of Magnesium Supplementation on the Diagnosis of Gestational Diabetes Mellitus

Ashley Blaylock and Heidi Washburn

Introduction

Gestational diabetes mellitus (GDM) is a condition in pregnancy where women have high blood sugar levels due to insulin resistance (1). This is a disorder in which a person's cells have a diminished ability to respond to insulin, forcing the pancreas to produce more insulin in order to maintain normal blood sugar levels (2). Eventually, the pancreas stops being able to produce enough insulin to keep blood sugar within normal ranges. This condition is fairly common. Using the updated diagnostic criteria, it is estimated by an international multicenter study that 18% of pregnant women will be diagnosed with GDM during their pregnancy (3).

This high prevalence is a major concern because GDM causes risks for the mother and baby. Although abnormal blood glucose levels and insulin resistance tend to disappear after the pregnancy, these women have an increased risk of developing type 2 diabetes later in life (1). They also have increased risk of preeclampsia (pregnancy-induced high blood pressure), surgical delivery, and developing GDM in a later pregnancy.

GDM also increases risks of problems during birth and later in life for the children. For instance, it increases the risk of birth trauma, fetal hypoglycemia (low blood sugar), and fetal macrosomia (disproportional growth of the shoulders and trunk) (1). The children of women with GDM have higher risks of developing obesity, prediabetes, and type 2 diabetes.

Many lifestyle and genetic factors influence an individual's risk of acquiring GDM. For instance, magnesium is a mineral that influences the cell's response to insulin (2). It helps relay insulin's message to the cell. It is involved in initiating the reaction that allows glucose to enter the cell. Therefore, it is concerning when data shows that the dietary intake of magnesium for Americans of all ages is below the recommended amounts according to the 2005-2006 National Health and Nutrition Examination Survey (2).

While the literature provides much information about diabetes, GDM, and the effects of magnesium on type 2 diabetes, there is little research regarding the impact of magnesium on GDM. Our study is intended to fill this gap. Our objective is to determine the effect magnesium supplementation has on pregnant women with regards to GDM. As our null hypothesis, we will state that a magnesium supplement will have no effect on the incidence of GDM diagnosis when compared to a placebo control. However, we expect that magnesium supplementation will decrease the incidence of GDM diagnosis.

Literature review

Magnesium and Type 2 Diabetes

There have been several studies done to assess the effect of dietary magnesium on insulin resistance. In a longitudinal study following 5000 American young adults for 20 years, it was found that that high magnesium diets were significantly correlated with the decrease of diabetes incidence compared to low magnesium diets (4). The study measured type 2 diabetes and excluded pregnant women from the study. While this was significant, it is impractical to conclude that magnesium was the only cause of the decreased diabetes incidence. Magnesium rich foods are also rich in other nutrients. Is magnesium an essential nutrient in diabetes management, or were the findings of this study based on the other nutritional components of the high magnesium diets?

A double-blind, random, placebo-controlled trial found that a six month $MgCl_2$ supplement significantly increased insulin sensitivity compared to a placebo supplement (5). This study found that those participants at risk for diabetes who took the supplement had better glucose levels than those who took a placebo. They also had additional markers that indicated increased insulin tolerance. Another double-blind, random clinical trial (including 97

participants) found that the blood glucose and insulin levels were decreased in the supplement group as compared with the placebo group (6). Again, they excluded pregnant women from the study. It seems that magnesium supplementation is effective in reducing type 2 diabetes.

Other Populations

Several studies extrapolated the data from the general public to more specific populations. One study found that the relationship between magnesium and insulin not only applies to adults but to children: obese children who ate low magnesium diets had higher insulin resistance than their lean peers who ate high magnesium diets (7). While there was no intervention in this study, it gives us more evidence that there is a relationship between dietary magnesium and serum insulin levels among children.

A study analyzed blood samples from patients with metabolic syndrome but without diabetes. They found a significant correlation between BMI and blood magnesium levels: those with higher BMIs had lower blood magnesium levels (8). This difference was more pronounced for white people than for non-white people. However, another study analyzed women with polycystic ovary syndrome (PCOS), a condition that is often associated with diabetes. They found that there was no significant difference in serum magnesium levels between women with PCOS and age-matched, BMI-matched controls (9). One difference between this study and others is that none of the participants were found to have low levels of serum magnesium. This may indicate that those who already have adequate magnesium in their diets would not benefit from magnesium supplementation.

Pregnancy and Magnesium

In general, pregnant women generally have lower plasma magnesium levels compared to non-pregnant controls. One study found that women with Gestational Diabetes Mellitus (GDM)

had even lower levels of plasma magnesium (10). However, this still leaves the question: do low magnesium levels increase risk for GDM or does GDM cause low magnesium levels?

One study involving 997 women investigated the mechanism through which women without diabetes develop GDM during pregnancy. They found a relationship between GDM and TRPM6. This is closely linked to magnesium because magnesium is a cofactor for the insulin TRPM6 channel. In the study, they tested the HgA_1C of pregnant patients and measured the types of TRPM6 receptors that the women had. The presence of the TRPM6(V1393I) and TRPM6(K1584E) receptors are associated with increased HgA_1C levels in pregnant patients. The presence of TRPM6(V1393I) and TRPM6(K1584E) instead of the regular TRPM6 channels may predispose a pregnant women to hypomagnesemia. Thus, there may be genetic factors that predispose a woman to GDM. It was not determined whether supplementary magnesium would decrease a woman's chance of developing GDM if she had irregular TRPM6 receptors (11).

Methods

Study Design

This will be a placebo controlled, double-blind clinical trial. The methods of recruiting participants will be through convenience sampling, though we will randomize participants into the intervention and control groups. We will obtain a sample of at least 200 pregnant women though fliers and advertisement. We will hang up four posters each at BYU, WIC clinics, and OBGYN offices throughout Utah County. We will also put 100 fliers by each poster that pregnant women can take. These fliers will have information necessary to enroll in the study.

Sample

After making sure the participant qualifies, we will randomly assign each woman to either the intervention or control group. To qualify, the participants must be between 4 and 14

weeks of pregnancy, not have diabetes (either type 1 or type 2), and have at least one risk factor for GDM (including diagnosis of GDM or preeclampsia in a previous pregnancy, classification as overweight or obese, or diagnosis of hypertension.) We will provide the pills to the women in a double blinded manner and instruct them to take the supplement each day with their prenatal vitamins.

Procedures

Throughout the next several months we will send out biweekly emails reminding them to take their daily supplements. At 36 weeks gestation, we will send out emails asking if the women have given birth. If they have, we will ask them to answer a survey with questions such as "I took the vitamin supplement provided ____days out of seven each week", "were you diagnosed with gestational diabetes during this pregnancy", "have you had gestational diabetes in a previous pregnancy", etc. We will continue to send this email to those who have not responded every other week for the next six weeks (until 42 weeks gestation). After the end of eight weeks (44 weeks gestation), we will individually call those who have not responded to the online survey.

Analyzing Data

We will perform a chi squared test to determine whether or not the intervention led to a significant change in incidence of the diagnosis of GDM. This test will allow us to reject or fail to reject our null hypothesis that a magnesium supplement will have no effect on the incidence of GDM diagnosis when compared to a placebo control. We will analyze the treatment and control groups using the gathered demographic, risk factor, and pregnancy information. If the two groups are significantly different in one of these factors, we will control for these variables and

calculate further statistics. We hope that this information will enable us to better help pregnant woman minimize their risk for developing GDM.

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Budget

Expense	Cost
Posters (12)	$240
Fliers (300 sheets with 4 per page)	$25
Magnesium supplement (for 100 people)	$1000
Placebo (x100)	$800
Pill bottles and labels	$100
Research Assistant (50 hours)	$500
Gas money to distribute fliers	$30
TOTAL	**$2695**

*****This budget assumes that the primary researchers are being paid by a university. This would also cover the cost of a statistician, phones, buildings, and computer software to analyze data.