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Review Article

Treatment Approach in Gestational Diabetes Mellitus: A Narrative Review

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Abstract

Background: Diabetes, specifically gestational diabetes mellitus (GDM), has become a global concern, impacting one out of every ten pregnancies. While previously more prevalent in developed nations, GDM is now increasingly common in developing regions, presenting a growing public health challenge. Despite often resolving after delivery, GDM raises the risk of recurrence in subsequent pregnancies and elevates the long-term risks of cardiovascular disease and diabetes for both the mother and child.

Methods: This narrative review consolidates global recommendations and diverse guidelines on GDM management. It underscores the importance of a multidimensional approach, focusing on lifestyle modifications tailored to individual needs. Aerobic and resistance training, combined with personalized dietary adjustments, emerge as effective interventions. Pharmacotherapy may be necessary for about one-third of GDM cases where optimal glycemic control proves challenging.

Results: The review highlights the primary strategy of GDM management, emphasizing lifestyle modifications such as diet and exercise adjustments. It also discusses the role of pharmacotherapy when needed for glycemic control.

Conclusions: By providing comprehensive insights into diverse treatment approaches, this review aims to benefit healthcare professionals, researchers, and policymakers. The holistic approach advocated ensures optimal care for individuals with GDM, addressing immediate needs and safeguarding the long-term health of both mother and child. This synthesis contributes to a nuanced understanding of GDM management, aiding informed decision-making and policy formulation in maternal healthcare.

Keywords: Gestational Diabetes Mellitus, Pregnancy, Treatment, Insulin, Metformin, Glyburide.

Introduction

Diabetes affects one in ten pregnancies globally, with the majority of cases being attributed to gestational diabetes mellitus (GDM) [1]. While GDM was once considered a significant public health concern primarily in developed nations, it is now emerging as a challenge in developing countries. The South Asian region, Middle East, Western Pacific regions, North Africa, and many others are witnessing a rising prevalence of GDM, whereas its occurrence is comparatively lower in Europe [2].

GDM usually resolves post-delivery. However, women with a history of GDM are prone to its recurrence in subsequent pregnancies. In addition, they may confront an elevated risk of developing cardiovascular disease (CVD) and diabetes mellitus (DM) in the future, posing long-term implications for the well-being of both the mother and child [3].

Broadly, the specific risks linked to diabetes during pregnancy include spontaneous abortion, gestational hypertension, preeclampsia, fetal anomalies, neonatal hypoglycemia, fetal death, neonatal respiratory distress syndrome (NRDS), macrosomia, and hyperbilirubinemia [4].

The main goal of treating GDM is to regulate maternal blood sugar (BS) levels, aiming for normalization while minimizing the risk of hypoglycemia. Effectively managing GDM contributes to improved outcomes for infants and lowers the risk of adverse events [5].

A synthesis of global recommendations across diverse guidelines indicates that, as a primary intervention, aerobic training for a minimum of 3-4 sessions per week, totaling 50 minutes to 2.5 hours per week, with a daily upper limit of half an hour, coupled with resistance training at least twice a week, stands out as the most effective physical activity (PA) intervention for GDM. This is recommended alongside dietary modifications [6].

While many individuals can achieve target glucose levels through exercise and nutritional therapy, approximately one-third may require pharmacotherapy. Notably, even pregnant individuals with mildly elevated glucose levels, who do not meet standard GDM criteria, may benefit from appropriate treatment, leading to enhanced pregnancy outcomes [7]. The emphasis is on tailoring treatment approaches to address specific glucose management needs, ensuring comprehensive care for optimal maternal and fetal well-being [8]

In the management of gestational diabetes mellitus (GDM), lifestyle modifications involving diet and exercise are the primary approach. However, if optimal glycemic control is not achieved, pharmacologic treatment becomes necessary. Insulin is recommended as the first-line treatment when lifestyle changes prove insufficient. Oral hypoglycemic agents like metformin and glyburide are increasingly used. This treatment approach aims to balance glycemic control while minimizing hypoglycemic risks [8]. In managing GDM, successful treatment strategies encompass individualized prenatal care and fetal monitoring. If lifestyle adjustments prove insufficient, the evaluation of metformin or insulin prescriptions remains pertinent, even amid the coronavirus disease 2019 pandemic, given the potential correlation between coronavirus disease and other pregnancy complications, such as Preeclampsia, as indicated by prior research [9,10].

The goal of this narrative review is to explore and assess the different treatment approaches employed in the management of GDM. By synthesizing existing literature, the study aims to offer

a comprehensive understanding of the effectiveness, challenges, and outcomes associated with various interventions, including lifestyle modifications, medical nutrition therapy, and insulin therapy. The objective is to provide valuable insights that can inform healthcare professionals, researchers, and policymakers in optimizing care and outcomes for individuals with gestational diabetes mellitus during pregnancy.

Methods

In this narrative review, our objective is to examine and evaluate diverse treatment approaches utilized in the management of GDM. To accomplish this, we conducted a thorough search and retrieved pertinent English publications from various databases, including PubMed, Web of Science (WOS), Google Scholar, and Scopus. Our search was guided by specific keywords such as Gestational Diabetes Mellitus, Diabetes, Gestational Diabetes, Pregnancy, Treatment, Insulin, Metformin, and Glyburide.

Results

The treatment approach for GDM mandates a multidimensional strategy to uphold optimal maternal and fetal health. Delving into nutrition therapy, physical activity, and medical interventions, this triad of strategies demands nuanced consideration in the management of GDM.

Nutrition Therapy

The nutrition therapy for GDM involves daily meal planning to ensure adequate maternal and fetal nutrition while achieving glycemic targets. Studies suggest potential benefits of following the dietary approaches to stop hypertension (HTN) as well as GDM for reducing cesarean section deliveries, though evidence quality is considered low. Various dietary interventions have been explored, posing challenges in guiding specific clinical practices [11].

According to the global recommendations, women diagnosed with GDM are encouraged to promptly start a personalized nutritional plan and participate in physical activity to keep maternal fasting and post-meal blood glucose levels within recommended targets. An effective strategy to attain this objective involves modifying the type and timing of carbohydrate consumption, emphasizing low-to-medium glycemic index carbohydrates, and increasing the frequency of meals [12].

An individualized nutritional plan is required for GDM considering glycemic control, energy needs, pre-pregnancy body mass index (BMI), macronutrient ratios, and the mother's preferences, lifestyle, and activity levels. The HbA1c assay (Hemoglobin subunit alpha), commonly used to measure hyperglycemia in epidemiological research, showed a reversed relationship with BMI [13].

The American Diabetes Association recommends specific daily nutrient intake for pregnant women, emphasizing the importance of prioritizing certain fats and avoiding others.70 grams of protein, 175 grams of carbohydrates (around one-third of a 2,000 calories/day), and 30 grams of fiber are recommended daily for women during pregnancy as a minimum intake. Balancing both the quantity and quality of carbohydrates is crucial for managing glucose levels. Allowing a liberal intake of higher-quality carbohydrates has been associated with positive outcomes, including improved glucose levels and potential benefits for both mother and infant [14].

Physical Activity

Incorporating physical activity as a treatment for gestational diabetes mellitus (GDM) is recommended, particularly when initiated before and during early pregnancy, as it demonstrates a protective effect by lowering the risk of GDM development. After GDM diagnosis, exercise contributes positively to blood glycemic control, fostering enduring changes in health-related behaviors [15]. Widely recognized as an adjunctive therapy for managing type 2 diabetes in non-pregnant individuals, physical activity enhances blood sugar control by improving insulin sensitivity and increasing muscle glucose uptake stimulated by insulin [16]

Maternal physical activity is pivotal in managing and treating GDM, reducing complications, improving overall health for both mother and child. A personalized exercise program, overseen by qualified professionals, is essential for a safe and effective pregnancy approach [17]

The specific guidelines for physical activity as a treatment for women with GDM advocate engaging in moderate-intensity exercise for 30-60 minutes, three times a week. Research indicates that GDM women participating in over one hour of exercise per day experience a reduced risk of abnormal plasma glucose levels. However, there is limited evidence regarding the optimal duration and quantity of physical activity necessary to effectively manage elevated glucose levels in women with GDM [18].

In the absence of contraindications, current observational studies indicate that participating in physical activity during pregnancy is considered safe. Pregnant individuals can safely initiate and continue activities such as walking, low-intensity fitness exercises, cycling, and swimming. With guidance from their obstetrician, individuals are permitted to continue, though not commence, activities like strength exercises, yoga, tennis, running, and badminton. It is recommended for pregnant individuals to avoid participating in contact sports, skiing, horse riding, diving, and surfing [19].

Medical Treatment

Among the ongoing debate about medical interventions for gestational diabetes, challenges arise in some GDM cases. Factors such as language barriers, comprehension difficulties, cultural influences, or financial constraints pose obstacles to the safe and effective use of insulin during pregnancy. When dietary adjustments fall short of achieving glycemic goals, the discussion often shifts toward pharmacological interventions [20].

While studies predominantly advocate insulin therapy as the safest option, the consideration of orally administered medications like metformin or glyburide emerges, contingent upon individual circumstances and a thorough evaluation by healthcare professionals. However, their limited use as a first-line treatment stems from concerns about their potential to cross the placenta, raising uncertainties about the long-term safety of the offspring [21].

Insulin

Throughout pregnancy, insulin doses are regularly adjusted based on BS levels, symptomatic hypoglycemia, dietary intake, physical activity, compliance, and infections. Insulin dosage and the time of injection hinge on factors like gestational age (GA) and weight. The currently available types of insulin are categorized as follows [22]:

1- Rapid-Acting: Aspart (NovoLog)-Lispro (Humalog)

2- Short Acting: Regular Insulin

3- Intermediate Acting: NPH (Neutral Protamine Hagedorn)

4- Long Acting: Glargine (Lantus)-Detemir (Levemir)

5- Ultra-Long Acting: Degludec (Tresiba)

6- Premixed: NPH/REGULAR 70/30

The utilization of short-acting insulin in GDM has been associated with an elevated risk of hypoglycemia and potential variations in glycemic control. New experiences with aspart have been reassuring, although the use of lispro has been linked to an increase in birth weight and a higher occurrence of neonates classified as large for gestational age. In contrast, when considering intermediate- and longer-acting insulin, studies comparing detemir to NPH have revealed no notable differences between them in terms of perinatal outcomes and controlling BS. In addition, detemir has demonstrated a lower incidence of hypoglycemia in non-pregnant women diagnosed with diabetes [23,24]. Metformin exhibits a transfer from mother to fetus, and its long-term impact remains unclear. The Metformin in Gestational Diabetes trial, a randomized multicenter study involving women diagnosed with GDM, revealed that the primary outcomes of metformin on neonatal morbidity rates were nearly identical to those in the insulin group [25].

Glyburide

Glyburide, or glibenclamide, is an FDA-approved second-generation sulfonylurea for treating type 2 diabetes (T2D). Available in generic form, it serves as an adjunct to physical activity and diet. Effective in lowering blood glucose levels, it is typically prescribed in small daily doses [26].

Sulfonylureas are a class of medications that exert their action by binding to receptors on pancreatic beta cells. This mechanism has been making sulfonylureas a well-established and cost-effective option. Despite their affordability, predictability, and safety, the significant risk of hypoglycemia, a common side effect, restricts their widespread use. Weight gain is another prevalent side effect associated with the use of sulfonylureas [27].

The use of glyburide in gestational diabetes raises concerns based on meta-analyses revealing suboptimal short-term outcomes. Linked to higher birth weight, increased macrosomia, and greater neonatal hypoglycemia, glyburide prompts discouragement for further trials. Evidence suggests that when metformin or insulin is available, glyburide should not be the preferred choice for managing gestational diabetes due to its inferior performance [28]. A study involving women with GDM did not demonstrate any significant difference in perinatal complications including neonatal hypoglycemia, macrosomia, and hyperbilirubinemia between the use of glyburide and subcutaneous insulin. However, these results provide insufficient support for considering glyburide as the primary treatment option [29].

Metformin

Metformin, an oral antihyperglycemic agent, enhances glucose tolerance in T2DM. by reducing basal BS and postprandial plasma glucose levels. Its distinct mechanisms include decreasing hepatic glucose production, enhancing insulin sensitivity, and reducing intestinal glucose absorption. Metformin avoids hyperinsulinemia and hypoglycemia, unlike sulfonylureas. It doesn't alter insulin secretion but may decrease fasting insulin levels [30].

Metformin demonstrates positive maternal outcomes by addressing issues related to weight gain and pregnancy-

induced hypertension. While fetal outcomes pose challenges, including a higher incidence of preterm births and less severe neonatal hypoglycemia, metformin shows a slight advantage, particularly when used in conjunction with insulin as needed, for short-term management of gestational diabetes. Despite concerns about its elevated treatment failure rate and uncertain long-term safety, metformin remains a viable option [31].

The results of a meta-analysis indicated that in women diagnosed with GDM, there were no noticeable differences in short-term maternal outcomes between those treated with glyburide and those administered insulin. However, the glyburide group showed a higher incidence of neonatal hypoglycemia compared to the insulin-treated group [32].

Certain women dealing with gestational diabetes and requiring medical intervention may face challenges hindering the safe and effective use of insulin during pregnancy. In such situations, considering oral medication as an alternative is plausible after discussing known risks and emphasizing the need for more comprehensive long-term safety data for offspring. Nevertheless, exercising careful consideration is paramount, and it is advisable to avoid using metformin during pregnancy in cases of preeclampsia, hypertension, or for those at risk of intrauterine growth restriction due to potential complications like acidosis or growth restriction associated with placental insufficiency [33,34].

Conclusion

The multifaceted management of GDM necessitates a comprehensive strategy, blending lifestyle adjustments, personalized nutrition, and moderate-intensity exercise. While medical interventions such as insulin, metformin, and glyburide offer tailored options, insulin retains its prominence. This holistic approach aims to ensure optimal care for individuals with GDM by addressing both immediate needs and long-term maternal and fetal well-being.

Conceptualization

Study concept and design: A. F. Y., G. C., S. A. R. N., and B. F.; data acquisition: G. C., S. A. R. N., and B. F.; data analysis and interpretation: A. F. Y., G. C., and B. F.; drafting the manuscript: A. F. Y., G. C., and S. A. R. N.; critical revision of the manuscript for important intellectual content: S. A. R. N., and B. F.; statistical analysis: G. C., S. A. R. N., and B. F.; administrative, technical, and material support: A. F. Y., G. C., S. A. R. N., and B. F.; study supervision: A. F. Y., G. C.,B. F., and S. A. R. N.

Conflict of Interest

The authors confirm no conflicts of interest, financial support, or employment related to this research. They have no personal financial interests, shares, stocks, patents, consultation fees, or unpaid memberships in organizations. No editorial board members or reviewers from this journal are associated with the study.

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