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Preconception optimization of glycaemic control in diabetes

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Abstract

The prevalence of Diabetes Mellitus is increasing worldwide. In developing countries 25% of adult females with diabetes are in the reproductive age. Thus in developing countries increased number of pregnancies are complicated by diabetes. Uncontrolled diabetes in pregnancy is associated with increased risk for both mother and foetus. These risks can be minimized by good control of diabetes before and during pregnancy. Management in the preconception period is discussed in this review article. Detailed management involves general advice of lifestyle modification followed by specific details of screening for complications of diabetes. Changes in the drugs for both glycaemic control and other co-morbid conditions are discussed. The recommended insulin regimen in the preconception period and monitoring of glycaemic control by self-monitoring of blood glucose (SMBG) and HbA1C has also been highlighted.

Keywords: Preconception, Diabetes mellitus, Glycaemic control, Pregnancy.

Introduction

The prevalence of Diabetes Mellitus continues to rise worldwide. International Diabetes Federation predicts a 55% increase in diabetes prevalence by 2040. In developed world more than 50% of diabetics are above the age of 65 and only 8% of adults are less than 44 years of age, the childbearing age. In contrast in developing countries 25% of adults with diabetes are in the reproductive age.[1]

Thus in developing countries increased number of pregnancies are complicated by diabetes.

Risks associated with diabetes during pregnancy

Pregnancies of women with diabetes are regarded as high risk for both mother and foetus. Miscarriage/abortion, pre-eclampsia and pre-term labour is more common in women with preexisting diabetes.[2] The rate of caesarian section is also higher in diabetic pregnancies. Diabetic retinopathy[3] and possibly diabetic nephropathy[4] may also worsen during pregnancy. Congenital malformations, macrosomia, birth injury, perinatal mortality and postnatal hypoglycaemia are more common in babies born to mothers with preexisting diabetes. These risks can be minimized by good control of diabetes before and during pregnancy.[5]

Management in the pre conception period

Almost all guidelines recommend a multi-disciplinary approach in diabetic patients who are contemplating pregnancy. They should be counseled about the importance of strict glycaemic control prior to conception. This should be achieved by informing the women that foetal organogenesis occurs during the first 7 weeks of intrauterine life some of which occurs before missing the first menstrual period emphasizing the importance of a planned pregnancy.

Diabetic women with an HbA1C >8% should be discouraged from becoming pregnant. Strongly advise women with HbA1C >10% not to get pregnant. Spontaneous miscarriages and foetal malformations are low when the HbA1C is modestly raised and increases rapidly with higher HbA1C levels (Figure).

The possibility of pregnancy should be identified by direct questioning at each clinic visit in all women of child - bearing age with diabetes.

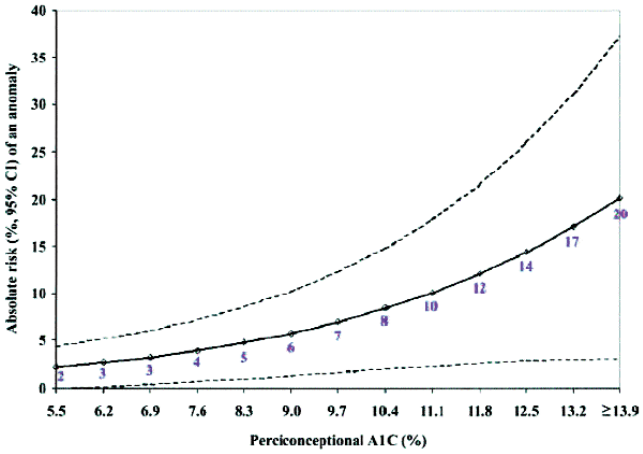

Figure: Risk of Foetal Anomaly Relative to Periconceptional A1C.

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Contraception

Contraception should be recommended until optimal diabetic control has been achieved. The contraception methods are the same as in the general population but in the presence of vascular complications, estrogen containing contraceptive pills should be avoided.[7]

Health Promotion in the pre conception period

Women planning to conceive should be encouraged to stop smoking after discussing consequences of smoking during pregnancy.

They should also be asked to stop alcohol consumption.

BMI should be calculated and if overweight or obese weight reduction prior to conception should be discussed. Obesity is an independent risk factor for delay in conception and for foetal abnormalities and adverse pregnancy outcomes.[6]

Folic acid supplementation is advised for at least three months before conception and to be continued for up to 3 months after conception.[9] Other nutrient supplementation like iron, calcium and vitamin D should also be considered particularly in the developing world.

Dietary advice in the pre conception period

Intrauterine growth and development are dependent upon adequate nutrition throughout pregnancy. Extremes of birth weight have long-term consequences.

Dietary advice should be appropriate with personal needs and culturally acceptable. Carbohydrate monitoring remains the key aspect in achieving glycaemic control. A balanced diet which includes fruits, vegetables, whole grain, legumes and milk is recommended for good health.

Physical activity in the pre conception period

Physical activity is encouraged because it has beneficial effects on insulin resistance in type 2 diabetic patients. Women on insulin regimen management of hypoglycaemia resulting from physical activity should be discussed and appropriately prevented.

Screening for Diabetic Complications

All diabetic women planning pregnancy should be screened for complications of diabetes, as these may accelerate during pregnancy and may change the outcome of pregnancy. In the case of advanced complications, specialist opinion should be sought from a diabetologist/endocrinologist with special interest in diabetes in pregnancy. A complete medical and obstetrical history should be obtained.

Retinal Assessment

Retinal assessment should be done by a diabetologist, ophthalmologist or using a digital camera with mydriasis using tropicamide unless they have had an annual assessment in the last six months.[7] The women who are contemplating pregnancy should be advised to defer rapid optimization of their diabetes until retinal assessment and treatment has been completed. There is a risk of progression of retinopathy during pregnancy which can be reduced through gradual improvement in glycaemic control rather than aggressive approach.

Renal assessment

Renal assessment should also be done by measuring serum creatinine, estimating e-GFR and measuring urine micro albumin. If serum creatinine is raised, e-GFR is less than 45 ml/minute or urinary albumin creatinine ratio is greater than 30 mg/mmol, consider referring to a nephrologist before going ahead with conception.[7] In the presence of overt diabetic nephropathy there is increased risk of permanent deterioration in maternal renal function and poor obstetric outcomes. In less severe diabetic nephropathy there is a risk of transient deterioration of renal function during pregnancy.

Cardiovascular assessment

Blood Pressure should be monitored at the initial assessment and anti-hypertensives appropriate to the pregnancy should be prescribed.

Coronary artery disease if untreated is associated with high maternal mortality during pregnancy. Preexisting coronary artery disease needs assessment and optimization of medications by the cardiologist prior to conception.

Thyroid function assessment

Thyroid function test should be assessed in all type 1 diabetics prior to conception and also in all patients known to have thyroid disorders both hypothyroidism and hyperthyroidism.

Glucose lowering agents in pre conception period and during pregnancy

Insulin remains the agent of choice for use in the pre conception period and during pregnancy. Metformin has been extensively studied in pregnancy. Metformin does not cross the placenta and there appears to be no teratogenic effects of this drug.

Among the sulphonylureas, glyburide/glibenclamide has been studied. It was considered safe until recently when some reports of adverse outcomes of using this drug in

3rd trimester has appeared. National Institute for Health and Care Excellence (NICE),[7] Canadian Diabetes Association (CDA)[9] and other bodies suggest that metformin may be used alone or as an adjunct to insulin in the pre conception period. All other oral and parenteral anti-diabetic agents should be discontinued before pregnancy and should be substituted by insulin.

Short acting human insulin and rapid acting insulin analogues (Aspart and Humalog) have been proven safe during pregnancy and are categorized as category B for pregnancy. Isophane insulin (NPH) and long acting insulin analogue Detemir is also a category B drug for pregnancy and can be safely used. Consider continuing long acting insulin analogue glargine (category C) in women with diabetes who have established good control of diabetes before pregnancy on it.

Glucose control is better achieved when using insulin regimen that mimics normal physiology. Basal bolus regimen also called multiple daily insulin (MDI) regimen, a combination of long acting and rapid acting insulin is the preferred regimen. Basal bolus regimen allows for flexibility as regards dose and timing of insulin. Thus it facilitates achievement of glucose targets, less hypoglycaemia and less basal insulin limiting excessive weight gain. Women on pre mixed insulin regimen should be shifted to basal bolus regimen preferably in the pre conception period. Subcutaneous insulin infusion (SCII) in type 1 diabetic patients if started earlier is recommended to be continued in the pre conception period and during pregnancy.

Drugs used in diabetes for co morbid conditions and complications

Anti-hypertensives

Angiotensin converting enzyme inhibitors and angiotensin receptor blockers/antagonist should be discontinued before conception. In a large cohort study of pregnancy ACE inhibitors use in the 1st trimester was associated with an increased risk of major congenital malformations.

Calcium channel blockers have the potential to cause foetal hypoxia and should be used with caution.[10]

These anti-hypertensives should be stopped in the pre conception period and replaced with drugs like methydopa, labetolol, diltiazem, clonidine and prazosin.

Lipid lowering drugs

Statins should be discontinued before pregnancy. Congenital malformation has been reported with statins and there is also concern that decreased cholesterol synthesis may affect foetal development.[11] The data on the use of Niacin and Fibrates during pregnancy is very limited so it should be stopped in the pre conception period.

Monitoring of glycaemic control during the pre-conception period

HbA1C should preferably be done monthly in the pre conception period. International Diabetes Federation (IDF) recommends best possible glycaemic control before pregnancy aiming for an HbA1C of < 6.5% or < 7% if on insulin.[10] American Diabetic Association (ADA) suggests an HbA1C target of < 7% prior to conception to minimize risk.[12]

Self-monitoring of blood glucose (SMBG) is essential with a mixture of fasting levels, pre meals and post meals. Ketone testing should be offered to type 1 diabetics who are planning conception. Ketone testing is recommended during hyperglycaemia and during periods of illness.

The target of blood glucose levels should be individualized but generally in patients with preexisting type 1 or type 2 diabetes, the pre meal glucose should be less than 90 mg/dl and two hour post meal less than 120 mg/dl. These are glycaemic targets during pregnancy and efforts should be made to attain them before pregnancy.

Hypoglycaemia risk is increased with tight control of diabetes so the management of hypoglycaemia should be comprehensively discussed including glucagon injections in case of severe hypoglycaemia in home setting.

Conclusion

Pre-conception optimization of glycaemic control in diabetics is essential to minimize the risk associated with uncontrolled diabetes to the mother and foetus. This involves general health promotion, lifestyle modification and screening for diabetic complications of retinopathy and nephropathy. Medications used for diabetes management are changed to insulin preferably using basal bolus regimen. Monitoring of diabetes control is much more intensive with tighter goals of blood glucose levels and HbA1C.

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