

COUNSELLING A PATIENT WITH CHRONIC ILLNESS BEFORE PREGNANCY

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ABSTRACT

As the reproductive age of women increases, women of reproductive age are exposed to more diseases and medications that are potentially related to adverse pregnancy outcomes. The approach to primary prevention of such outcomes is discussed. By minimizing the risks related to the diseases and the medications *before* conception, the best control of the medical condition and optimized pharmacotherapy is achieved when conception eventually occurs.

Key Words: *Preconception counselling, risk assessment, maternal education, folic acid supplementation, diabetes mellitus, obesity, dyslipidemia, seizure disorder, drug exposure*

INTRODUCTION

The usual preventive medical practices in obstetrics involve blood tests and imaging *during* pregnancy. However, preconception management (or counselling) involves identifying and modifying risks related to maternal health and pregnancy outcome *prior* to pregnancy.

Preconception counselling (PCC) has developed because of an unsatisfactory rate of perinatal mortality–mortality in the first year of life due to congenital malformations, and prematurity and related diseases, both of which can be reduced with PCC. Furthermore, with the aging mother, there is an increased risk of maternal disease and associated medication use. Of all fertile women, some take drugs that are known teratogens and some have pre-existing medical conditions) that could adversely affect pregnancy if not appropriately managed before conception. Of course, there is also a need to identify conditions for which it may be too late to manage prenatal care.

Examples of conditions that require PCC include: need for folic acid supplementation, obesity (high body mass index [BMI]), diabetes mellitus, hypercholesterolemia, epilepsy and use of antiepileptic (anticonvulsant) drugs, maternal phenylketonuria, autoimmune disorders (e.g., systemic lupus erythematosus, inflammatory bowel disease), use of teratogenic drugs (e.g.,

isotretinoin, warfarin), and harmful lifestyle (e.g., smoking, drinking, drug abuse).

Why Are All Women Not Receiving PCC?

There are a number of barriers to having all women receive PCC: social, lifestyle and financial barriers, including insufficient support and reimbursement for health promotion; caregiver limitations, with lack of training and skills regarding health promotion, as well as poor communication among practitioners; and lastly, patient-associated barriers. It is important that a care provider include PCC at any encounter with a woman of reproductive age to ensure that she is periodically examined, is evaluated for sexually transmitted disease, is counselled on contraception, and receives appropriate disease and health maintenance monitoring.

Components of PCC

The 3 essential components of PCC are maternal risk assessment, maternal education, and initiation of appropriate intervention(s). Maternal risk assessment is straightforward and begins with a thorough history and physical exam. This involves a BMI assessment; immunization, medical and surgical history; documenting the genetic history of both parents; identification of current medications, substance use and environmental and occupational exposures; obstetric and

gynaecological history, noting family planning intent and pregnancy spacing; testing for sexually transmitted diseases; and a socioeconomic, educational and cultural assessment.

Education of the patient begins with discussing her lifestyle. Does she use contraception; does she use it properly? What support does she need to be more compliant with current therapies or better managed? Discussion of exposures should include the medications being taken, including non-prescription, self-selected and alternative medicines, as well as substances of abuse. Concerns regarding the teratogenicity of select products and medicines need to be considered. Finally, there also needs to be a discussion about the bidirectional effects of pregnancy and pre-existing conditions, such as depression, epilepsy, immune disorders.

PCC interventions are customized for the patient and include counselling for lifestyle modification, such as cessation of harmful habits and minimizing toxic exposures. Screening tests may be needed for genetic disorders or for diseases (e.g., HIV). Vaccinations should be updated (measles, mumps, rubella, varicella). And for women with chronic diseases, adjustments in their care may be required. Medications can be changed to those with a better safety profile, and treatment and control of disease optimized before pregnancy is considered. In some cases a woman may need to be referred to a specialist or specialized facility for additional care.

Examples of PCC

Folic Acid Supplementation

Folic acid facilitates the production and maintenance of new cells. It is essential during rapid cell division and growth. Folic acid supplementation is the PCC intervention that has the most evidence-based support. In pregnancy, folic acid supplementation prevents up to 75% of neural tube defects.¹ It can also help prevent other abnormalities, such as heart defects, urinary tract anomalies, oral clefts, limb defects, and pyloric stenosis.

Maternal red blood cell (RBC) folate levels need to be at or above 900 nmol/L. The commonly needed dose ranges from 0.4 to 5 mg per day, should be started at least 3 months before

conception² and continued for at least 3 months after conception, when neural tube closure occurs.

Fortification of flour with folic acid is mandatory in countries around the world, including Canada and the US, but not across Europe. In 2006, 40% of reproductive-age women in Ontario, Canada, had RBC folate levels under 900 nmol/L and 20% had levels below 700 nmol/L.³ Strategies to improve supplementation led to significant improvement, with only about 10% of women having folate levels below 900 nmol/L. This is an example of a very successful preconception intervention.

It should be noted that higher folic acid doses, i.e., 5 mg, may be needed for special populations. These include young obese women and women with epilepsy or those treated with antiepileptic drugs. Folic acid supplementation should be advised for every woman of reproductive age at every encounter.

Diabetes Mellitus

Women with pre-existing diabetes mellitus carry the risk of giving birth to children with congenital abnormalities. Congenital malformations account for 30-50% of cases of perinatal mortality in offspring of women with insulin-dependent diabetes mellitus.^{4,5} A significantly increased risk of malformations has also been reported.⁶ Examples of congenital problems include macrosomia, large-for-gestational age, neonatal hypoglycaemia, respiratory distress syndrome, orofacial clefts, cardiovascular defects, oesophageal/intestinal atresia, hypospadias, limb reduction defects, spine malformations, and polydactyly.^{4,5}

Evidence for PCC in diabetes mellitus comes from a meta-analysis conducted by Ray and colleagues.⁷ The pooled rate of major and minor anomalies was lower among preconception glycemic control recipients (2.1%) than non-recipients (6.5%) (RR = 0.36, 95% CI 0.22-0.59).

Because many women with diabetes neither plan their pregnancy nor achieve adequate glycemic control before conception, strategies are needed to improve access to preconception counseling programs.

General interventions for diabetic women of childbearing age include a healthy diet and

exercise, folic acid supplementation, optimal glycemic control and pre-conception recognition of its importance during pregnancy, and when pregnant, appropriate prenatal screening (including a fetal echocardiogram). Euglycemia is important before and during pregnancy, underlining the importance of PCC.

Insulin is the most widely used medication, and has a good safety profile, in pregnancy. Sulfonylureas, specifically glyburide, have not been associated with congenital abnormalities in human studies. Glyburide is increasingly used in pregnant women with type 2 diabetes.

Obesity

Obesity can be associated with a number of comorbidities, such as type 2 diabetes, hypertension, hyperlipidemia, and coronary heart disease. Pregnancy-related risks in the obese woman include infertility (polycystic ovary syndrome), gestational diabetes mellitus, gestational hypertension, thromboembolic events, and an increased rate of caesarean section. Fetal risks include congenital abnormalities, such as neural tube defects, prematurity, and perinatal mortality.

Interventions begin with a healthy diet and regular exercise, together with formal nutritional counselling and folic acid supplementation. Annual BMI calculation is suggested for women of reproductive age. Ideally, pregnancy should be deferred until optimal weight is achieved. In severe cases, bariatric surgery may be considered.

Dyslipidemia

In pregnancy, cholesterol is essential for central nervous system development. On the other hand, hypercholesterolemia in the mother has been shown to relate to plaque formation in the fetus.⁸

There is no evidence as of yet regarding the long-term outcomes of the children of mothers who were taking statins during their pregnancy. Hypercholesterolemia in these children may be confounded by genetics, as well as by their mother's dyslipidemia during pregnancy. Hypercholesterolemia is usually asymptomatic, and may become apparent only when early

coronary heart disease develops. Intervention begins with dietary and lifestyle changes, to which lipid lowering drugs can be added. Drugs include statins, fibrates, ezetimibe, natural products (e.g., red yeast, which contains phytosterols and lovastatin⁹), and some medications currently in development, including monoclonal antibodies. Where there is a family history of premature heart disease (under 55 years of age), treatment with statins is suggested to commence at a young age.¹⁰

Although statins are not approved for use in pregnancy by Health Canada or the US Food and Drug Administration, published studies show no increased risk of birth defects.¹¹⁻¹³ A recent meta-analysis of teratogenic effects in both animals and humans, notes that no pattern of congenital anomalies could be observed in humans.¹⁴ The reviewed animal studies showed conflicting results, with congenital defects observed where doses much higher than those in humans were used. If a statin is indicated, pravastatin may be an option, as its hydrophilic properties may limit placental transfer to the fetus.¹⁵ However, because definitive studies are not available, the U.K. National Institute for Health and Care Excellence (NICE) recommends to stop statins 3 months prior to conception.¹⁶ Good PCC suggests screening for coronary heart disease in women with familial hypercholesterolemia, recommending lifestyle modifications in nutrition and exercise, and prescribing pharmacological therapy as needed.

Seizures and Anticonvulsants

With about 0.5 to 1% of the Canadian population¹⁷ and 7 to 8 out of 1000 women at reproductive age having a seizure disorder,¹⁸ this is the most common serious neurological complication during pregnancy. Pregnancy may increase the frequency of seizures. Seizures can adversely affect pregnancy outcome and increase the risk of malformations and dysmorphism when compared to healthy women. Anticonvulsants have been shown to increase the incidence of spontaneous abortion, low birth weight, developmental disabilities, neonatal haemorrhagic disorders (related to vitamin K deficiency), and perinatal death.¹⁹ Valproic acid, carbamazepine, and phenytoin have all been associated with

teratogenesis, including neural tube defects, cardiac anomalies, and negative cognitive outcomes. The possible mechanism for these effects may relate to reduction in folic acid levels and vitamin K deficiency. The newer agents, lamotrigine and levetiracetam, have so far not exhibited significant risks in pregnancy.

Management of reproductive-age women with seizure disorders includes referral to a neurologist for optimal seizure control. In such cases PCC should be done early. The drug that best controls the seizures is the one of choice.

Monotherapy with a safe drug option at the lowest possible dose is preferred. It is recommended to defer conception until seizures are well controlled. Treatment should include folic acid supplementation and withdrawal of

drugs may be considered only after 2 years of being seizure-free.²⁰

Drug Exposure in Pregnancy

Women and healthcare providers tend to overestimate the teratogenic risk of medications. The default safety position is to consider every drug a potential teratogen, even if data indicates otherwise. The message is usually to avoid medications “to be on the safe side”. Yet, untreated maternal conditions may also adversely affect pregnancy outcomes, e.g., diabetes mellitus, depression, seizure disorders.

The following table outlines specific drugs, exposures, and conditions which are proven to be harmful to the fetus.

TABLE 1 Harmful Exposures in Pregnancy

Drugs	Other Exposures	Maternal Conditions	Intrauterine Infections
retinoic acid (Accutane)	heavy alcohol abuse	diabetes mellitus	toxoplasmosis
warfarin	toluene	hyperthermia	rubella
valproic acid	mercury	hypotension	varicella
methimazole	lead		
misoprostol	radiation		

SUMMARY

Evidence-based PCC is effective in improving maternal and fetal health.^{21,22} PCC is indicated in order to prevent fetal exposures and unnecessary confusion and anxiety in the woman. Preconception counselling should be standard primary care and as routine as prenatal care. PCC helps to identify specific risks and to individualize care. Preconception timing can be crucial and every opportunity used to accomplish PCC. Multidisciplinary, collaborative care may be necessary. Although favorable pregnancy outcomes cannot be guaranteed, when a pregnancy is planned, many risk factors can be reduced and modified to enhance pregnancy outcomes. Examples include: optimization of diet,

weight, and exercise; discontinuation of smoking and drinking; controlling chronic medical conditions; starting supplementation with multivitamins and folic acid; and ensuring proper immunization.

There are many benefits of PCC: to promote healthy pregnancy *before* the pregnancy has occurred; to avoid abrupt discontinuation of drug treatment once pregnancy has been diagnosed; to increase the rate of planned pregnancies and decrease unnecessary terminations; have fewer hospitalizations and adverse pregnancy outcomes; and as a result of many of these benefits to the mother and fetus, to realize cost savings at the personal and societal level.

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