Diabetes in women of childbearing age

Contraceptive options and pregnancy planning

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For women with diabetes, optimal glycaemic control, particularly in the periconception period, is associated with improved pregnancy outcomes. It is important that women with diabetes plan pregnancies so that measures can be taken to achieve optimal metabolic control before conception. A key feature of pregnancy planning is effective contraception.

Key points

- **Effective contraception in women with diabetes is important to reduce the risk of unintended pregnancies and adverse pregnancy outcomes.**
- **Long-acting reversible contraceptives such as intrauterine devices and long-acting subdermal implants are highly effective and suitable for most women with diabetes.**
- **Optimisation of glycaemic control before conception is essential to reduce the risk of fetal abnormalities and adverse pregnancy outcomes.**
- **Screening for diabetes-related complications and optimising maternal blood pressure should occur before conception; medications should be reviewed before conception to avoid teratogenic agents.**
- **High-dose (5mg daily) folic acid should commence at least one month before conception.**

Type 1 and type 2 diabetes carry significantly elevated risks of adverse fetal outcomes, including congenital malformations, miscarriage, preterm delivery, macrosomia and perinatal mortality.[1] Maternal risks of pregnancy include pre-eclampsia and worsening of diabetes-related complications. The first weeks of pregnancy (when a woman may not know she is pregnant) are particularly important because diabetic embryopathy develops during this period.[2]

Women with diabetes have high rates of unintended pregnancy, despite having regular medical care.[3] Women need to know what the risks of pregnancy are and what risks may be preventable by planning a pregnancy. The use of effective contraception is especially important in women with diabetes to enable optimal pregnancy outcomes. Women should be advised to avoid pregnancy by using contraception until metabolic control has been achieved, that is: glycated haemoglobin (HbA_{1c}) less than or equal to 53 mmol/mol (7%) for women with type 1

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diabetes and less than or equal to 42 mmol/mol (6%) for women with type 2 diabetes.[4] Screening for diabetes complications, particularly retinopathy, renal function, microalbuminuria and hypertension, should also occur before conception. Women with diabetes should start higher-than-normal doses of folic acid (5 mg daily) before pregnancy because the risk of neural tube defects is increased.[5] In addition, vaccination status, smoking cessation, alcohol intake and body mass index should be optimised, and medications associated with potential teratogenicity should be changed to agents that are safer in pregnancy.

Contraceptive options for women with diabetes

The reasons why women with diabetes have unplanned pregnancies are complex.[6] For some women this involves a lack of knowledge about their fertility status or effective methods of contraception. Studies have demonstrated that women with diabetes are less likely to receive contraceptive counselling or prescriptions for birth control.[3] For others, the contraceptive methods chosen may not be used or are not effective. Some women do not use contraception, despite not wanting a pregnancy, because they are concerned about potential side effects. The goal is an effective contraceptive method without side effects. Efficacy is highest for long-term contraceptive methods, somewhat less for short-term hormonal therapies and lowest for barrier or behavioural methods.[7] The efficacy and safety of long-acting reversible contraceptive (LARC) methods warrant their consideration as first-line prevention of unintended pregnancy for women with diabetes. Guidelines for contraception state that women with diabetes that is insulin requiring or those with nephropathy, retinopathy, neuropathy or other vascular disease, should be advised to consider the most effective LARC methods, which provide a highly reliable and effective method of contraception (a failure rate less than one per 100 women per year of use).[7]

The levonorgestrel-releasing intrauterine system (LNG-IUS) is an effective, safe and convenient form of LARC (five years). Low but detectable circulating levels of progestin in LNG-IUS users have raised concerns that glucose control, lipid profile and blood pressure may be negatively affected. However, these concerns have not been substantiated in high-quality clinical trials. The data suggest that the LNG-IUS is safe to use in patients with diabetes, hypertension or hyperlipidaemia.[7] Overall the failure rate is low (0.2 pregnancies per 100 woman per year of use).[7]

Copper-medicated intrauterine devices are approved for use in Australia for up to 10 years and have an excellent safety profile and low failure rate (0.8 pregnancies per 100 woman per year of use).[7] Prospective trials examining copper-medicated intrauterine device use in women with type 1 and type 2 diabetes have found no increased risk for pelvic inflammatory disease, pregnancy or discontinuation rates.[8,9]

Contraceptive implants provide long-term, highly effective, convenient and reversible contraception. The subdermal implant contains 68 mg of etonogestrel. It is approved for three years of use and provides excellent efficacy throughout its use. In a study of metabolic effects of the subdermal implant in women with diabetes there was no adverse effect on the lipid profile. Carbohydrate metabolism was unchanged over the two-year study period and no aggravation of vascular lesions was noted.[10] Another study has shown that etonogestrel implants do not significantly increase the risk of cardiovascular disease.[11] Some small studies have shown lower serum etonogestrol concentrations in women with a body mass index more than 30 kg/m^2. Although none of the women had a level below that which is believed to reliably suppress ovulation, there have been some concerns that the lower concentrations may indicate a need to replace the implant sooner than the licensed three years in women who are obese.[12] Failure rate is low (0.05 pregnancies per 100 woman years of use).[7]

Women with diabetes should start higher-than-normal doses of folic acid (5 mg daily) before pregnancy because the risk of neural tube defects is increased.

Many women prefer the option of oral contraceptives. During the past 30 years, the oestrogen and progestin dose of oral contraceptives has been reduced fivefold and 25-fold, respectively, reducing the metabolic side effects and morbidity while retaining pregnancy protection. Today, almost all combination oral contraceptives contain a low oestrogen dosage of ethinyl estradiol (20 to 40 pg), but the formulations and dosage of the progestin component vary widely. Studies in healthy women have demonstrated a dose-dependent deterioration in glucose tolerance and lipid profile associated with cardiometabolic risk with increasing progestin dosage and potency.[13,14] Current low-dose combination preparations, whether containing the new progestins or the older preparations in lower doses, have been shown in prospective studies to have minimal effect on glucose tolerance, insulin secretion or glucagon levels in women with insulin resistance syndromes.[15] Although there may be some differences in metabolism of the oral contraceptive in women who are obese, contraceptive efficacy appears to be maintained because progestin levels do not drop below the level needed to suppress ovulation. Failure rates are reported as nine pregnancies per 100 woman years of use in typical users, although this may be as low as 0.3 per 100 woman years of use in perfect users.[7]

For women with diabetes who have no vascular disease, the advantages of combination oral contraceptive methods generally outweigh any theoretical or documented risks associated with these options.[7] A recent study found that the absolute risk of thromboembolism among women with type 1 or type 2 diabetes using hormonal contraception is low.[16] However, because oestrogen increases the risk of clotting, caution must be used when prescribing combination oral contraceptive methods for women with diabetes in whom vascular comorbidities have developed or in those who smoke. In patients who have evidence of end-organ damage or who have had diabetes for more than 20 years, or patients who have multiple

Resources for GPs and patients

The Australian website Pregnancy and Diabetes contains useful information for women and clinicians, including a prepregnancy checklist, about diabetes and pregnancy: http://pregnancyanddiabetes.com.au

Faculty of Sexual and Reproductive Healthcare. UK medical eligibility for contraceptive use, 2016: www.fsrh.org

cardiovascular risk factors, combination therapy is usually not recommended unless other contraceptive options are not available or acceptable.[7]

Progesterone-only pills are less commonly used due to the requirement of needing to be taken at the same time every day to ensure effectiveness. They are reported to have similar failure rates compared with combined oral contraceptive pills. There may be less thrombophilia risk, but cardiovascular risk may still be elevated in women with multiple cardiovascular risk factors.[7]

Barrier methods have a much higher actual use failure rate compared with perfect use because of the requirement of contraceptive application before coitus.[7] A higher risk of pregnancy or the required motivation for successful use may not make barrier methods an acceptable contraceptive method for many women with diabetes, although they do provide some protection against sexually transmitted infections (failure rate 18 pregnancies per 100 woman years of typical use condoms).[7]

Conclusion

Care and counselling of all women of childbearing age with diabetes should include a discussion of pregnancy intentions and contraception. Resources for both GPs and patients are shown in the Box. Discussion should include that pregnancy outcomes can be improved by pregnancy planning. Pregnancy planning enables optimisation of diabetes control, screening for diabetic complications before conception and review of medication safety in pregnancy. High-dose folic acid (5 mg daily) should be started before conception. The choice of contraception will be guided by patient preference, presence of cardiovascular complications and risks for thromboembolism. LARC methods are effective for women with diabetes and should be considered first line.

Women with diabetes need to know what the risks of pregnancy are and what risks may be preventable by planning pregnancy. The reasons why women have unplanned pregnancies are complex.[5] For some women it involves a lack of knowledge about their fertility status or effective methods of contraception. For other women, the contraceptive method chosen may not be used or are not effective. Some other women do not use contraception, despite not wishing to be pregnant, because they are concerned about potential side effects. The goal is an effective contraceptive method without side effects. Efficacy is highest for long-term contraceptive methods, somewhat less for short-term hormonal therapies and lowest for barrier or behavioural methods. **ET**

References

1. Murphy HR, Bell R, Cartwright C, et al. Improved pregnancy outcomes in women with type 1 and type 2 diabetes but substantial clinic-to-clinic variations: a prospective nationwide study. Diabetologia 2017; 60: 1668-1677.
2. Tennant PW, Glinianaia SV, Bilous RW, Rankin J, Bell R. Pre-existing diabetes, maternal glycated haemoglobin, and the risks of fetal and infant death: a population-based study. Diabetologia 2014; 57: 285-294.
3. Schwarz EB, Postlethwaite D, Hung YY, Lantzman E, Armstrong MA, Horberg MA. Provision of contraceptive services to women with diabetes mellitus. J Gen Intern Med 2012; 27: 196-201.
4. Cheung NW, Conn JJ, d'Emden MC, et al. Position statement of the Australian Diabetes Society: individualisation of glycated haemoglobin targets for adults with diabetes mellitus. Med J Aust 2009; 191: 339-344.
5. Chitayat D, Matsui D, Amitai Y, et al. Folic acid supplementation for pregnant women and those planning pregnancy: 2015 update. J Clin Pharmacol 2016; 56: 170-175.
6. Earle S, Tariq A, Komaromy C, et al. Preconception care for women with type 1 or type 2 diabetes mellitus: a mixed-methods study exploring uptake of preconception care. Health Technol Assess 2017; 21: 1-130.
7. Faculty of Sexual and Reproductive Healthcare (FSRH). UK medical eligibility for contraceptive use. London: FSRH; 2016. Available online at: www.fsrh.org/standards-and-guidance/uk-medical-eligibility-criteria-for-contraceptive-use-ukmec (accessed July 2018).
8. Kimmerle R, Weiss R, Berger M, Kurz KH. Effectiveness, safety, and acceptability of a copper intrauterine device (CU Safe 300) in type I diabetic women. Diabetes Care 1993; 16: 1227-1230.
9. Kjos SL, Ballagh SA, La Cour M, Xiang A, Mishell DR, Jr. The copper T380A intrauterine device in women with type II diabetes mellitus. Obstet Gynecol 1994; 84: 1006-1009.
10. Vicente L, Mendonca D, Dingle M, Duarte R, Boavida JM. Etonogestrel implant in women with diabetes mellitus. Eur J Contracept Reproductive Health Care 2008; 13: 387-395.
11. Merki-Feld GS, Imthurn B, Seifert B. Effects of the progestagen-only contraceptive implant Implanon on cardiovascular risk factors. Clin Endocrinol 2008; 68: 355-360.
12. Faculty of Sexual and Reproductive Healthcare (FSRH). CEU statement: weight and contraception. London: FSRH; 2017. Available online at: www.fsrh.org/standards-and-guidance/documents/ceu-statement-weight-and-contraception-april-2017 (accessed July 2018).
13. Godsland IF, Crook D, Simpson R, et al. The effects of different formulations of oral contraceptive agents on lipid and carbohydrate metabolism. N Engl J Med 1990; 323: 1375-1381.
14. Wang Q, Wurtz P, Auro K, et al. Effects of hormonal contraception on systemic metabolism: cross-sectional and longitudinal evidence. Int J Epidemiol 2016; 45: 1445-1457.
15. De Leo V, Fruzzetti F, Musacchio MC, Scolaro V, Di Sabatino A, Morgante G. Effect of a new oral contraceptive with estradiol valerate/dienogest on carbohydrate metabolism. Contraception 2013; 88: 364-368.
16. O'Brien SH, Koch T, Vesely SK, Schwarz EB. Hormonal contraception and risk of thromboembolism in women with diabetes. Diabetes Care 2017; 40: 233-238.

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