Gestational Diabetes in General Practice

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SUMMARY

The role of the general practitioner in the diagnosis and management of the gestational diabetic is defined. Recognition of this condition is important for improving the perinatal mortality; as is advice regarding steroid contraception; and as a means of predicting the development of overt diabetes. Methods of diagnosis are briefly commented upon.

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This article sets out to establish the significance of gestational diabetes and attempts to define the role of the general practitioner in its diagnosis and management. Gestational diabetes refers to abnormal glucose tolerance during pregnancy, which reverts to normal in the puerperium.[1] It is a condition which can be confirmed only in retrospect, i.e. after delivery, and which is usually asymptomatic. The diagnosis of the gestational diabetic is based on blood sugar levels obtained after a loading dose of glucose. The values for abnormality vary from centre to centre, and depend upon fasting, 1- and 2-hour blood sugar levels, subsequent to the oral administration of either 50 or 100 g of glucose. For purposes of the present discussion, a gestational diabetic is regarded as one in whom the fasting, 1-hour and 2-hour venous, true, blood sugar levels exceed 120, 180 and 140 mg/100 ml of glucose, respectively.

AETIOLOGY OF THE GESTATIONAL DIABETIC

The aetiology of the gestational diabetic is not germane to the present discussion and will not be commented upon, except for two features which are relevant to its diagnosis and treatment. Firstly, it has been shown that the acute release of insulin in gestational diabetics is sluggish, and that they exhibit marked peripheral resistance to insulin.[2,3] The combination of these two factors results in a relative state of hyperglycaemia, and consequently hyperinsulinism, comparable to that obtaining in obese diabetics. It is the absence of acute insulin release during the initial phase of the glucose tolerance test which differentiates this pathological state from the compensatory hyperinsulinism normally found during late pregnancy.

Secondly, the diabetogenic influence of pregnancy is progressive, and becomes more apparent later in pregnancy. This has a significant relation to diagnosis.

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RELEVANCE OF GESTATIONAL DIABETES TO THE GENERAL PRACTITIONER

Immediate Perinatal Result

It is a well-established fact that the perinatal mortality in patients destined to develop diabetes, is considerably greater than it is in patients without this predisposition. Thus, in a recent survey of the literature, Mestman *et al.*[4] noted that the perinatal mortality in the 5 years preceding the diagnosis of overt diabetes, varied from 15% to 40%. Conversely, the recent reduction in the stillbirth and neonatal mortality rate in established diabetics to figures well below 10%, has been brought about by consistent control of the blood sugar. Adequate control has had a beneficial effect even on the perinatal morbidity associated with the pregnant diabetic. If carbohydrate tolerance is achieved early enough in pregnancy, a decrease in congenital abnormalities commonly associated with the diabetic state can be anticipated.[5,6]

The probable season for this improvement relates to the maternal hyperglycaemia - fetal hyperinsulinism theory. Briefly, it is known that a direct relationship exists between the blood sugar levels in the mother and in the fetus, and that provided the plasma glucose of a normal mother stays within the physiological limits, a maternal-fetal plasma glucose difference of less than 20 mg/100 ml is maintained.[7] Maternal glycaemia, therefore, indirectly stimulates the developing beta cells of the fetal pancreas. Depending upon the degree of maternal glycaemia, a state of fetal hyperinsulinism may arise. This effect has been more marked in neonates of diabetic mothers, than in those born to normal women.[8] Under fasting conditions, although the supply of glucose from the mother is greatly diminished, hyperinsulinism (having been stimulated previously) often persists, and may be responsible for severe intra-uterine fetal hypoglycaemia. This is particularly true of infants born to diabetic or prediabetic mothers.[7]

The maternal hyperglycaemia - fetal hyperinsulinism theory is also said to account for the increased fetal mass noted in pre- and overt diabetics. The mechanism involved is conversion of the excessive carbohydrate to body fat.

In short, maternal hyperglycaemia resulting in fetal hyperinsulinism probably accounts for the characteristic overweight baby produced in the prediabetic years, and may be responsible for the unpredictable intra-uterine deaths and symptomatic neonatal conditions associated with profound hypoglycaemia.

Consistent control of the blood sugar in these women—and not the factor X which is responsible for its elevation—results in a marked decrease in the birth mass and a similar improvement in the perinatal mortality and morbidity. As restoration of normal glycaemia has improved

the perinatal result in overt diabetics, it is not surprising that the same is true for the gestational diabetic.[9] Therefore, early recognition and early treatment of gestational diabetes will improve the immediate perinatal result.

How does one treat the gestational diabetic? The medical management during pregnancy is essentially the same as that of an established diabetic, the objective being to achieve normoglycaemia throughout pregnancy. In the past, control of the diabetes has been vaguely inferred, and consequently authors have differed about the degree of control required. More recently, Karlsson and Kjellmer[5] noted a marked improvement in perinatal survival if blood sugar levels were kept consistently below 100 mg/100 ml. For example, the perinatal mortality was 4% when the blood sugar was kept below this level. In patients who had a blood sugar level consistently above 150 mg/100 ml, the mortality rate increased to 23,6%. These figures are not related to the severity of the peripheral vascular complications, and refer specifically to blood sugar control. The main difference in the treatment of overt and gestational diabetics is that in the latter condition it is not necessary to rely on insulin. The gestational diabetic invariably produces adequate amounts of insulin, and dietary restriction with supplementation by biguanides, is usually perfectly adequate.[10]

The second difference involved in the management of the gestational diabetic is that the pregnancy is allowed to continue to term.[11] Induction of labour is only recommended for post-datism or for other obstetrical complications. This more liberal approach to the termination of pregnancy is possible because the gestational diabetic very infrequently suffers from peripheral vascular disease —a condition associated with decreased placental perfusion. In overt diabetics, premature induction of labour is usually recommended for this reason. The mode of delivery is based entirely upon obstetrical considerations.

Contraceptive Advice

Oral contraception is the most effective form of contraception today. Preparations containing both an oestrogen and a progestogen are the most reliable. The oestrogen used, in particular mestranol, is thought to affect carbohydrate metabolism adversely.[12] For example, Szabo *et al.*[13] reported abnormal glucose tolerance tests in their gestational diabetics within 4-8 months of starting treatment. Of those who developed this abnormality, none showed metabolic adjustment after prolonged usage. The same authors reported 3 patients in whom diabetes was precipitated after the use of oral contraceptives. Others[14] maintain that the diabetogenic effect of these steroids is less noticeable when sequential preparations are used, while Posner *et al.*[15] believe that, although an abnormality in carbohydrate metabolism does occur subsequent to the taking of some of the oral contraceptives, glucose tolerance invariably returns to normal after a period of time. This is said to be the result of hypertrophy and hyperplasia of the islets of Langerhans, and correlates well with the clinical observation of raised insulin levels in patients taking steroid contraceptives.[16]

It would be wrong to over-emphasise the harmful effect of the steroid contraceptives on carbohydrate metabolism, since unlike pregnancy and adrenal steroids (where insulin secretion itself is affected), the oestrogen present in the pill merely decreases the sensitivity of the peripheral tissues to the hypoglycaemic effect of insulin.[15] Nevertheless, since there is doubt as to whether this altered carbohydrate metabolism reverts to normal with the cessation of therapy, or can precipitate overt diabetes, the consensus is that potential diabetics should be excluded from this method.

Therefore, the second benefit that would result from the detection of gestational diabetes, is that aggravation of a latent diabetic state would be averted.

Ideally, gestational diabetics should be offered mechanical forms of contraception, such as the intra-uterine device. If, however, the pill needs to be given, preparations containing progesterone should be used. If these cannot be tolerated, a low-dosage, combined preparation should be prescribed, excluding, if possible, those contraceptives which contain mestranol. Gestational diabetics on steroid contraception should have 6-monthly or annual glucose-tolerance tests.

It is pertinent to note that oral contraception is said to have little effect on diabetic control in established diabetics.[17]

Prediction of Overt Diabetes

Prospective population surveys, such as those conducted in Birmingham, have proved that one can predict the development of overt diabetes in susceptible populations.[19] It is equally well established that diabetes is responsible for much blindness, deafness, cardiovascular and renal disease. What is not agreed upon, however, is whether the early recognition of diabetes and its treatment will help in the prevention or amelioration of the disease itself and the complications resulting from it.

By screening for diabetes, it will be possible to classify patients into 3 classes, namely; biochemically normal; overtly diabetic; and potentially diabetic. The first 2 classes do not constitute a problem—the normal patients obviously do not require treatment, and the newly-discovered diabetics would be managed according to accepted practice. There remains the core of potential diabetics who do not qualify for treatment, but for whom the risk of developing diabetes late in life is nevertheless very great. Should these patients be informed of this abnormality, or should they be left in ignorance? Experience with Papanicolaou smear screening for cervical cancer serves as a useful example. It is known that many cases of dysplasia and carcinoma *in situ* do not progress to invasive carcinoma — yet those who do present with this histological abnormality are more prone to the development of invasive cancer. Provided the patient is not lost to follow-up it is not necessary to inform her of the potential of this abnormality. Any progression or recurrence of the disease will be detected at an annual examination.

Similarly, it is not essential to inform a potential diabetic of their diathesis, since annual blood tests will indicate whether the potential abnormality has progressed to overt disease. Reverting to the question as to the value

of treating potential diabetics, it is worth noting that control of the blood sugar level, and not the cause of the biochemical abnormality, has resulted in a marked improvement in the perinatal mortality rate of pregnant diabetics.

The diabetogenic stress of pregnancy frequently enables one to predict the development of overt diabetes. O'Sullivan[20] noted that of 137 gestational diabetics 7,1% developed clinical diabetes within 6 months, and no fewer than 28,5% of these were found to be diabetic when retested 5 years later. Therefore, by screening pregnant patients for diabetes, gestational diabetics will be detected, some of whom will later develop overt diabetes. Although some authors[21] feel that there is no point in making an early diagnosis because the issue is unaffected, neither is there proof to the contrary.[22] By instituting dietary control, and when necessary, additional antidiabetic therapy, one may be able to exert a beneficial effect on the pathogenesis of this disease and reduce, if not prevent, its associated long-term morbidity. One should give the patient the benefit of this approach, since the years spent in waiting for proof are irretrievable.[22]

In summary, the diagnosis of gestational diabetes could be of advantage to the patient in the following 3 respects: it could result in an improvement of the immediate perinatal mortality; it could serve as an important guide in contraceptive practice, especially in populations known to have a high incidence of diabetes; and it could enable one to institute early treatment for diabetes, thereby possibly reducing the incidence and degree of diabetic vasculopathies and other associated complications.

HOW, WHEN AND WHO?

How. Recent diabetic screening surveys have suggested that glycosuria is a most unreliable method of diagnosing diabetes.[23,24] This is particularly true during pregnancy. For example, in a personal survey[25] of diabetes among pregnant Natal Indians, it was shown that no fewer than 35% of established diabetics presented with aglycosuria, and that only 18,4% of pregnant subjects with glycosuria were found to be diabetic. More accurate and reliable information would be obtained if blood sugar estimations were performed 2 hours after a carbohydrate meal or glucose load. Although a full glucose tolerance test is better than a single blood sugar reading, the following classification of blood glucose levels after a 50 g glucose load is thought to be thoroughly reliable:[26] (*a*) levels below 135 mg/100 ml are probably indicative of normal carbohydrate balance; (*b*) blood sugar levels from 135 to 199 mg/100 ml indicate a high risk of florid diabetes; and (*c*) values over 200 mg/100 ml are indicative of definite florid diabetes.

Screening of a population into these 3 groups can be easily and conveniently achieved with the use of the Dextrostix test strip.[27]

When. Gestational diabetes can be diagnosed only when the patient is pregnant, as carbohydrate tolerance is rapidly restored to normal in the early puerperium. Furthermore, the earlier the diagnosis is made, the sooner can perinatal morbidity and mortality be predicted and prevented. Since the diabetogenic effect of pregnancy is progressive, one should screen for diabetes during the first, second, and third trimesters. This can be conveniently arranged by instructing patients to present themselves at the surgery or clinic about 2 hours after a high carbohydrate meal. Finger-prick samples of blood and the accurate application of the Dextrostix test strip provides the answer within 1 min.

Who. Every pregnant woman has her urine tested for the presence of reducing substances at every antenatal visit, the objective being to diagnose diabetes. The incidence of gestational diabetes is 8 times greater than that of overt diabetes. It is, therefore not an infrequent condition although its incidence will vary with the population group served. O'Sullivan[20] noted that 1 out of every 116 patients attending their unit were gestational diabetics. In deciding upon a screening programme, priority should be given to testing for conditions known to be prevalent. For example, the incidence of diabetes among the Eskimos is known to be extremely low, whereas some 50% of Pima Indians over the age of 35 are known to have diabetes.[28]

The comparable figure among Indians (Hindu) in South Africa is 27%.[29] Further, there are *certain* individuals who are more prone to develop this condition, and who should be selectively screened. Examples are patients who have a family history of diabetes, women who have had large babies, or who have suffered unexplained perinatal loss, or who have been delivered of infants with congenital abnormalities.

Finally, it should be decided whether it is fair to concentrate on screening the younger female population. Though the incidence of diabetes in the two sexes varies with age, the over-all incidence of diabetes is greater in women than in men.[17] Further, female diabetics over the age of 50 suffer more frequently from complications, such as coma, blindness and arterial disease, than men of a comparable age.[17] By screening them during their early reproductive years we may be able to prevent the later development of much morbidity.

CONCLUSION

It may therefore be concluded that gestational diabetes is a very real condition for the general practitioner.

Early diagnosis and treatment of this condition will help to improve the perinatal mortality of women suffering from this condition at a stage when the disease is still asymptomatic. Secondly, recognition would enable one to guide patients as to the best means of contraception. Thirdly, by screening the patient at risk, one would be in a position to institute prophylactic treatment, and thereby hope to influence the otherwise inevitable development of diabetogenic angiopathy and associated conditions.

The detection of this condition can be accurately, cheaply and easily achieved with minimal inconvenience to the patient. In order to avoid unnecessary psychological stress, the patient need not know that the blood test is for the detection of diabetes.

The need for such a survey would depend upon the incidence of diabetes in the community, and among individuals in one's practice.

Finally, although it is of no immediate benefit to the patient, early recognition of the gestational diabetic would allow for the study of the pathogenesis of this disease and aid research workers in their objective of curing this disease.

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