SPECIAL ARTICLE

UPDATE ON MANAGEMENT OF HYPERTENSION IN PREGNANCY — MEDICAL ASPECTS

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What is Hypertension in Pregnancy?

Or in what context does hypertension occur during pregnancy? First some terms defining conditions/ diseases where hypertension occurs in pregnancy.

1. Hypertension peculiar to pregnancy.
   Pregnancy-induced hypertension, pre-eclampsia (PE), toxaemia. A multisystem disease with onset after 24 weeks of gestation (excluding hydatidiform mole) where there is hypertension, proteinuria, central nervous system irritability, hepatic and renal functional abnormalities and consumption coagulopathy (1). More simply, it is hypertension, proteinuria and oedema occuring after the 24th week of gestation.
2. Hypertension not peculiar to pregnancy.
   (a) Pre-existing but not necessarily pre-diagnosed.
   or (b) Developing during pregnancy.
3. Pre-eclampsia superimposed on pre-existing hypertensive disorders.
4. Eclampsia — when the pregnancy induced or aggravated hypertensive state induces convulsions.

When is Hypertension in Pregnancy?

To understand the influence of pregnancy on blood pressure (BP) measurements at different stages of gestation, one must realise that in 40% of normal and hypertensive pregnancies, both the systolic and diastolic BP fall by 5 to 10 mm Hg during the second trimester only to rise again in the third trimester(2). Hence BP readings in the prepregnant state and in the first trimester are important data to obtain.

The obstetrician is concerned with the patients' BP for forty weeks but the physician has to contend with it for the rest of the patients' lives. In population-based studies, BP of more than 140/90 mm Hg (phase 5) on more than two occasions in the recumbent, resting position constitute hypertension. When is hypertension to the obstetrician? It is known that the higher the BP the greater the risk of foetal and maternal morbidity and mortality. The American Obstetrical Committee has recommended a BP of 130/80 mm Hg as being the upper limit of normal at any time during pregnancy with a rise of 30 mm Hg systolic or 15 mm Hg diastolic BP being considered abnormal regardless of the absolute values obtained (3).

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Classification of Hypertension in Pregnancy

1. Hypertension peculiar to pregnancy
   A. Pre-eclampsia: mild, moderate, severe depending on BP readings, proteinuria and other manifestations.
   B. Eclampsia.
2. Hypertension not peculiar to pregnancy
   A: Pre-existing (not necessarily pre-diagnosed) Diastolic BP greater than 90 mm Hg before 20 weeks gestation without proteinuria.
   1. Chronic essential hypertension
   2. Secondary hypertension:
      — chronic renal.
      glomerulo, pyelo-nephritis
      renal artery stenosis
      — cardiovascular.
      coarctation, SLE
      — endocrine
      Conn's, phaeochromocytoma
      — others

   B. Developing during pregnancy e.g. acute glomerulonephritis.
3. Pre-eclampsia superimposed on pre-existing hypertensive disorders.

Pre-eclampsia may be diagnosed during pregnancy whenever at least two of three non-specific signs, i.e. hypertension, proteinuria and oedema, are present (4). If present before 20–24th weeks, hydatidiform mole must be excluded. In PE, the diastolic hypertension is prominent and the systolic rarely exceeds 160 mm Hg. A systolic pressure of more than 200 mm Hg indicates toxaemia of pregnancy superimposed on essential hypertension (EH). Proteinuria should be more than 300 mg/day to be significant. It is a non-selective proteinuria (5) and completely reversible (6). Oedema is significant only if generalised because pedal or pretibial oedema is found in 20–80% of uncomplicated pregnancies (7,8). Chesley (9) defined PE as "severe" when one or more of the following were present: BP more than 160 mm Hg systolic, 100 mm Hg diastolic, proteinuria more than 5 gm/day, oliguria, visual disturbances or pulmonary oedema.

The physician may be asked to see a patient and decide which category of hypertensive disorder of pregnancy she has. It may be impossible to distinguish clinically between PE, essential or secondary hypertension, renal disease and combinations of these separate entities. The stress of pregnancy may reveal latent hypertension present in the patient especially in the last trimester when the BP temporarily rises. Thus in the second half of pregnancy when BP rises without other evidence of PE, this could be regarded as latent EH unmasked by pregnancy and in a high proportion, permanent EH will develop in later life (10).

Hypertension Workup

If the patient does not have unequivocal PE, then causes of hypertension not peculiar to pregnancy will have to be investigated for. Labile hypertension may rarely be due to a phaeochromocytoma. Family history of EH and PE may be helpful. For kidney disease, a knowledge of past or present haematuria, dysuria, loin pain, urine protein, pyuria, casts, renal function may help. Palpating femoral pulses, auscultating for renal bruits and establishing evidence for chronic hypertension in the fundi and heart are mandatory. The degree of proteinuria may indicate severity of the PE or hypertension. In fact the nephrotic syndrome in pregnancy is most commonly caused by PE (11,12). One would not expect significant proteinuria in EH unless the BP is greater than 180/110 mm Hg. For renal function, since for each 50% reduction in glomerular filtration rate, serum creatinine and blood urea double, a rise in serum creatinine from 0.5 to 1.0 mg per 100 ml or in urea from 16 to 32 mg per 100 ml, indicates severe reduction in the glomerular filtration rate even though these values may be considered normal in the non-pregnant female.

Serum uric acid levels have been said to be useful markers for PE. Its rise is not due to increased production but to decreased renal clearance. In PE, the serum uric acid is usually above 4.5 mg per 100 ml and some authors report higher values with more severe PE. Patients with hypertension on diuretics alone rarely raise their uric acid levels beyond 6.5 mg per 100 ml. More reliable information is gained from serial values than from isolated measurements; a rise of greater than 0.1 mg per 100 ml per week at any stage of gestation should be considered abnormal (13). Other authors feel that it provides little useful information (14, 15).

Therefore in early pregnancy, the task is to decide if the patient has essential or secondary hypertension. Age and family history of hypertension may indicate. After 20 weeks gestation, there is the added problem of PE alone, or PE on pre-existing hypertension. Retrospectively, if the BP remains abnormal more than 6 months postpartum, the diagnosis would be pre-existing hypertension with or without superimposed PE. Pre-eclampsia is rarely followed by permanent increase in BP except in patients who already have hypertension or are destined ultimately to develop it. The specific renal lesion of glomeruloendotheliosis in PE disappeared after four weeks to two years following parturition (16, 17).

Course of Hypertensive Pregnancy.

Whatever the aetiology of hypertension in pregnancy, increasing BP results in decreasing effective placental blood flow. With superimposed proteinuria, this diminished placental blood flow is more severe. Both these factors increase the risk of placental infarct, intrauterine foetal growth retardation and intrauterine death.

If in the second trimester, BP falls spontaneously, the foetal salvage rate is good. Should it rise further, salvage is poor and the prognosis is serious if the mother in addition fails to gain weight and develops proteinuria.

Pre-eclampsia is two to seven times more common in patients with EH than in normotensive patients and if it occurs before 32 weeks gestation, almost 75% of infants are lost.

Poor Prognostic Factors

Poor prognostic factors in hypertensive pregnancy are (2):

1. Elderly mothers with long established hypertension.
2. Initial BP greater than 180/110 mm Hg plus proteinuria.
3. No fall in BP by mid-second trimester.
4. Large increase in BP in third trimester.
5. Failure of mother to gain weight normally.
6. Development of proteinuria and PE before 32 weeks gestation.

Effect of Hypertension on Mother.

The maternal mortality is less than 1% and is due to a sudden rise in BP resulting in cerebral haemorrhage, acute left ventricular failure or malignant hypertension. If severe PE continues there is a high risk of eclampsia. There is no permanent deterioration in the EH as a result of pregnancy unless it is complicated by PE, in which case in about one-third of the patients, the hypertension is worsened permanently.

For subsequent pregnancies, the risk of PE is as great as in the first pregnancy. The earlier the onset of PE, the greater is the possibility of PE in the next pregnancy, and the older the patient, the greater is this risk.

Relationship of PE and EH.

"It is believed that the stress of pregnancy acts as a screening test for EH and that women predisposed to EH show a rise of BP during the last trimester and are particularly liable to develop PE." (2)

"A toxaemic pregnancy brings to light a latent tendency to hypertension and pre-fixes the time of onset of the disorder." (10) The fact that permanent hypertension follows PE more frequently in older women is due to these patients being nearer the age at which EH usually becomes manifest.

Treatment of the Hypertension.

While attention is paid to the diastolic BP to keep it below 90 mm Hg, specific therapeutic measures will depend on several factors including:

(a) period of gestation
(b) state of maternal health, and
(c) well-being of the foetus in utero.

Essential Hypertension. (and Secondary Hypertension)

Antihypertensive therapy prevents complications of hypertension and there is unequivocal evidence that treatment of hypertension in pregnancy does not worsen, and in most cases, improves foetal survival. These patients should have their BP maintained below 140/90 mm Hg with whatever antihypertensive regimen is best suited to them. Most patients on long-term

therapy will be on methyldopa, a diuretic, propranolol and hydralazine alone or in combinations. These drugs should be continued through the pregnancy. Diuretics are not contraindicated in pregnancy when there is a clear indication for their use.

Pre-eclampsia.

Pre-eclampsia or toxaemia of pregnancy is more than hypertension in pregnancy. The variable clinical presentations of toxaemia are well known and range from fulminant toxaemia with convulsions, thrombocytopenia, consumptive coagulopathy, azotemia and hypertension to systemic manifestations with/without renal involvement and hypertension. Some patients may be normotensive or only minimally hypertensive.

The only specific treatment for PE/eclampsia is termination of the pregnancy. The use of antihypertensive drugs aims to buy time for the baby to reach maturity in utero so that a few more weeks in utero might give the infant a better chance of survival ex utero. This must be balanced with the fact that in severe PE, procrastination may prove ill-advised since severe disease itself may kill the foetus. Thus normalising BP is only one facet of management. Foetal and maternal well-being must also be monitored and managed.

The most important feature in the prevention and treatment of PE is the recognition that a rise in BP greater than 30 mm Hg in systolic or 15 mm Hg in diastolic during pregnancy is significant and that the development of proteinuria is always an indication for hospitalisation. Therapy for mild PE (BP less than 140/90 mm Hg) is bed rest and sedation with or without diuretics. With higher BP and more severe PE, antihypertensive therapy must be instituted. Common drugs used are methyldopa and hydrallazine. Beta-adrenergic blocking agents have been used effectively in PE. There are favourable reports with atenolol in a placebo-controlled trial (18) and in women unresponsive to methyldopa (19); with metoprolol (21) and with labetalol (22, 23).

Antihypertensive Agents.

In 1982, a survey of 645 Australian Fellows of the College of Obstericians and Gynaecologists with regard to their "Attitudes to the management of hypertension in pregnancy" was carried out in Australia (24). The choice of antihypertensive drugs was not uniform. Methyldopa received the widest support. This was the drug used in the original Oxford controlled trial and has remained as a popular, safe and beneficial agent. The use of beta-blocking drugs to control hypertension is a more recent concept — with use of oxprenolol in Sydney and labetalol in Perth. The survey also showed that the Fellows seniority influenced aspects of management. Sedation was considered less important by young obstetricians. Diuretics are not used by the majority in the management of PE, but may be continued as part of a regimen of antihypertensive therapy in early pregnancy.

Methyldopa.

In EH, most authors would agree that methyldopa is the oral medication of choice. Initial dosage is 750 mg/day increasing to 3 gm daily. Occasionally it is necessary to add oral hydralazine (25). In an uncontrolled series reported by Kincaid Smith et al (26) and in a controlled study by Redman et al (27), impressive foetal survival rates were demonstrated when these patients were treated with methyldopa. (Methyldopa has been in use for over 15 years with documented safety and value.)

In PE, Ferris (3) would still consider using methyldopa although Rivlin et al (28) would use hydralazine as the drug of choice and makes no mention of methyldopa. Followup studies of the children born of mothers taking methyldopa throughout pregnancy have revealed normal mental and physical development up to five years of age (29).

Hydralazine.

This is a vasodilator and it can be given orally, intramuscularly or intravenously. Dosage is 25 to 50 mg every six hours. It has also been in use for over 15 years with a good safety record and is considered the antihypertensive agent of choice in PE by some authors (28, 30). It remains an effective agent for use in hypertensive crisis.

Adrenoceptor Antagonists.

The initial use of beta blockers in pregnancy was associated with some hesitation. There are now a number of controlled studies demonstrating their safety for mother and foetus (31). Most experience has been with propranolol, oxprenolol, metoprolol, atenolol and pindolol. Recent evidence shows that some of these beta blockers may have the beneficial effects of preventing proteinuric deterioration of hypertension in pregnancy, of diminishing the incidence of severity of respiratory distress in the newborn and counteracting platelet adhesions in PE (32).

Labetalol shows promise for use in pregnancy as uteroplacental flow is not impaired, a beneficial effect of lung maturation is suggested and platelet consumption in PE is reduced (31).

Adverse effects on the foetus (growth retardation, cardiorespiratory depression, hypoglycaemia, hyperbilirubinemia) formerly attributed to beta blockers are more likely related to poorly controlled hypertension.

More comprehensive reviews of various hypertensive agents used in pregnancy can be found in the literature (31, 33, 34)

Conclusion

The overall management of hypertension in pregnancy rests with the obstetrician in close cooperation with the physician. Hypertension in pregnancy has implications for both maternal and foetal welfare. Extrapolation from concepts of mechanisms operating in hypertension in general to pregnancy-related hypertension is not justified. Normalising BP in pregnancy should not be at the expense of compromising uteroplacental perfusion. While centrally acting sympatholytics are still useful in modulating the mothers' response to stimulation of the adrenergic nervous system, attacking the peripheral effector organ (alpha and beta adrenoceptor antagonists and vasodilating agents) now seems the preferred way of effective BP control.

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