Conservative management of severe proteinuric hypertension before 28 weeks' gestation

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Summary

Forty-five patients with severe proteinuric hypertension who presented before 28 weeks' gestation were managed conservatively by bed rest, antihypertensive treatment, betamethasone administration after 26 weeks' gestation, and intensive fetal and maternal monitoring. Eleven patients presented before 24 weeks and their babies all died; 34 patients presented at or after 24 weeks and 13 of their babies survived (38%). The indications for delivery were intrauterine death (13), fetal distress (9), deterioration in the mother's condition (17), and maternal complications — pulmonary oedema in 3 cases and pleural effusion in 1. One patient went into spontaneous labour and one was induced at 34 weeks. At postpartum follow-up examination all the mothers in the group that had presented before 24 weeks were found to have underlying diseases, compared with 42% of those who had presented between 24 and 27 weeks.

The low incidence of maternal complications and the relatively good survival rate of 38% indicate that there is a place for conservative management in patients with severe proteinuric hypertension presenting at 24 weeks or later. Termination of the pregnancy should, however, be seriously considered in those patients presenting before 24 weeks' gestation.

Patients and methods

All patients with severe hypertension (defined as two blood pressure readings of > 160/110 mmHg at least 6 hours apart) and proteinuria (defined as proteinuria > 3 + on the Ames dipstick) who were admitted to the Tygerberg Hospital special care obstetric unit were included in the study. The gestational age was assessed by dates and extrapolation from an early ultrasound scan, if possible, and expressed as completed weeks.

Management comprised an initial period of stabilisation lasting 24 hours that entailed strict bed rest and the administration of magnesium sulphate if eclampsia was thought to be imminent. The blood pressure was controlled with intravenous dihydralazine to maintain a diastolic blood pressure < 110 mmHg. Initial laboratory screening comprised measurement of haematocrit, platelet count, serum concentrations of urea and electrolytes, and liver function tests, together with cultures of the urine and estimation of the creatinine clearance rate. If the initial period of stabilisation was successful, oral antihypertensive treatment was started, initially with a-methyldopa to a maximum dose of 3 g daily. We attempted to keep the diastolic pressure between 90 and 100 mmHg, and if a-methyldopa was ineffective prazosin was used to a maximum dose of 18 mg daily. At 26 weeks' gestation, 12 mg betamethasone was given intramuscularly and the injection repeated 24 hours later. A single 12 mg injection was given weekly thereafter. This was done because Liggins and Howie failed to show any demonstrable benefit of the steroid after 7 days, and in patients with severe proteinuric hypertension timing of the delivery is uncertain. Lamont et al. showed that there were advantages for the fetus if mothers with severe proteinuric hypertension were given steroids. After 26 weeks' gestation non-stress tests were carried out three times daily. Laboratory tests were repeated weekly or if the clinical condition of the patient changed. The patients were weighed daily and strict intake and output charts were kept. The aim was to prolong pregnancy to 34 weeks' gestation, after which the infant would be delivered.

Indications for delivery in those patients who did not reach 34 weeks' gestation were divided into two groups, fetal and maternal. Fetal indications included a positive stress test, abruptio placentae, or intra-uterine death. Maternal indications comprised deterioration in the mother's condition defined as uncontrollable hypertension, excessive weight gain with ascites, or deteriorating renal function and the occurrence of complications of the disease, such as pulmonary oedema. If labour started spontaneously it was not suppressed.

All the babies that were discharged home were considered neonatal survivors. If a neonate died, even after 28 days, it was

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still included in the perinatal mortality for the purposes of this study.

Postpartum follow-up visits took place at 2, 4 and 6 weeks. If the blood pressure reading at 6 weeks was > 140/90 mmHg chronic hypertension was diagnosed. If proteinuria was still present after 3 months intravenous pyelography was done and renal biopsy was carried out.

Results were analysed by Student's t-test to compare means of normally distributed data. P values of < 0.05 were considered significant.

Results

Forty-five patients (16 primigravids and 29 multiparas) who fulfilled the criteria for admission to the study were seen during the 2-year period 1 February 1984 to 31 January 1986. Eleven patients were admitted at less than 24 weeks’ gestation, 12 were admitted at 24 to 25 weeks’ gestation, and 22 were admitted at 26 to 27 weeks’ gestation. The perinatal survival is shown in Table I.

**TABLE I: PERINATAL SURVIVAL IN PATIENTS MANAGED CONSERVATIVELY WITH SEVERE PROTEINURIC HYPERTENSION PRIOR TO 28 WEEKS’ GESTATION**

<table>
<thead>
<tr>
<th>Gestational age on admission (wks)</th>
<th>No. of patients</th>
<th>No. of babies discharged home</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 + 25</td>
<td>12</td>
<td>4 (33.3%)</td>
</tr>
<tr>
<td>26 + 27</td>
<td>22</td>
<td>9 (40.1%)</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>13 (28.9%)</td>
</tr>
</tbody>
</table>

Thirteen babies died in utero, 9 of whom weighed less than 500 g. Nine babies, developed repeated late decelerations during fetal heart monitoring, which in 1 case were caused by abruptio placentae, of which no other signs or symptoms were present. Seventeen pregnancies were terminated because of deterioration in the mother’s condition; 3 patients developed pulmonary oedema and 1 a pleural effusion. One went into labour spontaneously and 1 was induced at 34 weeks.

No baby survived if the mother had been admitted before 24 weeks’ gestation. For the purposes of this article it is therefore suggested, as the likelihood of poor fetal outcome in subsequent pregnancies is high, every effort should be made to diagnose any underlying conditions and control them before the next pregnancy. Where a specific disease is not diagnosed, prophylactic low-dose aspirin might be useful for these patients.

The role of antihypertensive drugs could not be evaluated in this study. Antihypertensive treatment is, however, advantageous for the mother because it prevents complications such as cerebral haemorrhage. The part that antihypertensive treatment plays in helping the fetus is less clear. Silverstone et al. found that hypertension was an important cause of mid-pregnancy intra-uterine death. Redman et al. showed that the incidence of mid-trimester abortions was reduced when methyldopa was used for moderate hypertension. For these reasons antihypertensive treatment is advocated in these patients.

In the group where survival was possible — that is, at or after 24 weeks’ gestation on admission — there was no way of predicting the outcome from the routine investigations (measurements of blood pressure, haematocrit, blood urea and uric acid concentrations, or urine creatinine clearance rate).

**Discussion**

Little has been written about severe proteinuric hypertension in the mid-trimester. Neonatal survival is poor with only 13-28% survivors. In this study the survival rate was 28% in all patients, but 38% in those at or past 24 weeks’ gestation on admission.

No babies survived if the mothers presented before 24 weeks. This group also had a high incidence of underlying diseases, which were found to be present in all 7 cases followed up. With such a poor prognosis, termination of pregnancy is worth considering. It would save prolonged admissions to hospital with little hope of success, and certainly reduce the risks to the mothers. More effort should then be made to diagnose any underlying conditions and control them before the next pregnancy. Where a specific disease is not diagnosed, prophylactic low-dose aspirin might be useful for these patients.

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The 38% neonatal survival rate gives hope for the fetus but one must not forget the long-term problems that these babies may suffer such as cerebral palsy, bronchopulmonary dysplasia, or retinopathy of prematurity. Yu et al. reported the outcome of extremely low-birth-weight infants — that is less than 1 000 g — and found a 29% incidence of major disabilities. In addition, although the percentage of survivors was greater in babies who were small for gestational age, these babies had a higher incidence of major disabilities. Unfortunately patients with severe proteinuric hypertension in the mid-trimester tend to have poor obstetric histories, as shown in this and other studies. Conservative management at or after 24 weeks’ gestation is therefore suggested. As the likelihood of poor fetal outcome in subsequent pregnancies is high, every effort should...
be made to ensure optimal intra-uterine and neonatal care because there may not be another successful pregnancy.

From a maternal point of view conservative management may be dangerous, as suggested by Sibai et al., but similar complications were not encountered in the present study. The explanation for this is unknown, but could be related to the intensive monitoring of the patients and prompt delivery when necessary.

We conclude that conservative treatment of severe proteinuric hypertension at or after 24 weeks' gestation is advantageous for the baby and carries little risk for the mother, provided that she can be intensively monitored in a special care unit.

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REFERENCES


Plasma volume expansion in pregnancy hypertension

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Summary

Stabilised human serum 500 ml was infused intravenously over 90 minutes in 14 hypertensive women in late pregnancy, and the haemodynamic changes were investigated and compared with those in 7 similar women who were not treated. There was a significant mean increase of 1.85 l in plasma volume, a decrease in diastolic and systolic blood pressure, and an increase in central venous pressure (CVP), pulse pressure and pulse rate in the treated group at 2 hours but not in the control group. After 24 hours most of the observations were not significantly different from the pretreatment levels except the CVP and pulse rate measurements which were still significantly raised. The CVP measurements in the hypertensive women before treatment were relatively low compared with those reported in normal women in late pregnancy. It is suggested that there may be an under-filling of the circulation in pregnancy hypertension and that plasma volume expansion may have an important therapeutic effect by increasing cardiac output and renal and uterine blood flow.


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Hypertension is a common complication of pregnancy and remains an important cause of perinatal morbidity and mortality. These patients appear to have relative hypovolaemia, generalised vasoconstriction, increased peripheral and systemic vascular resistance and a low cardiac output.

It has been suggested that at least in some cases these haemodynamic changes may be due to 'under-filling' of the circulation due to a low total circulating albumin with a low central venous pressure (CVP) and reduced venous return. It has also been suggested that this 'under-filling' of the circulation may be due to an increased capillary permeability to proteins resulting in leakage of albumin and fluid from the intravascular to the extravascular space. With the hypovolaemia and decreased cardiac output there may be a decrease in blood flow to both the kidneys and the uterus, which may have serious consequences.

The mean plasma volume of women with hypertension in pregnancy is approximately 15% (500 - 600 ml) less than that of normal pregnant women at comparable gestational age. In Europe it is generally believed that the hypovolaemia is secondary to vasoconstriction, whereas in some USA centres the reduction in blood volume is regarded as the primary change and vasoconstriction is considered to be secondary and patients may be treated with blood volume expansion. It is postulated that pre-eclampsia is primarily caused by failure of the blood volume to increase appropriately and that the relatively reduced blood volume results in a condition resembling 'chronic shock'. The 'chronic shock' results in poor organ and tissue perfusion, which may be exacerbated by the increased blood viscosity which occurs in pre-eclampsia.

Various workers have used plasma volume expanders in hypertensive patients and have claimed that renal and possible placental perfusion may be improved by such treatment. Some workers also believe that plasma volume expansion can reverse the disease process, at least temporarily, so that preg-