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Improve in foetal growth with treatment of maternal hypertension in pregnancy

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Summary

1. A highly significant inverse relationship was found between blood pressure in untreated hypertensive subjects in late pregnancy and birth weight.
2. Reversal of this intrauterine growth retardation was achieved in 19 patients by treatment of hypertension with oxprenolol.
3. No adverse effects from oxprenolol were found in the patients or in their babies.

Key words: birth weight, blood pressure, hypertension, oxprenolol.

Introduction

Hypertension in the pregnant woman, whether it occurs de novo or is known to precede pregnancy, is associated with an increased incidence of placental insufficiency and intrauterine growth retardation (Brosens, 1977), of premature delivery, abruptio placenta and antepartum haemorrhage and of intrauterine and perinatal death (Friedman, 1976). Low birth-weight babies have an increased risk of developing a number of potentially life-threatening complications in the early neonatal period, as well as long-term behavioural and intellectual problems (Stewart, 1977; Hardy & Mellits, 1977).

In an effort to reduce the morbidity and mortality associated with hypertension in pregnancy, we have been conducting a prospective study and present here the results of therapy with the non-selective β-adrenoreceptor blocking agent, oxprenolol.

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Methods

A sample of 19 pregnant women with moderately severe hypertension was treated with oxprenolol. Criteria for entry into the treatment group consisted of a sitting diastolic blood pressure (phase 4, Korotkoff sounds) of greater than 95 mmHg on at least two occasions 24 h apart or greater than 100 mmHg on at least two occasions 8 h apart. All blood pressure measurements were made with a Hawkesley Random Zero sphygmomanometer; the recorded blood pressure in each instance was the average of two readings taken at least 1 min apart after 10 min sitting quietly. Therapy was adjusted as necessary to maintain sitting diastolic blood pressure at or below 80 mmHg. Wherever possible, plasma volume was measured at 25–28 weeks and again at 33–36 weeks gestation. Foetal growth in utero was assessed by ultrasound and foetal wellbeing in the third trimester by serial urinary oestriol excretion, cardiotocography and where indicated, oxytocin challenge testing.

Results

The mean stage of commencement of therapy was 29 weeks gestation, excluding four patients who were transferred from another anti-hypertensive agent in early pregnancy. Sitting blood pressure at commencement of therapy was 148/102 ± 3.5/1.5 (SEM) mmHg. Blood pressure control was satisfactory by conventional standards, most patients while on therapy being within the normal range for pregnancy for our hospital, although at the upper end of that range. The mean sitting diastolic blood pressure reached 90 mmHg on two occasions only. Maximum daily dosage of oxprenolol used in any patient was 480 mg. In approx. 30% of patients it
was necessary to add hydralazine to the treatment regimen, whereas one patient was also treated with α-methyl-dopa.

Duration of pregnancy at delivery was 38 ± 0.4 weeks. 26% (five) patients went into labour spontaneously, 42% (eight) were electively induced and 32% (six) were delivered by lower segment caesarian section. There were no still-births or perinatal deaths. Birth weight of babies was 2984 ± 170.6 g, placental weight 540 ± 28.5 g. Mean Apgar score of babies at 1 min after birth was 8 and at 5 min 9.5. No baby had hypoglycaemia, respiratory depression or bradycardia attributable to neonatal β-adrenergic receptor blockade. 50% of babies were monitored intrapartum. These showed no evidence of foetal distress.

Discussion

It is apparent from these results that the theoretical dangers of β-adrenergic receptor blockade in pregnancy were not realized. There was not an increased incidence of premature labour or of neonatal complications attributable to β-adrenergic receptor blockade. It has been suggested, largely as a result of animal experimental results, that β-adrenergic receptor blocking agents are transported selectively across the placenta and that their effects are more marked and prolonged in the foetus (Truelove, van Petten & Willes, 1973; van Petten, 1975). From our results, it is clear that this is not the case for oxprenolol, which has not been extensively studied before. Previous anecdotal reports implicating propranolol as the cause of neonatal hypoglycaemia, respiratory depression or bradycardia have not taken account of the intercurrent events in the patients studied, which could well have caused the complications described (Fiddler, 1974; Reed, Cheney & Fearon, 1974; Gladstone, Hardof & Gersony, 1975).

Fig. 1 shows the relationship between untreated hypertension and birthweight in the Royal North Shore Hospital for a 12-month period ending on 31 December 1975. Only patients who were delivered of live infants and who were not treated with anti-hypertensive drugs were included. This control group had milder hypertension than those in the present treatment group, but even in this control group it is apparent that there is a highly significant inverse relationship between birth weight and maternal blood pressure \((r = 0.588, P < 0.001)\). If these blood pressure levels were extrapolated to the higher starting levels in our treatment group, as shown by the arrow at the right side of the figure, the expected birth weight would have been only 2120 g, much lower than was achieved after therapy with oxprenolol.

Normal birth weight at term for the population under study is 3507 ± 35.7 g whereas estimated foetal weight for our normal population at 38 weeks gestation is 3238 ± 37.4 g. The patients studied, therefore, still had smaller babies than normal \((P < 0.05)\). As was stated earlier in the discussion, on two occasions mean diastolic blood pressure of the group reached 90 mmHg and the mean birth weight of the babies from the treatment group falls on the regression line for birth weight at blood pressures between 90 and 95 mmHg. We feel, therefore, that this effect on the birthweight is still due to hypertension and that treatment, if more rigorously applied to reduce diastolic blood pressure to normal levels for pregnancy would have corrected more completely the effect of hypertension.

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References


