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Increased incidence of respiratory distress syndrome in babies of hypertensive mothers

T R J Tubman, M D Rollins, C Patterson, H L Halliday

Abstract

There is controversy over the effect of hypertension in pregnancy on the incidence of neonatal respiratory distress syndrome. We investigated the association between maternal hypertension and the incidence of respiratory distress syndrome in 268 very low birthweight babies of less than 34 weeks' gestation.

A lower incidence of respiratory distress syndrome was associated with growth retardation and membrane rupture >24 hours. Maternal hypertension was associated with an increased incidence of respiratory distress syndrome. We used the multiple logistic regression model to control for confounding variables, as the maternal and neonatal factors associated with respiratory distress syndrome were not evenly distributed between the two groups.

After adjustment for birth weight, gestational age, growth retardation, and membrane rupture >24 hours, the risk of developing respiratory distress syndrome was significantly greater in babies of hypertensive mothers. Significance was lost when labour before delivery and mode of delivery were taken into account. The increased incidence of respiratory distress syndrome in babies of hypertensive mothers may be due to the absence of labour before delivery because of the greater likelihood of caesarean section.

The effect of hypertension in pregnancy on the incidence of neonatal respiratory distress syndrome remains controversial. A number of studies have supported the widely accepted view that maternal hypertensive disease protects against the development of respiratory distress syndrome.[1–3] Some workers have found an increase in the incidence of respiratory distress syndrome,[4 5] however, and others no change in the incidence[6] among babies born to hypertensive mothers. Most of these studies have involved small numbers of subjects and not all have attempted to adjust for confounding variables. We investigated the association between maternal hypertension and the incidence of respiratory distress syndrome in a large group of very low birthweight babies (birth weight ≤1500 g) of less than 34 weeks' gestation.

Patients and methods

This study was performed in the Royal Maternity Hospital, Belfast, which is a high risk, university based obstetric unit, having approximately 4000 deliveries per year. Many of these are referred from other centres in Northern Ireland for specialist perinatal care. The hospital has a neonatal unit with provision for seven intensive care and 11 special care cots.

We used an established database of information on more than 600 liveborn babies with birth weight ≤1500 g who were managed in Royal Maternity Hospital from 1978 to 1988. Using this, we first excluded all babies of 34 weeks' gestation or greater, whose risk of developing respiratory distress syndrome was likely to be low. From the remainder we identified all babies (n=134) who had been born to mothers who had hypertension in pregnancy (diastolic blood pressure persistently greater than or equal to 90 mm Hg).[7]

A group of 134 babies also ≤1500 g birth weight and <34 weeks' gestation, born to normotensive mothers, was used for comparison. These were randomly selected from the database, matching only for year of birth to allow for the effects of improved outcome associated with the development of newer forms of treatment.

Information on mothers and their babies was obtained from review of patient hospital records. We recorded the following maternal and neonatal factors: presence of labour before delivery, mode of delivery, membrane rupture >24 hours, antenatal steroid administration, infant's sex, birth weight, gestational age, and growth retardation (birth weight less than 10th centile for gestational age). Infant gestation was based upon menstrual dates, early ultrasound scans where performed, and clinical judgment by medical staff in the neonatal unit. Respiratory distress syndrome was defined as the presence of tachypnoea >60/minute, sternal recession and expiratory grunting, need for supplemental oxygen, and a radiological picture of diffuse reticulogranular shadowing with an air bronchogram.[8] The severity of respiratory distress was judged by maximum fraction of inspired oxygen required, need for mechanical ventilation, and presence of grade 3/4 radiographic changes.[9] Information on lecithin-sphingomyelin ratios was available in only 28% of cases and was not used as part of our definition of respiratory distress syndrome.

Preliminary statistical analyses were performed using the Z, χ^2, and Mann-Whitney U tests for independent samples. Significance levels, where quoted, are for two tailed tests. We used the multiple logistic regression model to study the association between maternal hypertension and the incidence of respiratory distress syndrome, controlling for the confounding effects of other variables.

Royal Maternity Hospital, Belfast
T R J Tubman
M D Rollins
H L Halliday

Department of Epidemiology and Public Health, The Queen's University, Belfast
C Patterson

Correspondence to:
Dr T R J Tubman,
Neonatal Intensive Care Unit,
Royal Maternity Hospital,
Grosvenor Road,
Belfast BT12 6BB,
Northern Ireland.

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Results

Maternal and neonatal factors associated with respiratory distress syndrome are shown in tables 1 and 2. Babies who developed respiratory distress syndrome were of significantly lower birth weight and gestational age than those who did not. A significantly lower incidence of respiratory distress syndrome was associated with membrane rupture >24 hours and growth retardation. Antenatal steroid administration, presence of labour before delivery, delivery by caesarean section, and male sex were not associated with a difference in the incidence of respiratory distress syndrome; it was significantly more common in babies born to hypertensive mothers (table 3).

We determined the distribution of these factors within the two study groups (table 3). Babies in the hypertensive group had a mean gestational age two weeks greater than the normotensive group but had a similar mean birth weight. All cases of membrane rupture >24 hours occurred in the normotensive group. Most of the normotensive mothers had vaginal deliveries whereas most hypertensive patients were delivered by caesarean section, a small number after a preceding period of labour. A greater proportion of growth retarded babies came from the hypertensive group. There was no difference in the proportion of boys or incidence of antenatal steroids.

We performed multivariate analysis using the

Table 1 Incidence of maternal and neonatal factors in relation to the occurrence of respiratory distress syndrome: hypertensive group (n=134)

	Respiratory distress syndrome (n=87)	*No respiratory distress syndrome (n=47)*	*p Value*
Mean (SD) gestation (weeks)	29·7 (2·0)	31·4 (1·5)	<0·0001
Mean (SD) birth weight (g)	1093 (234)	1229 (214)	<0·001
No (%) with membrane rupture >24 hours	0	42 (89)	0·0001
No (%) undergoing labour	8 (9)	9 (19)	NS
No (%) having caesarean section	80 (92)	42 (89)	NS
No (%) with growth retardation	33 (38)	34 (72)	<0·001
No (%) having antenatal steroids	13 (15)	7 (15)	NS
No (%) boys	34 (39)	19 (40)	NS

Table 2 Incidence of maternal and neonatal factors in relation to the occurrence of respiratory distress syndrome: normotensive group (n=134)

	Respiratory distress syndrome (n=69)	*No respiratory distress syndrome (n=65)*	*p Value*
Mean (SD) gestation (weeks)	27·6 (2·4)	29·2 (2·2)	<0·0001
Mean (SD) birth weight (g)	1083 (259)	1250 (219)	<0·0001
No (%) with membrane rupture >24 hours	12 (17)	30 (46)	<0·001
No (%) undergoing labour	56 (81)	55 (85)	NS
No (%) having caesarean section	20 (29)	13 (20)	NS
No (%) with growth retardation	4 (6)	13 (20)	<0·05
No (%) having antenatal steroids	10 (14)	14 (22)	NS
No (%) boys	34 (49)	31 (48)	NS

Table 3 Distribution of maternal and neonatal factors within the study groups

	Hypertensive (n=134)	*Normotensive (n=134)*	*p Value*
No (%) with respiratory distress syndrome	87 (65)	69 (51)	<0·05
Mean (SD) gestation (weeks)	30·3 (2·0)	28·4 (2·4)	<0·0001
Mean (SD) birth weight (g)	1140 (236)	1164 (254)	NS
No (%) with membrane rupture >24 hours	0	42 (31)	<0·0001
No (%) undergoing labour	17 (13)	111 (83)	<0·0001
No (%) having caesarean section	122 (91)	33 (25)	<0·0001
No (%) with growth retardation	67 (50)	17 (13)	<0·0001
No (%) taking steroids	20 (15)	25 (19)	NS
No (%) boys	53 (40)	70 (52)	NS

Table 4 Odds for babies of hypertensive mothers developing respiratory distress syndrome relative to babies of normotensive mothers

Adjusted for:	*Relative odds of respiratory distress syndrome*	*95% Confidence intervals*	*Likelihood ratio χ^2 (df=1)*
No factors	1·7	1·1 to 2·9	4·99*
Birth weight, gestation	3·7	1·9 to 7·3	15·79**
Birth weight, gestation, growth retardation	3·8	1·9 to 7·6	15·43**
Birth weight, gestation, growth retardation, membrane rupture >24 hours	2·3	1·1 to 4·9	5·06*
Birth weight, gestation, growth retardation, membrane rupture >24 hours, labour	1·4	0·6 to 3·2	0·54
Birth weight, gestation, growth retardation, membrane rupture >24 hours, delivery	1·6	0·7 to 3·7	1·16
Birth weight, gestation, growth retardation, membrane rupture >24 hours, labour, delivery	1·4	0·6 to 3·2	0·46

*p<0·05, **p<0·001.

*Table 5 Incidence and severity of respiratory distress syndrome where present**

	Hypertensive (n=87)	*Normotensive (n=69)*
No (%) with grade 3/4 radiographic changes	55 (63)	47 (68)
No (%) needing mechanical ventilation	66 (76)	56 (81)
Mean (SD) maximum fraction of inspired oxygen	0·62 (0·24)	0·68 (0·24)

*There were no significant differences in the variables between the hypertensive and normotensive groups.

multiple logistic regression model to investigate further the association between hypertension and respiratory distress syndrome, adjusting for the confounding effects of gestational age, birth weight, growth retardation, and membrane rupture >24 hours. After this adjustment, there was still a significant association between maternal hypertension and respiratory distress syndrome (table 4). However, when mode of delivery and/or the presence of labour before delivery were also included in the model the association was no longer significant.

Severity of respiratory distress, as judged by radiographic changes, maximum fraction of inspired oxygen, and need for mechanical ventilation was similar in both hypertensive and normotensive groups (table 5). Babies in the hypertensive group who developed respiratory distress syndrome had a significantly greater survival rate (67/87, 77%) than the normotensive group (37/69, 54%).

Discussion

Although it is commonly stated that maternal hypertension is protective against the development of respiratory distress syndrome,[10] the evidence for this is conflicting.[1–6] As many factors affect the incidence of respiratory distress syndrome it is important to control for the influence of these when assessing the effect of a single variable, such as maternal hypertension. Most studies have involved small numbers of patients and some have not controlled for the effect of confounding variables.

Respiratory distress syndrome was significantly more common in babies of hypertensive mothers before correction for confounding variables (65% compared with 51%). After adjustment for confounding variables the incidence of respiratory distress syndrome remained higher in the hypertensive group, until mode of delivery and labour before delivery were taken into account. These two factors are consequences of maternal hypertension, in that pre-eclampsia often leads to emergency caesarean section without a preceding period of labour. Respiratory distress syndrome is more common after hypertensive pregnancies but the reason may simply be that the incidence of caesarean section is increased and a period of labour before delivery before birth is reduced. Alternatively, caesarean section and absence of labour may simply be acting as markers for hypertension. The available data did not allow us to distinguish between these alternatives.

There was no difference in the severity of respiratory distress syndrome between the two groups, though mortality was lower in babies in the hypertensive group who developed respiratory distress, perhaps due to the significantly greater mean gestational age of these babies (table 3).

This study supports other evidence to suggest that respiratory distress syndrome is more and not less common in babies of hypertensive mothers.[4 5] Little information on this subject exists in the literature. More research is therefore needed, preferably in the form of a large randomised controlled trial to determine whether different policies for labour and delivery of hypertensive mothers are associated with significant differences in the incidence of respiratory distress syndrome in their babies.

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