

Normal physical and mental development of 6-year-old children whose mothers were treated antenatally with prednisolone

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83 prednisolone-treated and 57 control children of a previous study demonstrating benefits of antenatal steroid prophylaxis of IRDS were re-examined at the age of 6 years. The prednisolone children were slightly higher and heavier, but no significant differences between steroid and control groups were noted in any other characteristics including IQ, psychosocial development, EEG, ophthalmology and audiology. The results confirm the finding that antenatal steroid prophylaxis has no long-term hazards to the fetus.

Antenatal administration of glucocorticoids has been shown to decrease the incidence and severity of idiopathic respiratory distress syndrome (IRDS). Although the acute side-effects proved to be insignificant, considering animal experiments in which cortisol had an adverse effect on fetal growth at the cellular level, there has been some speculation concerning hazards to later development. Based on follow-up studies, MacArthur et al. [3] and Veszeloyszky et al. [4] concluded that antenatal betamethasone therapy did not affect intelligence and cognitive development of the offspring until the age of 4 years.

Here we provide further evidence that somatic and intellectual development of 6-year-old children was not influenced by antenatal glucocorticoid treatment.

MATERIAL AND METHODS

In 1973–75 the mothers of 107 neonates, mainly prematures, at risk of IRDS, received antenatally 30 mg/day prednisolone for 3 days. In the same department the next born infant of similar birth weight and of the same sex, gestational age and route of delivery was chosen as matched control to each of the babies. Maternal steroid premedication proved to be effective in decreasing the morbidity and mortality of IRDS [2].

In 1979–82 the children of the original study were reexamined at the age of 6 to 6 4/12 years.

Out of the 107 pairs, 89 steroid-treated and 83 controls survived the neonatal period. Two steroid-treated and one control died at a later age, thus 87 of the premedicated and 82 of the controls could be asked to cooperate. In fact 83 (95.4%) steroid-treated and 57 (69.5%) control children appeared. Out of the originally matched pairs 41 could be examined, but the distribution according to sex, gestational age and perinatal history of the rest was very similar in the two groups. There were no significant differences in the social state of prednisolone and control children. Thus all the 140 subjects were involved in the final evaluation. The perinatal data by sex and treatment groups are shown in Table I.

TABLE I
Perinatal data by treatment groups and sex (mean \pm SD)

Data	Prednisolone n = 83	Control n = 57	P
Gestational age at birth, week			
Boys	33.8 \pm 2.7	34.2 \pm 2.9	NS
Girls	32.6 \pm 2.4	34.3 \pm 2.9	<0.05
Both sexes	33.2 \pm 2.6	34.3 \pm 2.9	<0.05
Birth weight, g			
Boys	2.193 \pm 611	2.090 \pm 529	NS
Girls	2.029 \pm 466	2.070 \pm 465	NS
Both sexes	2.113 \pm 546	2.079 \pm 492	NS

TABLE II

The most important findings in the prednisolone-treated and control children at the age of 6 years.

Mean \pm SD or percent of subjects affected;

	Prednisolone n = 83	Control n = 57	P
Height, cm	118.3 \pm 7.3	115.2 \pm 4.7	<0.02
Weight, kg	21.6 \pm 1.4	20.5 \pm 1.2	<0.05
Head circumference, cm	51.4 \pm 2.0	50.9 \pm 1.8	NS
Chest circumference, cm	57.4 \pm 3.1	56.3 \pm 3.3	NS
IQ mean	98 \pm 15	96 \pm 13	NS
IQ 70-90	11 (13.2%)	8 (14.0%)	NS
<70	2 (2.4%)	0	NS
Social immaturity	11 (13.2%)	7 (12.3%)	NS
Speech difficulties	26 (31.3%)	19 (33.3%)	NS
Pathological EEG	3 (3.6%)	3 (5.3%)	NS
Pathological ophthalmology	14 (16.9%)	7 (12.3%)	NS
audiology	1 (1.2%)	2 (3.5%)	NS

At reexamination the investigators were not aware of the group to which the subject belonged.

The characteristics assessed were as follows:

medical history based on health certificates and on the mother's report,
body measurements (height, weight, head circumference, chest circumference),
psychologic tests (Budapest-Binet, Bender, Goodenough),
developmental history as reported by the mother,
EEG,
ophthalmology,
audiology.

RESULTS

The results were evaluated for boys and girls separately, but no significant differences were noted. Similarly, the findings in the 41 originally matched pairs did not differ from those of the rest, thus only the cumulative data of the total of 83 prednisolone-treated and 57 control children are given in Table II.

As shown by the figures, the prednisolone children were slightly higher and heavier, but there was no difference in head and chest circumference between the two groups. No significant difference was found in the mean IQ values, however, 2 versus 0 cases of mental retardation with an IQ of less than 70 were discovered in the steroid treated group. No significant differences between the groups were noted in the frequency of speech difficulties (mainly stammer and stutter), social immaturity leading to delay of school admission, and number of pathologic EEG, ophthalmological and audiological findings. Squint was the most common eye abnormality, no retrolental fibroplasia was observed.

None of the measures of development or health reported by the mothers discriminated between the prednisolone and the control groups at the 5% level. According to the interviews the children were walking on the average by 16.3 and 15.8 months of age, respectively, and had had a total of 24 and 22 diseases up to 6 years of age. An almost identical proportion of the mothers was satisfied with development of the child in the two groups (70 versus 73%).

DISCUSSION

Although the number of children reexamined did not permit a detailed analysis according to gestational age and birth weight groups, and according to perinatal events, the mean

values of these measures suggested that the groups of prednisolone treated and control children were comparable. Our study did certainly not fulfill the requirements of a complete follow-up evaluation [1]; it had however, two advantages:

1. The control group consisted of the originally matched control infants. Thus a series of perinatal variations could be excluded.

2. Reexamination was performed after the 6th birthday in each case, which was the longest follow-up reported in the literature.

The results fully confirm the finding that antenatal maternal steroid treatment does not affect the physical and psychosocial development of children [3, 4]. The only significant difference was found in height and weight of the subjects, for which we have no explanation. However, even this difference was in favour of the prednisolone-treated group, thus from the practical point of view steroid prophylaxis of IRDS has probably no long-term hazards to the fetus.

ADDENDUM

Since submitting this manuscript a collaborative study on "Effects of antenatal dexamethasone administration in the infant" (*J Pediatr* 104: 259, 1984) has been published. The results of this meticulous 3-year follow-up fully agree with our ones, including the slightly greater weight and height of the children in the steroid group.

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