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Antepartum glucocorticoid treatment: The effect of prednisolone on umbilical blood glucose, plasma free fatty acids and individual free amino acid levels

By

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Blood glucose, plasma free fatty acid and individual free amino acid levels were measured in the cord blood of preterm newborns whose mothers had received prednisolone treatment to prevent RDS. No significant differences were found in either of the metabolites between the prednisolone treated and the control group of comparable gestational age and birth weight. The results suggest that corticosteroid treatment has no gross adverse effect on fuel homeostasis.

While studying the effect of hydrocortisone administered to pregnant ewes for inducing preterm delivery, Liggins and Howie [9] noted that a few premature lambs had less than the expected degree of atelectasis. On this observation has been based the steroid treatment of mothers in premature labour for the prevention of RDS in their offspring. The concept has been supported by a number of animal and human studies [1] and obstetricians now are frequently using glucocorticoids to prevent RDS. In view of the promising results but not knowing with any certainty the hazards to mother and fetus, the physician may have difficulty in deciding whether or not to use steroids in a given patient.

There is a long list of adverse effects of corticosteroid therapy, such as growth retardation, impaired central nervous system development, disturbed materno-fetal glucose transfer, abnormal glucose metabolism, etc. [16]. On the other hand, the effects of glucocorticoids on the human fetus during the third trimester are not well documented. There are few follow-up studies [2, 5, 15] and no documentation of the immediate untoward effects of prophylactic glucocorticoid treatment on blood or plasma metabolites of the human fetus is available.

Since therapeutic doses of glucocorticoids have a well-known effect on protein and carbohydrate metabolism [17] and substrate (amino acid, lipid and carbohydrate) deficiency has been suggested [6] to delay surfactant synthesis in the preterm newborn, the maintenance of normal levels of metabolites in the fetal

circulation despite cortisone administration seems to be essential.

We have therefore compared the blood glucose, plasma free fatty acid and individual free amino acid level in the cord blood of two groups of premature babies, with or without maternal prednisolone treatment.

Material and Methods

A total of 107 mothers in premature labour received 45 to 60 mg prednisolone and a randomly selected group of 107 preterm infants of comparable gestational age and birth weight served as controls. The clinical results of the study are published simultaneously [7]. Blood samples were taken from the umbilical vein immediately after birth. Blood glucose was estimated by the orthotoluidine method [12], plasma free fatty acids by the method of Dalton und Kowalsky [4].

Plasma was deproteinized by sulphosalicylic acid and plasma free amino acids were estimated by ion exchange chromatography using an Beckman Multichrom automatic amino acid analyser.

Results

Gestational age, birth weight, blood glucose and plasma free fatty acid levels are shown in Table I. Mean gestational age and mean birth weight were similar in the two groups. Mean blood glucose concentrations were almost the same. Newborns previously exposed to the effect of corticosteroid had somewhat lower plasma free fatty acid levels in cord blood, but the difference did not reach the level of significance.

Mean plasma concentrations of 17 individual amino acids are seen in Table II. With the exception of phenylalanine no significant differences were found between the two groups and combined concentrations of 17 amino acids were also very similar.

The following correlations were made: blood glucose levels against plasma free fatty acid values, blood glucose levels against free amino acid concentrations and free fatty acid values against free amino acids. A significant correlation was found only between blood glucose levels and free fatty acid values in the treated group ($r = 0.699$; $p < 0.01$).

Discussion

It is well-recognized that glucocorticoids increase the production of glucose by the liver [3]. This gluconeogenic effect has generally been ascribed to accelerated protein catabolism [10] resulting in augmented availability of precursor amino acids [14]. In acute experiments a single dose of glucocorticoid has been observed to increase plasma alanine concentration in children [11] and in rats [13]. In a recent study, [17] a 40% increment was observed in plasma alanine after administration of 2 mg/day dexamethasone for 3 days. These observations suggest that even a short glucocorticoid treatment may lead to considerable distortion in amino acid homeostasis.

The effect of maternal glucocorti-

TABLE I

Gestational age, birth weight, blood glucose and plasma free fatty acid (FFA) levels in the two groups of infants. Mean ± S.E.
Values in parentheses show the range for the relevant parameter

	Prednisolone-treated	Control	P
Gestational age, week	34 (28—36)	32 (28—36)	
Birth weight, g	2088 (1350—3300)	1926 (1300—2450)	
Blood glucose, mg/dl	73±6	76±9	NS
Plasma FFA, μmol/l	371±24	589±136	NS
n	19	16	

TABLE II

Individual and total plasma amino acid levels in the treated and in the control group of preterm babies. Mean ± S.E.

	Prednisolone-treated	Control	P
Taurine	266±26	269±25	NS
Aspartate	62±4	95±13	NS
Citrulline	11±2	14±3	NS
Proline	222±20	187±14	NS
Glycine	283±17	324±92	NS
Alanine	420±58	452±31	NS
Cystine	103±13	109±9	NS
Valine	267±28	266±11	NS
Methionine	28±2	31±3	NS
Isoleucine	62±8	76±5	NS
Leucine	147±8	159±9	NS
Tyrosine	63±5	62±6	NS
Phenylalanine	106±10	141±15	<0.01
Lysine	352±59	353±38	NS
Ornithine	140±11	159±26	NS
Histidine	95±16	56±10	NS
Arginine	76±6	87±10	NS
Total	2627±210	2735±67	NS

coid treatment on induction of fetal enzymes has not been investigated systematically. However, a 12 1/2 week old fetus of a prednisolone-treated mother exhibited a high phosphoenolpyruvate carboxykinase activity, a key enzyme of hepatic gluconeogenesis [8]. Augmented gluconeogenesis from amino acid substrates is probably accompanied by protein catabolism which is undesirable in the immediate postnatal period, when the intake of nutrients is already curtailed. In fact Ghadimi et al. [6] postulated that substrate lack could contribute to the deficient surfactant synthesis in RDS.

In the present study the cord level of all the metabolites measured was practically the same in both the treated and the control group. It would not, however, be correct to conclude that glucocorticoids in the dose given to the mothers had no effect on fetal glucose and amino acid metabolism. The number of cases was small and only a few plasma metabolites could be measured. The estimation of hormone levels, especially that of glucocorticoids in cord blood, should be included in further studies. Despite the difficulties created by the intravenous treatment of RDS (glucose and bicarbonate infusions, etc.), observation of the postnatal changes of these metabolites would also be informative. Finally, with all these reservations, it can be said that maternal prednisolone administration had no gross effect on cord blood glucose, plasma free fatty acid and free amino acid levels.

References

1. Avery, M. E.: Pharmacological approaches to acceleration of foetal lung maturation. Brit. med. Bull. **31,** 13 (1975).
2. Baden, M., Bauer, Ch. R., Colle, E., Klein, G., Taeusch, H. W., Stern, L.: A controlled trial of hydrocortisone therapy in infants with respiratory distress syndrome. Pediatrics **50,** 526 (1972).
3. Cahill, G. F. J.: Action of adrenal cortical steroids on carbohydrate metabolism. In: Christy, N. P. (Ed.): The Human Adrenal Cortex. Harper and Row Publishers, New York 1971.
4. Dalton, C., Kowalsky, C.: Automated colorimetric determination of free fatty acids in biological fluids Clin. Chem. **13,** 774 (1967).
5. Fitzhardinge, P., Eisen, A., Lejtényi, C., Metrakos, K., Ramsay, M.: Sequalae of early steroid administration to the newborn infant. Pediatrics **53,** 877 (1974).
6. Ghadimi, H., Arulanantham, K., Desai, L.: Unitary concept for prevention and treatment of respiratory distress syndrome. Lancet **2,** 126 (1973).
7. Horváth, I., Méhes, K., Fias, I., Szmodits, Sz.: Prevention of respiratory distress syndrome by antenatal maternal steroid medication. Acta paediat. Acad. Sci. hung. **17,** (1976).
8. Kirbi, L., Hahn, P.: Enzyme induction in human fetal liver Pediat. Res. **7,** 75 (1973).
9. Liggins, G. C., Howie, R. N.: A controlled trial of antepartum glucocorticoid treatment for prevention of RDS in premature infants. Pediatrics **50,** 515 (1972).
10. Long, C. N. H., Katzin, B., Fry, F. G.: Adrenal cortex and carbohydrate metabolism. Endocrinology **26,** 309 (1940).
11. Pagliara, A. S., Karl, I. E., De Vivo D. C., Feigin, R. D., Kipnis, D. M Hypoalaninemia: a concomitant of ketotic hypoglycaemia. J. clin. Invest. **51,** 1440 (1972).
12. Price, J. D.: A simple rapid method for determining glucose in blood or plasma. Analyst **92,** 198 (1967).
13. Ryan, W. L., Carver, M. J.: Immediate and prolonged effects of hydrocortisone on the free amino acids of rat skeletal muscle. Proc. Soc. exp. Biol. (N. Y.) 114, 816 (1963).
14. Smith, O. K., Long, C. N. H.: Effect of cortisol on the plasma amino nitro-

gen of eviscerated adrenalectomized diabetic rats. Endocrinology **80**, 561 (1967).
15. Taeusch, H. W. J., Wang, N. S., Baden, M., Bauer, C., Stern, L.: A controlled trial of hydrocortisone therapy in infants with RDS. II. Pediatrics **52**, 850 (1973).
16. Taeusch, H. W. J.: Glucocorticoid prophylaxis for respiratory distress syndrome: a review of potential toxicity J. Pediat. **87**, 617 (1975).
17. Wise, J. K., Hendler, R., Felig, Ph.: Influence of glucocorticoids on glucagon secretion and plasma amino acid concentrations in man. J. clin. Invest. **52**, 2774 (1973).

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