

NEONATAL DIABETES INSIPIDUS DUE TO MATERNAL LITHIUM THERAPY DURING PREGNANCY

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Summary

Lithium, given during pregnancy led to a temporary diabetes insipidus in a premature newborn, although the drug was discontinued one week before birth. The urinary concentrating defect was shown to be partially nephrogenic, partially central in origin. Lithium toxicity in this infant was triggered by the low salt diet of the mother.

Introduction

Lithium carbonate is widely used in the long-term treatment of manic-depressive psychosis and the drug is sometimes continued during pregnancy. Lithium ions diffuse freely across the placenta and this can lead to lithium toxicity in utero.

Case history

A newborn premature baby of four days was referred for failure to thrive. The mother had a manic-depressive psychosis and was treated with lithium carbonate from the 28th week of gestation. Serum lithium was monitored at weekly intervals. At 32 weeks a value of 2.05mEq/L was obtained and the therapy was discontinued for three days. At 34 weeks the serum lithium was 1.25mEq/L and a salt poor diet was prescribed because of oedema. Two weeks later serum lithium reached 3.3mEq/L, and the drug was stopped. At 37 weeks the baby was born, her birth weight was 2700g. On admission the physical examination of the baby revealed poor sucking reflexes and generalized hypotonia. A cardiac murmur was present. She weighed 2300g, i.e. birth weight less 20 per cent. Urine output was very high: 450ml/24h, i.e. 200ml/kg per 24h. Urine osmolality was less than 200mOsm/kg water. A total fluid input of 240ml/kg was necessary to make the baby grow. The baby's blood contained 0.05mEq/L of lithium at day 12. Slowly an improving appetite was noted together with decreasing fluid needs and urine output. The renal concentration defect disappeared completely after two months. The intravenous urography and cystography did not reveal any abnormality.

Methods

Fluid deprivation of six to eight hours was performed several times. Measurement of urinary and plasma osmolality and urinary sodium excretion was performed. Antidiuretic hormone (DDAVP - Desmopressin) was given by nasal insufflation three times: a dose of 2.5 to 5 μ g was used, twice after a period of fluid deprivation. The urinary osmolality was monitored. A percutaneous renal biopsy was performed.

Results

Table I shows the urinary and plasma osmolality after fluid deprivation on day 14, 20, 26 and 41 after birth. The urinary osmolality remained low and the plasma osmolality rather high, the serum sodium did not increase.

TABLE I. Effect of fluid deprivation on urinary and plasma osmolality and on serum sodium

age days	fluid deprivation hours	urinary osmolality mOsm/kg H ₂ O	plasma osmolality mOsm/kg H ₂ O	plasma sodium mEq/L
14	6*	70	280	134
20	8	150	320	141
26	8	172	287	139
41	7,30	265	290	139

* reduction of fluid intake only

In Table II the results of the DDAVP tests are given. An increase of the urinary osmolality of more than 50 per cent is seen at days 13 and 27; at day 44 a better result is achieved.

TABLE II. Effect of DDAVP on urinary osmolality

age days	fluid deprivation hours	urinary osmolality after fluid deprivation mOsm/kg H ₂ O	urinary osmolality maximum after DDAVO mOsm/kg H ₂ O
13	0	55	380
27	9	420	640
44	11	330	740

The renal biopsy did not reveal any lesions on light microscopy. With the electron microscope irregularities in the shape of the nuclei of the collecting ducts were seen. The tubules contained an increased number of lysosomal inclusions.

Discussion

Several typical aspects of lithium intoxication are present in this infant. The marked hypotonia and poor sucking [1–3] are neuromuscular effects probably caused by alterations of neural ion transport or by inhibition of an adenylycylase mediated neurotransmitter [4]. A ventricular septum defect has been reported in association with lithium intoxication although other congenital malformations of the heart, myocardial dysfunction and atrial flutter seem to occur more often [5–7]. As the mother of our patient was not treated with lithium during the first trimester of pregnancy the ventricular septum defect cannot be considered as a teratogenic effect of lithium.

A transient diabetes insipidus in a child born to a mother on chronic lithium therapy was first described by Mizrahi et al [3]. The authors considered the renal concentrating defect as nephrogenic although an increase of more than 50 per cent in the urinary osmolality was noted after vasopressin administration. We consider the renal concentrating defect in our patient as partially nephrogenic, partially as central. The concentrating ability of the kidney changes with age: the maximum osmolality in the newborn is much lower than in adults and increases rapidly after birth: urine osmolality after water deprivation ranges from 500 to 700mOsm/kg H₂O at birth compared to 1200mOsm/kg H₂O in adults [8]. An osmotic threshold of 282mOsm/kg H₂O is suggested for healthy full-term babies and of 291mOsm/kg H₂O for premature babies. In our patient the urinary osmolality remained very low after fluid deprivation 14 days after birth although the osmotic threshold was reached, the serum sodium did not increase.

The increase of the urinary osmolality after vasopressin indicates that the diabetes insipidus in our patient is partially central and not only nephrogenic. The concentrating defect persisted for almost two months although serum lithium was undetectable after 14 days.

Lithium is handled by the kidney in a manner similar to that of sodium. A low sodium diet will thus increase the tubular reabsorption of sodium and lithium and lead to lithium toxicity as occurred in our patient. Lithium probably interferes with adenylycylase activated by antidiuretic hormone (ADH) or with cAMP activity. The hypothalamic-pituitary release of ADH also depends on cAMP generation by adenylycylase stimulation and this mechanism could account for the central diabetes insipidus in lithium toxicity.

Finally the long-term effect of lithium in this newborn may be explained by the slow transfer of the ion from the intracellular space but more specifically by the immature glomerular filtration rate.

All neonates born to mothers treated with lithium carbonate should be monitored carefully. Recognition of a lithium induced diabetes insipidus in the newborn prevents dehydration.

References

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