

Oral desmopressin in neonatal diabetes insipidus

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SUMMARY A neonate with cranial diabetes insipidus was successfully treated with oral desmopressin. The patient had a midline cleft lip and palate and we obtained a more consistent response using the oral route than using the usual nasal route.

Desmopressin has been the treatment of choice for cranial diabetes insipidus since its introduction in 1972.¹ It is usually administered through the nose by nasal catheter or spray, but in a neonate with gross deformities of the oral and nasal cavities it is difficult to maintain a consistent response using this route.

Case report

A female infant was born at 38 weeks' gestation, birth weight 2060 g (<third centile), with a midline cleft lip and palate. The cleft extended into the left nostril and there was free communication between the oral and nasal cavities to either side of an apparently well formed nasal septum. Her head circumference was 29.0 cm. (<third centile); there were no other dysmorphic features.

The baby fed well at the outset on formula milk. At the age of six days she developed bilateral purulent conjunctivitis due to simultaneous gonococcal and chlamydial infections. This was successfully treated with frequent saline washouts, intravenous cefotaxime, oral erythromycin, and topical tetracycline. On day 8 she was noted to be hypernatraemic, the plasma sodium concentration rising to 158 mmol/l by day 12, but with normal concentrations of potassium and urea. At this time the plasma osmolality was 319 mOsm/kg H₂O when the urine osmolality was 65 mOsm/kg H₂O on a random sample.

Oral intake was by now more than 230 ml/kg/day and urine output greater than 100 ml/kg/day. Cranial diabetes insipidus was provisionally diagnosed and confirmed by giving desmopressin 400 ng intramuscularly after which the plasma sodium concentration fell from 164 mmol/l to 135 mmol/l, the plasma osmolality fell from 329 mOsm/kg H₂O to 284 mOsm/kg H₂O and the urine osmolality rose to 156 mOsm/kg H₂O from 65 mOsm/kg H₂O.

Treatment was started with desmopressin intranasally 1 µg twice daily through the intact nostril, but the child's facial anatomy made it difficult to administer with accuracy and consequently her weight varied greatly from day to day. Hypernatraemia persisted and urine output remained excessive (fig 1).

At the age of 33 days desmopressin was given orally in a dose of 5 µg daily, increasing to twice daily to control her urine output adequately. On this regimen weight gain was appropriate (fig 1), and the plasma electrolyte concentrations and osmolality returned to normal. Urine osmolality was measured on all specimens passed over a 24 hour period, and the results suggested that the duration of action of the oral desmopressin was about six hours (fig 2).

Because of the presence of a preservative, chlorbutol 0.5%, in the nasal preparation we at first decided to use the injectable solution by the oral route. There are, however, no reports of adverse effects from enterally administered chlorbutol and therefore we changed to using the nasal solution. This preparation comes in oversized phials containing 2.5 ml (250 mg) of desmopressin which was diluted to 10 ml with physiological saline. Using an oral syringe, 0.2 ml (5 µg) of the solution was given

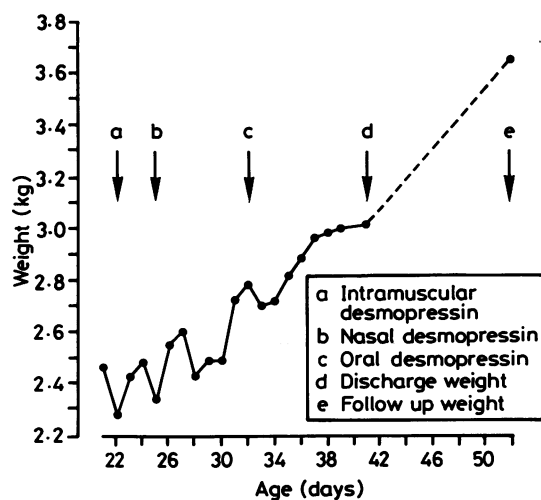


Fig 1 Daily weight after treatment with desmopressin.

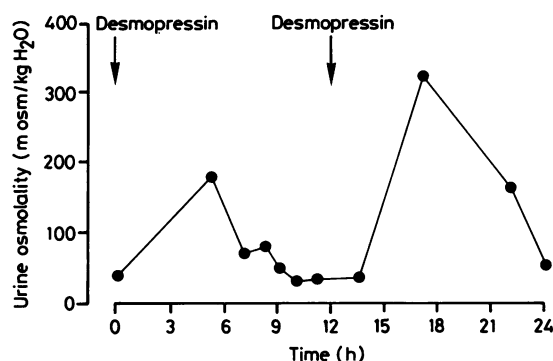


Fig 2 Effect of oral DDAVP on urine osmolality. Times of passing individual urine samples (●); time oral desmopressin given (↓).

into the oropharynx twice daily. This dose is about 10 times greater than the appropriate nasal dose.

Electrolyte concentrations remained within normal limits and she was discharged at the age of 41 days weighing 3140 g. At follow up at the age of 52 days plasma electrolyte concentrations were normal and she weighed 3660 g.

During her admission a computed tomogram of the brain showed that anteriorly the ventricles were poorly formed and the falx was absent. The cerebral hemispheres, corpus callosum, and cerebellum looked normal. Plasma concentrations of cortisol, thyroxine, and thyroid stimulating hormone were within normal limits.

Discussion

Pituitary hormone deficiencies in association with midline facial defects have been well described, in particular septo-optic dysplasia, the holoprosencephaly spectrum.^{2,3} Our patient had an extensive midline facial cleft with evidence from computed tomography of an intracranial midline defect.

Although the use of oral desmopressin has been reported in older children with cranial diabetes insipidus,⁴ we could find no reports of its use in neonates. In our patient oral desmopressin proved successful in maintaining normal plasma electrolyte concentrations and weight gain in the first months of life.

Although the effect of the oral desmopressin in the dose used seemed to last only about six hours we decided not to increase the size or frequency of the dose. This was to avoid water accumulation because plasma electrolyte concentrations and weight gain were normal. The period during which free water clearance remains negative can be expected to be prolonged by increasing the size of the oral dose.⁴

Although there was no evidence of other hormonal deficiencies in our patient, her pituitary function will be investigated.

The cost of the nasal preparation is about five times less than that of the injectable formula, but in neonates with cranial diabetes insipidus requiring treatment with desmopressin, the oral route is an effective alternative if the nasal route proves difficult to use.

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References

- Andersson KE, Arner B. Effects of desmopressin, a synthetic analogue of vasopressin, in patients with cranial diabetes insipidus. *Acta Med Scand* 1972;21:192.
- Haworth JC, Medovy H, Lewis AJ. Cebocephaly with endocrine dysgenesis. *J Pediatr* 1961;59:726.
- Benoit-Gonin JJ, David M, Feit JP, et al. 1978. La dysplasie septo-optique avec deficit en hormone antidiuretique et insuffisance surrenale centrale. *Nouvelle Presse Med* 1978;37:3327-31.
- Cunnah D, Ross G, Besser GM. Management of cranial diabetes insipidus with oral desmopressin (DDAVP). *Clin Endocrinol* 1986;24:253-7.

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