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ON THE OCCURRENCE OF MONO-SYMPTOMATIC NOCTURNAL ENURESIS IN CHILDREN TREATED WITH VALPROAT, AND ITS THERAPY WITH DDAVP

Aims of Study

The appearance of enuresis as a side-effect of therapy with Valproat has been long recognised. However, the possible reason for this phenomenon is so far not known. This study presents an extensive paediatric collective which developed mono-symptomatic nocturnal enuresis while being treated with Valproat (VPA). The effectiveness of dDAVP therapy in treating this side-effect casts new light on the possible aetiology of primary nocturnal enuresis (PNE).

Methods

From 1999 to 2002 17 patients with different forms of epilepsy were observed at the Clinic for Neuropaediatrics in Kiel and the Epilepsy Centre, Kork (m:f=8:9, age: 5 to 18 years, mean: 10 years). These patients, who were being treated with Valproat, had all developed typical mono-symptomatic enuresis nocturna, wetting their beds more than 3 times a week. None of the children was suffering from a urinary tract infection and/or anatomical abnormalities of the urinary tract. 10 of these patients were treated with 40µg dDAVP intranasaly in the evening.

Results

With respect to comparable patients, the frequency of enuresis as a side-effect of VPA therapy was about 0,6%. With mean VPA blood levels of 72 mg/l, all 17 patients were free of fits and their EEG was inconspicuous. In the synopsis of all cases it was possible to differentiate three courses:

In 7 cases enuresis persisted after conclusion of VPA therapy.

In 9 children taking VPA, therapy of the enuresis with dDAVP was started. 6 of these patients became completely dry, in 3 the number of wet nights was reduced by more than 50%. To date, 4 out of these 9 patients were also able to stop dDAVP medication after VPA therapy was ended without reoccurrence of enuresis.

In one patient the successful dDAVP treatment of enuresis was discontinued after the EEG had normalised. The reappearance of EEG signs that suspected seizures again led to administration of VPA medication - and to enuresis. Therapy with dDAVP was again effective.

Conclusions

As already described by other authors, mono-symptomatic nocturnal enuresis is a relatively frequent side-effect of VPA therapy. In the present study it was possible for the first time to demonstrate the good response of this enuresis to dDAVP. This fact has far-reaching consequences for understanding the aetiology of primary nocturnal enuresis (PNE) and the efficacy of dDAVP in its therapy. It contradicts the widely accepted opinion that a nocturnal ADH – deficit causes nocturnal enuresis. Neither is the postulated decreased functional bladder capacity of the enuretic child compatible with the findings described here, since VPA has no effect either on urine production or on bladder capacity. Rather, the data (again) focus interest on the central nervous system with regard to both the aetiology of PNE and to understanding the effects of dDAVP in its therapy. The influence of VPA on the sleep pattern and on arousal is undisputed. At the same time an increasing number of findings show that dDAVP besides its known V2-mediated renal effect, also has a second central target which, like VPA, influences sleep and arousal and evidently antagonises the effects of VPA on the same central structures.