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Desmopressin and psychiatric effects

Introduction

Desmopressin (Minrin®) was granted a marketing authorisation in 1974. Desmopressin is a synthetic vasopressin analogue with prolonged antidiuretic activity, but little pressor effects. It is indicated: *for diagnosing and treatment of central vasopressin sensitive diabetes insipidus, treatment of polyuria and polydipsia resulting from removal of the pituary gland, estimation of "renal concentration ability", and for treatment of nocturnal enuresis.*
Common adverse drug reactions include headache and gastrointestinal complaints. Post-marketing surveillance revealed emotional reactions in children and isolated cases of allergic (skin) reactions [1].

Reports

Untill 1 June 2004 Lareb received 43 reports concerning desmopressin use. Among these reports were 8 cases of psychiatric reactions while using desmopressin (table 1). In patient D a positive rechallenge was observed twice.

Table 1. reports of psychiatric ADRs associated with the use of desmopressin

Patient, Sex, age	Drug indication	Dose	ADR	Concomitant medication	Time to onset	outcome
A, F, 6	nocturnal enusesis	0.01 mg nasal	nervousness	xylometazoline	2 weeks	unknown
B, F, 11	nocturnal enusesis	0.01 mg nasal	agitation, nervousness	-	2 days	unknown
C, M, 12	nocturnal enusesis	0.01 mg nasal	restlessness	clonidine	2 weeks	unknown
D, M, 8	nocturnal enusesis	0.2 mg oral	aggression, personality change	xylometazoline	3 days	recovered after withdrawal, positive rechallenge
E, F, 82	?	0,1 mg oral	confusional state	-	?	?
F, M, 10	nocturnal enusesis	0,1 mg oral	sleep walking	lactulose sirup	3 days	recovered after withdrawal
G, M, 9	nocturnal enusesis	0.2 mg oral	personality disorder		1 day	recovered after withdrawal
H, M, 5	nocturnal enusesis	0.2 mg oral	psychotic disorder, aggression	paroxetine tamsulosine bicalutamide nicardipine isosorbide carbasalate-calcium	2 weeks	unknown

Other sources of information

Literature

Several case reports on psychiatric adverse drug reactions in children using desmopressin for nocturnal enuresis were published [2,3]. Von Gontard and Lehmkuhl [2] presented two cases of an 5-year-old boy and a 7-year-old girl who experienced hypermotoric behaviour, loss of concentration, pseudohallucinations, and anxiety. The symptoms resolved after cessation of desmopressin.

Vic *et al.* [3] decribe a 8-year-old boy who was using desmopressin. As soon as he gets a rhinal infection treated by antibiotics he started suffering from paresthesias, desorientation, photophobia and obnubilation. In the hospital hyponatremia was diagnosed and treated and the desmopressin was withdrawn after which he recovered without sequelae.
Paranoid psychosis was reported after desmopressin therapy for Alzheimer's disease [4].

Databases

The reports on desmopressin in the Lareb database are stratified by agegroup and psychiatric ADRs in table 2.

Table 2. Lareb reports on desmopressin with and without psychiatric ADRs by age group

		Age	
		<12 years	>12 years
ADR	psychiatric	8	1
	not psychiatric	9	24

One report is excluded because of unknown age

The number of children (0-12 years) with psychiatric ADRs is higher (odds ratio 21, 95% CI 2.3 - 195) than would be expected among these desmopressin reports if patients of all ages would be equally susceptible to psychiatric ADRs.

In the 4th quarter of 2003 the WHO database contained 1087 reports concerning 1911 ADRs on desmopressin. The most frequently reported ADR is hyponatraemia with 244 cases (ROR 77.5, 95% CI 67.2-89.5). In the system organ class psychiatric disorders the ADRs: thinking abnormal, nervousness, confusion, concentration impaired, personality disorder, paroniria, aggressive reaction, and emotional lability are disproportionally reported.

Mechanism

No direct mechanism to psychiatric effects was proposed in literature. If an effect on the central nervous system is involved, impermeability of the blood brain barrier to desmopressin in adults [5] could be an explanation for the small number of reports with psychiatric ADRs from this age group. Another, more plausible, hypothesis is that these pyschiatric ADRs occur as a secondary effect to hyponatriemia, although not reported to Lareb.

Conclusion

Lareb has received eight cases of psychiatric ADRs in mainly young patients using desmopressin, mainly for indication nocturnal enuresis. Case reports in literature and data from the WHO database support this association.

References

1. Dutch SPC Minrin®. (version date 9-3-2004) http://www.cbg-meb.nl/IB-teksten/06684-13958-18923.PDF.
2. von Gontard A, Lehmkuhl G. Desmopressin side effects. J Am Acad Child Adolesc Psychiatry 1996;35(2):129-30.
3. Vic P, Queinnec C, Durelle-Caillard P, Broch C, Blondin G, Blayo M, Broussine L. Troubles du comportement chez un enfant traité par desmopressine pour énurésie. Arch Pediatr 2000;7(10):1128-9.
4. Collins GB, Marzewski DJ, Rollins MB. Paranoid psychosis after DDAVP therapy for Alzheimer's dementia. Lancet 1981;2(8250):808.
5. Sorensen PS, Vilhardt H, Gjerris F, Warberg J. Impermeability of the blood-cerebrospinal fluid barrier to 1-deamino-8-D-arginine-vasopressin (DDAVP) in patients with acquired, c ommunicating hydrocephalus. Eur J Clin Invest 1984;14(6):435-9.