Virus-cell systems in which activity of DSCG was examined

Virus	Classification	Cell system
Pox virus	Vaccinia	CEF
Herpes virus	Herpes simplex	CEF
Picornavirus	Poliovirus 2	HEP ₂
Orthomyxovirus	Influenza A/PR/8 (H ₂ N ₂)	CAM ₂
Paramyxovirus	Influenza A/Hongkong (H ₂ N ₂)	CEF/CAM
Metamorphovirus	Parainfluenza 1 (Sendai)	CEF/CAM
	Respiratory syncytial (RS)	HEP ₂

CEF = chick embryo fibroblast; CAM = chorioallantoic membrane.³

bodies was observed after incubation of the mixtures for one hour (concentration of DSCG up to 1.95 mmol/l).

In-vivo experiments in mice—These included intracerebral inoculation of a mouse-adapted strain of polio virus type 2 at various dilutions and the intranasal and contact infection of mice with influenza and parainfluenza viruses. The drug was administered by mouth, subcutaneously, intranasally, and by aerosol at various dose levels up to 500 mg/kg/day. No antiviral activity was observed, nor did it affect the symptoms of the infections in the mice.

Comment

These limited studies did not show that DSCG had antiviral activity. While the drug has been shown to be remarkably non-toxic in laboratory and clinical use, we found that the upper non-toxic concentration of DSCG in vitro was about 7.8 mmol/l (4 mg/ml). Above this point signs of toxicity were usually apparent.² In contrast, the most effective concentration used by Penttinen *et al*¹ in their in-vitro studies of inhibition of virus-induced cytopathic effects was 19.5 mmol/l (10 mg/ml). While their results are obviously interesting and of significance for further investigation into exacerbation of asthma associated with virus infections, the level of drug to be used and the methodology and design of future experiments is most important.

¹ Penttinen, K, Arnio, A, and Hovi, T, *British Medical Journal*, 1977, 1, 82.

² Cox, J S G, *et al*, *Advances in Drug Research*, 1970, 5, 115.

³ Fazekas de St Groth, *et al*, *Journal of Hygiene*, 1958, 56, 415.

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Serum sodium and osmolality during carbamazepine treatment in children

Carbamazepine is an anticonvulsant used in treating different epileptic disorders in all age groups. It has an antidiuretic activity similar to that of the antidiuretic hormone.¹⁻³ The risk of hyponatraemia and low plasma osmolality during carbamazepine treatment in adult patients is related to the dose and blood concentration of the drug. We present here our findings in paediatric patients in these respects.

Patients, methods, and results

Twenty-eight patients attending the paediatric clinic of Malmö General Hospital for control of epileptic disorders were reviewed. Their average age was 12 years (range 6-18), the average daily dose of carbamazepine 650 mg (range 100-1400), and the average duration of therapy 36 months (range 2-113). Eleven of the children were taking carbamazepine only and 17 carbamazepine in combination with other anticonvulsants. Eighteen children with an average age of 11 years (range 3-18) under treatment with other anticonvulsants only, mainly phenytoin, were reviewed for comparison.

A serum sample was taken from each patient and analysed for carbamazepine and electrolyte concentrations. Serum osmolality was measured by

means of the depression of freezing point technique. Carbamazepine concentration was measured by gas chromatography using cyheptamide as an internal standard.

The results are summarised in the table. The mean serum sodium concentration was 143 (141-146) mmol (mEq)/l in children on carbamazepine only, 142 (141-145) mmol (mEq)/l in children on carbamazepine together with other anticonvulsants, and 142 (140-145) mmol (mEq)/l in children treated with other antiepileptic drugs only. The corresponding figures for serum osmolality were 285 (279-294), 288 (281-297), and 286 (278-297) mmol (mOsm)/kg respectively. None of the patients had hyponatraemia and no lowering of the serum osmolality was registered. No correlation was found between the daily dose of carbamazepine and serum sodium.

Details of patients on carbamazepine

Case No	Age (years)	Sex	Carbamazepine treatment		Cpss (μmol/l)	Serum Sodium (mmol/l)	Serum osmolality (mmol/kg)	Other drugs
			Duration (months)	Daily dose (mg)				
1	12	M	30	1400	27	141	284	P
2	13	M	67	1200	32	142	284	P
3	10	F	11	1200	30	143	289	P
4	16	M	113	1000	27	145	284	P, E
5	12	M	8	900	23	142	297	P
6	18	M	48	800	27	141	287	P
7	8	F	48	800	16	141	287	P
8	16	F	42	800	35	142	288	P
9	7	F	52	800	24	144	294	P, N
10	15	M	91	800	25	143	296	P, E
11	16	M	21	600	27	142	284	E
12	6	M	18	600	36	143	281	P
13	11	M	20	600	18	142	293	P
14	15	M	2	600	28	146	288	—
15	11	M	42	600	41	144	279	—
16	9	M	45	600	42	143	284	—
17	8	F	11	500	27	143	285	P, D
18	8	M	84	500	20	143	288	P, D
19	12	F	12	500	38	143	291	—
20	12	F	24	500	31	141	282	—
21	14	M	22	400	29	141	281	—
22	11	M	35	400	31	143	284	—
23	11	M	2	400	24	143	286	—
24	10	M	3	400	16	142	292	P
25	9	M	13	400	34	142	294	—
26	7	F	15	400	32	144	287	—
27	17	M	42	200	31	144	283	—
28	16	F	50	100	14	143	286	—

Cpss = Carbamazepine steady-state concentration. P = Phenytoin. E = Ethosuximide. N = Nitrazepam. D = Diazepam.

Conversion: SI to traditional units—Cpss: 1 μmol/l ≈ 0.24 μg/ml. Serum sodium: 1 mmol/l = 1 mEq/l. Serum osmolality: 1 mmol/kg = 1 mOsm/kg.

Comment

The antidiuretic action of carbamazepine has been used in the treatment of diabetes insipidus.¹⁻³ Henry *et al*⁴ have shown that this action is not confined to patients with diabetes insipidus. A high daily dose of carbamazepine may induce hyponatraemia in adults with other diseases. Furthermore, elderly patients with cardiovascular disease may be particularly vulnerable.⁵ We did not find any significant abnormalities in serum sodium or serum osmolality in children treated with carbamazepine alone or in combination with other anticonvulsants for epileptic disorders. Apparently with the dose of carbamazepine commonly required to ensure good control of a convulsive disorder in children there is hardly any risk of hyponatraemia. Nevertheless, in children with symptoms such as confusion, weakness, or lethargy while on carbamazepine, hyponatraemia should be considered.

¹ Braunhofer, J, and Zicka, L, *Medizinische Welt*, 1966, 17, 1875.

² Kimura, T, *et al*, *Journal of Clinical Endocrinology and Metabolism*, 1974, 38, 356.

³ Wales, J K, *Lancet*, 1975, 2, 948.

⁴ Henry, D A, *et al*, *British Medical Journal*, 1977, 1, 83.

⁵ Stephens, W P, *et al*, *British Medical Journal*, 1977, 1, 754.

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