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SYNTHETIC LYSINE VASOPRESSIN IN HERPETIC NEURALGIA

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Abstract. Acute cases of severe herpes zoster pain, in contrast to cases of slight or moderate pain, have been successfully treated with 5 IU of synthetic lysine vasopressin intramuscularly. If the duration of the pain exceeds at least 2 weeks, the effect is less favourable. Blanching of the face and slight gastrointestinal discomfort were unwanted reactions.

In the older literature there is mention that posterior pituitary hormones can be of use in the treatment of herpes zoster pain (4). In this connection Pituitrin and Pitressin are mentioned, both being a mixture of oxytocin and vasopressin, contaminated with neurophysins. From the literature it is difficult to glean further specifications of dosage, duration of treatment, and duration of effect of these posterior pituitary hormones. We therefore initiated a clinical trial in order to elucidate which fraction of the posterior lobe hormones might be responsible for this effect. It was planned that synthetic lysine vasopressin, synthetic oxytocin, neurophysin-1 and -2 should be tested. The clinical testing started with synthetic lysine vasopressin (Postacton, Ferring).

MATERIAL AND METHODS

In order to be able to evaluate the effect, patients in severe pain were primarily included in the study. These patients experienced excruciating pain, lasting almost continuously and disturbing sleep to a varying degree. Analgesics gave slight, brief relief, or failed completely. Pain could usually be categorized into either or both of two components, a more deep pain, and a more superficial one of burning type and/or itching. In 5 cases the affected area corresponded to the first trigeminus area with swelling of the eyelid but without involvement of the eye itself. Patients with pain lasting 1 week or less were designated acute cases, while patients who first came to treatment after at least 2 weeks of pain were arbitrarily categorized as chronic cases (no patients had pain lasting between 1 and 2 weeks). The material is presented in Tables I and II.

Vasopressin was given to 8 patients with slight or moderate pain (3 men and 5 women, age range 19–79 years), 3 of whom had previously been treated with the same agent because of severe pain (cases 4, 9 and 27 in Table I).

In addition, vasopressin was given to a 65-year-old woman with untreated trigeminal neuralgia, and to an 82-year-old man with tabes dorsalis and lancinating pains. Unfortunately both of these patients were only observed for half an hour after the injection. Vasopressin was also injected in 3 other patients, who had severe pain caused by skeletal metastasis, Raynaud's gangrene and osteoporosis, respectively.

Postacton (synthetic lysine vasopressin, Ferring, Malmö, Sweden) was given intramuscularly in a dose of 5 IU. Only in isolated cases was another dose, of 10 IU, given a few days after the first injection. Several patients in the group of acute cases visited us again, once or twice, after a primarily successful result, in order to receive another injection. The interval between treatments was usually 1–2 days. The effect of therapy was based solely upon the patient's own statement, since no objective methods are available to estimate the patient's appreciation of any difference in the pain.

Vasopressin has other well-known effects which make it impossible to carry out a double-blind placebo investigation. The increased gastrointestinal peristalsis especially would cause subjective complaints, and the pallor of the face would immediately make it clear to an investigator that the patient has received a vasopressin injection.

RESULTS

Patients with severe pain

Acute cases. In 23 out of 24 cases with deep pain and in 20 out of 21 cases with superficial pain, the neuralgia disappeared completely, or almost completely, within 1 hour (Table I). With one exception (case 6), this favourable effect was

Table I. *Results of vasopressin on pain in the group of acute cases*

Case no.	Age (y.)	Sex	Nos. of injections	Days between onset of symptoms and 1st injection	Effect on pain: Deep	Effect on pain: Superficial	Duration of effect (h)
1	19	♂	1	2	++		>16
2	29	♂	1	6	++	+(+)	>24
3	30	♂	2	2	++	++	17
					++		>20
4	32	♂	1	7	++		>21
5	37	♀	1	4	++		10
6	48	♂	2	4	++	++	24–48
					0	0	
7	50	♀	2	7	++ A	++ A	>15
8	53	♀	1	7	++	++	12
9	55	♀	1	7	++	++	12
10	56	♀	1	7		++	>48
11	58	♀	2	4	++	0	16
					++	0	12
12	59	♀	2	3	++	+	>48
						++	
13	60	♀	1	5	++	++	14
14	60	♂	2	6	0		
					0		
15	60	♂	3	5	++	+	>12
					++	++	15
					++		>15
16	62	♂	1	2	++	++	>48
17	63	♀	2	3	++	++	>24
					+		
18	64	♀	2	3	++		3
					++		3
19	64	♂	1	3		++	>12
20	66	♀	2	2	+(+)		9
						++	>48
21	68	♀	1	7	++	++	>24
22	70	♀	2	4		++ A	>24
23	71	♀	1	4	++	++	>23
24	72	♀	1	5	++	+	6
25	73	♀	2	1	++	++	>24
					++	++	7
26	73	♂	3	3	++	++	
					++	+	>24
27	79	♀	1	7	+(+)		>24

No sign in columns 6 or 7 denote absence of pain.
++ Complete disappearance of pain.
+ Almost but not complete disappearance of pain.
0 No or insignificant effect.
A Effect after 10 IU, but not after 5 IU, vasopressin.

also obtained in patients who were given repeated injections of vasopressin.

In most cases the patients experienced the disappearance of the pains shortly after the vasopressin injection. The shortest period of freedom from pain was 3 hours. The most usual period of freedom from pain was between 12 and 24 hours, and an even longer period was not infrequent. It was difficult to evaluate whether the pain-free period could last several days, because of the natural course of the disease. In a few cases the superficial pain reappeared somewhat earlier than the deep pain. Before the vasopressin injection, the pain had usually been continuous. After the injection, sleep usually returned to normal, in contrast to the sleeplessness which was caused by the pain. The eruptions were not affected. The eyelid swelling disappeared in 2 cases in which the first trigeminal root was involved. Itching, which was the predominant symptom

Table II. *Results of vasopressin on severe pain in the group of chronic cases*

Symbols as in Table I

Case no.	Age (y.)	Sex	Nos. of injections	Days between onset of symptoms and 1st injection	Effect on pain		Duration of effect (h)
					Deep	Superficial	
28	32	♀	1	30	0	0	
29	37	♀	1	14	++	++	>21
30	48	♀	1	16		0	
31	50	♂	1	90	++		>48
32	53	♀	3	18	++		4
					++		3
					+		4
33	56	♀	1	14	++	+	>48
34	65	♂	1	14	0	0	
35	66	♀	1	180		++	>48
36	66	♀	1	14		++	>48
37	67	♀	2	35	+	+	6
					+	+	24
38	70	♂	3	90	0	0	
39	71	♂	2	14	++	++	>24
					++	++	>48
40	75	♀	1	17	0	0	
41	86	♀	1	14		0	

in 1 case (case 10), disappeared in all cases where it was present.

Chronic cases. The number of chronic cases who obtained considerable relief from injection of vasopressin was relatively fewer than the alleviated acute cases, as can be seen from Table II.

Thus, deep pain was relieved in 6 out of 10 cases and superficial pain in 6 out of 12 cases.

Acute cases with slight or moderate pain. In this group ($n = 8$) the effect of vasopressin on the pain was nil, or insignificant, in striking contrast to the effect obtained in patients with severe pain.

Other cases. In 1 patient with trigeminal neuralgia, 1 patient with tabes dorsalis, and 1 patient with skeletal pain caused by cancer metastasis, and a case with Raynaud's gangrene, vasopressin had almost no effect whatsoever.

DISCUSSION

The obvious and well-known general effects of vasopressin such as blanching of the face and gastrointestinal peristalsis makes a double-blind placebo investigation pointless. The results of this investigation show that vasopressin has an early and favourable effect on severe pain in acute cases of herpes zoster. The deep pain disappeared completely, or nearly so, in 23 cases out of 24, and the superficial burning pain in 20 of 21 cases. This relief from pain could furthermore be reproduced after repeated injections. The duration of freedom from pain lasted, in most cases, between 12 and 24 hours. In cases with slight or moderate pain, the effect, if any, was doubtful. In cases of pain lasting at least 2 weeks, the effect was less constant.

The reason for this finding is completely unknown. It seems difficult to explain vasopressin's effect on pain by its antidiuretic, vasopressor or corticotrophin-releasing action. The biological half-life of these effects is a matter of minutes. The duration of relief from pain lasted several hours, and it therefore seems doubtful to assume the effect of vasopressin as being a primary one. The possibility remains that a primary effect may induce a secondary and longlasting mode of action. This, however, is pure speculation.

Vasopressin releases ACTH, directly or indirectly, from the anterior pituitary but even this does not offer an explanation. Repeated ACTH injections of 15–20 units several times per day have certainly been observed to give a dramatic relief of pain in acute cases of herpes zoster (1–3, 5–6) but vasopressin in the dosage used here

does not release such amounts of ACTH. Furthermore, the effect of ACTH was first seen 24 hours after the first injection, whereas the effect of vasopressin occurs even within 1 hour.

Trials are proceeding, to eliminate disadvantages and increase the duration of the effect on pain by using other forms of administering vasopressin and by studying vasopressin analogues, which theoretically might extend the duration of action and reduce side reactions.

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