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Plasma and CSF Levels of Immunoreactive β-Endorphin in Algic Peaks of Patients with Herniated Intervertebral Discs

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A. B. MORALES, F. VIVES, I. ROS and F. MORA. *Plasma and CSF Levels of Immunoreactive β-Endorphin in Algic Peaks of Patients with Herniated Intervertebral Discs.* Rev. esp. Fisiol., 44 (1), 21-26, 1988.

Plasma and CSF levels of beta-Endorphin (β-End) were measured by radioimmunoassay in three groups of human subjects. The first group consisted of healthy adults, and only plasma β-End was determined. The second group consisted of patients showing non-painful neurological diseases. The third group consisted of patients suffering from acute pain due to herniated intervertebral discs. In the last two groups, β-End levels were measured in plasma and CSF. The results showed that plasma levels of β-End were similar in the first two groups of patients. In contrast, patients with acute pain showed significantly increased levels of β-End in plasma. CSF levels of β-End did not show significant differences among the groups. The results suggest that the increase in plasma levels of β-End was a consequence of the stress produced by acute pain.

Key words: Beta-Endorphin, Algic peaks, Herniated intervertebral discs, Acute pain, Stress.

Since their discovery (12) opioid peptides have been associated with antinociceptive mechanisms (8, 15, 25). Thus, beta-Endorphin (β-End) has shown analgesic effects when injected peripherally or centrally (21). Also, an increase or decrease on the levels of β-End in plasma and CSF have been reported in patients suffering from pain (19, 22). Thus, acute pain has been shown to produce an increase while chronic pain a decrease in plasma and CSF β-End (14). These data, however, are not conclusive since opposite results have also been reported (1, 4, 17, 22). This controversy may partially be due to the fact that the neurological or general diseases subserving the pain syndrome could also produce by themselves an alteration in the levels of β-End.

The present work tries to clarify this problem studying the levels of β-End in plasma and CSF in patients suffering from an acute pain syndrome without any other neurological or systemic disorder. Herniated intervertebral disc (HID)

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patients do not often have any neurological disorder apart from the pain syndrome produced by the neural compression. In consequence, we have selected a group of patients with HID at the moment of an acute algic peak. The changes in the levels of β-End in plasma and CSF in these patients would be, at least theoretically, a direct consequence of the pain syndrome.

Materials and Method

Subjects. — Analysis of β-End in plasma and CSF was performed in three different groups of patients. The first group consisted of healthy adults, in whom only plasma β-End was determined. The second group consisted of 10 patients showing non-painful neurological diseases. Finally, the third group consisted of patients suffering from HID. These patients were hospitalized due to an algic peak along the course of their illness. CSF and blood samples were extracted from a group of 195 patients suffering from pain syndrome. Samples were stored at −30° C until analysis. Following rigorous diagnosis criteria (neurological, radiological and biochemical) only 30 patients out of 195 were selected. All these patients showed a disc prolapse between L4-L5, without any other neurological alteration apart from the HID syndrome. Although patients were taking analgesics occasionally, medication was suppressed upon admission at the hospital 72 h prior to CSF and blood extraction. After diagnosis and extraction of samples the medication was resumed.

β-End assay. —Blood and CSF sample extractions were made between 9 a.m. and 1 p.m. Blood samples were collected in 5 ml EDTA tubes. Also 0.1 ml of Trasylol was added to each tube. CSF was collected via lumbar tap (Radiculography, myelography or simple lumbar puncture) into siliconized plastic tubes at the time of blood extraction. Measurements of β-End were performed by a commercially available radioimmunoassay (RIA). In order to avoid cross reactivity between β-End and β-Lipotropin (β-LPH), samples were purified through sepharose anti-β-LPH prior to RIA. Then, β-End was purified using orthodecasylil-silica columns, eluted with methanol and then the RIA was carried out per duplicate. Interassay variability was 12 percent and intraassay variability was 8 percent. Statistical analysis was performed by a Student's t test. Also, the correlation between plasma and CSF levels of β-End was analyzed by a linear regression test.

Results

The levels of β-End in plasma in the three groups studied were not different between healthy adults and patients with non-painful neurological diseases. However, the group of patients with HID showed higher levels than the other two groups (table I).

Table II shows the CSF levels of β-End in the second and third group of patients, and they were similar in both groups. The linear regression test showed no correlation between plasma and CSF levels of β-End ($r = 0.38$).

Discussion

Patients with HID have a chronic syndrome generally characterized by algic peaks alternating with longer asymptomatic periods. In this study, blood and CSF samples were extracted during the period of an algic peak in a group of those patients. The results obtained showed that plasma levels of β-End were significantly higher in the HID group

Table I. *Plasma levels (pmol/l) of β-Endorphin measured by radioimmunoassay in normal adults, in patients without pain and in patients with HID.*
Values on the bottom are mean ± SEM. Subjects of each group have the same number in table I and in table II. 21.2 vs 13.4, $P < 0.001$ and 21.2 vs 15.9, $P < 0.01$

Control group		No pain group		HID group			
1	16.0	1	15.4	1	10.7	16	19.1
2	13.6	2	21.7	2	38.4	17	31.5
3	16.2	3	9.1	3	14.0	18	13.2
4	15.3	4	6.8	4	15.4	19	19.6
5	13.9	5	19.5	5	34.0	20	19.3
6	14.8	6	9.6	6	22.1	21	22.0
7	13.0	7	15.7	7	29.4	22	33.0
8	14.6	8	14.3	8	11.6	23	17.5
9	10.5	9	23.5	9	30.1	24	34.0
10	12.2	10	23.2	10	31.7	25	11.1
11	12.8			11	15.7	26	20.2
12	12.1			12	14.9	27	28.2
13	11.0			13	11.4	28	20.0
14	14.1			14	17.0	29	22.8
15	10.5			15	11.0	30	16.6
13.4 ± 0.48		15.9 ± 1.9		21.2 ± 1.9			

Table II. *CSF levels (pmol/l) of β-Endorphin measured by radioimmunoassay in patients without pain and in patients with HID.*
Values on the bottom are mean ± SEM. No significant differences were found. Subjects of each group have the same number in table I and in table II.

No pain group		HID group			
1	12.2	1	33.8	16	—
2	26.2	2	27.4	17	—
3	28.0	3	30.3	18	21.8
4	—	4	25.0	19	—
5	—	5	34.0	20	25.0
6	35.0	6	—	21	34.0
7	32.0	7	26.0	22	31.0
8	17.0	8	27.0	23	23.0
9	26.8	9	39.0	24	19.6
10	25.0	10	11.0	25	31.0
		11	35.0	26	16.7
		12	21.7	27	25.0
		13	19.8	28	25.2
		14	26.4	29	30.6
		15	—	30	35.3
25.3 ± 2.6		27.0 ± 1.3			

than those of control patients. In contrast, CSF levels of β-End were similar in both groups. Since the HID patients do not suffer any neurological degenerative disorder or any other systemic disease, it may be suggested that the changes in plasma levels of β-End are a direct consequence of the pain syndrome.

The possible involvement of β-End in pain processes has long been discussed. In humans, it has been shown that chronic pain may be attenuated by electrical stimulation of periaqueductal and periventricular gray matter and this pain relief can be totally reversed by naloxone (11). Also, intraventricular administration of human β-End produces a prolonged state of analgesia (10). These observations support the concept that β-End in the CNS may in part mediate analgesia in man (24). Nontheless, whether or not the activity of β-End pathways in the CNS may be correlated to the levels of this peptide in the CSF is at present controversial (2, 5, 22). The fact that acute pain

does not induce detectable changes in the levels of β-End in CSF tends to discard that possibility.

As shown here, acute pain produces an increase in the levels of β-End in plasma but not in CSF. Therefore, peripheral β-End may have a role not directly related to pain. Other reports have shown that different stress situations, induced or not by acute pain, produce similar increases to the ones reported here, that is, an increase in plasma but not CSF β-End (3, 23, 25). These findings would suggest that peripheral β-End may be related to stress rather than to pain itself. In fact, stress is a very powerful stimulus for the release of ACTH and β-End from the hypophysis (3, 25). Also a role in glucocorticoid release (18), energy balance (7, 16) antihypertensive mechanisms (13) respiratory response (6, 20) and immuno response (9) has recently been suggested for β-End. Thus, the role of peripheral β-End could be in part complementary to that played by ACTH. If this were the case, the increase in plasma levels of β-End could be a direct consequence of the activation of the hypophyso-suprarenal axis induced by the stress produced by the acute pain.

In conclusion, we suggest that the increased plasma levels of β-End found in patients suffering from HID during the algic peaks are associated with stress more than with pain itself. Further studies, especially at biochemical levels, would be necessary in order to clarify the possible role played by this peripheral β-End.

Resumen

Se determinan los niveles de beta-endorfina (β-End) en plasma y líquido cefalorraquídeo (CSF) en tres grupos de sujetos. En el primero, formado por adultos sanos sólo se determina la β-End plasmática. El segundo grupo está compuesto por pacientes con alteraciones neurológicas no dolorosas, y el tercero por pacientes con síndrome doloroso agudo debido a hernia discal. En los dos últimos grupos se determina la concentración de β-End en plasma y LCR. Los resultados muestran que los niveles plasmáticos de β-End son similares en los dos primeros grupos de pacientes, mientras aumentan significativamente en los pacientes con dolor agudo. La concentración de β-End en CSF es similar en los grupos estudiados. Los resultados sugieren que las alteraciones en los niveles de β-End plasmática se deben al estrés producido por el dolor agudo.

Palabras clave: β-Endorfina, Hernia discal, Dolor agudo, estrés.

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