EPIDURAL β-ENDORPHIN IN TREATMENT OF PAIN

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ABSTRACT

Epidural administration of 3 mg of synthetic β-endorphin produced analgesia in 10 patients with intractable pain due to disseminated cancer. Mean onset of relief of pain was 24 ± 3 minutes and the mean duration of analgesia was 19 ± 3 hours.

The onset of analgesia produced by the epidural injection of β-endorphin was slower and the duration less than those observed after intrathecal injection.

KEY WORDS: ANALGESIA, epidural β-endorphin; PAIN.

WE HAVE REPORTED previously profound and long-lasting analgesia from the intrathecal administration of 3 mg synthetic β-endorphin, the most potent of the opioid peptides, in patients with intractable pain due to disseminated cancer.[1]

This communication is concerned with recent observations of analgesia produced by the epidural administration of synthetic β-endorphin in 10 patients with intractable pain from disseminated cancer. No respiratory depression, hypotension, hypothermia, or catatonia was observed.

METHOD

Synthetic β-endorphin 3 mg in 10 ml of physiological saline, sterilised by Millipore filter, was injected epidurally at the appropriate lumbar interspace. Ten patients with chronic intractable pain in the back, chest, abdomen, hip and thigh regions secondary to metastic malignancies were selected for study. Informed consent was obtained. Systemic analgesics were withheld at least five hours before adminsitration of β-endorphin. The visual pain scale was explained to each patient and baseline pain intensity was determined 30 min before the epidural injection. In a single-blind randomised trial one physician administered successively β-endorphin or physiological saline to seven patients; the others received only β-endorphin, without placebo.

The β-endorphin used here was synthesized as previously described,[1,2] by Dr. Nicholas Ling, Laboratories for Neuroendocrinology, The Salk Institute for Biological Studies, La Jolla, California.

RESULTS

All 10 patients reported relief of pain (Table I and Figure 1). Pain relief was obtained within a mean of 24.9 ± 3.4 minutes (range 9–45 min) after the epidural injection of β-endorphin. This was slower than that produced by the intrathecal

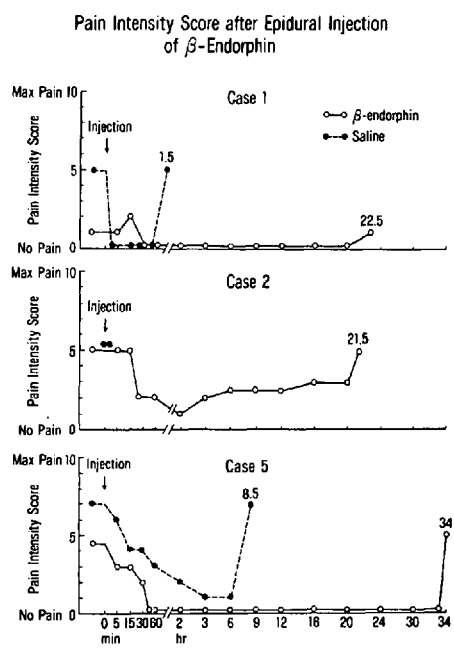

FIGURE 1 Intensity of pain (visual pain scale) as reported by three patients after epidural injection of either saline (●– – –●) or β-endorphin (○——○)

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TABLE I
EPIDURAL INJECTION OF β-ENDORPHIN (3 mg)

Patient number	Age	Sex	Body-weight (kg)	Previous analgesics (dose [mg] and no. of doses/day)	Pain relief after β-endorphin or placebo		
					Onset (min)	Duration (h)	Remark
1	53	F	42.5	Pent.* 15 × 5–6 (1M)	35′	22.5 [1.5]	1) nausea 2) vomiting 3) dysuria
2	63	M	62	Pent. 15 × 3–4 (3M)	25′	21.5 [0]	1) sleep 2) diarrhoae
3	40	F	41.5	Indomethacin 100 × 1 (1M)	9′	35	1) vomiting
4	50	M	55	Pent. 15 × 2–3 (3y)	30′	33.5 [19]	1) sleep
5	68	M	35.5	Pent. 15 × 3 Opiat 1 m l × 1† (2M)	45′	34 [8.5]	1) sleep
6	20	F	39.4	Pent. 30 × 2–3 (2M)	15′	21.5	1) chillness
7	48	M	45	Pent. 30 × 2–3 (2M)	30′	8.5	1) adbominal discomfort
8	51	M	50	Pent. 30 × 2 Opiat 1 m l × 2–3 (3M)	15′	6.5 [1]	
9	56	F	28	Pent. 15 × 5–6	30′	8.0 [1.5]	1) sleep
10	38	M	48	Pent. 15 × 6	15′	3.5 [1]	

*Pent. = pentoazocine
†Opiat = opium alkaloids 20 mg/mL
[ ]: Placebo

injection of β-endorphin 3 mg which produced rapid pain relief 1–5 minutes after the injection.[1,2] The mean duration of pain relief was 19.5 ± 3.7 h (range 3.5–35 h), which was shorter than that which had been produced by intrathecal injection (mean 33.4 h; range 22.5–73.5 h). The pattern of changes of intensity of pain in these patients is demonstrated in Figure 1. No effect or only a transient effect was found after injection of placebo in five of the seven patients (Table I) randomly selected for this part of the study. The epidural injection of β-endorphin caused no discomfort, except for patient 7 who had been suffering from abdominal discomfort for the past several weeks. No signs of respiratory depression, arterial blood-gas changes, hypotension, hypothermia, catatonia or muscle rigidity were observed. Four out of 10 patients slept during the procedure.

DISCUSSION

The intrathecal injection of opiates can be dangerous because of severe respiratory depression and/or apnoea which might not become evident until 6 to 15 hours after the injection.[3–7] Intrathecal injection of β-endorphin did not produce any such complication.[1,2] Epidural injection of morphine 2 mg, given to 10 patients with severe pain, was reported to produce relief

of pain which reached a peak in 10–15 minutes and was effective for 6–24 hours.[8] The incidence of respiratory depression with epidural narcotics appears to be low, but severe respiratory depression was reported in two patients after epidural meperidine.[9] Furthermore, cardiac arrest has been reported 45 min after 2 mg of morphine had been administered to an 85-year-old patient.[10] In our present clinical trial of epidural endorphin none of these respiratory or cardiovascular complications was observed.

Potential severe complications, such as paralysis, could occur from intrathecal or epidural injection of narcotics due to preservatives, stabilizers and/or antioxidants used in their preparation.[11] Another problem is that increasing the dosage of intrathecal or epidural narcotic results in only a slightly increased duration of analgesia compared to a lower dose. Besides, higher intrathecal doses have been associated with severe respiratory complictions[6,12] and dysuria.

A serious inherent disadvantage of epidural narcotics is the problem of tolerance. Administration for more than five days produced tolerance in chronic pain patients.[13] For instance epidural morphine 2 mg gave 8 to 12 hours relief of pain for the first five days, after which it became increasingly ineffective. Opiate withdrawal syndrome following intrathecal administration of morphine has also been reported recently.[14] Tolerance to β-endorphin after repeated epidural injections should be investigated in the future.

Opiate elimination from the cerebrospinal fluid is believed to occur by absorption through the choroid plexi and, therefore, opiates might pass into the 4th ventricle.[3] As in case of narcotics, epidural β-endorphin is assumed to diffuse into the cerebrospinal fluid through dura and arachnoid, and thus the concentration in the subachnoid space is less than that on intrathecal injection. This would explain the shorter duration and somewhat less complete relief of pain produced by epidural β-endorphin compared with intrathecal injection,[1,2] despite identical dosage (Figure 1).

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RÉSUMÉ

L'administration dans l'espace épidural de β-endorphin synthétique à la dose de 3 mg a produit de l'analgésie chez 10 patients souffrant de douleur irréductible causée par le cancer. La période d'installation de l'analgésie a été de 24 ± 3 minutes et sa durée moyenne a été de 10 ± 3 heures.

L'analgésie produite par l'injection épidurale de β-endorphin s'est installée plus lentement et a été d'une durée plus courte que celle qu'on a déjà observée après l'injection intrathécale.