CORRESPONDENCE

Hyperlgesic Response in a Patient Receiving High Concentrations of Spinal Morphine

To the Editor.—A recent article by Yaksh et al.1 demonstrated that the intrathecal administration of high concentrations of morphine in experimental animals resulted in a profound agitation response that was associated with hyperesthesia. We report here a hyperalgesic response in a patient with terminal cancer who required high doses of intrathecal morphine for the management of pain.

REPORT OF A CASE

A 68-yr-old woman suffering from recurrent pelvic squamous cell carcinoma presented with intractable pain in the distribution of the right sciatic nerve. The pain was refractory to high doses of systemic analgesics. She subsequently underwent the placement of an intrathecal catheter and an Infusaide® pump. During the patient’s remaining 9 months of life, intrathecal morphine was continuously infused for pain relief. The pain had been shooting in character and was initially controlled by intrathecal morphine 1 mg/day. However, recurrence of pain necessitated a gradual increase of morphine dosage over a 9-month period to a maximum of 68.4 mg/day delivered in a concentration of 38 mg/ml at a pump flow rate of 1.8 ml/day. Five months after the initiation of intrathecal morphine treatment (at a dose of 32 mg/day delivered in a concentration of 16 mg/ml at a pump flow rate of 2 ml/day), the patient started to complain of a new type of burning pain in the same lower extremity. Hyperesthesia was manifested in the whole extremity; there was no similar sensation in the other extremity. Burning pain was intermittent and refractory to increasing doses of intrathecal morphine; it was partially relieved by the addition of systemic methadone, amitriptyline, and ibuprofen. There was no evidence of thrombophlebitis in the extremity.

DISCUSSION

We did not observe similar hyperalgesic responses in three other patients who received comparable high concentrations of intrathecal morphine over 2-, 4-, and 10-month periods.

We cannot determine whether the hyperesthesia noted in this patient is analogous to that reported by Yaksh et al. or alternatively represents progression of the disease, inflammation, or other neurologic dysfunction.

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Pharmacokinetic Differences Could Explain the Lack of Reversal of Nitrous Oxide Analgesia by Low-dose Naloxone

To the Editor.—The recent report by Willer et al.1 is of interest; however, the conclusion that nitrous oxide does not produce its analgesic effects on the blink reflex through an interaction with the endogenous opioid system is open to question. The main problem is related to the effectiveness of naloxone as an opioid antagonist in the dose used and the manner of administration. We have shown that the effect of naloxone on nitrous oxide analgesia at doses below 2 mg, even when given as a bolus, decays rapidly and disappears within 10 min.2,3 This is not surprising because the concentration of naloxone in the brain rises and falls rapidly after intravenous administration.4 For this reason a low dose of naloxone given slowly over 2–4 min1 may not have been sufficient to antagonize the effects of nitrous oxide, which was given continuously and would be expected to have a constant high concentration at the opioid receptor. Apart from this, not all opioid receptors are equally susceptible to

REFERENCE

1. Moore PL: Nitroglycerin improves venous cunnocation. Anesthesiology 64:353, 1986 (Accepted for publication June 26, 1986.)