

Meniere-Like Syndrome following Epidural Morphine Analgesia

S. LINDER, M.D., A. BERGEAT, M.D., J. BIOLLAZ, M.D.

The demonstration that effective and prolonged pain relief can be achieved by injection of small doses of morphine into the epidural space¹ has led to increasing use of epidural morphine analgesia by clinicians, particularly in obstetrics and gynecology.^{2,3} Side effects attributed to epidural morphine administration are common, some irritating, others dangerous.⁴ We report here an unusual side effect, a Meniere-like syndrome, that appeared 6 h after a second dose of epidural morphine and was successfully treated with naloxone.

CASE REPORT

A 40-yr-old woman pediatrician (51 kg, 165 cm) was scheduled for abdominal hysterectomy under epidural anesthesia. Except for some minor surgery under general anesthesia a few years earlier, two conventional vaginal deliveries, and migraine headaches successfully treated with an ergotamine/caffeine preparation, the patient's medical history was unremarkable.

Using the loss of resistance technique, the epidural space was entered at L2-3 with a 16-G Tuohy needle, following an unsuccessful attempt at L3-4. The catheter was introduced 6 cm cranially without difficulty. An aspiration test revealed neither blood nor CSF. Following a test dose of 3 ml 2% lidocaine/1/200,000 epinephrine, 12 ml of a mixture of 2% lidocaine/0.5% bupivacaine with epinephrine was injected. The resulting sensory block extended to T3 on both sides.

The operation was uneventful (75-min duration, <300-ml blood loss, blood pressure stabilized with 2 l Ringer's lactate solution and 22.5-mg iv mephentermine sulfate). Postoperative analgesia was provided by epidural administration of 2 mg preservative-free morphine to which was added 50 µg fentanyl diluted in 10 ml normal saline. Six to seven hours later the patient reported motion sickness symptomatology and a mild migraine headache for which she insisted on having a Cafergot® suppository (ergotamine tartrate 2 mg, caffeine 100 mg, butalbital 100 mg, belladonna alkaloids 0.25 mg), her usual treatment at the onset of a migraine. The symptoms waned and the analgesia lasted 17 h. The next morning the patient received a second epidural injection of the morphine/fentanyl mixture. Six hours later she complained of a severe rotatory vertigo, followed by blurred vision (being unable to read), nausea, unilateral hearing loss, tinnitus, and a sensation of fullness in the ear. Blood pressure, pulse rate, and temperature were all in the physiologic range. The aforementioned ergotamine/caffeine medication was given without effect. The respiratory rate decreased from 15 to 12 breaths/min, but no sedation or miosis was observed. Finally, 10 h after receiving the second epidural injection of opioids

and, while the Meniere-like syndrome was still present, she complained of intense itching in the face, on the arms, and on the upper trunk for which she received a 0.1-mg naloxone injection. This dose remained ineffective and a second 0.1-mg dose was administered. The patient reported at that moment a dramatic improvement of her Meniere-like symptoms and the complete disappearance of her pruritus. Following the administration of incremental doses of up to 0.4 mg naloxone, all Meniere-like symptoms disappeared for half an hour. As soon as they reappeared, incremental doses of naloxone, up to 0.4 mg, were repeatedly given, and an infusion of 0.08 mg/h naloxone was started and maintained during 8 h. The Meniere-like symptomatology disappeared completely while the reemerging pain was satisfactorily treated with epidural 0.125% bupivacaine, 15 ml/h. Direct otoscopy was unremarkable. Further investigations were considered unnecessary after the prompt and lasting improvement obtained with naloxone.

DISCUSSION

Side effects attributed to morphine are common, possibly dose-related, and include nausea and vomiting, pruritus, urinary retention and, more rarely, early and late respiratory depression.⁴ Notwithstanding the absence of nystagmus, the clinical signs and symptoms presented by this patient (rotatory vertigo, nausea, unilateral hearing loss, tinnitus, and sensation of fullness in the ear) are highly suggestive of a Meniere syndrome. Signs or symptoms mimicking Meniere syndrome following epidural administration of opioids have, to our knowledge, not been previously reported, although some of them (vertigo, deafness) have been observed separately.^{5,6}

The normal otoscopy, the rapid and complete recovery following naloxone administration, the absence of premonitory signs, and the nonresponse to her usual treatment argue against a migraine equivalent syndrome and other etiologies of vestibular vertigo, such as pathology of the vertebrobasilar system, infectious labyrinthitis, or inner ear hemorrhage. Moreover, she was not taking any drug known to be toxic to the eighth cranial nerve. The rapid recovery, in a person who already had another stress related symptom complex (migraine headache), could suggest that the dysfunction might have been psychologic in origin (conversion reaction). The consistent symptomatology pattern does not fit, however, with conversion symptoms. It is conceivable that the patient presented a fortuitous Meniere syndrome, developed independently of the surgical procedure and epidural drug administration. Because Meniere syndrome is not known to regress so quickly; however, it is hard to refute a relationship between its appearance and epidural injections of mor-

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Address reprint requests to Dr. Linder: Hôpital d'Yverdon, CH 1400 Yverdon, Switzerland.

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phine and its disappearance following naloxone administration.

Somewhat puzzling is the fact that the full symptomatology only occurred following the second injection of epidural morphine, although motion sickness was already reported after the first injection. It should be recalled, however, that pruritus, a known side effect of extradural morphine, also appeared only after the second injection. The delayed appearance of the vestibular symptoms is best explained by the time lag that occurs between the injection of morphine into the epidural space and its intracranial spread,⁷ in particular in the endolymphatic system, which is connected with the CSF.

There is experimental evidence that the intracerebroventricular or intrathecal administration of opioids possesses irritant properties.⁸ In humans opioids have been shown to increase labyrinthine responsiveness,⁹ and a potential role of endogenous opioid peptides in the pathogenesis of motion sickness has been suggested.¹⁰ This suggestion is based on prophylactic and therapeutic effect of naloxone. These are indirect arguments, which coupled to the rapid and complete recovery following naloxone administration, argue for a direct pathogenic role of morphine in the manifestations presented by this patient.

Although lidocaine and bupivacaine, with their known CNS toxicity,¹¹ either alone or by interacting with morphine¹² might theoretically have played a role, the rather long delay between their administration and the symptomatology argue against such a role.

In conclusion, this case suggests that vestibular dysfunction may be added to the side effects associated with

epidural morphine analgesia and can be rapidly reversed by naloxone administration.

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Transient Systemic Arterial Hypotension and Cutaneous Flushing in Response to Doxacurium Chloride

DAVID L. REICH, M.D.*

Doxacurium chloride (BW A938U) is an investigational nondepolarizing neuromuscular blocking drug with a benzyliisoquinolinium structure and a duration of action

similar to that of pancuronium. Its ED₉₅ for neuromuscular blockade is 0.03 mg/kg, and it does not release histamine in doses up to 0.08 mg/kg.¹ Clinical studies of doxacurium have demonstrated cardiovascular stability following administration in healthy patients,² in children,³ and in patients anesthetized with sufentanil and midazolam undergoing cardiac surgery.⁴ Fifty-five patients have received doxacurium at our hospital as participants in an institutionally approved investigation for patients undergoing cardiac or major vascular surgery. Forty-five cardiac surgical patients⁵ and nine patients for abdominal aortic surgery received doxacurium without clinically significant

* Assistant Professor of Anesthesiology.

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Address reprint requests to Dr. Reich: Department of Anesthesiology, Box 1010, Mount Sinai Medical Center, One Gustave L. Levy Place, New York, New York 10029-6574.

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