7.5 mg EREM was not administered spinally because we did not attempt to aspirate CSF after administration of the drug. Our current system for safe EREM administration has safeguards that failed us and this patient. We use custom-assembled combined spinal–epidural kits with uniform assignment of syringes of different type and size filled with solutions with visibly different opacity (fig. 1). Because of this sentinel event, we are introducing additional safeguards to include withdrawal of EREM from the vial only after the spinal needle has been removed from the patient, and verbal confirmation of the drug and dose being given by two providers at the time the EREM is administered.

In conclusion, our practice of using a dose of EREM lower than recommended, the patient’s previous use of opioid and possible opioid tolerance, and her good health may have contributed to this outcome. In any case, this single example of intrathecal EREM is not presented to imply that this practice is safe: The pharmacokinetics of EREM in the spinal space have not been published, and this route of administration has not been adequately studied. Rather, we believe this case does imply that preservation of an acceptable patient recovery is possible with appropriate and thoughtful management of known accidental spinal administration of EREM.

References


In Reply:—We read with great interest the case report by Dr. Gerancher and Dr. Nagle about the effects of accidental spinal administration of extended release epidural morphine (DepoDur®; Pacira Pharmaceuticals, San Diego, CA). In their report, the authors note that no published pharmacokinetics data are available for this drug after intrathecal administration.

Pacira Pharmaceuticals, Inc., performed a study of the effects of DepoDur® on intrathecal administration to dogs during the drug’s development, which we would like to report. Adult male beagle dogs (n = 3, each group) were prepared with chronic intrathecal and epidural catheters. Animals received 30 mg DepoDur® in 3 ml by both routes, 7 days apart, in random order. Seven days after the last of the intrathecal and epidural dosing intervals, animals received an intravenous dose of morphine sulfate, 30 mg in 3 ml. All morphine treatments resulted in mild behavioral depression in arousal, muscle tone, and coordination; no animal required intervention. The rank order of time to onset was shortest for intravenous morphine sulfate, followed by intrathecal DepoDur® and then epidural DepoDur®. Duration was less than 10 h after intravenous administration and 48–72 h after intrathecal and epidural administration. Administration of morphine by all routes evoked mild bradycardia of similar onset and magnitude. Duration was shortest after intravenous administration; duration was similar after intrathecal and epidural administration. A mild decrease in blood pressure was observed after intravenous administration, whereas intrathecal and epidural administration were without effect. Respiratory rates were moderately diminished after all routes of administration. The duration of effect was similar after all routes. Body temperature was not affected after intravenous or epidural administration, whereas a modest decline was observed after intrathecal administration that resolved by 24 h.

Free morphine concentration after intravenous dosing declined to below detection limit by 24 h. In contrast, free morphine was detected for several days after intrathecal or epidural administration. The pharmacokinetic parameters for free morphine in the circulation were similar after intrathecal and epidural administration: Tmax was 6.5 ± 2.0 compared with 4.0 ± 1.0 h, Cmax was 39 ± 18 compared with 78 ± 6 ng/ml, t1/2 was 9.7 ± 3.2 compared with 10.3 ± 3.3 h, and AUC0–∞ was 727 ± 84 compared with 1,002 ± 150 ng·h·ml−1. In conclusion, after administration of DepoDur® intrathecally or epidurally to dogs, morphine release from the liposomal vehicle, as measured by serum pharmacokinetics of free morphine, was similar. No direct cerebrospinal fluid pharmacokinetics data have been collected after intrathecal administration of DepoDur®. In general, epidural and intrathecal DepoDur® resulted in prolonged and similar behavioral and physiologic effects. Pacira Pharmaceuticals never recommends intrathecal administration of DepoDur®, and the risk of respiratory depression from intrathecal injection is unknown.

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Reference


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