



FACTFINDERS FOR PATIENT SAFETY

PRESERVATIVE VS. PRESERVATIVE-FREE: STEROID CHOICE FOR EPIDURAL INJECTIONS

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MYTH: The administration of steroid formulations containing preservatives into the epidural space has been associated with neurological injury.

FACT: No adverse events have been documented from the administration of preservative-containing steroids into the epidural space; however, neurological injuries have been reported following intrathecal injection of these preservatives.

Concern for the use of preservative-containing steroid formulations may stem from potential problems associated with preservative-containing morphine administration into the epidural space [1].

Much of the literature about central nervous system toxicity related to preservative-containing steroids is related to intrathecal injection. Lima *et al.* investigated the clinical and histological changes associated with injecting methylprednisolone, with polyethylene glycol and myristilgama-picolinine chloride, into the intrathecal space of dogs [2]. The study demonstrated that the intrathecal administration of commercially available methylprednisolone led to no clinical changes but was responsible for causing histological changes in the spinal cord and meninges of the animals studied, with one animal presenting with necrosis of the spinal cord. Another animal study investigating the potential clinical and histological changes resulting from the injection of betamethasone with polyethylene glycol into the intrathecal space found no clinical changes [3]. However, histological changes were observed in the spinal cord and meninges of some dogs involved in this study.

A case report from 1977 described an obstetric patient who developed flaccid paralysis, with virtually complete recovery after 16 months [4]. The case reported inadvertent epidural administration of 40 mL of normal saline containing 1.5% benzyl alcohol. Notably, in this instance, an unintentional dural puncture occurred early in the procedure. This presumably resulted in a direct connection between the epidural and subarachnoid space, which may have accounted for the adverse event. This compromise of the dura may have caused intrathecal administration of the compound, although there is no definitive evidence in the case report to support this hypothesis. No similar epidural injection case reports have been published.

Despite concerns, no large-scale studies have demonstrated definitive neurotoxicity from preservatives in epidural steroid administration. As previously indicated, much of the literature on preservative-related risks is derived from studies involving intrathecal administration, where the findings remain equivocal [5,6].

Given the paucity of available evidence and the potential risk of dural puncture (approximately 0.5% to 1.8% per procedure, depending on the spinal level and technique [7-9]) and potential intrathecal injection, clinicians often err on the side of caution and prefer preservative-free formulations [10]. However, this raises another practical concern: the availability of these formulations. To date, dexamethasone is the only corticosteroid that major pharmaceutical manufacturers produce in a preservative-free formulation [11]. While compounding pharmacies may offer preservative-free formulations of other steroids, concerns about sterility persist, particularly in light of the fungal meningitis outbreak linked to contaminated compounded methylprednisolone [12].

Conclusions

- There is a paucity of literature comparing the safety of preservative-free to preservative-containing steroids, especially in the case of epidural steroid injections.
- There is a theoretical concern that preservative agents, if inadvertently administered intrathecally due to an adverse event during an epidural injection, may cause harm.
- If using preservative-containing steroids, we recommend taking all appropriate precautions to help ensure that the injectate remains epidural (*i.e.*, as confirmed by precise technique and contrast flow pattern identification, as detailed in the **IPSI Technical Manual and Atlas of Interventional Pain and Spine Procedures** [13]).

References

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