

# Inadvertent epidural injection of drugs for intravenous use. A review

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**Abstract :** *Introduction :* The frequency of inadvertent injection of drugs in the epidural space is probably underestimated and underreported, but it can cause serious morbidity and possibly mortality.

*Objective :* The aim of this review is to collate reported incidents of this type, to describe the potential mechanisms of occurrence and to identify possible therapeutic solutions.

*Methods :* We searched into medical databases and reviewed reference lists of papers retrieved.

*Results :* A list is reported of more than 50 drugs that were inadvertently injected into the epidural space. This list includes drugs which produce no, little or short-lasting neurological deficits, but also includes drugs that may be more etching and can result in temporary or even permanent neurological deficit.

*Discussion :* Most drugs do not lead to sequelae other than pain during injection or transient neurological complaints. Other drugs may have more deleterious consequences, such as paraplegia. Both the dose of the inadvertent injected drug and the time frame play an important role in the patient's outcome. "Syringe swap", "ampoule error", and epidural/intravenous line confusion due to inaccurate or absent colour coding of epidural catheters were the main sources of error. Preventive strategies, including non Luer-lock epidural injection ports, might increase safety.

**Key words :** Anesthesia ; epidural ; inadvertent ; accidental ; adverse ; toxic reactions ; prevention.

## INTRODUCTION

Bromage was one of the first to report cases of accidental injection into the epidural space in 1961 (1). In the last 25 years thoracic and lumbar epidural infusion to provide continuous analgesia have become increasingly popular (2). Simultaneously the incidence of epidural injection of unintended drugs has also increased. Most of our knowledge of inadvertent drug injection and its sequelae comes from case reports, and some of our knowledge comes from medico-legal reports, lawsuits and malpractice litigation. In most circumstances inadvertent administration of non-epidural

drugs into the epidural space will not contribute to significant neurological complications. However serious morbidity such as paraplegia or quadriplegia, sensory changes and bladder/bowel incontinence, may be the final disastrous outcome for the patient.

## METHODS

A computerized search was conducted of the Pubmed Medline, Embase, and Cochrane databases for North American and European English language literature for the period from 1951 to April 2011. The initial search terms were "epidural" and "(inadvertent or accidental)". We also searched for articles about litigation related to epidural anesthesia or analgesia, especially drug errors. Further reports were identified from reference lists of the papers retrieved.

## RESULTS

Our literature search yielded 57 articles of which 54 were case reports. Quite a number of papers were non-English written. They were partially taken into account when they had at least an English abstract. The first article about this subject

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was published in 1975 (3), the last one in July 2011 (4). Exact data about the true incidence of accidental epidural injection of drugs for non-epidural use cannot be retrieved from literature. Our literature search of inadvertent epidural injections is likely to represent a gross underestimation of the actual number of incidents that occur. In 2000 the Japanese Board of Anesthesiology questioned their members about this issue. 90% of Japanese anaesthesiologists replied, of which 54% had indeed experienced an inadvertent epidural injection, 18% even more than one (5). SZYPULA *et al.* investigated the litigation related to regional anesthesia from 1995-2007 (6). Of the 326 neuraxial claims, 264 (81%) were related to epidurals and only eight claims were due to "drug error".

The symptoms of wrongly injected drugs into the epidural space depend on the specific drug used. Some products produce intense pain during injection, others result in hypoventilation and respiratory insufficiency, prolonged neuromuscular blockade or tachycardia with hypertension. Severe sensory changes and bladder/bowel incontinence of varying duration can also occur. Potassium chloride and paraldehyde cause the greatest problems, ranging from intense pain during injection to permanent paraplegia, quadriplegia and even death. The rate of administration, the total dose and the concentration of the drug certainly play an important role in the final outcome. Bolus administration of a drug might lead to more severe complaints than continuous infusion. Unfortunately full recovery cannot be guaranteed. Table 1 lists the drugs accidentally administered epidurally.

## DISCUSSION

One can consider the epidural space as a human dustbin as virtually every drug or solution used in the hospital has been reported to have been injected epidurally.

### *The management of accidentally epidurally injected drugs*

When faced with an accidental injection of drugs into the epidural space, immediate and appropriate action is warranted. The administration of the wrongly injected drug has to be discontinued immediately and oxygen has to be administered, while intensive monitoring and frequent neurological exams are necessary. Depending on the patient's vital hemodynamic and respiratory parameters,

supportive therapy may be necessary, e.g. vasopressors, intravenous fluids, endotracheal intubation and mechanical ventilation. Further treatment depends on the complaints of the patient, the type of drug used and the amount given. There are no official guidelines on how to act in this scenario; the case reports in the literature offer different treatment options, but none of them are evidence-based. It is advisable to leave the epidural catheter in situ, as it seems logical to aspirate the catheter and discard as much of the wrongly injected medication as possible. Rinsing the epidural space with normal saline will dilute the drug given, but risks to spread it over a larger level. Local anesthetics can be injected via the epidural catheter to relieve the pain caused by the injected drug. Several case reports also suggest the administration of corticosteroids, intravenously, epidurally or both to avoid oedema of the myelum (7). Pruritus can be treated with antihistamines, and in case of an accidental epidural injection of metaraminol and ephedrine, beta blockers and nitrates can be administered intravenously (8, 9). Some advocate the use of an antidote via the intravenous route, eg. naloxone for opioids, intralipid for an overdose of local anaesthetics, neostigmine or sugammadex for muscle relaxants. However there is no hard evidence in the literature to support any of these manoeuvres.

### *Contributing factors and preventive measures*

Table 2 lists some factors contributing to inadvertent epidural administration of non-epidural drugs and possible preventive strategies. Although an analysis of claims against the National Health Service in England from 1995-2007 only found 8 claims due to drug errors it is likely that this is a gross underestimation and prevention is the mainstay to provide safe and effective epidural anaesthesia and analgesia in our patients. The use of an aspiration test, an appropriate pharmacological test dose, and fractionated dosing, while talking to the patient, monitoring vital parameters and adequately checking the resulting sensory and/or motor blockade after institution of the epidural catheter, may contribute in detecting wrongly injected drugs into the epidural space (10). The use of skilled personnel, adequate monitoring, one uniform epidural kit in the hospital and a dedicated anaesthesia block corner certainly creates a safer environment to avoid mistakes. Material and drugs should be adequately labelled and double checked. Epidural and intravenous drugs should also be physically separated and stored in different places. The use of

Table 1

Non-epidural drugs administered into the epidural space and effect on patient outcome

Drug	Effect
<i>Intravenous induction agents</i>	
• Thiopental (16, 17)	• Burning pain on injection
• Methohexital (18)	• Respiratory insufficiency requiring intubation
	• Severe hypotension
<i>Benzodiazepines and analgetics</i>	
• Diazepam (19)	• Increasing drowsiness
• Midazolam (20)	• Hypoventilation and respiratory insufficiency
• Acetaminophen (21)	• Hypotension
• Morphine (22-25)	
• Fentanyl (20)	
• Remifentanyl (26)	
<i>Muscle relaxants</i>	
• Succinylcholine (27)	• Prolonged neuromuscular blockade
• Pancuronium (28)	
• Vecuronium (29,30)	
• Rocuronium (4)	
• (Cis-)atracurium (31)	
<i>Antibiotics</i>	
• Cefazolin (32)	• Back pain during infusion
• Gentamycin (33)	
• Piperacillin/tazobactam (34)	
<i>Sympathomimetic drugs</i>	
• Ephedrine (9)	• Severe headache
• Metaraminol (8)	• Tachycardia, increased blood pressure
<i>Anti emetics</i>	
• Ondansetron (35)	• No effect detected
• Metoclopramide (36)	
<i>Etching drugs</i>	
• Potassium chloride (19, 37-40)	• Severe pain on injection
• Phenol (41)	• Motor and sensory block
• Ether (42)	• Bladder and bowel incontinence
• Magnesium sulphate (43)	• Respiratory insufficiency requiring intubation
• Paraldehyde (44)	• Sympathetic hyperreactivity
• 20% hypertonic saline (45)	• Generalised convulsion
	• Severe pruritus and hyperalgesia
	• Residual complete analgesia and paraplegia below Th. 7 resulting in death 6 months later
<i>Others</i>	
• Glucose (46)	• Severe pain on injection
• Insulin (47)	• Hypoglycaemia
• Paracetamol (48)	• Headache and vomiting
• Ranitidine (41)	
• Distilled H <sub>2</sub> O (49)	

uniform colour coded local anaesthetics further contributes to the final safety of the epidural procedure.

A regular updated protocol of postoperative epidural pain relief and a uniform local anaesthetic regimen helps avoiding drug errors. Restricting handling epidurals to dedicated nurses or pain team members further improves safety and sterility.

Nowadays, nearly all intravenous lines and epidural catheters are equipped with a Luer-lock syringe coupling system, which makes line confusion between epidural and intravenous lines more

likely. In other words, "If it can happen, it *will* happen." BLOCK *et al.* cited the Joint Commission's Sentinel Event Alert about 9 cases of tubing misconnections involving 7 adults and 2 infants (11). Death occurred in 8 of these instances and 1 resulted in permanent loss of function. They also mentioned US Pharmacopeia, the largest information source of tube misconnection related errors, which received 1600 reports of epidural to central or peripheral intravenous misconnections since 1999. Together with BLOCK *et al.* we plead for using a non-Luer-lock syringe coupling epidural system to

Table 2

Factors contributing to the inadvertent administration of non-epidural drugs into the epidural space and possible preventive strategies

Category
Syringe swap <ul style="list-style-type: none"> <li>• Same size</li> <li>• Unlabelled</li> <li>• Personnel swap</li> <li>• Similar location of syringes</li> </ul> Ampoule error <ul style="list-style-type: none"> <li>• Similar ampoule</li> </ul> Epidural/intravenous line confusion <ul style="list-style-type: none"> <li>• Unlabelled catheter</li> <li>• Unlabelled injection port</li> <li>• Inadequate knowledge</li> </ul>
Preventive strategies
<ul style="list-style-type: none"> <li>• Colour coding local anaesthetics</li> <li>• Bar coded local anaesthetics</li> <li>• Prefilled syringe by pharmacy</li> <li>• Non Luer-lock syringe coupling</li> <li>• Standardized colour coding</li> <li>• Handling of epidural catheters restricted to authorized personnel</li> <li>• Double check of local anaesthetics by both anesthetist and nurse</li> <li>• Epidural and intravenous drugs should be physically separated and stored in different places.</li> </ul>

further diminish the risk of accidental epidural administration of non-epidural drugs. It would also protect the patient from an accidental but potentially fatal intravenous administration of large doses of local anaesthetics. When manufacturers would agree to use a different coupling system for epidural use, the potential risk for administering intravenous medication epidurally (or vice versa) could be abolished, thus increasing the safety of the use of epidural catheters. This plea for different connection devices has been made before by other authors, suggesting reversing the female port at the end of the catheter into a male ending (12-14).

In November 2009, the National Patient Safety Agency of the United Kingdom issued a Patient Safety Alert. It recommends that, by April 2011, “*all spinal bolus doses and lumbar punctures should be performed using syringes, needles and other devices with safer connectors that will not connect with intravenous connectors*”, and that, by April 2013, “*all epidural, spinal and regional infusions and boluses should be performed with devices that use safer connectors that will not connect with intravenous Luer connectors or intravenous infusions spikes*” (15). These recommendations have triggered the industry to develop new devices (Neurax<sup>®</sup> device, B-Link, West Yorkshire, UK ; Safe Connect<sup>®</sup> device, B Braun, Melsungen, Germany ; Surety<sup>®</sup> device, InterVene Limited, Chesterfield, UK ; CorrectInject<sup>®</sup> device, Smiths

Medical, Hythe, Kent, UK). Hopefully this new development will further decrease or even abolish all problems with erroneous switches between intravenous lines and epidural catheters.

#### CONCLUSION

The technique of epidural anaesthesia and analgesia has stood the test of time and has proven to result in satisfactory pain relief. However, each technique has its price and complications and side-effects do occur still quite frequently. Inadvertent administration of non-epidural drugs into the epidural space inherits the potential for serious morbidity or even mortality. Etching drugs such as potassium chloride and paraldehyde can have serious and permanent neurological sequelae. A large amount of drug given as a bolus rather than as a continuous infusion can give severe complaints. There are no actual data on the true incidence of the problem. The large majority of articles found using our search strategy are case reports. However there are no trials or large scale studies to assess the effectiveness of the different treatment regimens we found in the literature. The main sources of error are “syringe swap”, “ampoule error”, and epidural/intravenous line confusion. Prevention should be the main defence strategy and constant human vigilance is therefore essential.

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