

disconnection.

A manufacturer has been consulted regarding a more streamlined prepackaged system along these lines which would preclude injection of solutions not intended for injection into the epidural space.

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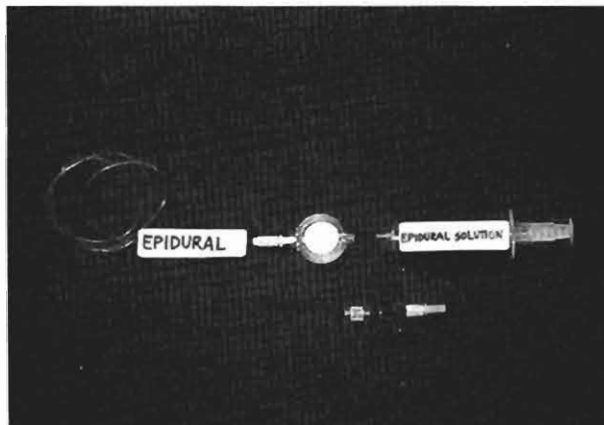


FIGURE 1

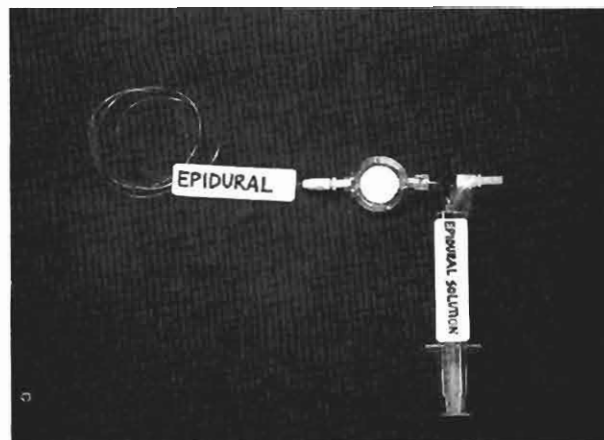


FIGURE 2

up immediately before use and not left standing<sup>1,4</sup>. Other methods described are diluting the propofol solution<sup>5</sup> and cooling the solution<sup>6</sup>.

A possible cause of this pain, not previously reported, may be due to substances released by propofol reacting with the inside wall of disposable syringes.

In a group of 100 ASA 1 and 2 patients presenting for elective orthopaedic or urological surgery, anaesthesia was induced with propofol, injected with a sterile, ground-glass syringe. All patients were pre-medicated with temazepam (10-20 mg) one to two hours before surgery. In each patient, a 20-gauge cannula (Venflon) was inserted into a dorsal hand vein without using local anaesthesia.

Propofol was the first drug injected and given at a rate of 10 ml over 10 to 15 seconds. After 10 ml, the injection was stopped and if the patient had not yet complained of any pain, they were asked if they had any pain or discomfort in their arm. Pain on injection was thus rated as: spontaneous complaint of pain; pain on questioning after 10 ml; or no pain. The injection of propofol was then continued as necessary. Any further signs of discomfort, such as grimacing or arm withdrawal, were noted.

The mean age of the patients was 60 years (range 14 to 88) and 40 were female. Sixteen patients (16%) complained of pain. Seven of these (7%) were spontaneous complaints during the initial 10 ml injection and nine complained of pain on direct questioning. The remainder (84%) had no pain. Twenty-four patients were under 50 years of age. In this group, eight (33%) complained of pain. Sixteen patients complained of pain (nine female, seven male).

Some studies have shown the incidence of pain on injection of propofol without lignocaine, into a dorsal hand vein, to be 59%<sup>2</sup>. In my group of patients, using a glass syringe, the incidence of pain was much lower (16%) with only 7% spontaneously complaining of pain.

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Fresenius Ex. 2006

Bass et al. v. Fresenius Kabi USA, IPR2016-00254

It may be that the pain is due to irritant substances formed when propofol comes into contact with the plastic of disposable syringes. This theory may be supported if previously described methods for reducing the pain are looked on as ways of either slowing down or preventing the reaction between the propofol and the plastic. These methods include cooling the propofol to 4°C<sup>6</sup>, diluting the propofol<sup>5</sup> and the addition of lignocaine to the solution. This latter method has been shown to be more effective if the solution is only mixed immediately before use<sup>1,4</sup>. It has been proposed that the reason for this is due to the propofol/lignocaine mixture being unstable, the lignocaine moving into a lipid phase, so reducing its free concentration<sup>1</sup>. It may just be that by drawing up the propofol immediately before use, there is a shorter contact time with the syringe.

Enquiries to manufacturers confirmed that propofol strips the silicone lubricant from the inside barrel of plastic syringes. Perhaps this is the cause of the pain. A controlled trial is planned.

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#### References

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2. Johnson RA, Harper NJN, Chadwick S, Vohra A. Pain on injection of propofol. Methods of alleviation. *Anaesthesia* 1990; 45:439-442.
3. Newcombe GN. The effect, on injection pain, of adding lignocaine to propofol. *Anaes Intens Care* 1990; 18:105-7.
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5. Stokes DN, Robson N, Hutton P. Effect of diluting propofol on the incidence of pain on injection and venous sequelae. *Br J Anaesth* 1989; 62(2):202-3.
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#### Inadvertent epidural overdose

bag was connected via a 3-way tap to a 50 ml syringe in a syringe pump, as shown in Figure 1. The Polybag was hung from a drip stand. It was used to refill the 50 ml syringe as required via the tap (Figure 2).

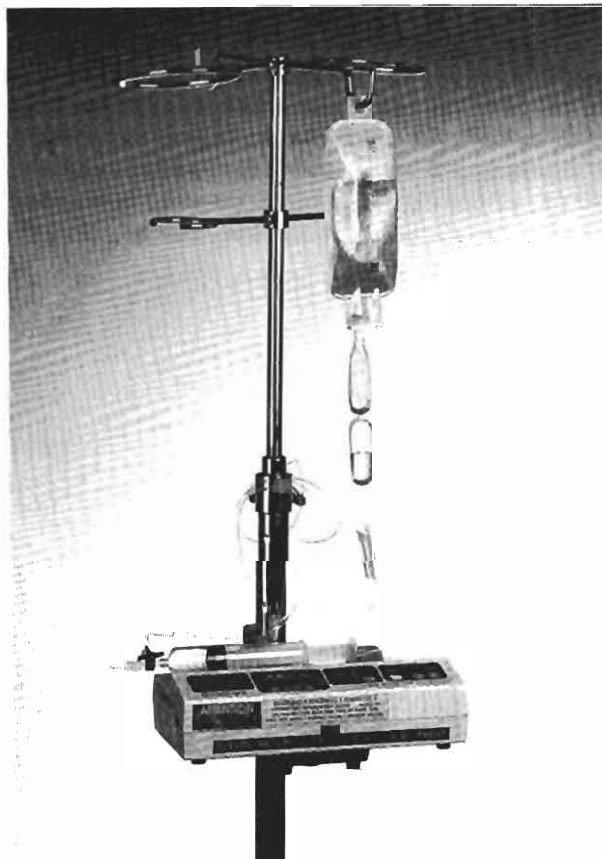


FIGURE 1

Excellent analgesia was provided for two and a half days, at an infusion rate of 5 ml/hr. No motor or sensory block was demonstrated, and the patient's observations were stable.

On the third postoperative night, the patient became oliguric despite an intravenous fluid bolus. Next