Massive subcutaneous emphysema after accidental removal of an intercostal drain

Editor—I congratulate the authors on the management of this difficult case of massive air leak after subclavian vein catheterization for permanent pacemaker insertion.3 This route of access is favoured by cardiologists for placement of pacing wires as it is thought to provide a more stable site with less chance of pacing wire migration.

I would like to raise another facet of the case, which was not raised in the report; namely prevention of the pneumothorax in the first place. Pneumothorax and other procedural complications related to needle insertions for central venous access can be almost completely eliminated by the routine use of ultrasound. This site can be accessed using ultrasound, particularly if screening is available.

It is widely recognized that complications related to needle insertions for central venous access can be almost completely eliminated by the routine use of ultrasound. This site can be accessed using ultrasound, particularly if screening is available to correct any catheter tip malposition.2 Despite the recommendations of NICE,3 based on a number of clinical publications, there remains reluctance in many centres to invest in appropriate ultrasound devices for this purpose, and it is the continued belief of many clinicians that they do not need the aid of such devices. A somewhat semantic debate continues in the correspondence columns about the cost effectiveness of ultrasound guided central venous catheterization.4

There is an attitude that such complications are minor (not to the patient) and an inherent risk of the procedure. The patient in this report must have suffered considerable stress, discomfort, and disability during convalescence, despite the reported eventual successful outcome. Analysis of this case suggests that the cost of the complication would be in the order of 15 days unnecessary stay on the ward at £300, plus 27 days on ITU at £1500 per day, for a procedure that otherwise would be done as a day-case or perhaps an overnight stay. Such costs total £46 000 and would obviously cause further disruption in terms of blocked beds for other cases. The high costs and excess length of stay after iatrogenic pneumothorax have been highlighted previously in a large survey of multiple acute hospitals in the USA.5 Ultrasound machines can be purchased for around £10 000–£15 000 apiece and running costs are low. When viewed in context their routine use make very good financial, legal and medical sense.

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1 Williams DJ, Jaggar SI, Morgan CJ. Upper airway obstruction as a result of massive subcutaneous emphysema following accidental removal of an intercostal drain. Br J Anaesth 2005; 94: 390–2
5 Zhan C, Miller MR. Excess length of stay, charges, and mortality attributable to medical injuries during hospitalization. JAMA 2003; 290: 1868–74

‘Paedfusor’ pharmacokinetic data set

Editor—Recently, several ‘open TCI’ systems (target-controlled infusion devices not requiring pre-filled propofol syringes) have been developed. In the near future some manufacturers of these systems will distribute such systems programmed with other pharmacokinetic data sets for propofol, and also data sets for other drugs such as remifentanil. One such set is the ‘Paedfusor’ pharmacokinetic data set for children. When we published the results of a study of the predictive performance of this data set, for brevity we did not publish the full pharmacokinetic details. We also omitted the non-linear kinetics used for children aged 13–16 yr.1,2 For the benefit of those who wish to use this model we have provided the full details in Table 1.

Table 1 ‘Paedfusor’ propofol pharmacokinetic data set

| Age 1–12 yr | V1=458.4xweight | k10=0.1527xweight−0.3 | k21=0.055 | k13=0.114 | k11=0.0033 | k40=0.26 |
| Age 13 yr | V1=400.0xweight | Other constants as above |
| Age 14 yr | V1=342.0xweight | k40=0.0678 |
| Age 15 yr | V1=284.0xweight | k40=0.0954 |
| Age 16 yr | V1=228.57xweight | k40=0.119 |

Maximum bolus size

Weight <15 kg: 3 mg
Weight <30 kg: 6 mg
Weight >30 kg: 12 mg

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Moles, weights and potencies: freedom of expression!

Editor—Rosenberg and Schug correctly remind us that there are 12.6% more molecules of bupivacaine in similarly expressed %wt/vol preparations of levobupivacaine (Chirocaine®) when...
compared with the racemate. They also correctly acknowledge that this difference was first highlighted in the British Journal of Anaesthesia in 1998. In that paper, the issue of regulatory changes to expressed formulations was first addressed and that an adjustment, equivalent to a reduction of 11% in the potency for the %wt/vol preparations of levobupivacaine when compared with racemate preparations that predated these changes, would be required. Although the discovery of this by Columb led to some initial concern, it became clear that, as this ‘error’ was systematic in the conduct of clinical toxicity and efficacy studies, the interpretation of any therapeutic implications would remain unaffected. However, Rosenberg and Schug incorrectly state that all authors have failed to consider the molar concentrations of levobupivacaine, when comparing it with bupivacaine and ropivacaine (Naropin®). Lyons and colleagues, using minimum local analgesic concentrations (MLAC), showed that a 2% potency difference existed between bupivacaine and levobupivacaine when expressed on a %wt/vol basis (MLAC %wt/vol 0.081 vs 0.083). However, a 13% reduction in potency occurred when taking the molarity of solutions into account (MLAC mmol litre⁻¹ 2.47 vs 2.87). In fact, from the outset, the first MLAC study comparing bupivacaine and lidocaine presented molar potencies in addition to usual %wt/vol. More recent studies have tended away from formally addressing the formulation issue, perhaps related to limited clinical importance of this, although Camorcia does discuss the molar potency issues relating to ropivacaine and levobupivacaine. Furthermore, the paper by McLeod, measuring the densities of local anaesthetics, tabulated the molar concentrations (mmol litre⁻¹) of commercially available ‘0.75%wt/vol’ solutions of bupivacaine, levobupivacaine and ropivacaine. Table 1, adapted from this paper, shows that the concentration of levobupivacaine 7.5 mg ml⁻¹ is 26.0 mmol litre⁻¹, and is indeed 12.6% greater than the concentration of bupivacaine (23.1 mmol litre⁻¹). However, Rosenberg and Schug are not consistent when translating molar concentrations between bupivacaine and levobupivacaine to studies comparing levobupivacaine and ropivacaine. Ropivacaine has a smaller propyl side chain and thus, a smaller molecular weight, compared with bupivacaine and levobupivacaine, which possess a larger butyl side chain. One mole of ropivacaine has a mass of 274 g and a mole of bupivacaine or levobupivacaine has a mass of 288 g. The difference of 14 g is accounted for by one carbon and two hydrogen atoms. Therefore, when taking molecular weights into consideration, a concentration of ropivacaine, expressed as %wt/vol or mg ml⁻¹, will have ~4.8% more molecules than racemic bupivacaine, and therefore 7–8% less than levobupivacaine. Again, we hope Table 1 may be useful for other researchers when considering these issues. Therefore, we suggest that in studies comparing the commercial solutions of bupivacaine racemate, levobupivacaine and ropivacaine, account may need to be taken of the differences in molarity attributable to differences in both molecular weights and presentation as base or hydrochloride. We also suggest that whilst the issues of molar potencies are of pharmacological interest, the limited clinical relevance of these formulation issues remains unchanged from that first published in the British Journal of Anaesthesia in 1998.

Table 1 Typical values for molecular weights and 0.75%wt/vol preparations

<table>
<thead>
<tr>
<th></th>
<th>Bupivacaine</th>
<th>Levobupivacaine</th>
<th>Ropivacaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free base mole (g)</td>
<td>288</td>
<td>288</td>
<td>274</td>
</tr>
<tr>
<td>Expressed mole (g)</td>
<td>324.5</td>
<td>288</td>
<td>310.5</td>
</tr>
<tr>
<td>Hydrochloride (mg ml⁻¹)</td>
<td>7.5</td>
<td>8.45</td>
<td>7.5</td>
</tr>
<tr>
<td>Molar (mmol litre⁻¹)</td>
<td>23.1</td>
<td>26.0</td>
<td>24.2</td>
</tr>
<tr>
<td>Molar difference (%)</td>
<td>0</td>
<td>+12.6</td>
<td>+4.8</td>
</tr>
<tr>
<td>Potency adjustment (%)</td>
<td>0</td>
<td>−11.2</td>
<td>−4.5</td>
</tr>
</tbody>
</table>

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6 Benhamou D, Ghosh C, Mercier FJ. A randomized sequential allocation study to determine the minimum effective analgesic concentration of levobupivacaine and ropivacaine in patients receiving epidural analgesia for labor. Anesthesiology 2003; 99: 1383–6

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Confidence with confidence intervals

Editor—We would like to congratulate Dr Sell and colleagues on their study that estimated the median effective dose (ED50) of ropivacaine and levobupivacaine for postoperative analgesia infused via an intrathecal catheter following hip replacement surgery. They used the minimum local analgesic dose (MLAD) modification of the minimum local analgesic concentration (MLAC) model for this study. It would appear, however, that they have reported spuriously tighter 95% confidence intervals (95% CI) than the data, as presented in Figure 1 of their article, suggest. Similar problems have been highlighted previously.

A problem with the analysis of up-down sequences is that the observations are not independent. Several approaches have been described to deal with this problem, the Dixon and Massey method being one of the more conservative approaches. For completeness we have included some suggested corrections for the Table including this method, independent pairs, a modified reversal analysis adjusted for testing interval, and probit regression, which we hope the authors and readers will find useful. In this instance we are not interested in the median effective dose (ED50) estimates, rather the 95% CI than the data, as presented in Figure 1 of their article, suggest. Similar problems have been highlighted previously.

The authors are to be commended for the use of the Figures that depict the data clearly and allow the reader to consider the data in detail. Re-analysis of the data suggests that the SD used to estimate the 95% CI approximated the testing interval (1 mg). Whilst this approach has been recommended for short sequences (nominal sample sizes of six or less) it is based on the assumption that the population SD is known, which is not generally the case. In any event, any estimate or assumption of SD should be considered in respect of the data as collected.