Expression of interleukin-6 messenger RNA in a rodent model of diffuse axonal injury

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Diffuse axonal injury has been identified in 50% of patients with severe non-missile head injury and is associated with persistent vegetative state and profound neurological disability. It is recognized that an immediate mechanical disruption of brain tissue is followed by cascades of cellular and biochemical reactions which are likely to account for as much cellular injury as the primary impact.1 Cells of the central nervous system, particularly astrocytes and microglia, can produce pro-inflammatory cytokines in response to a variety of stimuli and we have recently demonstrated a transcranial gradient of the cytokine interleukin-6 (IL-6) in patients with TBI or spontaneous subarachnoid haemorrhage. To determine the site and extent of this IL-6 production within the CNS, we have used in situ hybridization to label mRNA for IL-6 in rodent brains subjected to a weight-drop model of diffuse axonal injury23

We studied 11 male, Sprague–Dawley rats, weighing 300–350 g (seven trauma and four sham). After termination of isoflurane anaesthesia, the traumatized animals demonstrated delayed recovery (trauma 19 min, sham 7 min; P<0.01) in addition to loss of interest in their environment and forelimb flexion deformity. These animals were observed for 6 h before being killed. Sham animals demonstrated normal constitutive expression of IL-6 mRNA, as described previously.4 In five of the seven traumatized animals, an intense area of IL-6 mRNA labelling was found below the hippocampus. From sections prepared for morphological study, we found evidence of traumatic haemorrhage in this area. However, in brain sections used for in situ labelling, haemorrhage was no longer apparent, suggesting that induction of IL-6 mRNA may be a reaction to traumatic haemorrhage. Cells strongly expressing IL-6 mRNA were also seen in the dentate gyrus of these five animals. The number of these cells expressing IL-6 mRNA in the dentate and the number in the region below the hippocampus showed some correlation (r=0.44, P<0.05).

In three traumatized animals, evidence of tissue disruption was seen at the level of the pre-optic area. Specifically, there was tearing of the junction between the corpus callosum and septal region below. Cells expressing IL-6 mRNA could be seen on either side of the lesion, demonstrating co-localization of tissue damage and IL-6 expression.

Our results demonstrated IL-6 production in response to trauma at the cellular level. This inflammatory cytokine is clearly implicated in the response to CNS injury, but whether this response is neuroprotective or pathological remains to be established.

Keywords: brain, injury; polypeptides, cytokines; rat; model, rat

References

Effect of xenon on cytokine balance and adhesion molecule expression in an isolated cardiopulmonary bypass circuit

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Xenon is a noble gas with potent anaesthetic and analgesic properties. Despite being non-reactive, xenon is neither
chemically nor biologically inert. Xenon has many properties close to those of an ideal anaesthetic agent and despite its expense, its use in clinical anaesthesia is increasing. The reported haemodynamic stability of xenon anaesthesia makes it a suitable agent for patients undergoing cardiac surgery. There are few data on the immunomodulatory effects of xenon in humans.

Eight healthy volunteers each donated two 250-ml blood samples (SAGM anticoagulant and heparin 1000 u). These were used to prime two identical cardiopulmonary bypass (CPB) circuits and circulation was conducted under identical conditions, with strict control of pH, $P_{CO_2}$, $P_{O_2}$, flow and temperature. The membrane oxygenators were supplied with either 70% xenon in oxygen or oxygen-enriched air ($F_{O_2}$ 0.3). Samples of blood were obtained as follows: A= before exposure to the isolated bypass system (IBS); B, C and D=after 30, 60 and 90 min of IBS, respectively. Monocyte and lymphocyte HLA-DR expression and granulocyte adhesion molecules L-selectin, CD18 and CD11b were assayed using flow cytometry. Plasma pro-inflammatory cytokines IL-1β, TNFα and IL-8 and the anti-inflammatory cytokines IL-10, IL-1RA and TNF-SR2 were measured. Within- and between-group analysis was performed using ANOVA and $t$ tests.

There were no significant between group differences in any variable. Concentrations of IL-8 were increased significantly at time D (Fig. 1), indicating no alteration in immune response with xenon within an (in vitro) isolated CPB system.

**Keywords:** anaesthetics gases, xenon; immune response; polypeptides, cytokines; heart, cardiopulmonary bypass

**Acknowledgement**
We thank BOC Gases (UK) for supplying xenon and Polystan for supplying the CPB circuits. A. B. has a Research Fellowship from the Association of Anaesthetists of Great Britain and Ireland.

**Reference**

**Methylene blue in reperfusion syndrome inhibits the effects of nitric oxide**

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We have shown previously that the dye methylene blue reduces hypotension and inotrope requirements after graft reperfusion during orthotopic liver transplantation (OLT). This effect was mediated via improved cardiac function rather than vasoconstriction. In sepsis, the effects of methylene blue are thought to be mediated via inhibition of the effects of nitric oxide by inhibition of nitric oxide synthase and guanylate cyclase. Therefore, we have studied the effect of methylene blue on these systems in hepatic ischaemia reperfusion injury.

We studied 36 patients undergoing OLT. Patients were
allocated randomly to receive methylene blue 1.5 mg kg⁻¹ or an equivalent volume of normal saline i.v. by rapid bolus, 1 min before reperfusion. Blood samples were obtained at baseline and 5 and 60 min after reperfusion for measurement of plasma concentrations of nitrite and cGMP. Plasma nitrite and nitrate, the breakdown products of nitric oxide, were measured by conversion of nitrate to nitrite and measurement of plasma nitrite concentration using an Griess reaction. Plasma cGMP, an index of guanylate cyclase activity, was measured using an immunoassay technique. Results are given as median (range) and analysis was performed using the Mann–Whitney U test, Friedman’s test and least square correlation.

For all patients, there was a close correlation between nitrite and cGMP concentrations ($r=0.4$, $P=0.002$). Plasma nitrite concentrations (Fig. 2) were comparable between groups at all times. Nitrite concentrations decreased progressively with time in the control group ($P<0.0001$) but not in the methylene blue group ($P=0.4$, Friedman). cGMP concentrations were similar in both groups at baseline, but decreased in the methylene blue group ($P<0.001$) but not in controls ($P=0.2$). One hour after reperfusion, cGMP concentrations were significantly lower in the methylene blue group compared with controls (14.6 (2.7–42) vs 21.3 (13–37) pmol litre⁻¹; $P=0.008$).

We have demonstrated a progressive reduction in nitrite concentrations suggestive of decreasing plasma nitric oxide during OLT. cGMP concentrations correlated with nitrite concentrations at all times, consistent with nitric oxide exerting its action via guanylate cyclase activation in these patients. In the presence of methylene blue, there was a reduction in cGMP, but not in plasma nitrates.

**Keywords:** pharmacology, methylene blue; liver, transplantation; complications, reperfusion syndrome; pharmacology, nitric oxide

**Reference**

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**Table 1** Results of the halothane (hal.), caffeine (caf.), ryanodine and 4-CmC tests for patients with susceptible or equivocal diagnoses. Times from addition of 4-CmC to onset of contracture (Ot), contracture of 0.2 g (T0.2) and contracture of 1 g (T1) were recorded. 4-CmC did not produce contracture in muscle from patients diagnosed as not susceptible to MH.

<table>
<thead>
<tr>
<th>Patient</th>
<th>MHE</th>
<th>MHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>0.7</td>
<td>0.15</td>
</tr>
<tr>
<td>b</td>
<td>0.9</td>
<td>0.75</td>
</tr>
<tr>
<td>c</td>
<td>1.9</td>
<td>0.9</td>
</tr>
<tr>
<td>d</td>
<td>0.55</td>
<td>0.2</td>
</tr>
<tr>
<td>e</td>
<td>0.55</td>
<td>0.2</td>
</tr>
<tr>
<td>f</td>
<td>0.35</td>
<td>0.05</td>
</tr>
<tr>
<td>g</td>
<td>1.05</td>
<td>1.45</td>
</tr>
<tr>
<td>h</td>
<td>0.3</td>
<td>0.2</td>
</tr>
</tbody>
</table>

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**In vitro contracture produced by 4-chloro-m-cresol in muscle from patients attending for malignant hyperthermia diagnosis**

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Pharmacological challenge of excised muscle strips, the in vitro contracture tests (IVCT), remains the only validated diagnostic technique for malignant hyperthermia (MH) susceptibility. Susceptibility is diagnosed when there are abnormal responses to both halothane and caffeine tests and is excluded when responses to both drugs are normal. An equivocal diagnosis is made when the muscle responds abnormally to one drug only. Further tests with additional drugs (e.g. ryanodine) may resolve diagnostic uncertainty in some cases, but no such test has yet demonstrated absolute sensitivity and specificity. 4-Chloro-m-cresol (4-CmC) is used as a preservative in some pharmaceutical preparations of insulin, heparin and succinylcholine, for example. It has been found to affect the Ca²⁺ release channel of skeletal muscle sarcoplasmic reticulum and to cause time- and dose-dependent muscle contracture. We present our preliminary findings of the effects of 4-CmC on muscle from patients attending our unit for diagnosis of MH susceptibility.

Muscle biopsy and diagnostic IVCT were performed as described previously and, in addition, a ryanodine contracture test. Muscle strips surplus to diagnostic requirements were used for exposure to 4-CmC. After an equilibration period, 4-CmC 75 µmol litre⁻¹ was added to the muscle bath. Times from addition of 4-CmC to onset of contracture (Ot), contracture of 0.2 g (T0.2) and contracture of 1 g (T1) were recorded (Table 1). The tests were discontinued 30 min after addition of 4-CmC as the effect had reached a plateau by this time.

Muscle from two MH susceptible patients did not develop contracture when exposed to 4-CmC 75 µmol litre⁻¹. This raises doubts about the sensitivity of this particular procedure for a 4-CmC test for MH diagnosis.
Keywords: malignant hyperthermia; pharmacology; 4-chloro-m-cresol

References
2 Hopkins PM, Ellis FR, Halsall PJ. Br J Anaesth 1993; 70: 397–401
3 Tegazzin V, Scutari E, Treves S, Zorzato F. Anesthesiology 1996; 84: 1380–5

Profiling novel i.v. anaesthetic agents with a rat EEG model

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Methods for monitoring and controlling i.v. anaesthesia in rats using the burst suppression ratio (BSR) have been described previously.1 BSR is the percentage of time per 15-s epoch spent in suppression, where suppression is defined as an interval where the amplitude of the time-differentiated EEG signal stays within a –30 to 30 µV ms–1 window for at least 100 ms. Our aim was to compare the profile of two novel i.v. anaesthetics with standard agents. The first compound was Org 21465, a steroid anaesthetic which was submitted for phase I testing in 1996. The second was Org 25435,2 which is currently in the preclinical development phase. This was tested as the hydrochloride salt. Reference drugs tested were: etomidate, Saffan, propofol and thiopental.

Eighty-eight male Wistar rats (218–382 g) were chronically implanted with epidural EEG electrodes. Drug administration was via a tail vein. Two tests were performed: bolus injection of the drug over 10 s; and closed-loop, EEG-controlled infusion to maintain a BSR target for 1 h. The following variables were measured: mean bolus dose required to produce a peak value of 60% BSR; recovery time to return of the righting reflex after this bolus dose; mean infusion rate to maintain 60% BSR; and recovery time to righting after the end of the infusion (oversleep time). Results are shown in Figure 3.

Although Org 21465 was a very potent anaesthetic with a short duration of action after bolus injection, recovery after prolonged infusions was unacceptably long. Org 25435 had a better profile, with favourable recovery times after bolus injection and prolonged infusion.

Keywords: pharmacology, Org 25435; anaesthetics i.v.; monitoring, electroencephalography; rat

Reference
1 Vijn PCM, Sneyd JR. Br J Anaesth 1998; 81: 415–21
2 European Patent Application number 98305837.1

Effect of target-controlled infusion of propofol on the auditory evoked response, median frequency and spectral edge in humans

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New methods of drug delivery allow target-controlled infusion (TCI) to aim for a desired plasma concentration of propofol. We used this method to study the effect of three different doses of propofol on the auditory evoked response (AER) and the derived electroencephalogram (EEG) variables, median frequency (F50) and spectral edge (F95).

We studied 12 patients, aged 30–65 yr, in a crossover study performed before surgery. After premedication with morphine 10 mg and atropine 0.4 mg, anaesthesia was induced and maintained by TCI propofol infusion. After administration of vecuronium 0.1 mg kg–1, the trachea was intubated and the lungs ventilated with 66% nitrous oxide in oxygen to maintain a stable end-expiratory concentration of carbon dioxide of 4.5–5 kPa. Neuromuscular block was maintained with infusion of vecuronium. The AER and EEG were recorded throughout four consecutive 10-min periods.
Results for the EEG variables were more difficult to interpret. A linear relationship was demonstrated for F95 and log propofol dose, but spectral edge frequency increased with increasing propofol concentration (the opposite of the effect observed with increasing the dose of desflurane). There was no significant effect between F50 and log dose of propofol. This confirms the greater potential of the AER for measuring depth of anaesthesia as similar AER effects are seen for different anaesthetic agents whereas inconsistencies may occur in EEG variables.

**Comparison of esmolol and alfentanil on the auditory evoked response and haemodynamic response to intubation**

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The potent β-blocker esmolol obtunds the cardiovascular response to stress by actions on peripheral β-adrenoceptors. A recent study suggested that esmolol may have anaesthetic sparing properties, posing the question that some of its effects are produced by central reduction of the stress response rather than peripheral actions on the cardiovascular system. To explore this possibility, we have compared the effectiveness of esmolol and alfentanil in reducing the stress response to intubation, as reflected by the auditory evoked response (AER) and haemodynamic changes measured before and after intubation.

Patients aged 18–65 yr were premedicated with midazolam 10 mg, 30 min before induction of anaesthesia with propofol 2–3 mg kg⁻¹. After administration of vecuronium 0.1 mg kg⁻¹, a laryngeal mask airway was inserted and the patient’s lungs ventilated to maintain anaesthesia with 0.6% end-expiratory isoflurane and 50% nitrous oxide in oxygen for at least 5 min. Patients were allocated to one of five groups to receive an i.v. bolus of the study drug, 1 min before tracheal intubation: (1) control (n=13), 0.9% saline 5 ml; (2) low-dose esmolol (n=15), esmolol 1 mg kg⁻¹; (3) high-dose esmolol (n=10), esmolol 2 mg kg⁻¹; (4) low-dose alfentanil (n=14), alfentanil 20 µg kg⁻¹; and (5) high-dose alfentanil (n=10), alfentanil 50 µg kg⁻¹. The AER was recorded from electrodes at the vertex and inion and analysed off-line. Averaged AER responses representing 2.4 min (1024 sweeps) immediately

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**Table 2 Effects of target-controlled target propofol concentrations on AER and EEG variables (geometric means (95% confidence intervals))**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Propofol 2 µg ml⁻¹</th>
<th>Propofol 4 µg ml⁻¹</th>
<th>Propofol 6 µg ml⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pa latency</td>
<td>0.002</td>
<td>33.1 (31.0–35.4)</td>
<td>38.5 (36.0–41.1)</td>
</tr>
<tr>
<td>Pa amplitude</td>
<td>0.001</td>
<td>0.32 (0.24–0.43)</td>
<td>0.21 (0.16–0.28)</td>
</tr>
<tr>
<td>Nb latency</td>
<td>0.08</td>
<td>53.7 (50.4–57.2)</td>
<td>58.2 (54.7–62.0)</td>
</tr>
<tr>
<td>Nb amplitude</td>
<td>0.03</td>
<td>0.23 (0.17–0.31)</td>
<td>0.17 (0.13–0.23)</td>
</tr>
<tr>
<td>F50</td>
<td>0.67</td>
<td>2.66 (1.81–3.92)</td>
<td>2.16 (1.46–3.18)</td>
</tr>
<tr>
<td>F95</td>
<td>0.02</td>
<td>12.9 (11.1–15.1)</td>
<td>14.6 (12.5–17.0)</td>
</tr>
</tbody>
</table>

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**Table 3 Percentage change in Pa amplitude after intubation and mean (95% confidence intervals) changes in systolic arterial pressure (SAP) and heart rate (HR) in the five groups. Significantly different from zero *P<0.05, **P<0.01, ***P<0.001**

<table>
<thead>
<tr>
<th>Group</th>
<th>Pa amplitude (% change)</th>
<th>SAP (mmHg)</th>
<th>HR (Beats min⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline</td>
<td>56 (9–121) %***</td>
<td>26.8 (16.3–37.3)**</td>
<td>18.5 (13.4–23.7)**</td>
</tr>
<tr>
<td>Low-dose esmolol</td>
<td>16 (–16–61) %</td>
<td>20.9 (11.2–30.7)***</td>
<td>6.6 (1.8–11.4)**</td>
</tr>
<tr>
<td>High-dose esmolol</td>
<td>12 (–25–68) %</td>
<td>16.8 (4.8–28.8)***</td>
<td>9.2 (3.3–15.1)***</td>
</tr>
<tr>
<td>Low-dose alfentanil</td>
<td>47 (5–107) %*</td>
<td>3.1 (–7.0–13.3)</td>
<td>–1.8 (–6.8–3.2)</td>
</tr>
<tr>
<td>High-dose alfentanil</td>
<td>12 (–25–67) %</td>
<td>–2.3 (–14.3–9.7)</td>
<td>–0.2 (–6.1–5.7)</td>
</tr>
</tbody>
</table>

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**Reference**

before and after intubation were derived, enabling measurement of Pa amplitude. Analysis of variance and Student’s t test were used to compare the log-transformed data from these two periods for the saline, esmolol and alfentanil groups. Haemodynamic variables measured 1 min before and 1 and 5 min after intubation were subjected to similar statistical analysis but without log transformation.

The results are summarized in Table 3. Both esmolol and alfentanil blocked the AER response to intubation to the extent that the AER changes were not significantly different from zero. This has been reported previously for alfentanil

\(^2\)

and may be explained by its analgesic effects. The attenuation produced by esmolol is in keeping with an anaesthetic sparing effect

\(^1\)

and a central mechanism for this effect has to be considered.

**Keywords**: monitoring, evoked potentials; pharmacology, esmolol; sympathetic nervous system, esmolol; analgesics opioid, remifentanil; cardiovascular system, effects

**References**


**Does nitrous oxide affect closed-loop anaesthetic propofol?**

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We have described previously closed-loop infusion of propofol using the bispectral index (BIS) and a feedback control system.\(^1\) Nitrous oxide is used commonly as a supplement to propofol infusion to provide analgesia and additional hypnosis. We have evaluated introduction of nitrous oxide during closed-loop anaesthesia with propofol.

We studied eight volunteers (five males; aged 29–41 yr; weight 62–97 kg). An Aspect A1000 monitor recorded the raw EEG from bipolar leads (Fp1/Fp7 and Fp2/F8). BIS (V3.2) was obtained in real-time by the closed-loop control system running on a personal computer. Compared with the previous system,\(^1\) the proportional integral derivative (PID) controller gains and supervision rule-base have been improved. Target concentration of the built-in PK/PD model was regulated by the controller while the target site (effect site or plasma) was regulated by the supervision rule-base.

After a 5-min baseline EEG recording, the BIS target was set constantly to 65 during the 50-min closed-loop propofol infusion. Subjects breathed 50% nitrous oxide between the 20th and 35th minutes.

Anaesthesia was achieved in all subjects. Two subjects were anaesthetized during induction with minimum BIS values of 42.4 and 46.9. After some initial instability, stable anaesthesia was achieved after a mean time of 7.6 (sd 3.5) min. Mean measured BIS between the time of establishment of stable anaesthesia and 20 min (propofol only) was 62.9 (3.7); between 20 and 35 min (propofol and nitrous oxide), 62.6 (5.4); and between 35 and 50 min (propofol only), 62.6 (8.4). Addition of nitrous oxide did not prevent maintenance of the anaesthesia target, but its withdrawal was associated with moderate oscillation of BIS in three subjects (Fig. 4).

Our closed-loop system maintained anaesthesia during and after addition of nitrous oxide in volunteer subjects who were not subjected to painful stimulation.

**Keywords**: sedation; anaesthetics i.v., propofol; anaesthetics gases, nitrous oxide; monitoring, electroencephalography

**Acknowledgement**

Graseby Medical Ltd loaned the infusion pump and Dr Shafer gave some STANPUMP code.

**Reference**


**Closed-loop sedation during knee surgery under epidural anaesthesia**

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\(^1\)School of Electronic Communication and Electrical Engineering, University of Plymouth PL4 8AA, UK. \(^2\)Department of Anaesthesia, Derriford Hospital, Plymouth PL6 8DH, UK
We have reported previously computer-controlled closed-loop propofol sedation of volunteers. We have subsequently evaluated this system in patients undergoing reconstructive knee surgery during epidural anaesthesia. A lumbar epidural catheter was placed under local anaesthesia either before (n=4) or after (n=2) starting sedation, and a regional block established. The BIS target was initially set at 65 and then adjusted at clinical discretion. Closed-loop sedation was maintained throughout surgery.

We studied six male patients (ASA I–II, aged 25–39 yr, weight 70–100 kg). One other patient was entered into the study but sedation was not commenced because of technical difficulties (broken cable). Sedation at the initial BIS target was established in a mean time of 7.8 (SD 1.9) min. Subsequently, the error between measured and target BIS in the six patients after induction was –3.4 (10.5). Changes in patient position and other stimuli during placement of the lumbar epidural catheter in the first four patients were associated with rapid changes in BIS and variable levels of consciousness. In two patients, during surgery, when stimulation was confined to the leg (i.e. blocked by the epidural), measured BIS remained slightly deeper than target. The controller therefore gradually reduced the target propofol concentration until the patient suddenly ‘awakened’ (Fig. 5).

Although the closed-loop system was initially able to induce and maintain sedation, the response of the proportional integral derivative (PID) controller to persistent small errors caused progressive withdrawal of the sedative agent which gave clinically unsatisfactory sedation in two patients. We hypothesize that this may have been caused by establishment of natural sleep.

Keywords: sedation; anaesthetics i.v., propofol; anaesthetics gases, nitrous oxide; surgery, orthopaedic

Desaturation modelling in the ‘human patient’ simulator at the Bristol Medical Simulation Centre

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Bristol University Medical School, Bristol, UK

The Bristol Medical Simulation Centre uses a manikin and simulation software developed by Medical Education Technologies, Inc (METI). We investigated how realistically the METI system simulates normal physiology and chose to study one of the most fundamental emergencies in medicine—loss of airway and consequent interruption of the oxygen supply. We used the data-logging facility of METI to record the time course of decrease in arterial oxygen partial pressure (\(P_{aO_2}\)) and oxyhaemoglobin saturation (\(S_{aO_2}\)) after software imposition of 100% neuromuscular block. We did this at various settings of functional residual capacity (FRC) and fractional inspired concentration of oxygen (\(F_{I O_2}\)), at a fixed oxygen consumption (\(V_{O_2}\)) of 250 ml min\(^{-1}\) and pulmonary venous admixture (‘shunt’, \(Qs/Qt\)) of 2%. We compared times to 90% \(S_{aO_2}\) with those predicted by the model of Farmery and Roe. The METI system was consistently slower than the model of Farmery and Roe (Table 4).

On further examination, the corresponding time courses of decreases in \(P_{aO_2}\) were more closely aligned. Therefore, we examined for inconsistencies in the behaviour of the oxygen–haemoglobin dissociation curve using published standards. We plotted the decrease in METI values of \(S_{aO_2}\) with \(P_{aO_2}\) at different values of steady state pH and

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Table 4 Times to reach 90% desaturation (\(S_{aO_2}\)) using the METI system compared with those predicted by the model of Farmery and Roe. The METI system was consistently slower than the model of Farmery and Roe.

<table>
<thead>
<tr>
<th>FRC (ml)</th>
<th>(F_{I O_2})</th>
<th>Time for (S_{aO_2}) to reach 90% (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>METI</td>
</tr>
<tr>
<td>1530</td>
<td>0.21</td>
<td>90</td>
</tr>
<tr>
<td>2700</td>
<td>0.21</td>
<td>145</td>
</tr>
<tr>
<td>4000</td>
<td>0.21</td>
<td>195</td>
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<tr>
<td>1530</td>
<td>1.0</td>
<td>240</td>
</tr>
<tr>
<td>2700</td>
<td>1.0</td>
<td>420</td>
</tr>
<tr>
<td>4000</td>
<td>1.0</td>
<td>590</td>
</tr>
</tbody>
</table>

Reference


Acknowledgement

Graseby Medical Ltd loaned the infusion pump and Dr Shafer gave some STANPUMP code.

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Fig 5 Bispectral index (BIS) (top thin curve) and its target (top thick curve), and predicted plasma (bottom thin curve) and effect-site (bottom thick curve) propofol concentrations in a single subject. After initial over-sedation (arrow 1), the closed-loop system established stable sedation. Between 45 and 65 min, BIS remained below the target and the controller allowed plasma propofol concentrations to decrease. The patient then ‘awoke’ (arrow 2).


Page dimensions: 612.0x792.0

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\(\text{P}_{\text{aCO}_2}\) produced by altering ventilatory sensitivity to carbon dioxide. We discovered that: (i) arterial pH varied linearly with \(\text{P}_{\text{aCO}_2}\) rather than with the logarithm of \(\text{P}_{\text{aCO}_2}\), as described by the Sigaard-Andersen relationship, and (ii) that the oxygen–hemoglobin dissociation curve was not shifted by pH, as described by Bohr. We used the METI values of pH and \(\text{P}_{\text{aCO}_2}\) after the onset of apnoea to impose a Bohr shift on the time course of the METI \(\text{S}_\text{aO}_2\) values. This made the time course of the METI desaturations closer to those of the Farmery model, but did not entirely eliminate the discrepancy.

Without access to the METI software, we cannot begin to explain the deficiencies in the METI modelling but we feel that a model so heavily centred on anaesthesia should default to a more realistic simulation of such a fundamental emergency as loss of oxygen supply.

**Keywords:** computers, simulation; oxygen, saturation; model, computer simulation

**References**


**Psychomotor aptitude testing and the performance of obstetric epidural analgesia by anaesthetic trainees**

A. K. Dashfield*, J. C. Coghill* and J. A. Langton

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In previous work, we have described a positive correlation between the scores obtained by anaesthetists using a computerized psychomotor testing system and learning fibreoptic endoscopy using a video endoscope.\(^1\) Anaesthetists are required to learn a range of different psychomotor skills during their training and inherent psychomotor ability may be a determinant of how quickly these skills can be acquired and used successfully.

To test this hypothesis, we investigated anaesthetic trainees within our department learning to perform obstetric epidural analgesia. We studied 10 senior house officers who had no previous experience of performing obstetric epidural anaesthesia. All trainees completed the computerized psychomotor test ADTRACK 3 (AD3). This test has been extensively used and validated in the armed services to select candidates who are likely to be successful in pilot training.\(^2\) From the start of their obstetric training, a detailed record was kept of every obstetric epidural performed by each trainee. Failure was defined as failure to obtain satisfactory analgesia for any reason; this definition is similar to that used in previous work.\(^3\) All patients had a standardized technique for obstetric epidural analgesia with an initial bolus of 0.5% bupivacaine 10 ml followed by an infusion of 0.1% bupivacaine with fentanyl 2 \(\mu\)g ml\(^{-1}\) at a rate of 0–8 ml h\(^{-1}\) via the epidural catheter. The success rate of each trainee’s first 50 epidurals was then paired with his or her AD3 score. Data were analysed using Pearson’s correlation coefficient and linear regression.

We found that there was a significant post hoc correlation between mean failure rates for the second 25 epidurals and AD3 score \((r=-0.579, P=0.04)\)

We conclude that psychomotor abilities, as measured using the ADTRACK 3 computerized psychomotor test, appeared not to be determinants of the trainees’ early proficiency in obstetric epidural anaesthesia but may identify individuals who have a greater ability at a later stage in their training.

**Keywords:** anaesthetist, performance; anaesthetist, training; analgesic techniques, epidural; analgesia, obstetric

**Systemic absorption of cocaine during fibreoptic bronchoscopy**

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Intra-tracheal injection via the cricothyroid membrane has been shown to reduce coughing and distress associated with fibreoptic bronchoscopy under local anaesthesia.\(^1\) Cocaine is preferred to lidocaine for this route as it causes less cough and more profound anaesthesia.\(^1\) However, there is concern regarding the cardiac toxicity of cocaine,\(^2\) as this may potentiate the cardiovascular effects of bronchoscopy.\(^4\) The maximum safe dose of cocaine for topical anaesthesia to the nasal mucosa is 1.5 mg kg\(^{-1}\),\(^5\) but it is not defined for other routes of administration. The dose typically used

**Fig 6 Serum concentrations of cocaine (median, 95% confidence limits).**
via the intra-tracheal route varies between 100 mg and 200 mg (i.e. up to 5 mg kg$^{-1}$ for a 40-kg patient). In this study, we investigated if serum cocaine concentrations were increased significantly during fibreoptic bronchoscopy and at the time of discharge from the day-case unit.

A prospective study was undertaken in seven patients undergoing fibreoptic bronchoscopy. All patients received intra-tracheal injection of cocaine solution 125 mg (5 ml of 2.5%) in addition to lidocaine spray to the nose/pharynx. Venous blood samples were obtained for measurement of serum concentrations of cocaine at 5, 10, 20, 30, 60 and 120 min.

Serum concentrations of cocaine were increased significantly in all patients during and after bronchoscopy (Fig. 6). Median cocaine concentration at 10 min was 0.63 mg litre$^{-1}$, increasing to a peak of 1.88 mg litre$^{-1}$ at 60 min. At 120 min, when patients were discharged from the day-case unit, median cocaine concentration remained increased at 1.72 mg litre$^{-1}$.

We conclude that significant concentrations of cocaine were present during fibreoptic bronchoscopy and that this may contribute to the cardiovascular risk in patients with ischaemic heart disease. Cocaine concentrations were higher still at the time of discharge from the day-case unit. Patients should therefore receive a warning similar to that given after a day-case general anaesthetic.

**Keywords:** anaesthetics local, cocaine; pharmacology, cocaine; anaesthetic techniques, bronchoscopy

**References**

**Mortality and the use of pulmonary artery catheters**

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Pulmonary artery catheters in intensive care are controversial. Connors and colleagues$^1$ in 1996 used a propensity score to demonstrate increased mortality with their use in a multicentre US study. Applicability of this study to British intensive care has been questioned. Connors and colleagues disregarded therapeutic interventions. We have reviewed our intensive care database using similar statistical methods to Connors and colleagues to establish if there is an excess mortality directly attributable to pulmonary artery catheters.

Data were collected prospectively on all patients admitted to the intensive care unit between January 1991 and January 1998, including APACHE II score, patient characteristics, diagnosis and treatment (including inotropes and renal dialysis). A clinician’s (ATC) prediction of likely outcome was included at the time of patient admission. Actual outcome (survival data and duration of ICU stay) was subsequently entered. We used logistic regression to construct a propensity score$^2$ for pulmonary artery catheter insertion. Performance of the propensity score was tested by receiver operating characteristic (ROC) plotting. Logistic regression analysis was used to establish whether pulmonary artery catheter was an independent predictor of mortality after correction for propensity score. In addition to studying the whole data set, we examined subgroups stratified for APACHE II score at admission (<20, 20–25 and >25).

We studied 4186 patients aged more than 16 yr. Overall mortality was 293 of 2333 patients without pulmonary artery catheters and 794 of 1849 patients with pulmonary artery catheters ($P<0.0001$, chi-square). The ROC plot for propensity score (Fig. 7) showed good discrimination ($W=0.88, P<0.0001$). For the whole data set, propensity score was predictive of mortality (odds ratio 45.0 (95% confidence intervals 34.7–58.3)) but pulmonary artery catheter was not (odds ratio 1.08 (0.87–1.33)). The results were similar in the three subgroups, and in none was pulmonary artery catheter independently predictive of mortality. Odds ratios for predictive values of propensity scores were: APACHE II <20, 79.3 (45.8–136.7); APACHE II 20–25, 14.8 (8.2–26.3); and APACHE II >25, 6.7 (4.7–9.7).

These results demonstrate that in our series of 4186 consecutive intensive care patients, the risk factors for pulmonary artery catheter insertion, but not pulmonary artery catheters themselves, were associated with excess mortality. These results are at variance with those of Connors and colleagues.

**Keywords:** intensive care, audit; complications, mortality; equipment, catheters pulmonary artery
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Fig 8 A preoxygenation period of 3 min was sufficient to enable the five breathing system filters (BSF) tested to achieve close to their equilibrium level of moisture-conserving performance.

References
2 Rosenbaum PR, Ruben DB. Biometrika 1983; 70: 41–55

Moisture output of breathing system filters during the first 3 min of simulated use

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Breathing system filters (BSF) are recommended for use in anaesthesia. The moisture-conserving performance of BSF varies widely. It has been demonstrated that BSF with a high moisture output significantly reduce the incidence of adverse airway events compared with BSF with a low moisture output in non-smoking patients during over-pressure with desflurane. In that study, it was assumed that the moisture-conserving performance of the BSF had reached equilibrium after a preoxygenation period of 3 min before over-pressure. We tested this assumption by measuring the moisture output of BSF during the first 3 min of simulated use.

Simulated use was achieved with a test rig ‘expiring’ air fully saturated with water vapour at 34°C, and ‘inspiring’ dry air through the BSF under test. An approximately square-wave of flow was used with a tidal volume of 0.5 litre, frequency of 10 bpm and an I:E ratio of 1:1. One-way valves in the test rig separated inspiratory and expiratory flows. Relative humidity and temperature of the inspiratory air was measured for 3 min. From these data, the moisture content of the end-inspired air was calculated for each breath. The test was repeated five times for five types of BSF.

Differences between the BSF were evident from the first breath. The moisture content of the end-inspired air after 3 min for the five BSF varied from 6.4 to 27.8 mg litre−1 (Fig. 8). Although the moisture content of the end-inspired air was still increasing at the end of the test, the increase was small (only approximately 0.1 mg litre−1 per breath).

Keywords: equipment, breathing filters

Use of dextrose to produce isobaric solutions of bupivacaine and bupivacaine–opioid combinations at 37°C

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The density of intrathecally administered agents may be an important factor in determining their spread within the subarachnoid space. However, only recently have the densities of these agents and that of human CSF been established with enough accuracy at body temperature to allow direct comparison. We have determined the dextrose concentration required to produce isobaric solutions of plain bupivacaine and bupivacaine–opioid combinations at 37°C.

The densities of 0.5% plain bupivacaine (Astra and Antigen) were determined at 37°C (±0.01°C) using a density meter (DMA 450, Paar Scientific Ltd) incorporating a mechanical oscillation technique and accurate to ±0.00001 g ml−1. Bupivacaine solution (8 ml) was added to 2 ml of several saline–dextrose combinations, calculated to produce final dextrose concentrations from 0 to 10 mg ml−1, and their densities measured. In order to simulate clinically used intrathecal mixtures, Antigen bupivacaine 8 ml was then added to 2 ml of the same saline–dextrose combinations containing either diamorphine 500 µg ml−1 or fentanyl 10 µg ml−1 and their densities measured. Mean density was calculated from five measurements. Data were analysed using two-way ANOVA and linear regression. Mean densities were compared with known densities of subgroups of human CSF, allowing estimation of baricity.

Undiluted bupivacaine solutions and bupivacaine mixed with saline–opioid combinations were hypobaric at 37°C. Astra and Antigen bupivacaine differed significantly in their densities over the range of dextrose dilutions (P<0.0001), and dextrose produced solutions of predictable density (Fig. 9). Opioids had a small but significant effect (P<0.0001) on density.

All dextrose concentrations were well below that of commercial hyperbaric bupivacaine, but could produce both hyperbaric and isobaric solutions. Using Antigen 0.5%
bupivacaine, dextrose concentrations of 2.5 mg ml$^{-1}$ and 3 mg ml$^{-1}$ produced isobaric solutions for term pregnant and pre-menopausal women, respectively. An isobaric solution for males or post-menopausal females can be produced using dextrose 4 mg ml$^{-1}$. Although both plain (hypobaric) and heavy (hyperbaric) bupivacaine are used intrathecally, the use of true isobaric solutions with spread being unaffected by gravity, may be useful in future research and clinical practice.

Acknowledgement
We thank SIMS Portex for funding this research.

Keywords: anaesthetics local, bupivacaine; analgesics opioid; physics, baricity

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2 Richardson MG, Wissler RN. Anesthesiology 1996; 85: 326–30

Predictors of cerebral oxygenation during warm cardiopulmonary bypass

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Jugular bulb oxygen desaturation ($S_jO_2 < 50\%$) has been detected in 17–84% of patients during rewarming from cold cardiopulmonary bypass (CPB). $S_jO_2$ desaturation and increased arterial jugular oxygen content difference ($AjDO_2 > 6$ ml dl$^{-1}$) during rewarming have been associated with impaired cognitive function after CPB. In this study, we have evaluated changes in jugular bulb oxygenation during warm CPB (temperature 34–37°C) using pH stat strategy.

We studied 20 patients undergoing coronary artery bypass grafting. Retrograde cannulation of the jugular bulb was performed and intermittent samples were obtained before CPB, 5, 20, 40, 60 min during CPB, before the end of CPB and after CPB. $S_jO_2$ and jugular bulb oxygen tension ($P_jO_2$) were measured and $AjDO_2$ and oxygen extraction ratio (OER) were estimated. Only two patients (10%) were desaturated at any time during CPB. Stepwise multiple regression analysis was performed between all measurements of $S_jO_2$, $P_jO_2$, OER and $AjDO_2$, and mean arterial pressure, CPB temperature, haemoglobin concentration (Hb) and arterial carbon dioxide tension ($P_aCO_2$) during CPB. $S_jO_2$, $P_jO_2$ and OER were dependent mainly on $P_aCO_2$ and Hb during CPB, and $AjDO_2$ was dependent only on $P_aCO_2$ (Table 5).

Desaturation in 10% of patients compared with 17–84% suggests that cerebral oxygenation is better preserved during warm CPB. The positive dependence of $S_jO_2$ and $P_jO_2$ on $P_aCO_2$ and Hb is consistent with the reported benefit of mild hypercapnia ($P_aCO_2 6.0–6.7$ kPa) and with the effect of excessive haemodilution.

Keywords: heart, cardiopulmonary bypass; brain, oxygen consumption; oxygen, saturation

Acknowledgements
We thank Professor W. W. Mapleson for statistical advice.

References

Table 5 Stepwise regression analysis between $AjDO_2$ (ml dl$^{-1}$), $S_jO_2$ (%), OER (%), $P_jO_2$ (mm Hg) and $P_aCO_2$ (mm Hg) and/or Hb (g dl$^{-1}$), for all measurements during warm CPB

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent variable</th>
<th>Regression coefficient (B)</th>
<th>SEM</th>
<th>t</th>
<th>P</th>
<th>95% CI for B</th>
</tr>
</thead>
<tbody>
<tr>
<td>$AjDO_2$</td>
<td>$P_aCO_2$</td>
<td>-0.11</td>
<td>0.02</td>
<td>-5.58</td>
<td>0.001</td>
<td>-0.15 to -0.07</td>
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<td>$S_jO_2$</td>
<td>$P_aCO_2$</td>
<td>0.89</td>
<td>0.13</td>
<td>6.72</td>
<td>0.001</td>
<td>0.62 to 1.14</td>
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<tr>
<td></td>
<td>Hb</td>
<td>1.83</td>
<td>0.89</td>
<td>2.01</td>
<td>0.04</td>
<td>0.06 to 3.60</td>
</tr>
<tr>
<td>OER</td>
<td>$P_aCO_2$</td>
<td>-0.86</td>
<td>0.15</td>
<td>-5.88</td>
<td>0.001</td>
<td>-1.15 to -0.57</td>
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<td></td>
<td>Hb</td>
<td>-2.42</td>
<td>0.99</td>
<td>-2.45</td>
<td>0.02</td>
<td>-4.38 to -0.46</td>
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<tr>
<td>$P_jO_2$</td>
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<td>1.01</td>
<td>0.10</td>
<td>9.80</td>
<td>0.001</td>
<td>0.81 to 3.54</td>
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<tr>
<td></td>
<td>Hb</td>
<td>2.15</td>
<td>0.70</td>
<td>3.07</td>
<td>0.003</td>
<td>0.76 to 3.54</td>
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</table>
Towards a ‘Mixifusor’? Simulating the addition of remifentanil to a target-controlled infusion of propofol

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The introduction of the commercial ‘Diprifusor’ system has transformed target-controlled infusion (TCI) from a research tool to a widely used clinical technique. We have used simulation technique to predict the consequences of adding remifentanil to a propofol TCI system.

Using the simulation software STANPUMP (http://pkpd.icon.palo-alto.med.va.gov/), we simulated a target-controlled propofol infusion set to achieved plasma concentrations of propofol of 4, 1, 3, 2, 2.5 and 0 µg ml\(^{-1}\) at 0, 20, 40, 60, 80 and 100 min, respectively. A second simulation predicted remifentanil concentrations which would occur if the 1% propofol syringe had contained remifentanil 40 µg ml\(^{-1}\) (i.e. 2 mg in 50 ml) (Fig. 10). These simulations assume no pharmacokinetic interaction between propofol and remifentanil.

Inspection of our simulations suggests that after an increase in propofol TCI target, effect-site remifentanil concentration overshoots and then stabilizes. This overshoot occurs while the effect-site propofol concentration is equilibrating with plasma. After a decrease in propofol TCI target, effect-site remifentanil concentration decreased by a greater proportion than the effect-site propofol concentration. During prolonged infusion, plasma remifentanil concentration decreased gradually as the TCI system reduced the rate of propofol infusion to reflect accumulation of the drug.

Stability studies have demonstrated the compatibility of propofol with lidocaine and alfentanil but there are no equivalent data for remifentanil. Furthermore, concoction of ad hoc drug mixtures may expose the responsible clinician to product liability although the practice is well established (e.g. droperidol–morphine mixtures for patient-controlled analgesia). Our simulations suggest that the use of a TCI propofol system with added remifentanil may expose the patient to rapid changes in remifentanil concentrations which are not related linearly to plasma propofol concentrations.

**Keywords**: analgesics opioid, remifentanil; anaesthetics i.v., propofol; anaesthetic techniques, target controlled

Comparison of intubating conditions after propofol and succinylcholine with those after propofol and remifentanil

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The technique of tracheal intubation under deep general anaesthesia using an i.v. induction agent supplemented with a high dose of a potent short-acting opioid has been reported previously. \(^1\) Remifentanil is a new, potent, short-acting opioid with a duration of action measured in minutes. \(^2\) These properties make remifentanil the opioid of choice to facilitate tracheal intubation, but subsequently allow rapid return of spontaneous respiration and airway reflexes.

In this prospective observer blind study, we evaluated intubating conditions, haemodynamic responses and resulting duration of apnoea in 60 healthy adult patients allocated randomly to one of three groups to receive a combination of propofol 2 mg kg\(^{-1}\) with bolus remifentanil 2 µg kg\(^{-1}\) or 4 µg kg\(^{-1}\), or succinylcholine 1 mg kg\(^{-1}\). After induction, the lungs were hand ventilated with 2% sevoflurane in 50% nitrous oxide in oxygen, and the trachea was intubated by an anaesthetist blind to the patient group. After intubation, patients were hand ventilated at 5 bpm using the gas mixture until resumption of spontaneous respiration.

Intubating conditions (mask ventilation, jaw mobility, vocal cord exposure, vocal cord position and movement) were graded by the anaesthetist on a three-point scale (1= optimal response and 3=unsatisfactory conditions) (Table 6).

In patients who received propofol and remifentanil 2 µg kg\(^{-1}\) or 4 µg kg\(^{-1}\), mean arterial pressure after induction decreased by 21% and 28%, respectively (**P**<0.05). Bradycardia of 35 beats min\(^{-1}\) was observed.

**Table 6** Grading of intubating conditions in the three groups (median (range)). *P*<0.05 between groups

<table>
<thead>
<tr>
<th>Mask ventilation</th>
<th>Jaw mobility</th>
<th>Vocal cord exposure</th>
<th>Vocal cord position</th>
<th>Movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Succinylcholine</td>
<td>1 (1–1)</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
<td>1 (1–2)</td>
</tr>
<tr>
<td>Remifentanil 2 µg kg(^{-1})</td>
<td>1 (1–2)</td>
<td>1 (1–1)</td>
<td>1 (1–2)</td>
<td>2 (1–3)*</td>
</tr>
<tr>
<td>Remifentanil 4 µg kg(^{-1})</td>
<td>1 (1–3)</td>
<td>1 (1–1)</td>
<td>1 (1–2)</td>
<td>1 (1–3)</td>
</tr>
</tbody>
</table>

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**Fig 10** Predicted concentrations of propofol in plasma (thick curve) and at the effect site (top thin curve), and of remifentanil at the effect site (bottom thin curve). For clarity, plasma remifentanil concentrations have been omitted.
in one patient in the 4 µg kg⁻¹ remifentanil group that was treated with atropine. Time to return to spontaneous respiration was mean 6 min in the succinylcholine group and 9 and 13 min, respectively, in the remifentanil 2 µg kg⁻¹ and 4 µg kg⁻¹ groups (P<0.05).

We have demonstrated that after remifentanil, intubating conditions were dose dependent, and were indistinguishable at the higher remifentanil dose from intubating conditions produced with succinylcholine.

Keywords: intubation tracheal; neuromuscular block, succinylcholine; anaesthetics i.v., propofol; analgesics opioid, remifentanil

References

Does addition of ankle block for day-case foot surgery improve patient satisfaction?

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Day-case foot surgery can be very painful after operation because of the bony involvement. A foot block can be given to reduce postoperative pain but may result in severe pain when it has worn off when the patient is at home.

We studied 42 ASA I or II patients undergoing day-case bony surgery to one foot (e.g. Mitchell’s, Keller’s), allocated randomly to one of two groups. All patients were anaesthetized using propofol, fentanyl, isoflurane and a laryngeal mask, with morphine and a non-steroidal anti-inflammatory given at the discretion of the anaesthetist. Those in the block group were given 0.5% plain bupivacaine 20 ml to three nerves at the ankle (superficial peroneal, deep peroneal and posterior tibial). No placebo block was given to the patients in the control group and therefore the anaesthetist was not blind. Patients were not informed of their allocated group.

Patients were discharged with routine oral analgesia. All were followed-up by telephone questionnaire on the first and second days after operation by one of the authors not present in theatre, who was thus blind to group allocation. Patients were asked the time after operation when they first felt pain, a verbal incremental pain score (1–10) to assess first night pain, pain at the time of interview on the first and again on the second postoperative day, together with a final satisfaction score (1=same again to 4=very bad). No patient consulted their general practitioner or accident and emergency department during the follow-up period. Three patients were excluded from analysis because overnight admission was needed (two in the block group and one in the control group).

We were surprised that despite those who received a block having a significantly longer time to first recall of pain, this did not affect pain severity experienced on the first night or overall satisfaction score (Table 7). These findings concur with those of Needoff, Radford and Costigan, who found no difference in pain beyond 6 h after foot surgery. We made no attempt to change anaesthesia or routine postoperative management (thus the lack of data before discharge from hospital). Also, we did not actively assess the effectiveness of each block, although many blocks must have worked given the data for time to first pain.

We conclude that ankle blocks are a good adjunct to early postoperative pain relief with no worsening of pain control when wearing off on the first postoperative night, but do not improve patient satisfaction.

Keywords: anaesthesia, day-case; anaesthetic techniques, regional; surgery, orthopaedic

Reference

| Table 7 Time after operation when patients first felt pain, pain score (1–10) on the first night after operation, pain at the time of interview on the first and second postoperative days and satisfaction score (1=same again to 4=very bad) in the block and control groups (mean (range) or median (range)); **P<0.01 (Mann-Whitney) |
|---|---|
| Foot block group | Control group |
| (n = 18) | (n = 21) |
| Age (yr) | 51 (21–77) | 57 (25–78) |
| Duration of anaesthetic (min) | 32 (20–45) | 39 (20–60) |
| Time to first pain (h) | 12 (0–24) | 5.5 (0–24)** |
| Median pain, first night (1–10) | 4 [1–10] | 5 [1–8] |
| Median pain, first postop. day (1–10) | 5 [2–10] | 5 [1–10] |
| Median pain, second postop. day (1–10) | 4 [1–9] | 3.5 [1–7] |
| Median overall satisfaction (1–4) | 1.0 [1–4] | 1.5 [1–4] |

Recovery profiles after day-case diagnostic gynaecological laparoscopy: comparison of two anaesthetic techniques over 1 week follow-up

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New drugs permit rapid recovery from anaesthesia but few data describe patient outcome after hospital discharge. In this study, we have compared prospectively, over 1 week, the recovery profiles of two anaesthetic techniques in 100 patients undergoing day-case diagnostic gynaecological laparoscopy.
Table 8 Recovery profiles of two anaesthetic techniques (inhalation (INH) or i.v.) in patients undergoing day-case diagnostic gynaecological laparoscopy. Statistical analysis was performed using the chi-square test

<table>
<thead>
<tr>
<th></th>
<th>INH (n=49)</th>
<th>I.v. (n=46)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required morphine in recovery (n)</td>
<td>2</td>
<td>9</td>
<td>0.018</td>
</tr>
<tr>
<td>Vomited during journey home (n)</td>
<td>5</td>
<td>0</td>
<td>0.02</td>
</tr>
<tr>
<td>Minor accidents on day 1 postop. (n)</td>
<td>5</td>
<td>0</td>
<td>0.02</td>
</tr>
<tr>
<td>Energy level returned to normal on day 1 (n)</td>
<td>8</td>
<td>20</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Patients were allocated randomly to receive an inhalation (INH) or i.v. anaesthetic technique (n=50 in each group). Group INH received a mean dose of fentanyl of 2.3 (sd 0.6) µg kg⁻¹, propofol 2.5 (0.7) mg kg⁻¹, 0.8% end-tidal isoflurane and 66% nitrous oxide in oxygen. The i.v. group received remifentanil 0.43 (0.13) µg kg⁻¹ min⁻¹, propofol 4.1 (1.1) mg kg⁻¹, air and oxygen. Tracheal intubation was facilitated by mivacurium 0.15 mg kg⁻¹ which was antagonized by glycopyrrolate–neostigmine. Analgesia comprised rectal diclofenac 100 mg and 0.25% bupivacaine 20 ml to the pouch of Douglas and incision sites at the end of surgery. Patients underwent a structured interview with the research nurse before operation and then daily for 7 days to establish PONV, pain, quality of life and effects to the community. Patients and the nurse were blind to the anaesthetic technique. Five patients were excluded after randomization: one for surgical and four for anaesthetic reasons (mivacurium apnoea, laryngospasm with re-intubation, hiatus hernia, study drug unavailable and hospital admission for urinary retention). We report the in-hospital phase of this study and 7 days after recovery. The groups were similar in patient characteristics and had similar Palazzo scores.¹

Times to extubation and duration of stay in each part of the three-stage recovery process were similar, as were pain and nausea scores in hospital and during the journey home. There was significantly less vomiting during the journey home in the i.v. group (Table 8). Over 7 days, pain and analgesic requirements were similar in both groups, as were nausea and vomiting. On day 1 after operation, there were less accidents and more patients felt their energy level had returned to normal in the i.v. group (Table 8) but there was no overall difference between the two groups in burden to the community in respect of general practitioner consultations, days off work by the patient or their partner, help at home or other use of social services. I.v. anaesthesia for diagnostic gynaecological laparoscopy reduced early morbidity but did not accelerate discharge from hospital.

Keywords: anaesthetics i.v., propofol; analgesics opioid, remifentanil; anaesthesia, day-case; surgery, laparoscopy

Acknowledgement
P. J. V. was supported by Zeneca and Glaxo-Wellcome.

Reference
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Measuring the cost of desflurane anaesthesia

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The cost of drugs is an important consideration for budget managers, but comparisons between inhalation anaesthetics are not straightforward. Simply comparing the cost of the liquids and scaling for MAC neglects the reduced inspired–expired differences of less soluble anaesthetics and the cost advantage this brings, especially in rebreathing systems. Weiskopf and Eger designed a method based on a model of anaesthetic uptake and distribution, and used it to compare the cost of anaesthesia with isoflurane and desflurane at different fresh gas flows¹; it has never been tested. We report results using a similar method, and have compared our calculations with actual measurements.

The model of uptake and distribution we have adopted is a revised version of Narkup,² assuming a five-compartment body based on Yasuda and colleagues’ results³ and recent solubility data.⁴ We also re-analysed our database of computer-controlled anaesthetics containing measurements of the amount of anaesthetic actually used to maintain 1.3 MAC end-expired in a closed system and the inspired concentrations generated. From this we calculated the amount that would have been used in an open system with a fresh gas flow of 6 litre min⁻¹.

Figure 11 shows the relative volumes of isoflurane and desflurane used at 1.3 MAC (i.e. 1.5% and 8% end-expired, respectively) with a fresh gas flow of 6 litre min⁻¹ and at basal fresh gas flows. Thick curves=data from patients; thin curves=calculations using Narkup; and broken curves=calculations by Weiskopf and Eger.¹

Keywords: anaesthetics volatile, desflurane; anaesthetics volatile, isoflurane
Obstetric anaesthetic charts: a national survey

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Since 1989, a minimum data set has been published by the Obstetric Anaesthetists Association (OAA)1 for use by obstetric anaesthetists to record data from general anaesthesia and regional anaesthesia and analgesia. In addition, the Royal College of Anaesthetists (RCA) have published an anaesthetic record set.2 In this survey, we have investigated how far these professionally developed word-based record systems have been incorporated into obstetric anaesthetic record systems and what additional details in the form of words, layout or diagrams have been incorporated. The OAA database of maternity units was used and consultant anaesthetists were requested to forward epidural and anaesthetic charts to one of the authors. Of 207 maternity units surveyed, there were 159 replies (77%); 142 charts were obtained and of these 11 were duplicates from hospitals within the same trust. The majority of labour ward anaesthetic records were for epidural analgesia and of these 14 (11%) included a general anaesthetic record. Separate forms for general anaesthesia were sent by 55 of these 14 (11%) included a general anaesthetic record. The majority of records used and consultant anaesthetists were requested to forward epidemic and anaesthetic charts to one of the authors. Of

<table>
<thead>
<tr>
<th>Item</th>
<th>Charts surveyed</th>
<th>RCA1</th>
<th>OAA2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Maternal details (e.g. parity)</td>
<td>80 (61%)</td>
<td>na</td>
<td>Present</td>
</tr>
<tr>
<td>2. Regional analgesia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Consent: verbal/written</td>
<td>269 (27%)</td>
<td>Present</td>
<td>na</td>
</tr>
<tr>
<td>(b) Type of block</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidural</td>
<td>131 (100%)</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Spinal</td>
<td>41 (31%)</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Combined (CSE)</td>
<td>19 (14%)</td>
<td>Present</td>
<td>na</td>
</tr>
<tr>
<td>(c) Entry site</td>
<td>109 (83%)</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>(d) Needle used</td>
<td>42 (32%)</td>
<td>Present</td>
<td>na</td>
</tr>
<tr>
<td>(e) Catheter (Y/N)</td>
<td>98 (74%)</td>
<td>Present</td>
<td>na</td>
</tr>
<tr>
<td>3. Graded intubation difficulty</td>
<td>22 (41%)</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>4. Outcome complications</td>
<td>72 (55%)</td>
<td>na</td>
<td>Present</td>
</tr>
</tbody>
</table>

from others. These corporate findings may assist future development of obstetric anaesthetic and analgesic forms.

Keywords: anaesthesia, obstetric; anaesthesia, audit; records, anaesthesia

Acknowledgement
This study was supported by an OAA grant and we thank all contributors.

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An audit of the use of alarms in anaesthetic monitoring

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Alarms are now a feature of almost all theatre monitoring equipment and cover a large number of monitored variables. A consensus has reported that alarms should be used in anaesthetic practice1 and that not using alarms is risky.2 We felt that if alarms are to be fully effective in improving patient safety, the anaesthetist should be aware of the alarm settings. Therefore, we carried out an audit of anaesthetists’ awareness of alarm settings in equipment used in theatres throughout the United Bristol Healthcare Trust.

Between December 1998 and April 1999, 51 anaesthetists of all grades (33 consultants, 16 SpRs, 2 SHOs) were approached once each in a ‘quiet’ period during either an emergency or elective procedure. We asked them if they could (without reference to the equipment) quote (or guess) their current alarm settings for oxygen saturation ($SpO_2$) (minimum), systolic arterial pressure (SAP) (minimum and maximum), heart rate (HR) (minimum and maximum),
inspired oxygen fraction ($F_{O_2}$) (minimum) and end-tidal carbon dioxide tension ($e'_{CO_2}$) (minimum and maximum). The actual alarm settings were recorded. Our enquiries also included whether the default alarm settings were being used and whether one or more alarms were disabled permanently. We also recorded the default alarm settings that were in use in the different theatres in the United Bristol Healthcare Trust.

Only one of the 51 anaesthetists was aware of all the alarm limits. Thirty-two (65%) were aware of the settings for $Sp_o_2$ and 26 (51%) for $F_{O_2}$. For all other variables, fewer than 50% of anaesthetists were aware of the alarm settings, with only nine (17%) being aware of the minimum setting for $e'_{CO_2}$. The 29 anaesthetists who relied on default settings were less aware of alarm settings than the 22 who had themselves set one or more alarms. Even among these 22, the level of awareness was still surprisingly low: less than 11 (50%) could quote their current settings for maximum HR, minimum SAP and $e'_{CO_2}$. The 29 anaesthetists who relied on default settings were less aware of alarm settings than the 22 who had themselves set one or more alarms. Even among these 22, the level of awareness was still surprisingly low: less than 11 (50%) could quote their current settings for maximum HR, minimum SAP and $e'_{CO_2}$, and only 16 (72%) could quote the setting for $Sp_o_2$, for which awareness was highest. Three anaesthetists had permanently disabled one or more alarms. There was an appreciable variation in default alarm settings throughout the trust, the most striking being a setting for minimum $F_{O_2}$ of 0.18.

One consequence of this audit has been a departmental agreement to standardize the default alarm settings on all anaesthetic machines throughout the trust (with the exception of the children’s hospital). We plan to re-audit in June 1999 to see if our anaesthetists are more aware of their alarm settings.

**Keywords:** anaesthetists, performance; equipment, alarms; anaesthesia, audit

**References**


**The ‘METI’ simulator at the Bristol Medical Simulation Centre**

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At the heart of the Bristol Medical Simulator Centre is the ‘METI’ manikin and associated software, developed by Medical Educational Technology Inc together with the University of Gainsville, Florida. It combines physical and software features that allow interfacing with real anaesthetic and monitoring equipment so as to provide ‘high fidelity’ simulation and promote suspension of disbelief that a real situation is in progress. Experienced operators and teachers on the simulator can and have provided very realistic scenario-based training to a variety of personnel of all grades of experience and seniority. Satisfactory scenario-based teaching requires careful preparation and scripting that can make allowance for aspects of the system’s performance that depart importantly from known realities. These departures render the system less than satisfactory for attempts at flexible, *ad lib* problem-based tutorial teaching. None the less, we have used this type of educational exercise with undergraduate medical students, posing the question, ‘This is what the simulator does—is it right?’ We do not have access to the controlling software and have to adopt a ‘black box’ approach to what is effectively free ‘beta testing’.

Events (such as administering a drug or imposing PEEP) are logged automatically, as are respiratory and haemodynamic data every 5 s. Other information (such as neuromuscular block) can be displayed and recorded manually. Study of this information has revealed several interesting anomalies, including the following.

1. With the manikin breathing air, $P_{a_{CO_2}}$ is typically approximately 4.5–5.3 kPa, but $P_{a_{CO_2}}$ is typically about 17.3 kPa, in defiance of the alveolar gas equation.

2. At the same time, and with pulmonary venous admixture (‘shunt’) set at zero, $P_{a_{O_2}}$ is typically 15.3 kPa, making it difficult to teach about abnormal pulmonary gas exchange when normal gas exchange cannot be simulated as a starting point.

3. When a ‘shunt’ is imposed, it is a ‘true shunt’, giving $P_{a_{O_2}}$ that is virtually insensitive to changes in $F_{O_2}$.

4. The resulting hypoxaemia in these conditions is accompanied by an increase in cardiac output, but without disturbance in systolic or diastolic arterial pressure.

5. When PEEP is imposed in software after a shunt has been set, $P_{a_{O_2}}$ increases and becomes somewhat more sensitive to $F_{O_2}$, and cardiac output decreases but lung volume does not change.

6. When PEEP is imposed by a ventilator without simultaneously imposing software PEEP, lung volume changes but the above effects do not take place.

7. When anaesthesia is induced with propofol, arterial pressure decreases but without change in CVP, which is in variance with classical teaching that induction of anaesthesia is accompanied by a major effect on venous capacitance.

8. Succinylcholine produces a brief, but otherwise plausible, dose-dependent decrease and complete recovery of neuromuscular transmission, except for the fact that relaxation is antagonized by prior administration of neostigmine.

9. Non-depolarizing neuromuscular blocking agents produce a plausible onset of relaxation, but recovery of neuromuscular transmission is followed only to approximately 40%, after which it switches abruptly to 100%. This anomaly then ‘infests’ the response to a subsequent dose of succinylcholine.

**Keywords:** computers, simulation; anaesthetist, training; model, computer simulation
Effect of midazolam on cilia survival

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Effective mucus transport depends on the interaction of mucus and respiratory cilia. In vitro experiments have shown that some anaesthetic agents used in intensive care significantly decrease cilia beat frequency.1 Although midazolam has no significant effect on human cilia beat frequency in vitro,2 other features of cilia also affect mucus transport. Loss of cilia, in particular, has been associated with impaired mucus transport in patients undergoing tracheal intubation.3 We have investigated the effect of midazolam on cilia survival, in terms of percentage cilia coverage, using rat tracheal half-rings and a method reported previously.4

Pairs of rat tracheal half-rings in culture (10% newborn calf serum in medium 199, in a humid atmosphere at 37°C) were exposed to midazolam 150 µmol litre–1 over a period of 5 days. Fresh half-rings were fixed in 2.5% glutaraldehyde for 1 h before dehydration in ethanol and critical point drying with carbon dioxide. The half-rings were mounted on aluminium stubs, coated with gold and examined with a scanning electron microscope at a magnification of x2000. Pairs of half-rings (exposed and control) were examined on days 1, 3 and 5. A digital image recording system collected nine contiguous images of ciliated epithelium from each half-ring. These were analysed using a customized image analysis script (Quantimet-570) where cilia abundance was quantified in terms of percentage area cover by a researcher blinded to the study treatment.

The slight increase in cilia coverage associated with midazolam was unexpected (Table 10) and of unknown significance.

Acknowledgements

J. K. was funded by Anaesthesia Research Plymouth and the University of Plymouth (Faculty of Science). Hilary Sanders kindly assisted with the statistical analysis.

Keywords: lung, cilia; hypnotics benzodiazepine, midazolam

Table 10 Percentage cilia cover (mean (SD)) of sets of 10 rat tracheal half-rings. Nine images were averaged for each half-ring. There was a significant difference between treatments (P=0.02); there were no effects caused by day or animal (P>0.05) (three-factor ANOVA for day, animal and treatment).

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>3</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>60.9 (10.9)</td>
<td>65.3 (8.8)</td>
<td>61.3 (14.6)</td>
<td>72.9 (10.8)</td>
</tr>
<tr>
<td>Midazolam</td>
<td>66.1 (9.4)</td>
<td>77.7 (9.6)</td>
<td>75.9 (11.1)</td>
<td></td>
</tr>
</tbody>
</table>

References

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Warm air sensation for assessment of sensory level after spinal anaesthesia

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Ethyl chloride spray and pinprick are the most frequently used methods of assessment of the level of sensory block after spinal anaesthesia, but are associated with pollution, expense (ethyl chloride), discomfort and risk of infection (pinprick). Recently, a gas jet method, involving delivery of oxygen 2 litre min–1 via a length of oxygen tubing held 1 cm from the skin, compared favourably with pinprick and ethyl chloride.1 We evaluated a new method of assessing sensory level based on warm sensation.

A respiratory gas humidifier (MR-730, Fisher and Paykel) was adjusted to give a constant flow of warm, humidified air at 40±0.2°C, which gave a pleasantly warm sensation when oxygen flow was maintained at 10 litre min–1 and held 1 cm from the patient’s skin. We studied 30 women undergoing elective Caesarean section under standard spinal anaesthesia. In the recovery room at the end of surgery, the upper sensory level was assessed in the midclavicular line independently by two anaesthetists. One used the warm air jet moving in a cephalad direction (i.e. numb to normal) and the other (blind to the first result) used ethyl chloride spray in the same way immediately afterwards. The sequence of testing was allocated randomly and results were recorded on a standard dermatome chart. Bilateral testing on 30 patients provided 60 comparisons between the methods.

Differences in sensory level detected showed a skewed distribution (Komolgorov–Smirnov test, P=0.001). There were no significant differences in dermatomal sensory level detected by the two methods using the Wilcoxon signed ranks test (median 0 (interquartile range difference 0–1); P=0.65). A plot of the limits of agreement between the two methods, as described by Altman and Bland2 (Fig.12), indicated that all but two of the 60 comparisons lay within the 95% limit of agreement (approximately 1.5 dermatomal levels about the median). As this range would not usually be clinically significant, we conclude that the warm air jet method compares favourably with the ethyl chloride method and that these could be used interchangeably.

Proceedings of the Anaesthetic Research Society
Weaning failure in two critically ill patients is associated with changes in myosin subtypes

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Generalized skeletal muscle weakness has been recognized as the predominant condition of weaning failure in critically ill patients. Several underlying mechanisms (e.g. critical illness polyneuropathy) have been suggested¹ but the causes remain obscure. Based on the results of mechanomyographic measurements using a double-pulse stimulation pattern with changing inter-stimulus intervals, we recently hypothesized intracellular changes other than muscle fibre loss as one contributing factor.² Accordingly, we present the results of myofibril analysis performed in muscle specimens from two critically ill patients during weaning failure.

Patient No. 1 was an 18-yr-old male liver transplant recipient who could not be weaned after 18 days of mechanical ventilation although he had recovered from postoperative ARDS. Patient No. 2 was a 24-yr-old female liver and kidney transplant recipient who had recovered from several postoperative SIRS–sepsis periods. Muscle specimens were obtained from the quadriceps femoris muscle (vastus medialis). We used sodium dodecyl sulphate-polyacrylamide gel electrophoresis to separate myosin heavy chain (MHC) isoforms³ and two-dimensional gel electrophoresis to separate tropomyosin (TM) and myosin light chain (MLC) isoforms.⁴ ⁵

The muscle specimen of patient No. 1 showed 35% MHC I, 23% MHC IIa and 42% MHC IIb. In the specimen of patient No. 2, the isoform distribution was 10% MHC I and IIa, and 90% MHC IIb. In both specimens, neither slow MLC nor slow TM isoforms were detected. All MLC and TM present were of the fast type.

In contrast with muscles of immobilized patients,⁶ those of the two critically ill patients expressed predominantly the anaerobic, fast-twitch, non-fatigue resistant MHC IIb isoform. This fibre type distribution shift commonly occurs within the first 2 yr after severe spinal cord injury.⁷ Moreover, as we could not detect slow MLC or slow TM isoforms, we must conclude that all MHC I were dysfunctional. Under this condition, the muscle is still able to contract but fatigues rapidly. Therefore, changes in myosin composition may be a possible explanation of weaning failure.

References

Pain scores after total hip arthroplasty: prospective, randomized, open comparison of two analgesic techniques

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Epidural techniques are used widely to provide postoperative analgesia after total hip arthroplasty (THA) but they may be associated with serious morbidity.¹ In this study, we determined if the combination of lumbar and sacral plexus block (LSPB) with i.v. patient-controlled (PCA) morphine produced similar analgesia to an epidural infusion after THA.

We decided that a 10-mm difference in mean pain scores was clinically significant and hence 24 patients were
Table 11 Pain scores in the lumbar and sacral plexus block (LSPB) (n=21) and epidural infusion (n=23) groups after total hip arthroplasty (THA). U values= two-sample Mann–Whitney U test of VAS data

<table>
<thead>
<tr>
<th></th>
<th>24 h at rest</th>
<th>24 h movement</th>
<th>48 h at rest</th>
<th>48 h movement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LSPB</td>
<td>Epidural</td>
<td>LSPB</td>
<td>Epidural</td>
</tr>
<tr>
<td>Median</td>
<td>24</td>
<td>43</td>
<td>39</td>
<td>58</td>
</tr>
<tr>
<td>Mean</td>
<td>24.5</td>
<td>39.1</td>
<td>42.3</td>
<td>56.4</td>
</tr>
<tr>
<td>SD</td>
<td>15.9</td>
<td>27.2</td>
<td>18.8</td>
<td>29</td>
</tr>
<tr>
<td>U value</td>
<td>0.06</td>
<td>0.04</td>
<td>0.22</td>
<td>0.86</td>
</tr>
</tbody>
</table>

required in each group (α=0.05, β=0.2). We studied 46 ASA I–III patients (mean age 64 (range 41–86) yr) presenting for primary, unilateral THA. Each patient received either LSPB or an epidural. A nerve stimulator was used to identify each plexus paravertebrally and 0.25% bupivacaine 30 ml with clonidine 75 µg was injected at each site. The lumbar epidural was established with 0.25% bupivacaine up to 20 ml. All patients received a standardized general anaesthetic. Postoperative analgesia was provided using either i.v. PCA morphine (1-mg bolus, 5-min lockout, no background infusion (LSPB group)) or an epidural infusion (0.167% bupivacaine up to 10 ml h⁻¹). Catheterization and DVT prophylaxis followed standard ward procedures. Pain scores were assessed on the first two days after operation using a 100-mm retrospective visual analogue scale (VAS).

After randomization, two patients failed to understand the VAS concept and were excluded. Patient characteristics were similar in the two groups as were mean anaesthetic time, mean total blood loss, mean time to mobilization and hospitalization periods, incidence of urinary catheterization and DVT, mean time to mobilization and hospitalization periods, incidence of urinary catheterization and DVT, mean time to mobilization and hospitalization periods, incidence of urinary catheterization and DVT. Interim analysis of the pain scores for the two groups is presented in Table 11.

There is currently insufficient statistical evidence to reject the null hypothesis. Thus far the two techniques have provided comparable postoperative analgesia after THA.

Keywords: pain, postoperative; surgery, orthopaedic; analgesic techniques, epidural; analgesic techniques, regional

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Bolus vs cumulative administration of halothane for contracture testing in malignant hyperthermia diagnosis

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One of two protocols for malignant hyperthermia (MH) diagnosis is followed by the majority of MH centres throughout the world. The first of these to be published was that of the European MH Group. The North American MH Group protocol took longer to evolve but is now quite similar to the European protocol. The main difference between the two is that, for the in vitro muscle contracture studies, halothane is added cumulatively in concentrations of 0.5%, 1% and 2% in the European protocol but is added as a single bolus concentration of 3% in the North American protocol. Consequent differences in describing the MH phenotype present a potential problem for collaborative molecular genetic studies. We have compared the two types of halothane tests in 102 consecutive patients attending for MH diagnosis.

The muscle biopsy procedure and in vitro contracture tests for diagnostic purposes (including a cumulative halothane test) were performed as described previously, according to the European MH Group protocol. Patients were classified as MH susceptible (MHS) if both halothane and caffeine tests were abnormal, MH equivocal (MHE) if one or other test was abnormal or MH negative (MHN) if both tests were normal. An additional muscle strip was used for exposure to a bolus of 3% halothane and the test considered positive if the tension generated was ≥0.7 g.

Patients were classified according to the diagnosis made using the European MH protocol (MHS, MHE or MHN) and the response to 3% halothane (positive or negative). MHS=MH susceptible if both halothane and caffeine tests are abnormal, MHE=MH equivocal if one or other test is abnormal and MHN=MH negative if both tests are normal

<table>
<thead>
<tr>
<th>3% bolus halothane result</th>
<th>European protocol diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>MHS</td>
</tr>
<tr>
<td>Negative</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

Incorporation of an equivocal diagnostic category in the
North American protocol, along similar lines to that in the European protocol, would improve concordance of phenotyping for research purposes without significantly increasing the potential error rate of phenotyping.

Keywords: malignant hyperthermia; anaesthetics volatile, halothane

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Pressure support ventilation in the anaesthetized patient using the laryngeal mask airway

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The aim of this study was to investigate the effects of pressure support ventilation (PSV) on the pattern of spontaneous respiration in patients breathing via a laryngeal mask airway (LMA). A small number of studies have been published using a fixed level of PSV via a tracheal tube in anaesthetized patients.1–3 These studies were designed predominantly to measure the effects of PSV on the work of breathing.

We studied eight unpremedicated ASA I patients undergoing general anaesthesia for elective peripheral orthopaedic surgery. No patient was obese or had dyspeptic symptoms. All measurements were made before the start of surgery. After induction of anaesthesia with propofol, anaesthesia was maintained with 1% end-tidal isoflurane and 60% nitrous oxide in oxygen via the LMA. The cuff of the LMA was inflated until no leak was detected by auscultation over the larynx during gentle manual ventilation. The patient was then allowed to breathe via a standard circle system during a period of stabilization. When a regular respiratory rhythm had been established, the patient was switched to a Siemens 900C ventilator and placed on 2 cm H2O of pressure support. After each subsequent 5-min period, pressure support was increased by 2 cm H2O, and this was continued until a significant reduction in ventilatory frequency was noted (<8 bpm) or a leak around the laryngeal mask was detected by auscultation. Pressure support was then decreased by 2 cm H2O. Airway pressure, flow, tidal volume, end-tidal carbon dioxide and tidal carbon dioxide excretion (\(V_{\text{CO}}\)) were displayed continuously on a chart recorder. Radial artery blood-gas values were obtained before starting PSV and again at the maximum PSV level achieved.

The maximum level of PSV was 6–14 cm H2O. No patient became hypoxic or haemodynamically unstable at any time. All patients showed a decrease in ventilatory frequency (mean change 11 (range 4–23) bpm), and all patients showed an increase in tidal volume (mean change 140 (range 75–532) ml). In six of eight patients, a decrease in arterial carbon dioxide occurred at the maximum level of PSV. Mean change was –0.46 (range –1.15 to 0.47) kPa. All patients developed an irregular respiratory pattern at some time as PSV was increased. This was reversible by decreasing PSV to its previous level. In four patients, PSV was increased deliberately when the respiratory rhythm became irregular: this resulted in a further increase in tidal volume and a return to regular breathing.

In the small number of patients studied so far, it appears that PSV partially overcomes the respiratory depressant effects of isoflurane anaesthesia in some patients. Further investigation is needed to ascertain the clinical usefulness of this technique.

Keywords: equipment, masks anaesthesia; ventilation, pressure support

Acknowledgement
We thank Dr R. Fletcher for the loan of equipment.

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