Within-breath arterial PO₂ oscillations in an experimental model of acute respiratory distress syndrome

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Tidal ventilation causes within-breath oscillations in alveolar oxygen concentration, with an amplitude which depends on the prevailing ventilator settings. These alveolar oxygen oscillations are transmitted to arterial oxygen tension, PaO₂, but with an amplitude which now depends upon the magnitude of venous admixture or true shunt, Qs/Qt. We investigated the effect of positive end-expiratory pressure (PEEP) on the amplitude of the PaO₂ oscillations, using an atelectasis model of shunt. Blood PaO₂ was measured on-line with an intravascular PaO₂ sensor, which had a 2–4 s response time (10–90%). The magnitude of the time-varying PaO₂ oscillation was titrated against applied PEEP while tidal volume, respiratory rate and inspired oxygen concentration were kept constant. The amplitude of the PaO₂ oscillation, ΔPao₂, and the mean PaO₂ value varied with the level of PEEP applied. At zero PEEP, both the amplitude and the mean were at their lowest values. As PEEP was increased to 1.5 kPa, both ΔPao₂ and the mean PaO₂ increased to a maximum. Thereafter, the mean PaO₂ increased but ΔPao₂ decreased. Clear oscillations of PaO₂ were seen even at the lowest mean PaO₂, 9.5 kPa. Conventional respiratory models of venous admixture predict that these PaO₂ oscillations will be reduced by the steep part of the oxyhaemoglobin dissociation curve if a constant pulmonary shunt exists throughout the whole respiratory cycle. The facts that the PaO₂ oscillations occurred at all mean PaO₂ values and that their amplitude increased with increasing PEEP suggest that Qs/Qt, in the atelectasis model, varies between end-expiration and end-inspiration, having a much lower value during inspiration than during expiration.

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Krogh and Lindhard, in 1914,¹ hinted that alveolar and arterial oxygen tensions, PaO₂ and Pao₂ respectively, could fluctuate during the respiratory cycle. Bergman, in 1961,² confirmed this hypothesis with an animal model using arterial saturation, Sargo, as a proxy for PaO₂. Although Bergman was not able to measure Pao₂ continuously, he hypothesized that fluctuations in Sargo, during the respiratory cycle might be due to the pulmonary shunt fraction (Qs/Qt) changing between the inspiratory and expiratory phases of the respiratory cycle. Further isolated studies over the past 30 yr have shown that oscillations in arterial oxygen tension, cotemporaneous with the respiratory cycle, do occur and that they are most apparent in the presence of hypoxaemia or significant venous admixture.³–⁴ The origin of these oscillations, with peak-to-peak amplitude denoted by ΔPao₂, are thought to be in the complex interaction between the continuous process of gas exchange and the tidal process of the ventilation respiratory cycle.⁵–⁷ We considered that if variations in Qs/Qt caused by atelectasis occurring during expiration and alveolar reopening during inspiration, did occur in the lung, then the amplitude of the oscillations would be sensitive to the application of PEEP when both the inspired oxygen fraction (FiO₂) and the ventilator settings were kept constant. We assessed the effect of PEEP on
Table 1 The effect of increasing (upper of each pair of rows) and decreasing (lower row) PEEP on blood gases, oxygen saturation, peak airway pressure, shunt fraction, cardiac output and arterial blood pressure. The mean (sd) is shown for seven animals unless indicated by a superscript number. Blood-gas values were corrected to 38°C. Statistical significance was assessed using the paired Student’s t-test (unpaired when n not equal). *P<0.05 from the postlavage value; **value of the variable at 0 PEEP significantly (P<0.05) altered by 2 kPa PEEP; ***Value of the variable during lung inflating at a given PEEP level significantly different (P<0.05) from the value during deflation. Otherwise no statistical differences were found.

<table>
<thead>
<tr>
<th></th>
<th>Before lavage</th>
<th>After lavage PEEP (kPa)</th>
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<tbody>
<tr>
<td></td>
<td>0</td>
<td>0.5</td>
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<tr>
<td>PaO₂ (kPa)</td>
<td>56.6 (2.5)</td>
<td>9.5 (0.7)*</td>
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<tr>
<td>PaCO₂ (kPa)</td>
<td>8.8 (1.3)</td>
<td>6.5 (1.1)*</td>
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<tr>
<td>SaO₂ (%)</td>
<td>100 (0)</td>
<td>82 (5.9)</td>
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<tr>
<td>Peak airway pressure (kPa)</td>
<td>1.7 (0.4)</td>
<td>2.8 (0.3)*</td>
</tr>
<tr>
<td>Shunt fraction (%)</td>
<td>6 (1)**</td>
<td>53 (16)*</td>
</tr>
<tr>
<td>Cardiac output (litre min⁻¹)*</td>
<td>2.4 (0.7)</td>
<td>2.1 (0.7)</td>
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<tr>
<td>Systolic pressure (kPa)*</td>
<td>20.6 (1.5)</td>
<td>13.4 (2.8)*</td>
</tr>
<tr>
<td>Diastolic pressure (kPa)*</td>
<td>15.8 (2.0)</td>
<td>8.5 (3.5)*</td>
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ΔPaO₂ in an experimental model of atelectasis [simulating acute respiratory distress syndrome (ARDS)] which developed moderate to severe levels of pulmonary shunt.

Methods and results

In seven adult female dogs (weight range 10.4–13.3 kg), anaesthesia was induced by i.v. pentobarbitone sodium (60 mg ml⁻¹) and maintained by infusion (60–180 mg ml⁻¹). The surgical preparation was performed as described elsewhere.

A prototype intravascular PO₂ sensor (IE Sensors, Salt Lake City, Utah, USA) was inserted into the aorta and left to stabilize. This Clark-type amperometric sensor had a 10–90% response time of 2–4 s. Fibre optic pulmonary artery catheters (Opticath Catheter; Abbott Critical Care Systems, Chicago, Illinois, USA) were used to measure mixed venous blood oxygen saturation continuously using the principle of reflectance spectroscopy (Oximetric 3; Abbott Critical Care Systems). Intermittent measurement of blood gases and pH were made using a blood-gas analyser (ABL 330; Radiometer, Copenhagen, Denmark), and the same blood sample was used to measure other blood variables by co-oximetry (OSM 3; Radiometer). Cardiac output, Q̇, was measured by thermodilution (Oximetric 3, Abbott Critical Care Systems). The value of Q̇/Q̇ was calculated conventionally using the Fio₂, blood gas and saturation data, assuming a respiratory quotient of 0.8.

Correct positioning of the PO₂ sensor in the aorta was assessed by observing the blood pressure tracing from the sensor’s blood sampling port and by a stable mean PaO₂. The PO₂ sensor was calibrated against drawn heparinized arterial blood using the blood-gas analyser. Inspired and expired oxygen concentrations were measured, at the end of the tracheal tube, using a respiratory Quadrupole mass spectrometer (VG Quadrupoles, Middlewich, UK).

Throughout the study, the mechanically ventilated animals received a constant mean (sd) inspired Fio₂ of 0.72 (0.01). Tidal volume and respiratory rate were kept constant during each individual study, but ranged from 0.25 to 0.30 litres and 11 to 13 breaths min⁻¹, respectively, between animals to maintain an end-expired carbon dioxide concentration of 4.7 (0.6) v/v. After surgery, a stabilization period of 1–2 h was allowed and baseline (prelavage) values were recorded (Table 1). Bronchopulmonary lavage was performed to deplete the lung surfactant, inducing a large pulmonary shunt. The lavage procedure was repeated, typically 10–20 times, until PaO₂ had decreased from 57 to 10 kPa (Table 1). This procedure produced a typical initial shunt fraction, Q̇S/Q̇, of 53% (sd 16%).

When the mean PaO₂ was stable, a set of observations was taken, followed by simultaneous venous and arterial blood samples. The time-varying PaO₂ signal was recorded over 30
breaths by computer. This procedure was repeated every 20 min with 0.5 kPa increments of PEEP from 0 to 2 kPa, followed by a return to zero PEEP (ZEEP) in decrements of 0.5 kPa.

Results (Table 1 and Fig. 1) are expressed as mean (SD), and the statistical analysis was by one-way analysis of variance with repeated measurements. When this analysis showed significance, post hoc comparisons of the means were made by Scheffé’s test. A P value less than 0.05 was considered as significant. Table 1 shows the overall effect of increasing and decreasing PEEP on blood gases, oxygen saturation, cardiac output, shunt fraction and arterial blood pressure. The table also shows the conventional pulmonary blood-flow shunt fraction calculated at each PEEP level. Bronchopulmonary lavage reduced the mean (prelavage) PaO₂ by 47 kPa and the mean PVR by 2.3 kPa. At the initial low mean PaO₂, 9.5 (0.7) kPa, the PaO₂ signal began to oscillate about its mean value with an amplitude of 1.2 (0.8) kPa, and both the mean PaO₂ and its oscillation amplitude began to increase as PEEP was imposed. Figure 1A shows typical results taken from a single animal study. It must be noted that the PaO₂(t) time-varying tracings presented in this figure are not related to each other on the time axis, and no physiological inference can be made from the time-phase differences of these traces. Figure 1B shows the effect of incremental changes on ΔPaO₂ (mean (SD)) for all the studies, as PEEP was firstly increased from 0 to 2 kPa and then decreased from 2 to 0 kPa. Each individual study showed the same effects of PEEP on ΔPaO₂ as those illustrated in Fig. 1, namely that (i) as PEEP was initially increased, both the mean PaO₂ and ΔPaO₂ increased; but that (ii) ΔPaO₂ began to decrease after a certain PEEP value was reached, although the mean PaO₂ continued to rise. This pattern was reversed as PEEP was reduced back to its baseline (ZEEP) level. In all instances, the PaO₂ oscillations followed the ventilator frequency, and appeared to become maximal at the end of inspiration and minimal at the end of expiration. There was also a transport lag between the ventilator inspiratory–expiratory phases and the PaO₂ oscillations.

Comments

There were two main findings of this study. First, an experimental animal model of ARDS was associated with significant oscillations in PaO₂ linked with the respiratory cycle. Secondly, the peak-to-peak amplitude of these fluctuations, ΔPaO₂, was dependent upon the level of PEEP applied to the damaged lungs, the magnitude of the amplitude increasing up to 3 kPa with increasing PEEP. The true in vivo PaO₂ oscillations were probably considerably greater than this because the intravascular PaO₂ sensors had a 10–90% response time of only 2–4 s. This would have attenuated the rapidly changing true in vivo arterial Po₂ signals. A rough calculation of the true magnitude of the PaO₂ oscillations can be derived from the knowledge of the Po₂ sensor response time, the respiratory rate, by approximating the inspiration:expiration ratio to 1:1 and then using the formula of Arieli and Van Liew⁹ to calculate the attenuation of the physiological PaO₂ signal due to the sensor membrane. This rough calculation suggests that the in vivo PaO₂ peak-to-trough oscillations are up to three times greater than those recorded by the IE Sensors Inc. intravascular Po₂ sensors, shown in Fig. 1A.

Both Purves and the Kreuzer group, in the 1960s and 1970s, reported respiratory-induced oscillations in arterial Po₂ in animal models. These were a direct consequence of tidal ventilation fluctuations in alveolar gas oxygen tension, and had the same period as the ventilator setting. An increase in tidal volume or a decrease in ventilation frequency led to an increase in the amplitude of the PaO₂ oscillations. These early studies ruled out the possibility that the effects of cyclical variations in arterial pressure, or blood flow, could produce the measured PaO₂ fluctuations. In
Within-breath $P_{O_2}$ oscillations

contast to our own animal ARDS model, these earlier studies investigated these $P_{A_{O_2}}$ oscillations only in the healthy lung.

Our own findings confirm those of previous authors, such as Bergman’s report in 1961\textsuperscript{2} of oscillations in arterial oxyhaemoglobin saturation, $S_{A_{O_2}}$, (when haemoglobin was not fully saturated) and, more recently, those of Elwell et al. in 1996,\textsuperscript{11} which demonstrated that oscillations in arterial saturation occur with the induction of mild hypoxia. The results of Elwell et al. were explained by Lovell et al. in 1997,\textsuperscript{11} who showed that changes in ventilator settings could alter the $S_{A_{O_2}}$ oscillations. Bergman showed that the amplitude of the $S_{A_{O_2}}$ oscillations diminished as haemoglobin became saturated, but he was not able to measure $P_{A_{O_2}}$ on-line.\textsuperscript{2} However, on the basis of his $S_{A_{O_2}}$ studies, he hypothesized that the most likely explanation of his results was that pulmonary shunt varied during the respiratory cycle as a result of the lung collapsing during expiration and then reopening during positive-pressure inspiration.

Two problems need to be faced. These are that (i) the $\Delta P_{A_{O_2}}$ amplitudes observed in our study were larger than would be expected in healthy lungs; and (ii) current knowledge suggests that $P_{A_{O_2}}$ oscillations on the steep part of the oxyhaemoglobin association/dissociation curve are buffered by the shape of the curve describing the relationship of oxygen content with $P_{O_2}$. Significant $P_{A_{O_2}}$ oscillations in this steep part of the curve could be caused by: (i) the presence of inhomogeneity in the lung ventilation–perfusion ratio induced by the pulmonary lavage; (ii) different degrees of atelectasis occurring in the lung during the inspiratory and expiratory phases of the respiratory cycle (the Bergman hypothesis); or (iii) a combination of both mechanisms, as they do not exclude one another.

We consider that, during inspiration, more alveoli are recruited, with a decrease in venous admixture (during inspiration) and consequently an increase in both the mean $P_{A_{O_2}}$ and the $P_{A_{O_2}}(i)$ time-varying oscillatory signal. During expiration, these recruited alveoli could collapse and contribute to an increased shunt fraction and, thus, a decrease in mean $P_{A_{O_2}}$. When PEEP was increased sufficiently to induce permanent recruitment during the expiratory phase, the overall $P_{A_{O_2}}$ amplitude would decrease and the mean $P_{A_{O_2}}$ rise. On the other hand, if shunt fraction was constant during both the inspiratory and expiratory phases of respiration (the conventional view of $Q_S/Q_T$) then the $\Delta P_{A_{O_2}}$ oscillations would not appear at all at low mean $P_{A_{O_2}}$ values because of the buffering capacity of oxyhaemoglobin in this region of the dissociation curve.

It now seems clear that $P_{A_{O_2}}$ oscillations occur in the atelectatic lung, and that the application of PEEP not only elevates the mean arterial $P_{A_{O_2}}$ but also affects the magnitude of the $P_{A_{O_2}}$ oscillations superimposed on this mean. The effect of these oscillations in the clinical care setting is not clear.

Acknowledgements
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Spasmolytic effects of prostaglandin E₁ on serotonin-induced bronchoconstriction and pulmonary hypertension in dogs

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In this study, we simultaneously evaluated the spasmolytic effects of prostaglandin E₁ (PGE₁) on serotonin-induced bronchoconstriction and pulmonary hypertension. Eleven mongrel dogs (8–12 kg) anaesthetized with pentobarbital were assigned to two groups: saline (n=4) and PGE₁ (n=7). Bronchoconstriction and pulmonary hypertension were elicited with serotonin 10 μg kg⁻¹ + 1 mg kg⁻¹ h⁻¹ and assessed as the percentage change in bronchial cross-sectional area (BCA) measured by bronchoscopy and pulmonary vascular resistance (PVR), respectively. Thirty minutes after starting the serotonin infusion, saline or PGE₁ 0 (saline), 0.01, 0.1, 1.0 or 10 μg kg⁻¹ i.v. was given. %BCA and %PVR (basal=100%) were assessed before and 30 min after serotonin, and 30 and 60 min after saline (saline group) or 5 min after each dose of PGE₁ (PGE₁ group). In the saline group, pulmonary hypertension and bronchoconstriction were stable. In the PGE₁ group, PGE₁ at ≥0.1 μg kg⁻¹ significantly decreased %BCA and 10 μg kg⁻¹ almost fully reversed the constriction (from mean (SEM) 56.2% (4.9%) to 94.4% (3.7%)), %.PVR was significantly decreased at 10 μg kg⁻¹ (from 230% (24%) to 176% (11%)) only. We suggest that PGE₁ may produce bronchodilation rather than pulmonary vasodilation.

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Prostaglandin E₁ (PGE₁) relaxes not only vascular smooth muscle but also airway smooth muscles.¹ It has been reported that 60–90% of PGE₁ is inactivated after one passage through the pulmonary circulation in dogs, cats, rabbits and humans.² Its rapid metabolism in the lung may limit its clinical use, so previous investigators have examined inhalational administration of PGE₁ (see reference ³ for details): it has been found that (i) this may be more effective than i.v. administration for antagonizing airway constriction; (ii) PGE₁ has bronchodilating effects in asthmatic patients but not in healthy volunteers, but it was concluded that inhalation of PGE₁ is unsuitable for therapeutic use in asthmatic patients as airway irritation occasionally induced bronchoconstriction; (iii) inhalation of PGE₁ per se sometimes produces bronchial constriction, as coughing and bronchospasm were observed in one of six asthmatic volunteers, but bronchodilation was observed in the remaining volunteers.

We have previously demonstrated that PGE₁ reverses histamine-induced bronchoconstriction dose-dependently.² A multicentre clinical trial has shown that liposomal PGE₁ improved oxygenation, increased lung compliance and decreased ventilator dependency in patients with acute respiratory distress syndrome (see reference 2). These findings suggest that i.v. PGE₁ may be effective in airway constriction.

PGE₁ has been reported to be useful for treating pulmonary hypertension.³ In addition, several reports suggest that it may reduce experimental pulmonary hypertension⁴. However, Priebe reported that PGE₁ had no beneficial cardiopulmonary effects in a canine model of acute pulmonary hypertension.⁵ The spasmolytic effects of PGE₁ in pulmonary hypertension thus remain controversial.

Serotonin (5-hydroxytryptamine, or 5HT) increases smooth muscle tone via 5HT receptors at low concentrations and via β-adrenoceptors at high concentrations.⁶ Hence it simultaneously produces bronchoconstriction and pulmonary hypertension.

In this study, we examined whether PGE₁ reversed 5HT-induced bronchoconstriction and pulmonary hypertension.

Methods and Results
Following approval of our study protocol by the Animal Experiment Committee of the University of Hirosaki, 11
mongrel dogs (8–12 kg) were anaesthetized with i.v. pentobarbital 30 mg kg\(^{-1}\) + 10 mg kg\(^{-1}\) h\(^{-1}\) and paralysed with pancuronium 0.2 mg kg\(^{-1}\) h\(^{-1}\). The trachea was intubated using a special tracheal tube (Univent tube; Fuji System, Tokyo, Japan) with an additional small lumen for insertion of a superfine fibreoptic bronchoscope (outer diameter 2.2 mm; OES Angiofibrescope AF type 22A; Olympus, Tokyo, Japan). The lungs were mechanically ventilated with oxygen using a respirator (Servoventilator 900C; Siemens AB, Elema, Sweden) and the end-tidal carbon dioxide concentration maintained at 4.0–4.5%. A pulmonary artery catheter (CCO thermodilution catheter Model 139H 7.5F; Baxter Healthcare Corporation, CA, USA) was inserted through a sheath into the femoral vein to monitor pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP) and cardiac output and to administer drugs and fluid (lactate Ringer’s solution at 4 ml kg\(^{-1}\) h\(^{-1}\)). Cardiac output was measured continuously using a Vigilance monitor (Model V12; Baxter Healthcare, Corporation, Irvine, CA, USA). The femoral artery was cannulated to monitor systemic arterial pressure.

Airway tone was evaluated as bronchial cross-sectional area (BCA) determined by our bronchoscopic method as previously reported.\(^2\)\(^7\) Briefly, the BCA at the third bifurcation of the right lung was continuously monitored through the bronchoscope, and the area during the end-expiratory pause was measured using image analysis software (NIH Image program written by Wayne Rasband at the US National Institutes of Health). Pulmonary vascular tone was assessed as pulmonary vascular resistance (PVR). Changes in BCA and PVR were expressed as a percentage of the basal value before 5HT infusion.

Bronchoconstriction and pulmonary hypertension were elicited with 5HT infusion (10 μg kg\(^{-1}\) +1 mg kg\(^{-1}\) h\(^{-1}\)) via the pulmonary artery catheter. Thirty minutes later, when stable pulmonary hypertension and bronchoconstriction was achieved, seven dogs were subsequently given each dose of PGE\(_1\) in the following order: 0 (saline), 0.01, 0.1, 1.0 and 10 μg kg\(^{-1}\) (PGE\(_1\) group) and four dogs were given saline only (saline group). BCA and PVR were assessed before and 30 min after the 5HT infusion started and 5 min after administration of each dose of PGE\(_1\) in the PGE\(_1\) group. At least 15 min elapsed between each administration. In the saline group, these variables were assessed before and 30 min after the 5HT infusion started, and 30 and 60 min after saline i.v.

Arterial blood (6 ml) was collected through the femoral artery catheter into syringes containing EDTA simultaneously with BCA and PVR assessment, immediately centrifuged at 3000 r.p.m. (1700 g) for 10 min at −10°C and then the plasma was separated and kept frozen at −70°C until catecholamine assay. Plasma catecholamine concentrations were determined by high performance liquid chromatography with electrochemical detection. The assay coefficients of variation for epinephrine and norepinephrine were 3.31% and 2.93%, respectively.

Data are shown as mean (95% confidence interval) except in Figure 1. Statistical analyses were performed by repeated measure ANOVA followed by Fisher’s protected least significant difference test. P<0.05 was considered significant.

5HT decreased %BCA by 40–60% and increased %PVR to about 230% (Figure 1). In the saline group, these values persisted until the end of the experiment. In the PGE\(_1\) group, PGE\(_1\) 10 μg kg\(^{-1}\) produced a significant reduction in %PVR (Figure 1A). In contrast, %BCA increased dose-dependently, such that PGE\(_1\) 10 μg kg\(^{-1}\) almost fully reversed the constriction produced by 5HT (Figure 1B). Plasma epinephrine increased significantly from 165 (104–227) to 277 (50–503) pg ml\(^{-1}\) after PGE\(_1\) 10 μg kg\(^{-1}\) i.v.

5HT did not significantly change systemic haemodynamic variables, while PAP was significantly increased. PGE\(_1\) 10 μg kg\(^{-1}\) significantly decreased the following haemodynamic variables during 5HT infusion: systemic vascular resistance from 4274 (3345–5202) to 3338 (2608–4067, P<0.01) dynes s cm\(^{-5}\) and mean arterial pressure from 127 (90–164) to 110 (78–143, P<0.01) mm Hg, whereas mean PAP did not change significantly (decreasing from 34 (28–39) to 31 (24–37) mm Hg).
Comments

Our results data show that PGE$_1$ attenuated 5HT-induced bronchoconstriction. Similarly, we have previously observed that PGE$_1$ also antagonized histamine-induced bronchoconstriction. As PGE$_1$ is a an EP$_2$ receptor agonist, adenylate cyclase is activated to increase intracellular cAMP concentrations which produces airway smooth muscle relaxation. Therefore, increased intracellular cAMP may contribute to the observed spasmyotic effects.

In the present study, plasma epinephrine slightly but significantly increased after administration of PGE$_1$, 10 µg kg$^{-1}$. This suggests that PGE$_1$-induced systemic vasodilation increases sympathetic activity although PGE$_1$ attenuates arterial baroreceptor reflexes. As circulating catecholamine concentration is one of the most important factors controlling airway tone, catecholamine release may also be involved in the observed bronchodilation. However, as PGE$_1$ 0.1 and 1.0 µg kg$^{-1}$ produced significant bronchodilation without increases in plasma catecholamines, PGE$_1$ may have direct bronchodilatory effects.

PGE$_1$ has been used clinically for the treatment of pulmonary hypertension. Fullerton and colleagues have also shown a direct relaxant effect of PGE$_1$ on isolated rat pulmonary artery rings. In the present study, PGE$_1$, 10 µg kg$^{-1}$ significantly attenuated pulmonary hypertension although at ≤1.0 µg kg$^{-1}$ PGE$_1$ was ineffective. However, as the catabolism of PGE$_1$ in the lungs of dogs is about six times that in humans, clinically relevant doses may not attenuate pulmonary hypertension. Consistent with this, several reports suggest that PGE$_1$ does not attenuate pulmonary hypertension by pulmonary vasodilation.

In conclusion, the present study indicates that clinically relevant doses of PGE$_1$ may produce direct bronchodilation, but not pulmonary vasodilation.

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References


Influence of airway-occluding instruments on airway pressure during jet ventilation for rigid bronchoscopy

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We measured changes in airway pressure ($P_{aw}$) caused by microsurgical instruments introduced into a rigid bronchoscope during high frequency jet ventilation (HFJV). With approval of the

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High frequency jet ventilation (HFJV) for rigid bronchoscopy is a convenient method that gives optimal visibility and easy access of diagnostic and surgical instruments to the airway, mainly because HFJV does not require a sealed airway. In contrast, the rigid bronchoscope must be kept open to the surrounding atmosphere to allow passive exhalation of the insufflated gas. Unless the egress of gas is impaired, inadvertent airway pressure (Paw) elevation and lung distension are unlikely. However, there is a risk of airway obstruction when instruments are introduced into the bronchoscope. A newly developed probe for tracheobronchial endosonography, recently introduced for scanning of mediastinal structures, to assess lung tumours and affected lymph nodes, is such an instrument. The tip of this probe has an expandable balloon which is filled with water as a transmission medium. To obtain the image, the balloon is expanded until sufficient contact is achieved between probe and airway wall. During inflation of the balloon, the airway is progressively obstructed; there is a risk that air will be trapped in the lung supplied by the obstructed airway. The purpose of this study was to assess proximal and distal Paw during progressive airway occlusion caused by intermittent inflation of the endosonography probe.

Methods and Results
Following approval by the institutional ethical committee and informed consent, 10 adults undergoing elective diagnostic or interventional tracheobronchial endoscopy and endosonography under general anaesthesia were enrolled. All patients received total intravenous anaesthesia with propofol, remifentanil and succinylcholine. HFJV was applied with an AMS 1000 jet ventilator (Acutronic Medical Instruments, Hirzel, Switzerland) via the jet port at the proximal end of a rigid bronchoscope (Karl Storz, Tuttingen, Germany). Monitoring consisted of electrocardiography, non-invasive measurement of arterial pressure and pulse oximetry.

After insertion of the rigid bronchoscope, the endosonography probe was placed in the main left bronchus, where the artificial airway obstruction was to be created. Proximal and distal Paw were measured with sensors derived from standard intravascular pressure measurement equipment, consisting of transducers and water-filled tubing. The proximal Paw sensor was located in the tip of a steel tube with an internal diameter of 1.0 mm, which was introduced into the light guide channel of the bronchoscope. The distal Paw was measured through a Cavafix Certo 358 catheter (B. Braun, Melsungen, Germany), internal diameter of 1.1 mm, which was placed with its tip into the left mainstem bronchus 10 cm distal to the tip of the bronchoscope. The validity of intratracheal Paw measurement as an approximation for alveolar pressure was shown in previous investigations. Both transducers were placed at the xiphoid level.

Airway obstruction was created by gradually filling the balloon of the endosonography probe, so that obstruction increased steadily from 0% to 100% over an 8 s period (Figure 1). Paw was recorded throughout the balloon expansion. Three specific levels of obstruction, 0%, 50%
and 90%, were evaluated further. The measurements were performed under two different driving pressure (DP) settings (2.0 and 3.0 atm); all other variables, such as F\textsubscript{I.O}, (1.0), inspiration duration (50%) and frequency (100 cpms) remained unchanged. From the continuous P\textsubscript{aw} tracings we measured peak inspiratory pressure (PIP) and end-expiratory pressure (EEP).

Changes of P\textsubscript{aw} during progressive airway obstruction were analysed using nonparametric analysis of variance for repeated measurements (Friedman test) followed by paired Wilcoxon’s signed rank tests with Bonferroni correction. Proximal and distal P\textsubscript{aw} values without obstruction were compared using Wilcoxon’s signed rank test. The level of significance was set at P=0.05. Continuous data are presented as mean (SD).

All patients had a pulse oximeter saturation of \(\geq90\%\) throughout the procedure. No lung injury or surgical emphysema was noted up to 4 h after the intervention. Biometric and clinical data of the patients are summarized in Table 1.

![Fig 1](image1.png) Proximal (dotted line) and distal (solid line) airway pressure (P\textsubscript{aw}) in patient no. 6 during increasing obstruction of the airway: Period A: apnoea during zeroing of both pressure sensors; period B: beginning of expansion of endosonography probe balloon; period C: complete occlusion of the airway.

![Fig 2](image2.png) Proximal and distal P\textsubscript{aw} during 50% and 90% obstruction of the airway and a driving pressure of 2.0 atm (upper segment) and 3.0 atm (lower segment). Values are expressed as mean±SD; *Significantly different from P\textsubscript{aw} without obstruction (P<0.025). †Pressure amplitude significantly different from that without obstruction (P<0.025).

During jet ventilation with a DP of 2.0 atm (Figure 2), gradual obstruction of the left mainstem bronchus resulted in a progressive increase of proximal PIP from 7.5 (2.6) to 9.5 (3.5) mm Hg (P=0.0008). In contrast, proximal EEP remained unaffected by airway obstruction (1.8 (2.6) and 1.9 (2.5) mm Hg). Without airway obstruction, there was no difference between distal and proximal PIP, or between distal and proximal EEP. Gradual airway narrowing did not affect distal PIP, but caused a highly significantly increase of distal EEP compared with the unobstructed airway lumen, from 2.5 (3.4) to 5.4 (3.6) mm Hg (P=0.0005). With a DP of 3.0 atm, these effects on P\textsubscript{aw} were more pronounced: proximal PIP increased from 9.7 (3.7) to 13.0 (5.1) mm Hg (P=0.0001), proximal EEP decreased from 3.2 (2.9) to 1.8 (1.8) mm Hg (P=0.0001), distal PIP did not change and distal EEP increased significantly from 3.2 (3.6) to 8.0 (4.3) mm Hg (P<0.0001).

**Comment**

HFJV is a convenient method of ventilation for rigid bronchoscopy, but P\textsubscript{aw} must be monitored continuously, especially if additional instruments are inserted into the bronchoscope. These devices may cause some airway obstruction: the recently introduced endosonography probe causes near complete airway obstruction.4 We have shown that both PIP and EEP were affected by the degree of airway obstruction and by the applied DP: proximal PIP and distal EEP increased significantly, while proximal EEP and distal PIP remained unaffected. P\textsubscript{aw} alterations were more pronounced with a DP of 3.0 atm than at 2.0 atm. Air trapping became significant when the obstruction occupied 50% of the original airway cross-sectional area. This corresponds to findings of Ayuso and colleagues, who found sufficient gas exchange with <50% of the cross-sectional area of the airway obstructed.6

**Table 1** Biometrical and clinical data (mean (SD)). VC=vital capacity; F\textsubscript{E}V\textsubscript{1}=forced expiratory volume in 1 s

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (females/males)</td>
<td>1/9</td>
</tr>
<tr>
<td>Age, yr (range)</td>
<td>66 (47–75)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>172 (5)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>77 (9)</td>
</tr>
<tr>
<td>VC, litres</td>
<td>3.6 (0.9)</td>
</tr>
<tr>
<td>F\textsubscript{E}V\textsubscript{1}, litres</td>
<td>2.5 (0.8)</td>
</tr>
<tr>
<td>F\textsubscript{E}V\textsubscript{1}, (% of VC)</td>
<td>68 (10)</td>
</tr>
</tbody>
</table>
The relevance of these findings for the routine application of HFJV during rigid bronchoscopy depends on factors such as jet flow, airway dimensions and degree of obstruction, and on the interaction between these factors. The increase in distal EEP during progressive airway obstruction may not necessarily be dangerous, since it was always less than the distal PIP observed without airway obstruction. The slight increase in proximal PIP is not likely to damage the lungs.

In summary, short-term near-total occlusion of the airway during jet ventilation beyond the tip of the rigid bronchoscope may slightly increase proximal peak \( P_{aw} \) and increase distal EEP. These effects depended on the degree of obstruction and the DP, but were never high enough to cause overinflation of the lung or even barotrauma. Nevertheless, careful and continuous monitoring of airway pressure (as used with modern jet ventilation equipment) and observation of the thoracic excursions during jet ventilation are indispensable during endoscopic instrumentation.

References


Transcranial magnetic-evoked potentials under total intravenous anaesthesia and nitrous oxide

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*Corresponding author

Magnetic stimulation of the cortex and recording of the motor-evoked potentials (MEPs) by electromyography (EMG) is a well proven method to assess the descending pathways of the spinal cord and detect neurological impairment. We have assessed, in 33 adult patients undergoing spinal surgery, the influence of four total i.v. anaesthesia regimens (TIVA) on this recording technique. In 20 patients, the effect of 50% nitrous oxide was also studied. MEP amplitudes, latencies and success rates of stimulation were obtained in the steady-state after induction of anaesthesia. Combinations of midazolam and ketamine, and alfentanil and etomidate had the least effect on MEPs. Propofol (in combination with alfentanil or ketamine) showed marked depression of the MEP amplitude and the lowest success rates of stimulation. The latencies did not change at all. The addition of nitrous oxide significantly depressed the registered MEPs and lowered the success rates.


Keywords: brain, electromyography; brain, evoked potentials; brain, cortex; anaesthesia, i.v.; anaesthetic gases, nitrous oxide

Accepted for publication: April 17, 2000
Recording motor-evoked potentials (MEPs) is regarded as a sensitive method of monitoring the integrity of descending motor tracts of the spinal cord. Muscle action potentials of the upper or lower limbs are the responses to the central stimulation. Good correlation between neurological deficits and MEP changes have been shown in animal models and in humans.

Electrical stimulation may be used, but we prefer single-pulsed magnetic stimulation which is not painful. Previous studies have shown that the sensitivity of MEPS is compromised by the suppressive action of many commonly used anaesthetics, but the results of human and animal studies are often conflicting. This study was designed to determine the effects of four i.v. anaesthetic techniques on MEPs recorded in patients undergoing spinal surgery.

Methods and results
The study was approved by the Ethics Committee of the Ruhr University Bochum. It included 33 adult patients of both sexes, ASA class I–II, mean age 51 yr, mean body weight 77 kg, who were due to undergo surgery for lumbar disc hernia. Patients with a history of seizure, with implants or neuropathy were excluded. The patients were allocated randomly to one of four groups, according to the combination of i.v. anaesthetic drugs to be used: alfentanil–etomidate (AE); alfentanil–propofol (AP); propofol–ketamine (PK); midazolam–ketamine (MK).

Prior to the administration of any drug, baseline MEP recordings were obtained. All patients then received midazolam 0.05 mg kg⁻¹ i.v. as premedication. Anaesthesia was induced by i.v. injection (lasting 30 s) of: in group AE, alfentanil 20 μg kg⁻¹ and etomidate 0.3 mg kg⁻¹; in group AP, alfentanil 20 μg kg⁻¹ and propofol 2 mg kg⁻¹; in group PK, propofol 2 mg kg⁻¹ and ketamine 2 mg kg⁻¹; in group MK, midazolam 0.1 mg kg⁻¹ and ketamine 2 mg kg⁻¹. Mask ventilation was started by a second anaesthetist at the first sign of unconsciousness or respiratory depression. Thereafter, a continuous i.v. infusion was started: in group AE, alfentanil 100 μg kg⁻¹ h⁻¹ and etomidate 0.6 mg kg⁻¹ h⁻¹; in group AP, alfentanil 100 μg kg⁻¹ h⁻¹ and propofol 10 mg kg⁻¹ h⁻¹; in group PK, propofol 10 mg kg⁻¹ h⁻¹ and ketamine 2 mg kg⁻¹ h⁻¹; in group MK, midazolam 0.1 mg kg⁻¹ h⁻¹ and ketamine 2–4 mg kg⁻¹ h⁻¹. Tracheal intubation was performed, facilitated by suxamethonium 1.5 mg kg⁻¹ after precurarization with atracurium 5 mg. If necessary, additional doses of etomidate, propofol or ketamine were injected before intubation. Ventilation of the lungs was maintained with 40% oxygen in air for 15 min. At this point, anaesthesia was regarded as being in a steady-state and MEP measurements were again taken. There was no muscle relaxation. Oscillometric blood pressure, heart rate, oxygen saturation and end-tidal carbon dioxide were controlled for each series of measurements.

After the steady-state measurements, 50% nitrous oxide was added and maintained for 10 min after reaching the desired end-expiratory concentration (five patients from each group) and MEP recordings obtained. This completed the study and the patients underwent the operation with enfurane in nitrous oxide–oxygen for maintenance of anaesthesia.

For the recording of MEPs, central stimulation was performed with a magnetic stimulator (Magstim 200, The Magstim Co., Wales, UK), which produces a maximum magnetic field of 1.5 Tesla. A single coil (diameter 14 cm) was placed over the vertex. Its best position was determined in the awake state and marked on the scalp. The stimulations were started at 30% of maximum power. Thereafter, the power was increased in steps of 5% until a response was observed (the brain stimulation threshold). Electromyographic responses (EMG) to stimulation were recorded in duplicate from the contralateral thenar muscles using subdermal paired needle electrodes. A Neuropack Four (Nihon Kohden, Tokio, Japan) was used to record MEPs. Stimulation threshold, success rates, latency and amplitude of the magnetic motor-evoked potentials were determined.

For statistical evaluation, the Wilcoxon test for matched pairs and the Kruskall–Wallis test were used. A P-value of <0.05 was considered statistically significant.

The results are presented in Table 1. Each drug combination produced a significant increase in threshold stimulation, but the MEP amplitude was not depressed by midazolam and ketamine (MK), or by alfentanil and etomidate (AE). The observed increase in amplitude in the midazolam/ketamine group was not significant. Combinations using propofol led to a considerable and significant reduction in the MEP amplitude. The MEP latencies were unaffected by each combination. When considering the success rates of obtaining a response to stimulation, the combinations midazolam–ketamine and alfentanil–etomidate were superior to both combinations using propofol (AP and PK). The addition of nitrous oxide had a pronounced depressive effect on MEPs. All patients recovered well after surgery.

Comment
Serious neurological deficits with postoperative loss of motor function in the limbs can complicate neurosurgical, orthopaedic or abdominal vascular surgery procedures. Animal studies have suggested that magnetic motor-evoked potential (MEP) monitoring is more sensitive than somato-sensory-evoked potential (SSEP) monitoring in detecting spinal cord injury. Combined neuromonitoring, consisting of SSEP and MEP may be useful.

The results of our study demonstrate that MEPs were least affected in the AE and MK groups. Etomidate, together with fentanyl, has been shown to allow MEP recording even in patients with pre-existing spinal neuropathy with a success
Table 1  Changes in motor-evoked potential amplitude, latency, threshold, and arterial blood pressure and heart rate, after application of four i.v. anaesthesia regimens and nitrous oxide. Amplitude, latency and threshold: mean (SEM); mean arterial pressure (MAP) and heart rate (HR): mean (SD)

<table>
<thead>
<tr>
<th></th>
<th>Group AE</th>
<th>Group AP</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Alfentanil–etomidate (n=9)</td>
<td>Alfentanil–propofol (n=8)</td>
</tr>
<tr>
<td></td>
<td>Before</td>
<td>Steady-state</td>
</tr>
<tr>
<td>Amplitude (μV)</td>
<td>245.1 (86.3)</td>
<td>229.5 (111.6)</td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>26.7 (1.1)</td>
<td>27.8 (1.0)</td>
</tr>
<tr>
<td>Threshold (%)</td>
<td>51.7 (2.6)</td>
<td>95.6 (4.4)</td>
</tr>
<tr>
<td>Success rate</td>
<td>79%±7.7%</td>
<td>1/8±12.5%</td>
</tr>
<tr>
<td>MAP</td>
<td>108.6 (11.3)</td>
<td>84.8 (6.2)</td>
</tr>
<tr>
<td>HR</td>
<td>81.0 (8.9)</td>
<td>64.6 (6.6)</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th></th>
<th>Group PK</th>
<th>Group MK</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Propofol–ketamine (n=8)</td>
<td>Midazolam–ketamine (n=8)</td>
</tr>
<tr>
<td></td>
<td>Before</td>
<td>Steady-state</td>
</tr>
<tr>
<td>Amplitude (μV)</td>
<td>300.1 (76.1)</td>
<td>72.4 (43.5)</td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>25.5 (0.9)</td>
<td>25.2 (1.8)</td>
</tr>
<tr>
<td>Threshold (%)</td>
<td>50.8 (2.8)</td>
<td>100 (0)</td>
</tr>
<tr>
<td>Success rate</td>
<td>5/8±62.5%</td>
<td>7/8±87.5%</td>
</tr>
<tr>
<td>MAP</td>
<td>101.3 (8.7)</td>
<td>93.4 (14.3)</td>
</tr>
<tr>
<td>HR</td>
<td>69.0 (7.7)</td>
<td>66.2 (6.6)</td>
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<table>
<thead>
<tr>
<th></th>
<th>Effect of nitrous oxide</th>
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<tbody>
<tr>
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<td>Before</td>
</tr>
<tr>
<td>Amplitude (μV)</td>
<td>345.6 (110.8)</td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>26.2 (0.7)</td>
</tr>
<tr>
<td>Threshold (%)</td>
<td>97.0 (2.1)</td>
</tr>
<tr>
<td>Success rate</td>
<td>11/20±55%</td>
</tr>
<tr>
<td>MAP</td>
<td></td>
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<td>HR</td>
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rate similar to the 77.7% of our AE group.2 Induction doses of etomidate, however, can lead to significant depression of the MEPs.3 In contrast to previous investigations on the effect of propofol on magnetically induced potentials in rats,4 our studies clearly indicate that propofol significantly affects MEP recordings. A similar result was obtained by Taniguchi et al.3 Ketamine seems to diminish the depressant effect of propofol when the alfentanil–propofol group is compared with the propofol–ketamine group, where propofol was applied in the same dosage. This might be due to a central excitatory effect, because ketamine, in a small dosage, was found to increase the MEP amplitude up to 120% from baseline.5 It seems possible that in our studies, ketamine, combined with smaller doses of propofol, might have achieved better results. We could also show a strong depressant effect of nitrous oxide on MEPs. The success rate of obtaining a response was low (55%). Nitrous oxide, in a concentration of less than 50%, had previously been recommended, although a depressant action had also been reported.5 None of our techniques affected the MEP latencies. In this study, MEP responses were recorded from intact motor pathways of the upper limbs. In the case of pre-existing neurological deficits and in the case of also monitoring the lower limbs, the results might have been slightly modified (e.g. with regard to the success rates), but certainly not completely different.

References

Motor block during patient-controlled epidural analgesia with ropivacaine or ropivacaine/fentanyl after intrathecal bupivacaine for Caesarean section†

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We compared patient-controlled epidural analgesia (PCEA) with ropivacaine alone or combined with fentanyl in terms of analgesic efficacy, motor weakness and side-effects in patients who had received spinal anaesthesia for elective Caesarean section. ASA I patients received combined spinal–epidural anaesthesia and were randomly assigned, in a double-blind study, into two groups after operation: group R (n=23) received PCEA ropivacaine 0.1%, bolus 5 mg, lock-out 15 min, 3 mg h⁻¹ background infusion, and group RF (n=24) received PCEA 0.1% ropivacaine/fentanyl 2 µg ml⁻¹ at identical settings. Pain and satisfaction on a 100 mm visual analogue scale (VAS) and side-effects were noted. Incidence of motor weakness (Bromage grade 1 or higher) was 48% (11/23) at 8 h in group R compared with 13% (3/24) in group RF (P=0.025). Pain scores on movement were lower in group RF at 8 and 12 h and at rest at 6 and 8 h (P<0.05 for each comparison). Analgesic consumption was less in RF (P=0.041), but there was no difference in time to first request for supplementary analgesia. Patient satisfaction with postoperative analgesia (mean (SD)) was higher in RF (79 (23) vs 57 (29) mm, P=0.045). Caution should be exercised using ropivacaine PCEA after spinal bupivacaine for Caesarean section, because its reputed motor-sparing property may be unreliable.

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Keywords: anaesthetic techniques, epidural; analgesia, patient-controlled; anaesthetics, local, ropivacaine; anaesthetics, analgesics, opioid; anaesthesia, obstetrics

Accepted for publication: March 30, 2000

Analgesic techniques for Caesarean section must be highly effective and yet allow early mobilization to enable these women to care for their babies. While patient-controlled epidural analgesia (PCEA) with local anaesthetics provides good analgesia, it causes motor weakness, limiting postoperative mobilization. Ropivacaine, the most recent amide local anaesthetic introduced into clinical practice, reportedly produces less motor weakness than bupivacaine. Ropivacaine epidural analgesia after spinal anaesthesia has not been reported. We compared PCEA ropivacaine alone or combined with fentanyl after Caesarean section under bupivacaine spinal anaesthesia, in terms of analgesic efficacy, motor weakness and side-effects.

Methods and results
After obtaining institutional ethics committee approval and written informed consent, 50 women scheduled for elective Caesarean section under regional anaesthesia were enrolled into the study. Excluded were patients other than ASA I, patients for whom a central neuraxial block was contra-indicated and those with a history of adverse reaction to any study medication. Patients were briefed preoperatively on visual analogue scales (VAS) and how to operate the PCEA.

After i.v. access had been established and an infusion of crystalloid commenced, all patients had a combined spinal– epidural (CSE) anaesthetic. The epidural space was identified at L2–3 or L3–4 using a loss of resistance to saline technique with the patient in a sitting position. Dural puncture was performed by a needle-through-needle technique with a Whitacre 26G needle; hyperbaric 0.5% bupivacaine 2.6 ml was injected into the intrathecal space. An epidural catheter was then inserted into the epidural space.

When surgery was complete, patients were randomized, by a sealed envelope technique, into one of two groups: group R (n=25) received PCEA 0.1% ropivacaine, bolus 5 mg, lockout 15 min, with 3 mg h⁻¹ background infusion.

†Presented in part at the Anaesthetic Research Society Meeting, St George’s Hospital, London, November 1998 and at the Obstetric Anaesthetists Association Annual Scientific Meeting, Liverpool, April, 1999.

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Group RF (n=25) received PCEA 0.1% ropivacaine/fentanyl 2 μg ml⁻¹, at identical settings to group R. The analgesic regimen was prepared by the anaesthetist managing the patient, who was not subsequently involved in data collection. It was commenced in the recovery room while the spinal block was still effective. Patients and nursing staff were blind to the group randomization.

Pain at rest and on movement (sitting forward) on a 100 mm VAS at 2, 4, 6, 8, 12 and 24 h, satisfaction with postoperative analgesia at 24 h (VAS) and the incidence of nausea and pruritus were recorded by the patients on a four-page individual patient diary. Dermatological sensory level was noted using ethyl chloride spray at the commencement of the study and at 8 h. Motor block was evaluated using a modified Bromage scale by nursing staff who were familiar with these assessments. If patients had inadequate analgesia, supplementary rescue analgesia with oral codeine 30 mg/paracetamol 500 mg was available. Total PCEA consumption was noted.

Postoperative monitoring consisted of hourly respiratory rate, pulse rate and non-invasive blood pressure measurements for 4 h and thereafter at intervals of 4 h. Hypotension was defined as systolic blood pressure <90 mm Hg. Sedation was assessed on a four-point scale: 0=fully alert, 1=drowsy, eyes closed occasionally; 2=asleep but roused easily on speaking to the patient; 3=profoundly sedated, roused by physical stimulation.

Data were analysed in GraphPad Prism™, version 2.0. Physical characteristics and satisfaction scores were compared using the unpaired t-test. VAS pain and total analgesic consumption were compared using the Mann–Whitney U-test. Contingency tables were constructed for categorical data and analysed by χ² analysis with Yates’ correction. The prospective study power calculation was based on analgesic data. Previous studies of women after Caesarean section indicated a standard deviation of the order of 30 mm in early postoperative pain scores. We took a VAS reduction of 25 mm to be clinically significant, hence 24 patients were required in each group to give an α value of 0.05 and a β value of 0.2.

Although 25 patients were enrolled in each group, only 23 in group R and 24 in group RF were deemed eligible for statistical analysis. One patient was withdrawn from each group because of technical difficulties with the epidural catheter. Another patient’s data were lost from group R because of PCEA provider pump failure. A further two patients were withdrawn from the ropivacaine group at 12 h because of profound, prolonged motor block. They were included in the analysis as the only missing data were at 24 h.

The two groups did not differ in age, weight or parity. Patients receiving ropivacaine alone had significantly higher VAS pain scores at 6 and 8 h at rest and at 8 and 12 h on movement. Total analgesic consumption was less in the RF group than in group R and no patient in RF requested supplementary oral analgesia compared with eight patients in group R (P=0.005). There was no difference in the time to first request for supplementary analgesia. Patients in group RF had significantly higher scores for satisfaction with their postoperative analgesia compared with group R (P=0.045) (Table 1).

The incidence of demonstrable motor weakness (Bromage grade 1 or above) was significantly higher (P=0.025) in group R than in group RF at 8 h but not at 12 h. When patients with Bromage grades 2 or 3 were analysed separately, there was no statistical difference. No patient was allowed to walk if any motor weakness was detected. The two patients in group R who were withdrawn at 12 h had fully recovered by 24 h. There was no difference between the groups in sensory level at 8 h. Pruritus was significantly more likely in group RF than in group R (P=0.033), but no patient requested treatment. There were no differences in the incidences of nausea, hypotension or sedation between the groups (Table 1).

Comment

This is the first report, to our knowledge, of epidural ropivacaine for continuing postoperative analgesia after spinal anaesthesia. The increasing use of CSE techniques increases the possibility of epidural administration of ropivacaine after spinal anaesthesia with bupivacaine. The principal finding is the unexpectedly high incidence and duration of motor block observed in patients receiving PCEA with ropivacaine. This observation differs from the initial clinical impression of ropivacaine, which suggested a motor-sparing effect.² However, a study of PCEA epidural 0.125% ropivacaine compared with 0.125% bupivacaine in labour found that they were clinically indistinguishable in terms of motor weakness.³

We chose a background infusion of ropivacaine 0.1%, believing that it would provide an acceptable balance between adequate analgesia and minimal motor block. In retrospect however, it is clear that we failed in this objective because we underestimated the pain produced by Caesarean section in our patients. In a randomized, double-blind study of three solutions of ropivacaine/fentanyl for PCEA after lower abdominal surgery, 0.05% ropivacaine/fentanyl 1 μg ml⁻¹ produced equivalent analgesia to 0.2% ropivacaine/fentanyl 4 μg ml⁻¹. However, the latter group had a 30% incidence of motor block, compared with none in those receiving the lower concentration of ropivacaine.⁴ Our choice of ropivacaine 0.1% could reasonably have been expected not to aggravate motor weakness. Moreover, recent work has shown that the relative potency of ropivacaine compared with bupivacaine is only 0.6 and the EC₅₀ for the minimum local anaesthetic concentration for ropivacaine in labour is approximately 0.16%.⁵ Hence, 0.1% ropivacaine should have been even less likely to produce motor block than 0.1% bupivacaine.

Although the difference is statistically significant only when patients with all grades of motor weakness are included, this unexpected finding is clinically important because even Bromage grade 1 weakness precludes
Table 1 Physical characteristics, analgesia, motor weakness and side-effects. All data are expressed as mean (sd) or median (interquartile range) except where stated

<table>
<thead>
<tr>
<th></th>
<th>Ropivacaine (n=23)</th>
<th>Ropivacaine/fentanyl (n=24)</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>32.4 (5.5)</td>
<td>28.5 (5.0)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80.4 (8.3)</td>
<td>82.0 (11.2)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Parity</td>
<td>1 (0–3)</td>
<td>1 (1–3)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Total PCEA ropivacaine consumption in 24 h (mg)</td>
<td>199 (23)</td>
<td>175 (15)</td>
<td>P=0.041</td>
</tr>
<tr>
<td>Supplementary oral analgesia, n (%)</td>
<td>8 (35%)</td>
<td>0 (0%)</td>
<td>P=0.005</td>
</tr>
<tr>
<td>Time to supplementary analgesia (h)</td>
<td>9.7 (2.7)</td>
<td>6.6 (2.4)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Pain VAS at rest, 6 h (mm)</td>
<td>20 (13–40)</td>
<td>8 (1–25)</td>
<td>P=0.039</td>
</tr>
<tr>
<td>Pain VAS at rest, 8 h (mm)</td>
<td>24 (19–35)</td>
<td>12 (2–5)</td>
<td>P=0.047</td>
</tr>
<tr>
<td>Pain VAS on movement, 8 h (mm)</td>
<td>54 (34–60)</td>
<td>35 (4–35)</td>
<td>P=0.045</td>
</tr>
<tr>
<td>Pain VAS on movement, 12 h (mm)</td>
<td>53 (30–70)</td>
<td>39 (20–55)</td>
<td>P=0.049</td>
</tr>
<tr>
<td>Patient satisfaction VAS (mm)</td>
<td>57 (29)</td>
<td>79 (23)</td>
<td>P=0.045</td>
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<tr>
<td>Motor weakness at 8 h, n (%)</td>
<td>11 (48%)</td>
<td>3 (13%)</td>
<td>P=0.025</td>
</tr>
<tr>
<td>Bromage score=1</td>
<td>6 (26%)</td>
<td>2 (8%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Bromage score=2</td>
<td>3 (13%)</td>
<td>1 (5%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Bromage score=3</td>
<td>2 (9%)</td>
<td>n.s.</td>
<td></td>
</tr>
<tr>
<td>Motor weakness at 12 h, n (%)</td>
<td>6 (26%)</td>
<td>2 (8%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Bromage score=1</td>
<td>4 (17%)</td>
<td>2 (8%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Bromage score=2</td>
<td>0</td>
<td>n.s.</td>
<td></td>
</tr>
<tr>
<td>Bromage score=3</td>
<td>2 (9%)</td>
<td>n.s.</td>
<td></td>
</tr>
<tr>
<td>Sensory level at baseline</td>
<td>T5 (T4–T10)</td>
<td>T6 (T3–T10)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Sensory level at 8 h</td>
<td>T11 (T10–L2)</td>
<td>T10 (T8–L1)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Pruritus, n</td>
<td>3</td>
<td>11</td>
<td>P=0.033</td>
</tr>
<tr>
<td>Hypotension, n</td>
<td>2</td>
<td>2</td>
<td>n.s.</td>
</tr>
<tr>
<td>Nausea, n</td>
<td>1</td>
<td>3</td>
<td>n.s.</td>
</tr>
<tr>
<td>Sedation score &gt;1, n</td>
<td>0</td>
<td>2</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Ambulation. Inadvertent intrathecal spread of ropivacaine (via the small dural hole created by the spinal component of the CSE) could possibly explain our observations, although there was no suggestion of dural puncture in any of our patients. Indeed, it has been shown that dural puncture with a 26 gauge Whitacre spinal needle before epidural injection (as in the present study) increases the caudal, but not the cranial, spread of epidural local anaesthetics. It is also possible that low thoracic placement of the epidural catheter may have been more appropriate. Repeated introduction of boluses of local anaesthetic into the lumbar area may not provide analgesia in the lower thoracic dermatomes, yet accumulation may increase the risk of motor weakness in the lumbar dermatomes. Although there is also greater sensitivity of neural tissue to local anaesthetics during the later stages of pregnancy, this is an unlikely explanation because patients in group RF did not have as much leg weakness as those in group R. However, it is noteworthy that patients in group R received a significantly higher dose of ropivacaine than patients in group RF over the duration of the study, presumably because their analgesia was less satisfactory than in group RF.

An alternative explanation is an interaction between the two local anaesthetics. An experimental model of profound nerve block under spinal anaesthesia found that combinations of amide local anaesthetics could produce unpredictable prolongation of the block. Although the mechanism is unclear, these investigators postulated that local anaesthetics could interact at the sodium channel to prolong effective duration. Whether this effect could be more pronounced on motor as opposed to sensory nerves is unknown.

In conclusion, we found a higher incidence of motor weakness after 8 h in patients receiving PCEA ropivacaine compared with a ropivacaine/fentanyl mixture after bupivacaine spinal anaesthesia. The reason for this finding is unclear, but further studies are indicated to clarify the optimum dose regimen of epidural ropivacaine and fentanyl after spinal anaesthesia. In the interim, caution should be exercised when administering epidural ropivacaine after bupivacaine spinal anaesthesia.

References

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3 Owen MD, d’Angelo R, Gerancher JC, et al. 0.125% ropivacaine is similar to 0.125% bupivacaine for labor analgesia using patient-controlled epidural infusion. Anesth Analg 1998; 86: 527–31

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