Effects of minor surgery and endotracheal intubation on postoperative breathing patterns in patients anaesthetized with isoflurane or sevoflurane

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We studied the effects of minor surgery and endotracheal intubation on postoperative breathing patterns. We measured breathing patterns and laryngeal resistance during the periods immediately before intubation (preoperative) and immediately after extubation following minor surgery (postoperative) in eight patients anaesthetized with sevoflurane and eight patients anaesthetized with isoflurane, breathing spontaneously through a laryngeal mask airway at a constant end-tidal anaesthetic concentration (1.0 MAC). In both sevoflurane-anaesthetized and isoflurane-anaesthetized patients, expiratory time was reduced and inspiratory and expiratory laryngeal resistance increased after surgery. In sevoflurane-anaesthetized patients, occlusion pressure \( (P_{0.1}) \) increased without changes in inspiratory time \( (T_I) \). Occlusion pressure did not change and \( T_I \) was greater in isoflurane-anaesthetized patients after surgery. Minor surgery may have a small but significant influence on breathing and increased laryngeal resistance following endotracheal intubation may modulate these changes. The difference in breathing pattern between sevoflurane and isoflurane may be a result of different responses of the central nervous system to different anaesthetics in the presence of increased laryngeal resistance.

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Breathing patterns in the immediate postoperative period can have some important clinical implications. For example, after surgery, a normal breathing pattern can be a criterion for extubation. Breathing patterns at this time are affected not only by anaesthetic and surgical factors but also by upper airway function. Our previous studies showed that breathing patterns after surgery are quite different from those before surgery. However, in these studies the breathing patterns were analysed in patients with a tracheal tube, and the contribution of changes in upper airway resistance produced by endotracheal intubation was not evaluated. Furthermore, most of these patients underwent thoracotomy or laparotomy which may place a load on the respiratory system and affect breathing patterns through load compensation mechanisms. The effects of endotracheal intubation on postoperative breathing patterns in patients after minor surgery have not been studied. Different volatile anaesthetics may also affect postoperative breathing patterns. The present study was performed to evaluate the breathing patterns after minor surgery in patients anaesthetized with either sevoflurane or isoflurane.

Methods

Subjects

Using sealed envelopes, 16 patients were allocated by block randomization to one of two groups of eight subjects each to receive either isoflurane (ISO group) or sevoflurane (SEVO group). All were to undergo elective minor surgery such as partial mastectomy or minor urological or ENT surgical procedures. None had clinical evidence of respiratory, cardiovascular, or neuromuscular disorders. Patient characteristics and the duration of surgery are given in Table 1. The ethics committee of the hospital approved the study, and informed consent was obtained from each subject.

Preparation of the subjects

All patients were pre-medicated with atropine 0.5 mg and midazolam 3 or 4 mg given i.m. 30 min before induction of anaesthesia. In the SEVO group, anaesthesia was induced with inhalation of sevoflurane by the single breath tech-
nique.\textsuperscript{11} In the ISO group, anaesthesia was induced with inhalation of oxygen with 66% nitrous oxide followed by gradual increases in inspired isoflurane concentration to reduce breath-holding and laryngospasm during anaesthetic induction. Ventilation was then manually controlled and administration of nitrous oxide was discontinued. In both groups, after the administration of succinylcholine (1 mg kg\textsuperscript{−1}), a laryngoscope was used to insert a polyethylene catheter (6-Fr; Multiple Purpose Tube, Atom Medical, Tokyo, Japan) into the trachea just below the vocal cords for the measurement of subglottic pressure (P\textsubscript{sg}), and a laryngeal mask airway (LMA\textsuperscript{‡}: size #3 or 4) was placed. Spontaneous breathing was then allowed to resume. End-tidal isoflurane and sevoflurane concentrations were monitored with a respiratory gas analyser (AS/3; Datex, Helsinki, Finland) and maintained constant (1.2% isoflurane and 1.7% sevoflurane, corresponding to 1.0 minimum alveolar anaesthetic concentration (MAC) in adult humans). Airflow (\(V\)) was measured by a pneumotachograph connected to a differential pressure transducer (TP-602T; Nihon Koden, Tokyo, Japan). End-tidal carbon dioxide tension (P\textsubscript{\(\text{CO}_2\)}) was measured using a side-stream capnometer (CAPNOX; Colin, Aichi, Japan). In addition to measurements of airway pressure at proximal end of LMA (P\textsubscript{mask}) and P\textsubscript{sg}, pressure difference between the P\textsubscript{mask} and P\textsubscript{sg} (P\textsubscript{delta}) was directly measured with a pressure transducer (23NB005G; IC sensors, Silicon Valley, CA, USA). These data were recorded on an eight-channel thermal recorder (WS-682G; Nihon Koden, Tokyo, Japan) and stored simultaneously in a personal computer with a sampling frequency of 50 Hz by a data logging software package (LABDAT 5.2 RHT-Infodat, Montreal, Quebec, Canada) for later analysis.

\textbf{Experimental procedure}

When the breathing pattern was unchanged, the ventilatory variables were measured before the operation while maintaining a constant anaesthetic level (1 MAC). After the steady-state breathing measurements, the occlusion pressure (P\textsubscript{0.1}) was obtained during an inspiratory effort against the airway occluded at end expiration for one breath. Then, vecuronium 8–10 mg was given and a cuffed tracheal tube (ID 7.0 mm for females and 8.0 mm for males) was inserted after removal of the LMA and the polyethylene catheter. During surgery, anaesthesia was maintained with isoflurane (1–3%) or sevoflurane (1–3%) with nitrous oxide (66%), and vecuronium intermittently as necessary.

After surgery, the tracheal tube was removed and the LMA and subglottic catheter were inserted again. Residual muscle paralysis was reversed by i.v. administration of atropine 1.0 mg and neostigmine 2.0 mg, and the patients were allowed to breathe spontaneously. Adequate reversal of neuromuscular block was confirmed by the presence of stable ventilation and by observing a normal train-of-four responses to the ulnar nerve stimulation.

When the breathing pattern was stable, the same ventilatory measurements as in the period immediately before the operation were repeated while maintaining the same anaesthetic level (1 MAC).

\textbf{Data analyses}

Using the software (ANADAT 5.1 and 5.2; RHT-Infodat Inc., Montreal, Quebec, Canada), durations of inspiration (T\textsubscript{I}) and expiration (T\textsubscript{E}), duty ratio (T\textsubscript{I}/T\textsubscript{tot}; T\textsubscript{I}+T\textsubscript{E}), respiratory frequency (RR), tidal volume (\(V_t\)), and minute volume (MV) were determined from the flow signal. To analyse the respiratory waveform in detail, T\textsubscript{E} was divided into the duration of active expiration (T\textsubscript{E-active}; period with the presence of expiratory airflow) and the duration of end-expiratory pause (T\textsubscript{E-pause}; period of no airflow before onset of inspiration) as evaluated by Byrick and Janssen.\textsuperscript{12}

As the presence of LMA contributes to the P\textsubscript{delta}, we estimated the resistive pressure decrease caused by the LMA. By measuring the pressure difference across the LMA passing 100% oxygen at a range of flow rates, we found that the resistance of the LMA (R\textsubscript{LMA}) varies with size and flow (\(V\)), and can be fitted by the following Rohrer’s equations for each LMA size; LMA of #4: R\textsubscript{LMA}:=0.077+0.093*\(V\) (kPa litre\textsuperscript{−1} s), LMA of #3: R\textsubscript{LMA}:=0.074+0.085*\(V\) (kPa litre\textsuperscript{−1} s). Trans-laryngeal pressure (P\textsubscript{larynx}) was, therefore, calculated by subtracting the R\textsubscript{LMA} \(\times \(V\) from the P\textsubscript{delta} for each flow rate. We calculated laryngeal resistance (R\textsubscript{larynx}) at a constant flow rate of 0.15 litre s\textsuperscript{−1} (R\textsubscript{larynx,0.15}) during inspiration and expiration in addition to R\textsubscript{larynx} at maximum inspiratory and expiratory flow rates (R\textsubscript{larynx,max}).

\textbf{Statistical analysis}

All values are given as median (10–90th percentiles). Comparison between the pre- and postoperative variables for each group and comparison between R\textsubscript{larynx} on inspiration and expiration were performed using the Wilcoxon Signed Rank test. Statistical differences were considered significant when P<0.05.

\begin{table}[ht]
\centering
\begin{tabular}{|l|c|c|}
\hline
 & Isoflurane & Sevoflurane \\
\hline
Number of patients & 8 & 8 \\
Sex (male/female) & 7/1 & 6/2 \\
Age (yr) & 45.0 (36–69) & 47.0 (40–72) \\
Height (cm) & 154.0 (152–173) & 156.5 (145–181) \\
Weight (kg) & 58.5 (49–76) & 58.5 (48–82) \\
Operation time (min) & 179.5 (145–227) & 157.5 (65–260) \\
\hline
\end{tabular}
\caption{Patient details data and operation time of isoflurane and sevoflurane groups. Values are expressed as median (range)}
\end{table}
Results

The two patient groups were similar with respect to physical characteristics (Table 1). The duration and the types of surgery did not differ between the groups.

Breathing patterns

Ventilatory variables and the values of $P\nCO_2$ obtained from each group before and after operation are shown in Table 2. In the ISO group, $T_i$ was longer ($P=0.008$) and $T_e$ shorter ($P=0.016$) after surgery while $RR$ did not change. In the SEVO group, $T_i$ did not change after surgery while $T_e$ was significantly less than before surgery ($P=0.008$), resulting in a slight, but significant increase in $RR$ ($P=0.016$). In addition to these changes, $P_{0.1}$ significantly increased after the surgery in SEVO group ($P=0.016$). In both groups, $T_e$ was less because $T_{e-pause}$ was less ($P=0.008$) (Fig. 1). $T_i/T_{tot}$ increased after surgery in both groups ($P=0.008$). No difference was observed in $V_T$, $MV$, and $P\nCO_2$ before and after the surgery.

Laryngeal airway resistances ($R_{larynx}$)

Figure 2 shows an example of $P_{larynx}-V$ relationships before and after surgery in one subject of the ISO group. The $P_{larynx}-V$ relationships were curvilinear both on inspiration and expiration, and a large amount of hysteresis was present particularly on inspiration. The slope of the postoperative $P_{larynx}-V$ curve, which represents translaryngeal airway resistance, was always greater than that of preoperative curve both on inspiration and expiration.

Changes of $R_{larynx}$ before and after surgery for each group are given in Table 3. Both $R_{larynx-0.15}$ and $R_{larynx-max}$ were significantly greater after surgery than before surgery both on inspiration ($P=0.016$, $P=0.016$ ISO group and $P=0.016$, $P=0.008$ SEVO group, respectively) and expiration ($P=0.023$, $P=0.039$ ISO group and $P=0.023$, $P=0.039$ SEVO group, respectively). There were no significant differences in the values of $R_{larynx-0.15}$ between inspiration and expiration in both the ISO and SEVO groups.

Discussion

The major findings of this study were as follows: (1) a significant shortening of $T_e$ and an increase in $T_i/T_{tot}$ were observed after surgery both during isoflurane anaesthesia and during sevoflurane anaesthesia; (2) $T_i$ increased only during isoflurane anaesthesia; (3) $P_{0.1}$ increased during sevoflurane anaesthesia but it did not change during isoflurane anaesthesia after surgery; and (4) $R_{larynx}$ significantly increased both during isoflurane anaesthesia and during sevoflurane anaesthesia. Thus, the results indicated that minor surgery with endotracheal intubation affects breathing patterns in postoperative period, and that sevoflurane and isoflurane had different effects.
**Postoperative breathing pattern**

Breathing abnormality, such as rapid shallow breathing with increase in central respiratory drive, has been reported to occur after upper abdominal and thoracic surgery.\textsuperscript{2,3,9,13,14} Postoperative pain relief did not normalize the breathing pattern after lower abdominal surgery.\textsuperscript{15} Tulla and colleagues found that minor surgery had a minimal effect on the breathing pattern.\textsuperscript{16} Postoperative breathing pattern may thus depend on the magnitude of the surgical stress, unrelated to pain. We observed no significant changes in \( V_t \), \( MV \), and \( P_{\text{ET}}^{\text{CO}_2} \) in our patients, but, this does not necessarily mean that minor surgery does not affect the breathing pattern at all. Detailed analysis of breathing pattern from a consistent shortening of \( T_e \) and increase in \( T_i/ \) \( T_{\text{tot}} \) after surgery in both the ISO and SEVO groups. The differences in \( T_i \) and \( P_{0.1} \) suggest that minor surgery may have different effects on respiratory control, depending on the different anaesthetic agents. The effects we found could also be caused by a time effect as the design of our study does not allow us to be sure that the changes found were related specifically to the effects of minor surgery. The respiratory depression caused by volatile anaesthetics decreases with time despite the same end-tidal concentration of volatile anaesthetics, and the degree of recovery from respiratory depression is different between different volatile anaesthetics.\textsuperscript{17}

There was a considerable difference in the values of \( P_{0.1} \) obtained before the surgery between the ISO and SEVO groups. Although the underlying mechanisms are unclear, the difference might be primarily a result of the different effects of the two agents on the central respiratory neural network, secondary to the difference in the shape of occlusion pressure waveform between the two groups. Thus, we should be cautious about comparing the \( P_{0.1} \) values of the two groups.

**Role of the larynx**

We examined the breathing pattern without bypassing the larynx, which is an internal variable resistance that may control respiratory timing.\textsuperscript{5} Respiratory timing is determined by interaction between central modulation and peripheral mechanics, and postoperative changes in respiratory timing may be affected by the laryngeal airflow regulation. Kuna, Insalaco and Woodson\textsuperscript{18} measured laryngeal adductor muscle activity in awake and sleeping human adults, and demonstrated that while awake, the level of phasic expiratory activity was directly related to \( T_e \) and expiratory \( R_{\text{larynx}} \), but the activity was absent in NREM sleep. We know of no study on laryngeal modulation of the respiratory timing in anesthetized humans. Although we did not measure laryngeal muscle action, we found no

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**Table 2** Ventilatory variables and \( P_{\text{ET}}^{\text{CO}_2} \) of each group before and after surgery. \( V_t \)=tidal volume; \( T_i \)=duration of inspiration; \( T_e \)=duration of expiration; \( T_{\text{active}} \)=duration of active expiration; \( T_{\text{pause}} \)=duration of end-expiratory pause; \( T_{\text{tot}} \)=respiratory cycle time; \( TVT_{\text{tot}} \)=duty ratio; \( R R \)=respiratory frequency; \( MV \)=minute volume; \( P_{0.1} \)=inspiratory occlusion pressure at 0.1 s; \( P_{\text{ET}}^{\text{CO}_2} \)=end-tidal carbon dioxide tension. Values are expressed as median (10±90%). *\( \text{P}<0.05 \) and **\( \text{P}<0.01 \), respectively, vs before surgery

<table>
<thead>
<tr>
<th></th>
<th>Isoflurane</th>
<th>Sevoflurane</th>
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<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>( V_t ) (litre)</td>
<td>0.23 (0.18–0.42)</td>
<td>0.23 (0.18–0.35)</td>
</tr>
<tr>
<td>( T_i ) (s)</td>
<td>0.87 (0.69–1.19)</td>
<td>1.05 (0.80–1.30)**</td>
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<tr>
<td>( T_e ) (s)</td>
<td>1.70 (1.48–2.36)</td>
<td>1.60 (1.18–2.01)**</td>
</tr>
<tr>
<td>( T_{\text{active}} ) (s)</td>
<td>1.23 (1.21–1.45)</td>
<td>1.29 (1.03–1.61)</td>
</tr>
<tr>
<td>( T_{\text{pause}} ) (s)</td>
<td>0.41 (0.28–0.92)</td>
<td>0.26 (0.15–0.41)**</td>
</tr>
<tr>
<td>( TVT_{\text{tot}} ) (s)</td>
<td>0.35 (0.27–0.42)</td>
<td>0.39 (0.34–0.51)**</td>
</tr>
<tr>
<td>( RR ) (breath min(^{-1}))</td>
<td>23.0 (18.1–26.1)</td>
<td>23.1 (19.4–29.2)</td>
</tr>
<tr>
<td>( MV ) (litre min(^{-1}))</td>
<td>5.01 (3.78–10.65)</td>
<td>4.97 (3.95–9.38)</td>
</tr>
<tr>
<td>( P_{0.1} ) (kPa)</td>
<td>0.17 (0.10–0.26)</td>
<td>0.20 (0.16–0.29)</td>
</tr>
<tr>
<td>( PV_{\text{CO}_2} ) (kPa)</td>
<td>5.33 (5.15–6.09)</td>
<td>5.47 (5.07–6.13)</td>
</tr>
</tbody>
</table>

**Table 3** Laryngeal airway resistances (\( R_{\text{larynx}} \)) of each group before and after surgery. Values are expressed as median (CI 10–90%) (kPa litre\(^{-1}\) s). *\( \text{P}<0.05 \) and **\( \text{P}<0.01 \), respectively, vs before surgery

<table>
<thead>
<tr>
<th></th>
<th>Isoflurane</th>
<th>Sevoflurane</th>
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<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>( R_{\text{larynx}} ) at maximum inspiratory flow</td>
<td>0.18 (0.04–0.22)</td>
<td>0.30 (0.22–0.75)*</td>
</tr>
<tr>
<td>( R_{\text{larynx}} ) at maximum expiratory flow</td>
<td>0.17 (0.05–0.24)</td>
<td>0.31 (0.17–0.64)*</td>
</tr>
<tr>
<td>( R_{\text{larynx}} ) at a flow of 0.15 litre s(^{-1})</td>
<td>0.16 (0.05–0.20)</td>
<td>0.22 (0.16–0.48)*</td>
</tr>
<tr>
<td>On inspiration</td>
<td>0.13 (0.04–0.21)</td>
<td>0.24 (0.13–0.45)*</td>
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difference in resistance between inspiration and expiration, unlike the awake condition.\(^{19}\) Laryngeal regulation of respiratory airflow under general anaesthesia is probably less than in conscious state and the larynx may not have had an important role in the modulation of respiratory timing in our quietly breathing anaesthetized subjects. We did find that laryngeal resistance had increased after the surgery, probably from changes such as laryngeal swelling produced by the endotracheal intubation.

**The influence of increased laryngeal resistance on the postoperative breathing pattern**

It is reasonable to consider that an increase in laryngeal resistance could affect breathing pattern after minor surgery. Flow limitation by increased laryngeal resistance could prolong both \(T\) and \(T_E\), reduce \(RR\), and decrease \(MV\). However, we did not find any reduction of \(RR\), and \(MV\) was well preserved. Compensatory mechanisms may be active. Although \(T\) increased in the ISO group, this prolongation did not accompany changes in \(P_{O_{2.1}}\). This could maintain \(V_T\) in the face of increased laryngeal resistance. In contrast, \(P_{O_{2.1}}\) increased without changes in \(T\) in SEVO group, suggesting that augmentation of neural drive has occurred. The compensatory mechanisms in response to a small increase in laryngeal inspiratory resistance during isoflurane anaesthesia seem to differ from those during sevoflurane anaesthesia, although we have no explanation for the difference between the two anaesthetic agents.

\(T/I\) consistently increased in both the SEVO and ISO groups after minor surgery in this study and this increase was mainly a result of significant shortening of \(T_E\). The increase in \(T/I\) was ascribed from shortening of \(T_{E-pause}\) and that the duration of active expiration did not alter after the surgery. It is likely that these changes are caused by the effects of minor surgery on respiratory control and for the shortening of \(T_{E-pause}\) may be compensation for the increase in expiratory flow resistance.

Minor surgery changes breathing pattern, affecting respiratory timing. This change in breathing pattern may result from an increase in laryngeal resistance caused by endotracheal intubation. There was also a slight difference in postoperative breathing pattern between sevoflurane and isoflurane, presumably because the central nervous system has different responses to different anaesthetics.

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**References**