Intravenous opioids reduce airway irritation during induction of
anaesthesia with desflurane in adults

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Desflurane is a halogenated ether with low solubility (partition coefficients: blood:gas, 0.42; oil:gas, 18.71),
giving rapid induction and emergence from anaesthesia.2–3
It has other valuable features, such as stability in soda
limes4–5 and negligible biotransformation to toxic metabo-
lites,6–7 and hence a low potential for hepatic and renal
toxicity. However, it can cause airway irritation when used for
the induction of anaesthesia in adults8–12 and children,
leading to coughing, apnoea, laryngospasm, copious secre-
tions and excitatory movements.13 14 We studied the ability
of intravenous opioids to reduce the airway irritation caused
by desflurane.

Patients

With hospital ethics committee approval and patient
consent, 180 adult ASA I and II patients aged between 18
and 65 yr who were scheduled for elective surgery entered
the study. The exclusion criteria were anaemia, a history
suggestive of malignant hyperthermia, a family history of
anaesthetic mishaps, severe lung disease, chronic cough
(cough occurring for at least 3 months of the year for 2
 successive years), obesity (body mass index >30 kg m−2),
previous exposure to desflurane, smoking, and medication
that could interfere with the study (e.g. anxiolytics). Patients
with a history of upper respiratory tract infection within 1
month of surgery were also excluded. Patients were
randomized to three groups (60 patients per group) to receive
morphine, fentanyl or saline before induction with desflur-
an. Randomization was by means of sealed envelope.

Methods

Monitoring included continuous ECG, pulse oximetry, non-
invasive blood pressure, end-tidal CO2 and expired
desflurane concentration (Hewlett-Packard Anaesthetic
Gas Module M1026A).

The opioids were given from a syringe containing either
fentanyl, morphine or saline made up to 10 ml (in saline if
necessary), prepared by an assistant who was not involved

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in the study. The anaesthetist administered the drugs over 1 min and was not aware of the contents of the syringe.

Saline (group C), morphine 0.1 mg kg\(^{-1}\) (group M) or fentanyl 1 \(\mu g\) kg\(^{-1}\) (group F) was given 2 min before preoxygenation with 100% oxygen at 6 litre min\(^{-1}\) for 3 min using a circle system with soda lime absorber. The oxygen flow was then reduced to 3 litre min\(^{-1}\) and nitrous oxide (50%) was started at 3 litre min\(^{-1}\). Desflurane 1% was started and increased by 1% after every six breaths. Every 10 s during this period, each patient was asked to open his or her eyes. The time when the patient failed to respond to this command was taken as the time of completion of inhalational induction.

We recorded the age, sex, weight, ASA status, diagnosis and the type of surgical procedure for each patient. The reading of the pulse oximeter before induction and the lowest reading obtained during induction were noted. The time between starting desflurane and loss of consciousness was calculated and the expired desflurane concentration at loss of consciousness was noted. Any coughing, apnoea, laryngospasm or excitatory movements were noted. Coughing was considered mild if there were 1–3 coughs, moderate if there were 4–7 coughs and severe if there were 8 coughs or more. Apnoea was noted as no breathing movements for more than 30 s.

If patients developed laryngospasm, i.v. propofol 2 mg kg\(^{-1}\) was given with the addition of i.v. suxamethonium 1 mg kg\(^{-1}\) if necessary. The patients were then ventilated using the mask with 100% O\(_2\) until saturation improved.

If apnoea and oxygen desaturation were present (Sp\(_O_2\), <90%, or a decrease of more than 5% from initial value), the lungs were ventilated via a mask until spontaneous respiration returned.

**Statistics**
Analysis of variance (ANOVA) was used to analyse parametric data and all non-parametric data were analysed using the Kruskal–Wallis and Mann–Whitney tests. A \(P\) value of <0.05 was considered significant.

**Results**
The three groups were comparable in age, sex, weight and ASA status (Table 1).

The induction times for the three study groups are given in Table 2, and were not significantly different (\(P=0.26\)).

The expired desflurane concentrations at loss of response to command are given in Table 2. The concentration was greater in the morphine group than in the control group (\(P=0.02\)).

The incidence of complications is shown in Table 3. Significant differences in coughing were found between the control and fentanyl groups (\(P=0.002\)) and between the

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**Table 1** Characteristics of the three groups

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Fentanyl</th>
<th>Morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>60</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Age (y) (mean)</td>
<td>43(21–65)</td>
<td>45(22–65)</td>
<td>46(17–65)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>56 (10)</td>
<td>55 (9.6)</td>
<td>58 (13.2)</td>
</tr>
<tr>
<td>ASA status</td>
<td>52, 8</td>
<td>56, 4</td>
<td>50, 10</td>
</tr>
<tr>
<td>Sex (M, F)</td>
<td>25, 35</td>
<td>19, 41</td>
<td>23, 37</td>
</tr>
</tbody>
</table>

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**Table 2** Time required for induction and the expired desflurane concentration at induction. Values with the same superscript are significantly different (\(P<0.05\))

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Fentanyl</th>
<th>Morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to loss of response to command (min)</td>
<td>4.0 (1.1)</td>
<td>3.8 (1.4)</td>
<td>4.0 (1.5)</td>
</tr>
<tr>
<td>Exhaled desflurane concentration at loss of response to command (%)</td>
<td>3.8 (1.1)</td>
<td>3.9 (1.2)</td>
<td>4.4 (1.5)</td>
</tr>
</tbody>
</table>

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**Table 3** Incidence of cough, apnoea, laryngospasm and excitatory movements during desflurane induction. Values with the same superscript are significantly different (\(P<0.05\))

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Fentanyl</th>
<th>Morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>25.0%(^{ab})</td>
<td>5.0%(^a)</td>
<td>8.3%(^b)</td>
</tr>
<tr>
<td>Apnoea</td>
<td>20.0%(^{c})</td>
<td>13.3%</td>
<td>5.0%(^{c})</td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>46.7%(^{d})</td>
<td>16.7%</td>
<td>8.3%(^{d})</td>
</tr>
<tr>
<td>Excitatory movements</td>
<td>11.7%(^{e})</td>
<td>3.3%</td>
<td>1.7%(^{e})</td>
</tr>
</tbody>
</table>
control and morphine groups (P=0.013). No differences were found between the morphine and fentanyl groups.

The difference in apnoea between the control and morphine groups was statistically significant (P=0.012). No significant differences were found between the control and fentanyl groups or the morphine and fentanyl groups.

Seven patients in the control group had laryngospasm. In one of these, oxygen saturation decreased to 70%. Two patients in the fentanyl group and one patient in the morphine group had laryngospasm without oxygen desaturation. There was a significant difference between the control and morphine groups (P=0.025). No differences were found between the control and fentanyl groups or the morphine and fentanyl groups.

There were more excitatory movements in the control group than in the morphine group (P=0.025), but the control and fentanyl groups and the morphine and fentanyl groups did not differ.

The blood pressure and heart rate changes in the three groups are given in Table 4. Overall there were no group differences and the magnitudes of the changes were not of clinical significance.

### Discussion

#### Expired desflurane concentration at the end of induction

The mean (SD) expired desflurane concentration at completion of induction in the control, fentanyl and morphine groups was 3.8 (1.1), 3.9 (1.2) and 4.4 (1.5)%, respectively. During the study, 50% N₂O was introduced together with desflurane. This could explain the lower expired desflurane concentration at the completion of induction, as the use of N₂O reduces the minimal alveolar concentration (MAC) of volatile anaesthetic.

This study showed a significant difference in the expired desflurane concentration at the end of induction between the control and morphine groups. This difference may have been the result of sedation cause by morphine.

No differences were found between the fentanyl and control groups. Fentanyl had a peak effect at 4–5 min. It may be that the effect of fentanyl was beginning to wear off (even though its duration of action is 20–30 min).

#### Time to loss of response to command

No differences were found between the three groups in the time taken to induction, which was approximately 5 min. This could be due to the slow, small increments in inhaled concentration in the study design because of the risk of laryngospasm.

Coughing occurs in 26–59% of patients during desflurane inhalation. 8–12 This is supported by our results. The control group had an incidence of coughing of 25.0%. Among the 14 patients who coughed, cough was mild in two, moderate in seven and severe in five. Morphine or fentanyl reduced the incidence of coughing. In the fentanyl group, all three patients had mild cough, whereas of the five patients who received morphine two had mild cough, two had moderate cough and one had severe cough.

Sevoflurane is often used for inhalational induction in both adults and children, with coughing in 16%. 17–19 The tidal volume induction technique may be associated with a greater incidence of airway complications compared with vital capacity induction. 17–19 Pretreatment with morphine or fentanyl reduces the incidence of airway complications below 10% during tidal volume induction using desflurane.

This study also supports the incidence of apnoea reported in the literature (13–35%), 8–12 with 20% in the control group. Pretreatment with morphine or fentanyl reduced the incidence of this adverse effect to 5 and 13.3%, respectively. These incidences are comparable with those reported for sevoflurane (16%). 17–19

The incidence of excitation is reported to be 24–43%, 8–12 and was 47% in this study. Pretreatment with morphine or fentanyl reduces the incidence to 8.3% and 16.7%, respectively. When sevoflurane is used for induction 12% of patients exhibit excitatory movements. 17–19 Morphine pretreatment reduces the incidence of excitatory movements to a comparable figure during desflurane inhalational induction.

Seven patients (11.7%) in the control group had laryngospasm during induction, similar to the reported incidence of up to 17%. 8–12 Three of these seven patients also had cough of moderate severity, two had apnoea and five had excitatory movements. One patient, a 31-yr-old ASA I man, had significant desaturation during induction. He also had excitatory movement but he did not cough or become apnoeic during induction. His blood pressure remained stable.
One patient in the morphine group had laryngospasm. He
did not cough or have apnoea or excitatory movements
during induction, or show arterial desaturation during the
episode. Two patients in the fentanyl group had laryngos-
spam with mild cough and excitatory movement. They did
not have apnoea or arterial oxygen desaturation during this
episode. Laryngospasm is reported in 3–8% of patients
induced with sevoflurane and a tidal volume induction

technique. Pretreatment with morphine or fentanyl
reduces the incidence of laryngospasm during desflurane
induction to a figure comparable with sevoflurane induction.

Conclusion
Pretreatment with morphine or fentanyl reduces the inci-
dence of airway irritation to a value similar to that value
reported with sevoflurane during inhalational induction of
anaesthesia. However, for direct comparison a randomised
study should be performed. With opioid pretreatment, desflurane can be considered for inhalational induction of
anaesthesia in adults.

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