INSPIRATORY TO END-TIDAL OXYGEN DIFFERENCE DURING NITROUS OXIDE ANAESTHESIA

J. P. BENGTSON, Å. HARALDSSON, A. BENGTSSON, B.-Å. HENRIKSSON AND O. STENQVIST

SUMMARY
In order to evaluate the value of the inspiratory to end-tidal oxygen concentration difference \((i_{O_2} - e_{O_2})\) as a monitor during general anaesthesia, we studied 40 orthopaedic patients allocated randomly to four groups: anaesthesia with enfurane or isoflurane in nitrous oxide with either spontaneous or controlled ventilation \((i_{O_2} - e_{O_2})\) followed an asymptotically increasing curve because of decreasing uptake of nitrous oxide. At 1 h, \((i_{O_2} - e_{O_2})\) approached the end-tidal carbon dioxide concentration \((e_{CO_2})\). During spontaneous ventilation, \((i_{O_2} - e_{O_2})\) correlated best with \(e_{CO_2}\). During controlled ventilation, there was a negative correlation between \((i_{O_2} - e_{O_2})\) and nitrous oxide uptake rate. Changes in oxygen uptake rate were reflected in \((i_{O_2} - e_{O_2})\), provided that the total ventilation volume was constant and the nitrous oxide uptake rate approached steady state conditions.

KEY WORDS

Breath-by-breath analysis of oxygen concentration has become available recently through improvements in paramagnetic oxygen analysers [1, 2]. In addition to the inspiratory oxygen concentration \((i_{O_2})\), fast response oximetry gives end-tidal oxygen \((e_{O_2})\) and the inspiratory to end-tidal oxygen concentration difference \((i_{O_2} - e_{O_2})\). In animal experiments, an increasing \((i_{O_2} - e_{O_2})\) was the most sensitive indicator of hypoventilation and exceeded the sensitivity of end-tidal carbon dioxide \((e_{CO_2})\) [3]. This finding has been confirmed during clinical anaesthesia [4]. \((i_{O_2} - e_{O_2})\) theoretically reflects metabolism, circulation and ventilation. During nitrous oxide anaesthesia, uptake of nitrous oxide influences the end-tidal oxygen concentration as the expiratory volume decreases by the nitrous oxide uptake [5]. The interpretation of \((i_{O_2} - e_{O_2})\) during anaesthesia is therefore complicated.

This study was undertaken to evaluate \((i_{O_2} - e_{O_2})\) as a monitoring variable during nitrous oxide anaesthesia.

MATERIALS AND METHODS
The study was approved by the Ethics Committee of the University of Göteborg.

\(i_{O_2}\) and \((i_{O_2} - e_{O_2})\) were measured between the Y-piece and the tracheal tube with a sampling paramagnetic analyser (Multicap, Datex Instrumentarium OY, Helsinki, Finland). The 10–90% response time was 150 ms, with a non-linearity error of less than \(\pm 1\%\) [2]. \(e_{CO_2}\) and inspiratory nitrous oxide concentration \((i_{N_2O})\) were measured by infrared absorption in the Multicap.

A circle absorber system (Monosorb, Siemens-Elema, Solna, Sweden) of total volume 4.5 litre with a graded standing bellows was used. Expiratory total ventilation \((V_e)\) was measured between the tracheal tube and the Y-piece with a turbine vane transducer sensor of stated accuracy of \(\pm 8\%\) (Ohmeda 5420, BOC Health Care Division).

Sampling gas from the gas analyser was returned to the circle system through a uni-directional valve placed before the absorption canister. The analyser was calibrated before and after each patient with a certified gas containing 3.0% carbon dioxide, 31% oxygen, 59% nitrous oxide and 7% nitrogen (AGA GAS AB, Stockholm, Sweden), and with 100% oxygen and 100% nitrous oxide. An anaesthetic agent monitor (Normac, Datex Instrumentarium OY, Helsinki, Finland) was calibrated according to the manufacturer's instructions, with a calibration gas. The displayed readings were within 0.05 vol% of the calibration gas. The oxygen and nitrous oxide flowmeters were calibrated with a Calibration Analyzer RT-200 (Timeter International Inc., Lancaster, PA 17601, U.S.A.). These flowmeters were checked also by the filling times of the Mylar bag used for the collection of excess gas.

Excess gas was collected every 10 min in a non-permeable Mylar bag connected to the spill valve. The gas pressure in the bag was measured during the collection period. When the pressure increased from \(-0.2\) to \(1.5\) cm H\(_2\)O, the bag contained a gas volume of 660 ml. The time needed for this pressure increase was recorded every 10 min until completion of surgery. The excess gas flow could thereby be calculated. The gas contained in the Mylar bag was then analysed for oxygen and nitrous oxide concentrations.
ventilation was controlled so that $\epsilon_{\text{co}_2}$, 4.5 vol% was obtained.

Six minutes after tracheal intubation, low flow anaesthesia was started. $Vfg_{\text{o}_2}$ was set according to body weight. Patients with a body weight of less than 70 kg received oxygen 250 ml min$^{-1}$, those weighing 70–100 kg received 350 ml min$^{-1}$, and for patients with a body weight of more than 100 kg, 500 ml min$^{-1}$ was used. $Vfg_{\text{N}_2\text{o}}$ was adjusted to maintain $\epsilon_{\text{N}_2\text{o}}$, 30 vol%. If the bellows were emptying, $Vfg_{\text{N}_2\text{o}}$ was increased by 50 ml min$^{-1}$. Either enflurane or isoflurane was given with an end-tidal concentration maintained at 1.2 or 0.85 vol%, respectively. If it became necessary to increase the depth of anaesthesia during the course of anaesthesia, thiopentone 50 mg was given i.v.

After obtaining informed consent, we studied 40 ASA group I and II patients undergoing knee arthroscopy who were allocated randomly to one of four groups:

- **Group ES.** Enflurane: end-tidal concentration maintained at 1.2 vol%. The patients breathed spontaneously after the initial 6 min described above.
- **Group EC.** Enflurane as in group ES, but ventilation controlled to maintain an end-tidal carbon dioxide concentration of 4.5 vol%.
- **Group IS.** Isoflurane: end-tidal concentration maintained at 0.85 vol%. Spontaneous breathing after 6 min.
- **Group IC.** Isoflurane as in group IS, but ventilation controlled to maintain an end-tidal carbon dioxide concentration of 4.5 vol%.

**Statistics**

Statistical significance was tested with ANOVA and Fisher’s PLSD test between groups during the first 1 h of anaesthesia, and with repeated measures ANOVA and Fisher’s PLSD test within each group in association with the start of surgery. Linear regression analysis was used when appropriate. Statistical significance was assumed for values of $P < 0.05$.

**RESULTS**

The mean age of the 40 patients was 36 yr and mean weight 78 kg; 11 were women.

After the initial 6 min of controlled ventilation, the mean ($\epsilon_{\text{o}_2}$) was 1.6–1.8 vol% in all groups (fig. 1). In the groups with continuous controlled ventilation, ($\epsilon_{\text{o}_2}$) increased gradually to 4.3 vol% at 60 min. In the groups with spontaneous ventilation (groups ES and IS) ($\epsilon_{\text{o}_2}$) increased rapidly to about 5.4 vol% at 10 min. At 60 min, the mean values were 6.5 and 5.9 vol% in groups ES and IS, respectively. At the first measurement with spontaneous ventilation (10 min after induction of anaesthesia) there were significant ($P < 0.05$) differences in ($\epsilon_{\text{o}_2}$) between the groups with spontaneous ventilation and those with controlled ventilation. These differences persisted throughout the first 1 h, with the exception of the measurements at 30 and 40 min. At these measurements, ($\epsilon_{\text{o}_2}$) in group IS was not significantly different from the
values in groups IC or EC. Group ES had greater values of \((i_o - E'_{o})\) than group IS at 30, 40 and 50 min \((P < 0.05\) in all cases).

Linear regression analysis was used between \((i_o - E'_{o})\) and \(\dot{V}N_{2}O\). The strongest positive association was found between \((i_o - E'_{o})\) and \(E'_{co2}\) in the two groups with spontaneous ventilation (fig. 2). The relationship was:

\[
E'_{co2} = 4.1 + 0.40 \times (i_o - E'_{o})
\]
\((r = 0.79, P < 0.001)\).

A negative association was found between \((i_o - E'_{o})\) and nitrous oxide uptake during controlled ventilation (fig. 3). Linear regression analysis gave the formula:

\[
\dot{V}N_{2}O = 468 - 65 \times (i_o - E'_{o})
\]
\((r = -0.70, P < 0.001)\).

With the start of surgery (mean time 22–25 min after induction of anaesthesia in all groups), \((i_o - E'_{o})\) decreased in the groups with spontaneous ventilation \((P < 0.05)\), whereas \((i_o - E'_{o})\) increased during controlled ventilation \((P < 0.05)\) (table I). Associated mean values for ventilatory frequency, tidal volume, \(E'_{co2}\), \(\dot{V}O_2\) and \(\dot{V}N_{2}O\) are given also in table I. During controlled ventilation, a change in \(\dot{V}O_2\) correlated significantly with a change in \((i_o - E'_{o})\) according to the formula:

\[
\Delta \dot{V}O_2 (\text{ml kg}^{-1} \text{min}^{-1}) = -0.01 + 0.20 \times \Delta (i_o - E'_{o})
\]
\((r = 0.55, P < 0.05)\).

**DISCUSSION**

Theoretically, one would expect \((i_o - E'_{o})\) to correlate positively with \(E'_{co2}\) and \(\dot{V}O_2\) and negatively with \(Ve\) and \(\dot{V}N_{2}O\). Assuming that the oxygram is an inversion of the capnogram and that the respiratory quotient is 1.0, \((i_o - E'_{o})\) should equal \(E'_{co2}\) during air breathing in steady state conditions. A respiratory quotient of less than 1.0 would result in an \((i_o - E'_{o})\) greater than \(E'_{co2}\). This is usually not the case during the first 1 h of anaesthesia with 70% nitrous oxide. At the start of a nitrous oxide anaesthetic, the uptake of nitrous oxide results in a difference between inspired and expired ventilatory volumes. The \(E'_{o}\) can therefore be greater than the \(i_o\) despite a normal uptake of oxygen from the lungs—that is \((i_o - E'_{o})\) has a negative value [5]. Subsequently, as \(\dot{V}N_{2}O\) decreases, \((i_o - E'_{o})\) increases. As the sum of the partial pressures of oxygen, carbon dioxide, nitrogen and anaesthetic gases must be constant, \(E'_{o}\) is dependent on \(E'_{co2}\) and on the end-tidal concentrations of anaesthetic gases. Thus \(E'_{o}\) decreases and \((i_o - E'_{o})\) increases with increasing \(E'_{co2}\) and \(E'_{N}_{2}O\).

A possible advantage of \((i_o - E'_{o})\) in monitoring compared with \(E'_{co2}\) is its greater sensitivity to increases or decreases in respiratory gas exchange. This is probably a result of the small buffering capacity in the body for oxygen. Therefore, acute hyperventilation is detected by the \((i_o - E'_{o})\) before \(E'_{co2}\) [3, 4].

In this study, the displayed \((i_o - E'_{o})\) correlated best with \(E'_{co2}\) during spontaneous ventilation and with \(\dot{V}N_{2}O\) during controlled ventilation. An approximation of the expected \((i_o - E'_{o})\) time course during nitrous oxide anaesthesia based on our results is:

\[
(i_o - E'_{o}) (\text{vol} \%) = E'_{co2} (\text{vol} \%) / 0.85 - 10 \times \dot{V}N_{2}O \text{ } t^{-0.5}
\]

where \(t\) represents time in minutes from the start of nitrous oxide anaesthesia.

The complexity of \((i_o - E'_{o})\) as a monitor was illustrated at the start of surgery. With spontaneous ventilation, the increased tidal volume and decreased \(E'_{co2}\) resulted in a decreased \((i_o - E'_{o})\). In contrast, during controlled ventilation an increased oxygen uptake and a decreased nitrous oxide uptake resulted in an increased inspiratory to end-tidal oxygen concentration difference.

**Table I**: Respiratory variables before and after the start of surgery (mean (SD)). BS = Last measurement before the start of surgery; AS = first measurement after the start of surgery; \(f\) = ventilatory frequency; \(VT\) = tidal volume

<table>
<thead>
<tr>
<th>Ventilation</th>
<th>Spontaneous (Groups ES + IS)</th>
<th>Controlled (Groups EC + IC)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BS</td>
<td>AS</td>
</tr>
<tr>
<td>(f) (b.p.m.)</td>
<td>21.8 (4.9)</td>
<td>23.8 (5.5)</td>
</tr>
<tr>
<td>(\dot{V}T) (ml)</td>
<td>172 (45)</td>
<td>257 (59)</td>
</tr>
<tr>
<td>(E'_{co2}) (vol%)</td>
<td>6.9 (0.9)</td>
<td>6.4 (1.1)</td>
</tr>
<tr>
<td>(\dot{V}O_2) (ml min^-1)</td>
<td>186 (51)</td>
<td>222 (46)</td>
</tr>
<tr>
<td>(\dot{V}N_{2}O) (ml min^-1)</td>
<td>283 (105)</td>
<td>182 (49)</td>
</tr>
<tr>
<td>((i_o - E'_{o})) (vol%)</td>
<td>7.0 (2.2)</td>
<td>5.8 (1.6)</td>
</tr>
</tbody>
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REFERENCES


