ACUTE VENTILATORY CHANGES DURING I.V.
INDUCTION OF ANAESTHESIA WITH THIOPENTONE OR
PROPOFOL IN MAN
Studies Using Inductance Plethysmography

R. M. GROUNDS, D. L. MAXWELL, M. B. TAYLOR, V. ABER AND
D. ROYSTON

Propofol (2,6 di-isopropylphenol formulated as an emulsion) has been shown to be a suitable agent with which to induce anaesthesia for short procedures and day case surgery (Cummings et al., 1984; Cummings and Spence, 1985; Redfern et al., 1985). However, a number of studies have shown that the administration of propofol is associated with respiratory depression characterised by periods of apnoea (Goodman, Carter and Black, 1985; Taylor et al., 1987). Interest lies in whether the mechanism of this respiratory depression is central in nature, as with opioid drugs which depress respiration by producing apnoea (Prys-Roberts and Kelman, 1967) or more peripheral in nature, as with drugs such as thiopentone (Jordan, 1982).

In an attempt to investigate the mechanism of the respiratory depression, we have compared the changes in ventilation during the induction of anaesthesia in two similar groups of patients, using ventilatory inductance plethysmography (VIP) (Respitrace Ambulatory Monitoring Systems Inc., New York). The use of VIP for the study of the respiratory effects of drugs has been described previously (Jordan, Jones and Pinto, 1979; Catling et al., 1980) and has the advantage that changes in resting lung volume can be recorded as well as changes in ventilation and the pattern of breathing.

SUMMARY
We have compared the acute ventilatory changes during induction of anaesthesia with equipotent doses of thiopentone and propofol in 12 premedicated female patients. Using ventilatory inductance plethysmography we have shown that both agents depress respiration to a similar and significant degree (P < 0.001). However, although the functional residual capacity was reduced in patients receiving propofol, it increased slightly after induction with thiopentone (P < 0.05).

PATIENTS AND METHODS
Twelve female patients (ASA Grade I) about to undergo elective minor gynaecological surgery were studied. All patients gave their written informed consent to inclusion in the trial, which had been approved by the hospitals ethics committee.

All patients received papaveretum and hyoscine as premedication which was given i.m. approximately 1 h before the induction of anaesthesia (< 50 kg: papaveretum 10 mg, hyoscine 0.2 mg; 50–70 kg: papaveretum 15 mg, hyoscine 0.3 mg; > 70 kg: papaveretum 20 mg, hyoscine 0.4 mg). Anaesthesia was induced with either thiopentone 4 mg kg⁻¹ or propofol 2.5 mg kg⁻¹. These doses have been shown to be equipotent (Grounds, Moore and Morgan, 1986).

Minute ventilation (\(\dot{V}_E\)) and its subdivisions (tidal volume (\(V_T\)), frequency (\(f\)), the time of inspiration (\(T_I\)) and expiration (\(T_E\)), the duty inspiratory cycle (\(T_I/T_{tot}\), where \(T_{tot} = T_I + T_E\))
and mean inspiratory flow ($V_t/Ti$)) were monitored with an inductance plethysmograph (VIP). Briefly, this consists of two elasticated bands containing coils of wire placed around the chest and abdomen. Movement of the chest wall and abdomen causes changes in the self inductance of the coil of wire which can be processed subsequently to produce a volume signal. Additionally, when the inductance plethysmograph is used in its d.c. mode, overall changes in lung volume (for example with changes in functional residual capacity (FRC)) also cause corresponding changes in self inductance, so that such changes can be estimated. At least 90 min before the start of any recordings, the VIP belts were attached to the thorax and abdomen of the patients to allow the belts to achieve thermal equilibrium.

Before induction, the inductance plethysmograph was calibrated against a spirometer using a single posture technique (Mannix et al., 1984) and compared with the tidal volumes obtained from simultaneous water-bell spirometry (for 20 breaths). The validation confirmed the accuracy of the plethysmograph and provided a tidal volume ratio (spirometer:plethysmograph) with which volume measurements could be corrected subsequently. Analysis of data from the inductance plethysmograph was carried out on-line by a microcomputer and used to display a breath-by-breath update of ventilation and its subdivisions on a monitor. In addition, all variables were recorded continuously on a chart recorder. Changes in FRC during induction were estimated from changes in the end-expiratory lung volume. Mean values of minute ventilation, its subdivisions, and of the end-expiratory volume were obtained for 1-min time periods starting 1 min before the beginning of the induction of anaesthesia and ending 3 min after induction. Changes in the FRC during induction were estimated by calculating the change in end-expiratory volume from that obtained just before induction.

On the patient's arrival in the anaesthetic room, an ECG was attached to the patient and an i.v. cannula inserted (under local analgesia) to a suitable forearm vein. A pulse oximeter was attached to one earlobe of each patient (Ohmeda Biol II). Before the induction of anaesthesia, the patients were asked to breathe 100% oxygen via a Magill anaesthetic breathing system for at least 3 min. Anaesthesia was induced using the equipotent doses of either thiopentone 4 mg kg$^{-1}$ or propofol 2.5 mg kg$^{-1}$ given over 30 s (by R.M.G.). The investigator making the VIP recordings (D.M.) was unaware of the induction agent which the patient received.

If any patient's airway became obstructed during the period of measurement, this obstruction was relieved by the supervising anaesthetist (M.B.T.) and that patient excluded from the trial. If apnoea occurred, ventilation was assisted only if the oxygen saturation measured by the pulse oximeter decreased to less than 90%; the patient was then excluded from the study. Although three patients were apnoeic for longer than 20 s, the measured oxygen saturation did not decrease to less than 90%; thus no patient required assisted ventilation.

The study was considered complete when either 4 min had elapsed from the start of the i.v. injection or the patient showed clinical signs of starting to waken. The patient was then given a further suitable dose of the initial i.v. induction agent and anaesthesia was continued using a suitable conventional general anaesthetic technique.

The statistical analysis was by analysis of variance, and Student's $t$ test where appropriate.

RESULTS

The demographic details of the patients studied are shown in table I. All patients were female. There were no significant differences between the groups for age, weight or height. The numbers of patients remaining apnoeic for longer than 20 s were: one patient in the thiopentone group (47 s) and two patients in the propofol group (21 and 52 s).

Table II shows the changes in ventilatory variables recorded by VIP. Changes in FRC are recorded as changes from baseline, where baseline was the mean value during the 1 min before induction.

<table>
<thead>
<tr>
<th>TABLE I. Demographic details of patients studied</th>
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<tr>
<td></td>
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<tr>
<td><strong>Thiopentone</strong></td>
</tr>
<tr>
<td>No. patients</td>
</tr>
<tr>
<td>Age (yr) (mean ± SEM)</td>
</tr>
<tr>
<td>Range (yr)</td>
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<tr>
<td>Weight (kg) (mean ± SEM)</td>
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<td>Range (kg)</td>
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<tr>
<td>Height (m) (mean ± SEM)</td>
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<td>Range (m)</td>
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TABLE II. Changes (mean ± SD) in minute volume, frequency of ventilation (f), tidal volume (VT), mean inspiratory flow rate (VT/TI), the duty inspiratory cycle (Ti/TTOT) and change in function residual capacity (δFRC) during induction of anaesthesia with either thiopentone or propofol. Significant effect of time (but not drug) on: VE (P < 0.001); VT/TI (P < 0.05); VE (P < 0.01). Significant interaction between drug and time for: FRC (P < 0.05)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Time (min)</th>
<th>0-1</th>
<th>1-2</th>
<th>2-3</th>
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<tbody>
<tr>
<td></td>
<td></td>
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<tr>
<td>VT (ml)</td>
<td>Thiopentone</td>
<td>325(121)</td>
<td>288(110)</td>
<td>239(100)</td>
</tr>
<tr>
<td></td>
<td>Propofol</td>
<td>378(185)</td>
<td>449(212)</td>
<td>229(200)</td>
</tr>
<tr>
<td>VT/TI (ml)</td>
<td>Thiopentone</td>
<td>16.2(5.5)</td>
<td>14.4(5.5)</td>
<td>13.7(10.4)</td>
</tr>
<tr>
<td></td>
<td>Propofol</td>
<td>16.2(5.5)</td>
<td>14.4(5.5)</td>
<td>13.7(10.4)</td>
</tr>
<tr>
<td>Ti/TTOT (litre min⁻¹)</td>
<td>Thiopentone</td>
<td>0.44(0.05)</td>
<td>0.420(0.08)</td>
<td>0.410(0.1)</td>
</tr>
<tr>
<td></td>
<td>Propofol</td>
<td>0.44(0.07)</td>
<td>0.385(0.11)</td>
<td>0.331(0.13)</td>
</tr>
<tr>
<td>δFRC (ml)</td>
<td>Thiopentone</td>
<td>0</td>
<td>-69(140)</td>
<td>59(197)</td>
</tr>
<tr>
<td></td>
<td>Propofol</td>
<td>0</td>
<td>-122(202)</td>
<td>-228(241)</td>
</tr>
</tbody>
</table>

Analysis of variance revealed significant decreases in minute ventilation (P < 0.01), tidal volume (P < 0.001) and mean inspiratory flow (P < 0.05) following induction with both agents. These decreases were always maximal between the 1st and 2nd minutes after the start of induction. These decreases were all significant with respect to time, but not to the drug used for induction. In the patients given propofol, tidal volume decreased at a later stage and the mean inspiratory flow recovered earlier than in the thiopentone group. Although, in both groups, induction was accompanied by a reduction in ventilatory frequency, this was small and not statistically significant. However, overall there were no statistically significant differences in the pattern of breathing between the groups.

Changes in FRC during induction have been displayed as changes from baseline. From these data, it can be seen that there was a slight increase (59-104 ml) in FRC in the thiopentone group in the 3 min following induction, but a reduction of 122-228 ml in FRC in the propofol group during the same period. The difference between the two groups during this period was significant (P < 0.05).

The contribution of abdominal movement to each tidal volume, and the degree of paradoxical movement, were also measured with the inductance plethysmograph. Although there were no differences in the contribution from the abdominal belt between the two patient groups, and there was a trend towards an increase in paradoxical movement with the onset of anaesthesia, none of the changes was statistically significant.

DISCUSSION

This study confirms previous work (Bellman and Pleuvry, 1981; Taylor et al., 1986) that propofol is a respiratory depressant and that, in equipotent anaesthetic doses, it is as potent a respiratory depressant as thiopentone. However, it should be appreciated that in the study by Grounds, Moore and Morgan (1986) of the equipotency of propofol and thiopentone, the patients were not premedicated with an opioid—as in this study. The depression of minute volume produced by equipotent doses of the two agents was similar, but unlike the study in rabbits by Bellman and Pleuvry (1981), we did not find that the depression of minute volume produced by thiopentone was almost solely as a result of depression of ventilatory frequency. The depression of minute volume with both agents was caused by a reduction in both tidal volume and ventilatory rate, confirming the earlier work of Taylor and colleagues (1986) in which ventilation was monitored using a pneumotachograph. Despite having an opioid premedication, neither group of patients exhibited an opioid type of ventilatory depression, in which tidal volume may be increased but ventilatory rate reduced (Smith et al., 1967; Hunter, Pleuvry and Rees, 1968).

In this study, we have used a non-invasive method (VIP) to monitor the changes in ventila-
tony pattern during the induction of anaesthesia. Changes in ventilation or the pattern of breathing may result from alterations in $V_T/T_I$ or $T_I/T_{tot}$. In normal subjects, $V_T/T_I$ may be taken as a reasonable reflection of central neuromuscular ventilatory drive and $T_I/T_{tot}$ reflects the action of the central timing mechanism (Derenne et al., 1976). Our results suggest that the ventilatory depression accompanying the induction of anaesthesia is caused by a decrease in central inspiratory drive rather than a change in central timing. When allied to the reports of an increased frequency of apnoea following propofol (McCollum, Dundee and Robinson, 1986, unpublished observations; Taylor et al., 1986), these data suggest that the mechanism of the apnoea is dissimilar to that of the opioid drugs (Prys-Robert and Kelman, 1967) when a decrease in the ratio $T_I/T_{tot}$ would have been anticipated. However, during the present study we examined changes during the peri-induction period. This time period was chosen because the equipotent induction doses for sleep between the two agents have been defined (Grounds, Moore and Morgan, 1986). A further study comparing the two agents during steady state infusions for anaesthesia may produce different conclusions. However, these equipotent steady state infusion rates for anaesthesia are unknown.

In this study, the FRC decreased in the patients who received propofol. This was an entirely expected change and is in accordance with previous work on other i.v. and volatile anaesthetic agents (Hewlett et al., 1974). However, in addition we have shown a slight increase in FRC in the first 3 min following i.v. induction of anaesthesia with thiopentone. This result was unexpected and would be very difficult to validate using conventional steady state helium dilution techniques for the measurement of FRC. Don, Wahba and Craig (1972) felt that the primary change in ventilatory mechanics during anaesthesia was “probably a mechanical phenomenon associated with an alteration of the position of the chest wall,” but this would not explain our findings of a small increase in FRC immediately after induction with thiopentone.

In conclusion, although propofol 2.5 mg kg$^{-1}$ may be a relatively large dose for induction of anaesthesia in patients who are premedicated, it is interesting to note that this appears to be no more depressant than an equipotent dose of thiopen-

 tone. However, there are reports of a higher frequency of apnoea following induction with propofol (McCollum, Dundee and Robinson, 1986, unpublished observations; Taylor et al., 1986), and this may provide an additional problem when propofol is used in a single dose technique for the induction and maintenance of anaesthesia for short procedures and day case surgery. However, ventilatory depression may confer some benefits when propofol is used, by continuous infusion, to provide sedation in patients requiring long term intermittent positive pressure ventilation in the intensive care unit. It would allow for easier and, therefore, better management of this group of patients.

ACKNOWLEDGEMENTS

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REFERENCES


Jones, J. G., and Pinto, D. J. (1979). Postoperative respiration monitoring; in Proceedings of the Third Inter-