PROPOFOL OR THIOPENTONE: EFFECTS ON INTRAOCULAR PRESSURE ASSOCIATED WITH INDUCTION OF ANAESTHESIA AND TRACHEAL INTUBATION (FACILITATED WITH SUXAMETHONIUM)

R. K. MIRAKHUR, W. F. I. SHEPHERD AND W. C. DARRAH

Propofol (2.6 diisopropylphenol), a non-barbiturate anaesthetic agent in an emulsion formulation, provides a smooth induction of anaesthesia without major adverse effect, and is associated with rapid clear-headed recovery (Cummings et al., 1984; Nightingale et al., 1984; Kay and Healy, 1985; MacKenzie and Grant, 1985). A previous study in non-intubated patients showed that the administration of propofol was associated with a significant decrease in intraocular pressure (IOP) (Mirakhur and Shepherd, 1985). In the present study, we have compared the effects of propofol on IOP with those of thiopentone in patients receiving suxamethonium, and in whom tracheal intubation was performed.

PATIENTS AND METHODS

Sixty adult patients, 16–83 years old, conforming to ASA grades I and II and scheduled to undergo elective ophthalmic surgery, were included in the study after obtaining the approval of the Hospital Ethical Committee, and the informed consent of the patients. Patients with pre-existing increases in IOP (glaucoma), hypertension, obesity (body weight greater than 120% of that expected for age) or those receiving any drugs likely to have an effect on IOP were excluded. Following premedication with diazepam 5–10 mg by mouth, 30 patients each received a dose of either propofol 2.0–2.5 mg kg\(^{-1}\) or thiopentone 4.5–5.0 mg kg\(^{-1}\) sufficient to induce sleep—as judged by the loss of eyelash reflex and failure to respond to verbal communication. This was followed by suxamethonium 1.0 mg kg\(^{-1}\) and the trachea was intubated 2 min later. Half the patients in each group received an additional smaller dose of the same induction agent (propofol 1.0 mg kg\(^{-1}\) or thiopentone 2.0 mg kg\(^{-1}\)) immediately before intubation. Both agents produced significant decreases in IOP which were slightly more marked with propofol. The administration of suxamethonium produced an increase in IOP in all groups, more so in those given thiopentone, in whom it exceeded the control values. Intubation of the trachea produced the greatest increase in IOP, averaging about 25% above control in all groups except in the group given the additional dose of propofol, in whom IOP remained below control values throughout the process of induction and intubation. Ten patients (33%) experienced pain on injection with propofol. A decrease in systolic arterial pressure of more than 30% was observed in 12 patients (40%) receiving propofol, compared with three (10%) of those given thiopentone.

SUMMARY

Changes in intraocular pressure (IOP) were studied in patients given propofol 2.1 mg kg\(^{-1}\) (n = 30) or thiopentone 4.9 mg kg\(^{-1}\) (n = 30) followed by suxamethonium 1.0 mg kg\(^{-1}\) and tracheal intubation. Half the patients in each group received an additional smaller dose of the same induction agent (propofol 1.0 mg kg\(^{-1}\) or thiopentone 2.0 mg kg\(^{-1}\)) immediately before intubation. Both agents produced significant decreases in IOP which were slightly more marked with propofol. The administration of suxamethonium produced an increase in IOP in all groups, more so in those given thiopentone, in whom it exceeded the control values. Intubation of the trachea produced the greatest increase in IOP, averaging about 25% above control in all groups except in the group given the additional dose of propofol, in whom IOP remained below control values throughout the process of induction and intubation. Ten patients (33%) experienced pain on injection with propofol. A decrease in systolic arterial pressure of more than 30% was observed in 12 patients (40%) receiving propofol, compared with three (10%) of those given thiopentone.
IOP was measured using a hand-held applanation tonometer (Perkins, 1965) in the eye not to be operated upon. Baseline (control) values of IOP were obtained before the induction of anaesthesia following instillation of 1% amethocaine. Further measurements of IOP were made after the administration of the propofol or the thiopentone, 1 and 2 min after the administration of the suxamethonium, and 1, 2 and 3 min after the intubation of the trachea. Heart rate and arterial pressure were measured and recorded at the same times using an ECG and an oscillometer (Dinamap), respectively. Note was also made of any pain on injection or any other side effects such as involuntary movements, tremor, hiccups etc. Based on these criteria, the induction of anaesthesia was classified as good, adequate or poor—depending on the observation of no, minor or severe side effects, respectively.

Analysis of variance was applied at each time point to determine the significance of the changes in IOP, arterial pressure and heart rate. When the overall F ratio was statistically significant, pairs of means were compared using Student’s t test.

RESULTS

The patients in the four subgroups were comparable with regard to age, weight and IOP (table I). This table also shows that the average induction doses were 2.1 mg kg\(^{-1}\) for propofol and 4.9 mg kg\(^{-1}\) for thiopentone. The average induction time was around 40 s, and in the majority the induction agent was injected to a vein on the dorsum of the hand. Values of IOP in the various groups are given in table II, with percentage changes shown in figure 1. The administration of the induction agent produced a significant (P < 0.0005) decrease in IOP which averaged around 40% with propofol and 31% with thiopentone: the differences were not significant between the groups. The administration of

<table>
<thead>
<tr>
<th>TABLE I. Physical characteristics of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propofol</td>
</tr>
<tr>
<td>One dose</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>n</td>
</tr>
<tr>
<td>Age (yr ± SD)</td>
</tr>
<tr>
<td>Weight (kg ± SD)</td>
</tr>
<tr>
<td>IOP (mm Hg ± SD)</td>
</tr>
<tr>
<td>Induction dose</td>
</tr>
<tr>
<td>Duration of induction (s ± SD)</td>
</tr>
<tr>
<td>Site of injection</td>
</tr>
<tr>
<td>Antecubital fossa</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE II. Intraocular pressures (mm Hg) during induction and intubation (mean ± SD).</th>
<th>Propofol</th>
<th>Thiopentone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (control)</td>
<td>12.1±3.11</td>
<td>13.0±4.07</td>
</tr>
<tr>
<td>After induction agent</td>
<td>7.6±3.59*</td>
<td>8.1±3.62*</td>
</tr>
<tr>
<td>1 min after suxamethonium</td>
<td>10.8±3.49**</td>
<td>12.9±4.27**</td>
</tr>
<tr>
<td>2 min after suxamethonium</td>
<td>11.7±4.18**</td>
<td>11.9±3.49**</td>
</tr>
<tr>
<td>After 2nd dose of induction agent</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1 min after intubation</td>
<td>15.5±4.72†</td>
<td>16.3±5.60†</td>
</tr>
<tr>
<td>2 min after intubation</td>
<td>15.5±4.26</td>
<td>13.7±4.22</td>
</tr>
<tr>
<td>3 min after intubation</td>
<td>11.4±3.99</td>
<td>12.1±4.42</td>
</tr>
</tbody>
</table>
suxamethonium produced an increase in IOP in all groups, the increase being slightly less in those given propofol, in whom the IOP remained less than baseline values in comparison with those receiving thiopentone. The absolute values of IOP were not significantly higher than baseline in any group, although the increase was significant ($P < 0.001$) when compared with the values obtained immediately before the administration of the suxamethonium in all groups. The administration of the second, smaller dose of the induction agent resulted in a decrease in IOP to about 27% below baseline in those given propofol ($P < 0.001$), and by about 8% in those given thiopentone. Tracheal intubation produced the greatest increase in IOP, averaging about 25% above baseline in all groups except that given the additional dose of propofol, in whom the IOP was significantly lower ($P < 0.05-0.001$) in comparison with all the other groups. IOP in the two-dose propofol group always remained less than baseline; the increases were significant ($P < 0.01$) in the other three groups.

Heart rates and systolic arterial pressures are given in tables III and IV. Although the administration of thiopentone tended to increase the heart rate slightly more than propofol, there were no significant differences in absolute heart rate amongst the groups, except in those given the second dose of induction agent, where patients given thiopentone showed a higher heart rate. Systolic arterial pressure decreased signifi-

Table III. Heart rate (beat min$^{-1}$) during induction and intubation (mean ± SD). Differences are significant between: (a) Propofol two doses v. thiopentone two doses at 2 min after suxamethonium ($P < 0.05$). (b) Propofol one dose v. thiopentone two doses before intubation ($P < 0.01$). (c) Propofol two doses v. thiopentone two doses after administration of the second dose of induction agents ($P < 0.01$). (d) Thiopentone one dose v. thiopentone two doses before intubation ($P < 0.05$).

<table>
<thead>
<tr>
<th></th>
<th>Propofol One dose</th>
<th>Two doses</th>
<th>Thiopentone One dose</th>
<th>Two doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (control)</td>
<td>81 ± 21</td>
<td>78 ± 12</td>
<td>75 ± 18</td>
<td>75 ± 13</td>
</tr>
<tr>
<td>After induction agent</td>
<td>88 ± 17</td>
<td>82 ± 11</td>
<td>84 ± 21</td>
<td>90 ± 9</td>
</tr>
<tr>
<td>1 min after suxamethonium</td>
<td>92 ± 15</td>
<td>84 ± 12</td>
<td>82 ± 22</td>
<td>92 ± 15</td>
</tr>
<tr>
<td>2 min after suxamethonium</td>
<td>87 ± 16</td>
<td>83 ± 11</td>
<td>82 ± 22</td>
<td>92 ± 17</td>
</tr>
<tr>
<td>After 2nd dose of induction agent</td>
<td>—</td>
<td>82 ± 12</td>
<td>—</td>
<td>95 ± 15</td>
</tr>
<tr>
<td>1 min after intubation</td>
<td>96 ± 19</td>
<td>91 ± 16</td>
<td>91 ± 20</td>
<td>99 ± 16</td>
</tr>
<tr>
<td>2 min after intubation</td>
<td>90 ± 17</td>
<td>88 ± 13</td>
<td>92 ± 27</td>
<td>97 ± 14</td>
</tr>
<tr>
<td>3 min after intubation</td>
<td>85 ± 13</td>
<td>85 ± 13</td>
<td>88 ± 21</td>
<td>94 ± 12</td>
</tr>
</tbody>
</table>
cantly \( P < 0.01 \) soon after the induction of
anaesthesia. The systolic pressures were signifi-
cantly lower \( P < 0.05 - 0.005 \) in those given
propofol immediately before and 3 min after
intubation. The administration of the second
dose of propofol did not result in any further
decrease in the average systolic arterial pressure.
The average peak heart rates and arterial pressures
following intubation were lower in those given
propofol, but the differences were not significant.

The incidence of side effects is given in table V.
Ten (33\%) patients given propofol complained of
modest to severe pain on injection. In most, the
drug had been injected to a vein on the back of the
hand. Forty percent of patients given propofol
showed a decrease in systolic pressure of greater
than 30\% in comparison with 10\% of those given
thiopentone. This required the administration of
500-1000 ml of lactated Ringer's solution to four
patients given propofol. Other side effects were
mostly minor in nature. There was no difference
in the overall quality of induction in the various
groups, nor were there any venous sequelae up to
24 h after injection—although the veins were not
solely used for the administration of the induction
agents.

**DISCUSSION**

The findings from the present study confirm the
results of previous investigations that the induc-
tion of anaesthesia with propofol or thiopentone is
associated with useful and significant decreases in
IOP, with propofol producing a marginally
greater effect (Joshi and Bruce, 1975; Mirakhur
and Shepherd, 1985). The present study was,
however, designed to assess the effects of these
agents on IOP in the face of two factors, the
administration of suxamethonium and tracheal

### Table IV. Systolic arterial pressure (mm Hg) during induction and intubation (mean ± SD). Differences are significant between: (a) Propofol two doses v. thiopentone two doses at 2 min after suxamethonium \( P < 0.05 \). (b) Propofol one dose v. thiopentone one dose 2 min after suxamethonium \( P < 0.05 \). (c) Propofol one dose v. thiopentone two doses 2 min after suxamethonium \( P < 0.001 \). (d) Propofol two doses v. thiopentone two
doses after 2nd dose of the induction agent \( P < 0.001 \). (e) Propofol two doses v. thiopentone two doses at
3 min after intubation \( P < 0.01 \).

<table>
<thead>
<tr>
<th></th>
<th>Propofol One dose</th>
<th>Propofol Two doses</th>
<th>Thiopentone One dose</th>
<th>Thiopentone Two doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (control)</td>
<td>152 ± 18</td>
<td>152 ± 17</td>
<td>154 ± 22</td>
<td>157 ± 16</td>
</tr>
<tr>
<td>After induction agent</td>
<td>124 ± 20</td>
<td>127 ± 18</td>
<td>132 ± 20</td>
<td>143 ± 14</td>
</tr>
<tr>
<td>1 min after suxamethonium</td>
<td>120 ± 23</td>
<td>128 ± 16</td>
<td>134 ± 33</td>
<td>145 ± 28</td>
</tr>
<tr>
<td>2 min after suxamethonium</td>
<td>124 ± 19</td>
<td>133 ± 17</td>
<td>144 ± 31</td>
<td>158 ± 34</td>
</tr>
<tr>
<td>After 2nd dose of induction agent</td>
<td>—</td>
<td>125 ± 15</td>
<td>—</td>
<td>163 ± 30</td>
</tr>
<tr>
<td>1 min after intubation</td>
<td>149 ± 27</td>
<td>153 ± 27</td>
<td>169 ± 34</td>
<td>177 ± 31</td>
</tr>
<tr>
<td>2 min after intubation</td>
<td>151 ± 29</td>
<td>143 ± 27</td>
<td>165 ± 36</td>
<td>174 ± 26</td>
</tr>
<tr>
<td>3 min after intubation</td>
<td>139 ± 31</td>
<td>132 ± 25</td>
<td>154 ± 33</td>
<td>168 ± 22</td>
</tr>
</tbody>
</table>
intubation, known to produce increases in IOP (Pandey, Badola and Kumar, 1972). It is clear that
the stimulus of intubation produces an increase in IOP which is even greater than that observed after
the administration of suxamethonium. In spite of
an initial decrease, the administration of suxa-
methonium and intubation of the trachea increased the IOP above the control values in three
out of the four groups, the increase being greater
in those patients in whom anaesthesia was induced
with thiopentone. However, IOP always remained
below baseline values when the induction dose of
propofol was followed by a smaller second dose of
propofol immediately before intubation. The
rational for administering a second dose of the
induction agent before intubation was based on the
observation that this technique helps to attenuate the increase in intracranial pressure
associated with intubation (Unni et al., 1984), and
it is known that the pressures in the eye and in the
central nervous system are affected similarly by a
number of factors. The usefulness of this
technique using propofol is further shown by the
observation of a rapid decrease in IOP once the
stimulating effects of intubation had abated. The
lack of protective effect of the second smaller dose
of thiopentone is surprising, but may be related to
the fact that the administration of thiopentone did
not cause such a marked decrease in IOP before inte-
butation. It may also be a result of the fact that
propofol, particularly the second dose, produces a
deeper and smoother sleep. Part of the beneficial
effect on IOP may also be attributable to a greater
reduction in systolic arterial pressure seen with
this agent.

Other factors such as central venous pressure or
carbon dioxide tensions in arterial blood could
have affected the results (Hvidberg, Kessing and
However, all patients were horizontal throughout
the period of study and ventilation was assisted or
controlled as soon as indicated using a non-
rebreathing circuit. Moreover, all groups would
be similarly affected and, in addition, this was
designed to simulate as closely as possible the
routine induction of anaesthesia.

It is true that the use of a non-depolarizing
neuromuscular blocking drug would not have
increased the IOP after the induction of anaes-
thesia, but suxamethonium was used as a challenge
to assess both the effects of propofol and the
usefulness of a second smaller dose of induction
agent before intubation. Moreover, it is likely that

Although other side effects of propofol are
generally minimal, significant and clinically impor-
tant hypotension occurs frequently. This is a
limitation to its use, particularly in elderly
patients. Thus it should be used with discretion,
or perhaps avoided, when a decrease in arterial
pressure would be particularly undesirable. How-
ever, hypotension responded to simple treatment
such as the infusion of 500–1000 ml of lactated
Ringer's solution.

In conclusion, propofol appears to be a suitable
agent with which to induce anaesthesia in
ophthalmic surgical patients, particularly if an
additional small dose is given immediately before
intubation.

ACKNOWLEDGEMENTS
The authors are grateful to the the nursing and technical staff
of the Eye Theatres for their help and co-operation with the
study, to I.C.I. for supplies of propofol and financial assistance
and to Miss Gillian Stewart for typing the manuscript.