Comparison of the incidence of complications at induction and emergence in infants receiving oral atropine vs no premedication

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We studied 120 patients less than 1 yr of age, allocated randomly to receive atropine 40 μg kg⁻¹ orally 1 h before operation (group A) or no premedication (group B). All patients underwent a standardized anaesthetic, including inhalation induction with halothane followed by atracurium 0.5 mg kg⁻¹, tracheal intubation and positive pressure ventilation. Monitoring during anaesthesia included heart rate, arterial oxygen saturation, temperature and airway conditions at induction and emergence. The incidence of a decrease in arterial oxygen saturation to 94% or less at induction and recovery was similar in both groups (30.5% at induction, 39% at extubation in group A; 31% at induction, 41% at extubation in group B). There were significantly more airway complications in group B both at induction and emergence (25% and 49%, respectively, compared with 9% and 25% in group A; P<0.015). Mean heart rate at induction and in the peroperative period was significantly higher in the group receiving atropine (P<0.001). There was an increased incidence of bradycardia (decrease in heart rate of ≥20%) at induction in the non-premedicated group (23% in group B compared with 10% in group A), but this was not statistically significant. We conclude that the incidence of airway complications at induction and emergence was reduced by orally administered atropine premedication.

Keywords: premedication, atropine; anaesthesia, paediatric; infants; airway, complications

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Since the days of ether and chloroform, anticholinergic drugs have been used as an adjunct to anaesthesia to reduce potentially troublesome airway secretions and prevent excessive vagal activity. With the advent of less irritant inhalation agents, this practice has been called into question, and as long ago as 1962 it was suggested that anticholinergic premedication in adults was unnecessary.1 2 Indeed, anticholinergic drugs are now rarely prescribed for adults before operation.3

It is widely accepted that children, although possibly not neonates,4 have higher vagal tone than adults, resulting in potentially more severe adverse airway and cardiac events associated with anaesthesia.5-7 This has resulted in many institutions routinely prescribing atropine as premedication to infants and children. Although this is safe practice,8 it may be unpleasant for the patient, causing dry mouth, pyrexia and tachycardia. Furthermore, tachycardia may make subsequent assessment of volaemic status and adequacy of anaesthesia difficult.9

Although the practice of premedication with atropine in young children is widespread it is certainly not universal and its value has been questioned recently.10 Paediatric anaesthetists who do not routinely prescribe atropine premedication have not reported an increased incidence of severe adverse sequelae.10 11 Our study was undertaken in two centres by anaesthetists with a regular commitment to paediatric anaesthesia. The aim was to determine whether atropine is still appropriate as premedication in infants or whether this practice may now be safely abandoned as it has been in adults. We studied the effect of atropine given as an oral premedicant in neonates and infants on the incidence of complications on induction and emergence.

Patients and methods

An initial pilot study was performed on 20 patients. The subsequent power analysis indicated a minimum sample size of 94 to detect a 5% difference in arterial oxygen saturation at 80% power. After obtaining approval from the Ethics Committee and informed parental consent, we studied 120 patients less than 1 yr of age, allocated randomly (using a random number generator) to receive
atropine 40 μg kg⁻¹ orally, 1 h before operation (group A) or no premedication (group B). The study was carried out at two centres, Great Ormond Street Hospital for Children and St George’s Hospital, London, UK. All patients were ASA I or II undergoing elective surgery which required tracheal intubation as part of the anaesthetic technique. Exclusion criteria were emergency surgery, significant cardiovascular or respiratory instability, pyrexia greater than 38°C, narrow angle glaucoma, atropine hypersensitivity and autonomic imbalance. Patients undergoing neurosurgical procedures and those with a history of previous airway problems during anaesthesia were also excluded. At the time of the preoperative anaesthetic assessment on the ward, heart rate and temperature were recorded.

Inhalation induction was used with incremental halothane (up to 5%) in oxygen (minimum FIO₂ 0.3) and nitrous oxide using a hand-held Ayre’s T-piece (Jackson-Rees modification). As soon as anaesthesia was achieved, i.v. access was obtained and tracheal intubation was facilitated with atracurium 0.5 mg kg⁻¹. Anaesthesia was maintained with halothane in oxygen (minimum FIO₂ 0.3) and nitrous oxide. Appropriate halothane concentrations were used according to clinical signs of depth of anaesthesia. Positive pressure ventilation to normocapnia was provided by a Nuffield Penlon 200 ventilator, with Newton valve attachment, via an Ayre’s T-piece. Analgesia was provided as analgesic suppositories and opioid analgesics.

In addition to the standard monitoring used continuously throughout anaesthesia, a trained observer, unaware of the patient’s premedication group, recorded the minimum heart rate achieved at any point during induction and in the peroperative period, maximum peroperative rectal temperature and minimum arterial oxygen saturation achieved at induction, in the peroperative period and at extubation. The pulse oximeter was an Ohmeda Biox 3740 and soft probe 8123-009 with an averaging time of 6 s and a pulse interval of 12 s. The anaesthetist, who was also blinded to the randomization, noted airway conditions at induction and extubation. Airway conditions assessed were: excessive secretions, breath-holding, cough and laryngospasm. Excessive secretions were defined as requiring application of more than one suction to see the larynx and achieve tracheal intubation. Breath-holding was defined as cessation of a regular breathing pattern during induction of, or emergence from, anaesthesia. The peroperative use of succinylcholine or atropine was also noted. At the end of surgery, neuromuscular block was antagonized with neostigmine 50 μg kg⁻¹ and atropine 25 μg kg⁻¹. The oropharynx was suctioned as routine and extubation was performed when the patient was breathing regularly and awake, and with airway reflexes fully restored.

All statistical tests were performed using the software SPSS for windows release 6.1.3 (Dec. 95). Data on normally distributed variables are presented as mean (sd). Comparison of these means was performed using a two-tailed Student’s t test for unpaired observations. Differences in proportions were compared by chi-square methodology. Statistical significance was indicated by P<0.05. The association between a range of baseline characteristics and the occurrence of an outcome event was examined using a multiple logistic regression with forward stepwise methodology.

**Results**

Patient characteristics in the two groups were similar (Table 1), except for duration of operation which was significantly longer in the group who received atropine (group A), despite randomization. Figure 1 illustrates the distribution of airway complications at induction between the two groups. These were more common in patients who did not receive premedication. Fifteen (24.6%) patients in group B compared with five (8.5%) in group A had one or more of the four complications (laryngospasm, cough, excessive secretions and breath-holding) (P=0.015).

| Table 1 Patient characteristics, surgical presentation and anaesthetic details in group A (atropine premedication) and group B (no premedication). Data are mean (sd) [range] or number. *P<0.05 compared with group A |
|-----------------|-----------------|-----------------|
| **Age (days)**  | **Group A** (n = 59) | **Group B** (n = 61) |
|                 | 111 [1-336]     | 127 [2-308]     |
| **Weight (kg)** | 5.4 [1.9]       | 4.6 [2.4]       |
| **Sex (M/F)**   | 26/23           | 40/21           |
| **FIO₂ (%)**    | 38              | 41              |
| **Peroperative temperature (°C)** | 36.7 [0.7] | 36.6 [0.6] |
| **Peroperative heart rate (beat min⁻¹)** | 146 [18] | 128 [20] |
| **Atropine on induction (n)** | 0 | 0 |
| **Intraoperative atropine (n)** | 3 | 4 |

**Fig 1** Airway complications on induction in patients premedicated with atropine and in those who received no premedication.

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175
compared with the resting preoperative observations both decrease in heart rate of more than 20% at induction

Change in peroperative heart rate (beat min⁻¹)

Decrease in heart rate ≥20% (n)

No. of patients with S\(\text{O}_2\) <94% on induction

Minimum S\(\text{O}_2\) on induction

No. of patients with S\(\text{O}_2\) <94% on extubation

Minimum S\(\text{O}_2\) on extubation

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<table>
<thead>
<tr>
<th>Change in heart rate on induction (beat per min⁻¹)</th>
<th>Group A (atropine) (n = 59)</th>
<th>Group B (no premed) (n = 61)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+14 (28)***, 12%</td>
<td>-10 (28)***, -7%</td>
</tr>
<tr>
<td>Change in peroperative heart rate (beat min⁻¹)</td>
<td>+15 (22)***, 13%</td>
<td>-1 (25)***, 0.2%</td>
</tr>
<tr>
<td>Decrease in heart rate ≥20% (n)</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>No. of patients with S(\text{O}_2) &lt;94% on induction</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Minimum S(\text{O}_2) on induction</td>
<td>86%</td>
<td>50%</td>
</tr>
<tr>
<td>No. of patients with S(\text{O}_2) &lt;94% on extubation</td>
<td>23</td>
<td>25</td>
</tr>
<tr>
<td>Minimum S(\text{O}_2) on extubation</td>
<td>50%</td>
<td>60%</td>
</tr>
</tbody>
</table>

**Fig 2** Airway complications on extubation in patients premedicated with atropine and in those who received no premedication.

Six (10%) patients in the group who received atropine and 14 (23%) in the unpremedicated group showed a decrease in heart rate of more than 20% at induction compared with the preoperative resting heart rate; this was not statistically significant. Mean heart rate increased compared with the resting preoperative observations both at induction (by 14 beat min⁻¹) and in the peroperative period (by 15 beat min⁻¹) in group A. Infants in group B demonstrated little change in mean heart rate (Table 2). This difference between groups was significant (P≤0.001).

There was no significant difference between groups in the number of patients with oxygen saturations less than 94%, or in the minimum arterial oxygen saturation at induction. The most profound desaturations on induction occurred in the unpremedicated group.

At emergence, airway complications occurred more commonly in group B, with 30 (49.2%) compared with 15 (25.4%) patients in group A having one or more of the four complications (P≤0.006). The type of airway complications seen on extubation in the two groups is shown in Figure 2.

There was no difference between groups in the number of patients with arterial oxygen saturations less than 94% or in the minimum arterial oxygen saturation at extubation (Table 2).

To examine the factors associated with an airway complication, a forward step multiple logistic regression analysis was performed. The following variables were entered into the analysis: operation type (three categories shown in Table 1); duration of operation; sex; gestational age at delivery (greater or less than 36 weeks); weight; use of additional atropine at induction or in the peroperative period; and use of succinylcholine at induction. This secondary analysis showed that the occurrence of airway complications at induction was associated with lower patient weight and the use of succinylcholine. At extubation, the occurrence of airway complications was associated with lower patient weight and gestational age at birth.

Discussion

In this study, performed by anaesthetists with a regular paediatric commitment, the incidence of complications was comparable with previous studies; approximately 30% and 40% of patients had arterial oxygen saturations of 94% or less at induction and extubation, respectively. These finding are similar to those of Laycock and McNicol who found that during induction of anaesthesia, 40% of children less than 1 yr had arterial oxygen saturations of 90% or less, whereas Kong and colleagues found that 27% of their patients (neonates and small infants weighing less than 5 kg) had decreases in arterial oxygen saturation of more than 5% from preoperative values during inhalation induction. Kong's group also showed that there was a significantly higher incidence of patient arterial desaturations when anaesthesia was performed by less experienced anaesthetists. It is possible that the incidence of complications in paediatric patients may be greater with less experienced anaesthetists and that in such circumstances atropine premedication affords a greater margin of safety.

Several routes of administration and doses of atropine are available. The dose chosen for this study was 40 pg kg⁻¹ orally, 1 h before operation, to reflect current practice in our hospitals. A study by Crean and colleagues compared atropine 40 pg kg⁻¹ orally with 20 pg kg⁻¹ i.m. and found no significant difference between the two doses, methods of
administration or clinical effect. More recent work by Gervais and colleagues has demonstrated variable cholinoreceptor occupancy after both oral and i.m. administration. Other workers have found similar clinical effects and serum atropine concentrations after oral, i.m. and i.v. atropine administration.

We compared oral atropine with no premedication to reflect local practice. Although most clinicians and nursing staff prefer to avoid the i.m. route, one survey suggests that parental objection is rare. There were significantly more episodes of arterial oxygen desaturation or bradycardia as a result of airway complications and attribute this to swift, appropriate airway management by experienced anaesthetists. Although the study did not dictate inspired oxygen content (F<sub>O₂</sub>), there was no difference between groups in F<sub>O₂</sub> (Table 1). Rapid intervention was allowed at the first sign of complications, and a few patients in each group required administration of succinylcholine and atropine (Table 1).

We suggest that serious sequelae could arise with less experienced anaesthetists. The three patients with severe arterial desaturations less than 70% at induction were all in group B, and two of the three were associated with excessive secretions. At emergence, eight patients had arterial oxygen saturations less than 80%; three of these were associated with excessive secretions and the remaining five were associated with one or more of the other three airway complications studied.

Mean difference in heart rate at induction compared with the peroperative period differed between the two groups, with patients in group A demonstrating increases of 14 and 15 beat min<sup>−1</sup> compared with little change in group B. Although highly statistically significant (P≤0.001), this mean increase in heart rate is unlikely to be clinically important. More interesting, however, was the fact that twice as many unpremedicated than premedicated patients had a decrease in heart rate of more than 20% at induction (Table 2). The most serious decreases in heart rate were associated with airway complications.

Secondary analysis by forward step multiple logistic regression indicated that the occurrence of airway complications at induction and emergence was associated with low patient weight. This is unsurprising. Although it would be interesting to examine this group further, the number of patients weighing less than 5 kg and suitable for this study was, unfortunately, small.

Halothane has for many years been the agent of choice for inhalation induction of anaesthesia in children. However, sevoflurane has recently gained in popularity. Despite this, as recently as 1998 the Association of Paediatric Anaesthetists of Great Britain and Ireland overwhelmingly rejected a motion proposing the replacement of halothane by sevoflurane. This was partly on the grounds of cost, but it was also noted that the longer duration of action of halothane might confer distinct advantages over sevoflurane, particularly during airway procedures. Thus it is likely that halothane will not be completely replaced by sevoflurane for inhalation induction of anaesthesia in the foreseeable future. We believe that atropine premedication will continue to serve a useful role in inhalation induction of anaesthesia of infants and children.

In summary, we found that although airway complications occurred in both groups, the incidence was significantly lower, both at induction and extubation, in the group who received atropine premedication.

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