CLONIDINE DOES NOT DELAY RECOVERY FROM ANAESTHESIA

S. BELLAÏCHE, F. BONNET, M. SPERANDIO, P. LEROUGE, G. CANNET AND F. ROUJAS

SUMMARY

Clonidine is known to reduce anaesthetic requirements and improve haemodynamic stability when given as premedication. This study, of 46 ASA I–II patients undergoing thyroid surgery, was designed to assess if clonidine interferes with recovery from anaesthesia. Patients were allocated randomly to three groups to receive, 2 h before surgery, flunitrazepam 1 mg, clonidine 150 μg, or both drugs. Anaesthesia comprised thiopentone, alfentanil, isoflurane and 70% nitrous oxide in oxygen. Recovery from anaesthesia was assessed using a clinical score, electro-oculographic measurements and reaction times to auditory stimuli. Psychomotor tests were performed the day before surgery and 30, 60, 120 and 240 min after arrival of the patient in the recovery room. Psychomotor performance was decreased significantly after operation in the three groups (P < 0.05) and returned to baseline at 240 min. There was no significant difference between the three groups. This study indicates that clonidine 150 μg orally before surgery does not delay recovery from anaesthesia.

KEY WORDS

Clonidine, an alpha₂-adrenergic agonist, has been used for premedication to improve haemodynamic stability during surgery [1, 2]. It also decreases requirements for anaesthetic agents [3] and induces sleep and sedation in laboratory animals and humans [2, 4]. It follows, therefore, that clonidine premedication might be expected to delay recovery from anaesthesia [2]. The aim of this study was to assess anaesthetic recovery in patients who received benzodiazepine or clonidine, or both drugs, as premedication.

PATIENTS AND METHODS

We studied 46 patients (ASA physical status I or II) undergoing thyroid surgery after informed consent and Ethics Committee approval had been obtained. Patients with hyper- or hypothyroidism and patients undergoing treatment with beta-adrenergic blocking agents or clonidine were excluded from the study. Patients were allocated randomly to three groups the day before surgery. Two hours before surgery, they received flunitrazepam 1 mg orally (group I), clonidine 150 μg orally (group II) or flunitrazepam 1 mg plus clonidine 150 μg (group III). The anaesthetic procedure was the same for the three groups: induction comprised thiopentone 5 mg·kg⁻¹ and alfentanil 0.02 mg·kg⁻¹; vecuronium 0.1 mg·kg⁻¹ was given to facilitate tracheal intubation. Anaesthesia was maintained with 70% nitrous oxide and 0.6% isoflurane (expired concentration, Multicap, Datex) in oxygen. During surgery, hypertension (systolic arterial pressure > 180 mm Hg) was treated with a 0.01-mg·kg⁻¹ bolus of alfentanil and hypotension (systolic arterial pressure < 80 mm Hg) was managed by reducing the concentration of isoflurane. Arterial pressure was monitored by an automated oscillotonometer (Dinamap, Critikon) and heart rate by ECG lead CM5.
Patients were studied on arrival in the recovery room by an independent observer. Recovery from anaesthesia was assessed using simple questions evaluating short-term memory, orientation and cognition (table I).

Psychomotor performance was assessed before and after operation, at 30, 60, 120 and 240 min after arrival in the recovery room, by two different tests. The first test comprised electro-oculography (EOG): the changes in an electrical field, created between periorcular electrodes by the movements of the eyes, were measured while the patient was invited to look alternately at one of two pin-shaped white targets fixed to a horizontal line, on a black background, and separated by an angular distance of 10° [5]. Three successive series of 10 to-and-fro movements of the eyes were recorded. In awake patients, jerking movements of the eyes produce rapid changes in voltage which are related linearly to changes in eye movements. A micro-computer converts changes in voltage to velocity of eye movement. The mean value of the peak velocity of 60 jerking movements was calculated for each period of measurements. Oscillations of smaller amplitude have been reported during anaesthesia or after administration of benzodiazepines [5-7].

The second test was based on measurement of motor reaction time (MRT) to 50 consecutive auditory signals, given to the patients by an automatic device at random intervals. The delay between each stimulus and a subsequent manual response (recorded electrically) was calculated. Results are expressed as mean values (SD). Statistical analysis comprised ANOVA for repeated measures and paired and unpaired t tests where appropriate. P < 0.05 was considered significant.

RESULTS

The three groups were comparable for patient characteristics, duration of surgery and the doses of anaesthetic agents (tables II, III). Recovery scores were decreased significantly after the end of anaesthesia and these returned to preoperative values 2 h later (table IV). There was no difference between the three groups. EOG showed a decrease in peak velocity of eye movement which was comparable in the three groups (fig. 1, table IV). The mean values of MRT (and the standard deviations) increased after operation in the three groups (fig. 2, table IV).

DISCUSSION

This study has shown that, with the tests used, premedication with oral clonidine 150 μg did not impair recovery from anaesthesia compared with flunitrazepam.

As the psychomotor tests used to evaluate recovery from general anaesthesia (EOG, MRT) do not improve with practice, they are considered reliable. When used for assessment of “street fitness” after ambulatory anaesthesia, this type of
TABLE IV. Sensorimotor parameters. EOG = Peak velocity of eye movements; MRT = mean motor reaction time; MRT SD = mean value of SD of reaction times. *P < 0.05; **P < 0.01; intragroup comparisons

<table>
<thead>
<tr>
<th>Clinical score</th>
<th>Before operation</th>
<th>After operation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>30 min</td>
</tr>
<tr>
<td>Group I</td>
<td>14.0 (0)</td>
<td>9.3 (4.9)**</td>
</tr>
<tr>
<td>Group II</td>
<td>14.0 (0)</td>
<td>10.6 (3.4)**</td>
</tr>
<tr>
<td>Group III</td>
<td>14.0 (0)</td>
<td>7.7 (5.0)**</td>
</tr>
<tr>
<td>EOG (deg. s⁻¹)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>266 (52)</td>
<td>135 (58)**</td>
</tr>
<tr>
<td>Group II</td>
<td>267 (23)</td>
<td>199 (64)*</td>
</tr>
<tr>
<td>Group III</td>
<td>249 (38)</td>
<td>162 (69)**</td>
</tr>
<tr>
<td>MRT (s 10⁻²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>26.2 (9.0)</td>
<td>39.2 (10.2)*</td>
</tr>
<tr>
<td>Group II</td>
<td>24.9 (5.5)</td>
<td>33.7 (9.5)**</td>
</tr>
<tr>
<td>Group III</td>
<td>22.6 (4.3)</td>
<td>44.4 (13.8)**</td>
</tr>
<tr>
<td>MRT SD (s 10⁻²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>7.1 (5.6)</td>
<td>12.1 (5.2)**</td>
</tr>
<tr>
<td>Group II</td>
<td>6.6 (2.3)</td>
<td>10.1 (4.9)*</td>
</tr>
<tr>
<td>Group III</td>
<td>7.8 (9.9)</td>
<td>13.2 (3.0)**</td>
</tr>
</tbody>
</table>

Fig. 1. Mean (SD) values before and after operation, for peak velocity of the electro-oculogram in the three groups of patients. □ = Flunitrazepam (group I); ■ = clonidine (group II); ○ = flunitrazepam + clonidine (group III). The performances were decreased significantly after operation (see table III), but there was no significant difference between the three groups.

Fig. 2. Mean (SD) values before and after operation, for mean time to response to auditory stimuli in the three groups of patients. □ = Flunitrazepam (group I); ■ = clonidine (group II); ○ = flunitrazepam + clonidine (group III). The performances were decreased significantly after operation (see table III), but there was no significant difference between groups.

test is usually thought to be too sensitive [8, 9]. In the current study, the sensitivity of these psychomotor tests was an advantage and allowed detection of small differences between groups.

Clonidine did not prolong awakening from anaesthesia in this study although it is known to possess sedative effects. Although recovery has been reported as more rapid after administration of clonidine [1, 2], in both those studies anaesthetic requirements were decreased, and this may explain a more rapid recovery. In contrast, Richards and colleagues reported prolonged recovery after oral premedication with clonidine and propofol–alfentanil anaesthesia [10]. In that
study, clonidine was given in a dose three times greater than that used here, and it was administered in combination with a benzodiazepine.

The sedative effect of clonidine is thought to result from an inhibitory effect on spontaneous and evoked activity of central monoaminergic systems involved in modulation of sleep and cortical arousal [11–13]. This effect is mediated by alpha2-adrenergic receptors [14] and is observed after administration of alpha2-adrenergic selective agonists such as azepexole or dexmedetomidine [15–17] and antagonized by alpha2-adrenoceptor antagonists such as idazoxan [15].

The discrepancy between the well known sedative properties of clonidine and the lack of prolongation of anaesthetic effect noted in this study may be explained by the complex mechanism of action of the drug. For example, the action of clonidine is only partly dose-related, as a ceiling effect has been documented [18]. This effect has been attributed either to an agonist–antagonist action at the alpha2-adrenergic receptor site [19] or to an alpha2-adrenergic agonist action of the drug [20]. Furthermore, a biphasic sleeping time dose–response curve has been documented [4]. In small doses, clonidine produced a small decrease in sleeping time in the rat, whereas doses > 0.1 mg kg⁻¹ significantly increased sleeping time [4]. In another study, large doses of clonidine potentiated the effect of inhalation anaesthesia and mimicked the effect of general anaesthesia on electrocortical activity, while a reverse action was reported with small doses [21]. Compared with previous studies [1, 2], we used a small dose of clonidine (about 2 μg kg⁻¹), which has been reported to induce sedation after extradural or parenteral administration [22]. Nevertheless, the hypnotic effect of clonidine may be insufficient to prolong significantly the duration of anaesthesia when compared with a benzodiazepine. However, our study does not exclude the possibility that, in comparison with a placebo or a larger dose of clonidine, significant prolongation of recovery might be demonstrable.

REFERENCES
17. Doze VA, Chen BX, Maze M. Dexmedetomidine pro-


