CLONIDINE DECREASES POSTOPERATIVE OXYGEN CONSUMPTION IN PATIENTS RECOVERING FROM GENERAL ANAESTHESIA

L. DELAUNAY, F. BONNET AND P. DUVALDESTIN

SUMMARY
Twenty ASA I patients, undergoing thyroid surgery were allocated randomly to receive at the end of surgery either an isotonic saline solution or clonidine 2 μg kg⁻¹ i.v. administered over 20 min. Oxygen consumption (VO₂) and carbon dioxide production (VCO₂) were measured during recovery in patients breathing spontaneously with a head canopy system. Clonidine was found to attenuate the increase in VO₂ and VCO₂ associated with recovery from anaesthesia. The effect of clonidine was associated with a reduction in shivering. Sedative and analgesic properties of clonidine may also contribute to the reduction in metabolic demand during recovery from anaesthesia.

KEY WORDS

Recovery from general anaesthesia is associated with shivering and increase in oxygen consumption (V̇O₂) which may result in hypertension and tachycardia [1–3]. Postoperative shivering is uncomfortable and its haemodynamic consequences may be harmful in patients with coronary artery disease [4]. It has been demonstrated recently that clonidine, an alpha-2 adrenergic agent, attenuated postoperative shivering [5]. The aim of this study was to assess if inhibition of postoperative shivering by clonidine is associated with a reduction in V̇O₂ and carbon dioxide production (V̇CO₂).

PATIENTS AND METHODS
We studied 20 patients ASA physical status I, undergoing thyroid surgery after obtaining informed patient consent and Ethics Committee approval.

Patients with hyper- or hypothyroidism were excluded from the study, in addition to those treated previously by β-adrenergic blocking agents, psychotropic drugs and alpha-2 adrenergic agonist agents. Patients were premedicated orally with lorazepam 1 mg. Anaesthesia was induced with thiopentone 5 mg kg⁻¹ and alfentanil 150–200 μg kg⁻¹. Vecuronium 0.1 mg kg⁻¹ was given to facilitate orotracheal intubation. Ventilation was controlled using a closed system (SA1 Draeger). Anaesthesia was maintained with 50% nitrous oxide and 0.6–1% isoflurane (expired concentration, Multicap Datex) in oxygen and additional bolus doses of alfentanil. At the end of surgery, isoflurane and nitrous oxide were stopped, fresh gas flow was increased to 6–8 litre min⁻¹ and the anaesthetic breathing system was opened. Patients were allocated randomly to two groups (n = 10 each) to receive either an isotonic saline solution (control group) or clonidine 2 μg kg⁻¹ i.v. injected over 20 min (clonidine group). At the end of the infusion, patients were transferred to the recovery room where measurements began. During the 60 min after arrival in the recovery room V̇O₂, V̇CO₂ and respiratory quotient (RQ) were measured with a head canopy system (Deltatrac metabolic monitor, Datex) while patients were breathing room air spontaneously. Measurements were performed every 1 min and values of V̇O₂, V̇CO₂ and RQ were expressed as the mean value of a 10-min period of measurements. Systemic arterial pressure and heart rate were measured every 10 min in the recovery room (Dinamap) and rectal temperature was noted (rectal sensor: Mon a therm).


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In order to assess the validity of $\dot{V}O_2$, $\dot{V}CO_2$ and RQ measurements in postoperative patients, these variables were measured in five healthy volunteers before and 20 min after a 15-min period of inhalation of 50% nitrous oxide in oxygen. $\dot{V}O_2$, $\dot{V}CO_2$ and RQ were identical before and 20 min after nitrous oxide inhalation in these healthy volunteers.

Measurements were performed by an independent observer, unaware of the solution administered. The observer recorded also the occurrence of shivering and evaluated patient sedation and pain on graded scales. **Sedation**: 1 = fully conscious and wake; 2 = drowsy; 3 = mostly sleeping but answering to verbal command; 4 = sleeping and awakened only by tactile stimulation. **Pain**: 1 = no pain; 2 = mild pain; 3 = moderate pain; 4 = severe pain.

Values are expressed as mean (SD). Data were analysed by ANOVA and Scheffé $F$ test to show differences at individual time points, and Mann–Whitney test for comparison of patient data. Fisher's exact test was used for comparison of shivering between the two groups. $P < 0.05$ was considered significant.

**RESULTS**

There was no difference in patient characteristics between the two groups (table I). Duration of surgery, rectal temperature on arrival in the recovery room and time to tracheal extubation were comparable for the two groups. $\dot{V}O_2$ was significantly greater in the control group on arrival in the recovery room compared with the clonidine group and then decreased significantly to reach values similar to those of the clonidine group 60 min later (fig. 1). The changes in $\dot{V}CO_2$ were similar to those of $\dot{V}O_2$ in the two groups while RQ remained constant throughout the study (fig. 1). Shivering occurred in five patients in the control group, but in only one patient in the clonidine group during the first 15 min of the study (ns). Shivering was considered mild in the placebo group and was minimal in one patient in the

<table>
<thead>
<tr>
<th></th>
<th>Control group ($n = 10$)</th>
<th>Clonidine group ($n = 10$)</th>
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</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>2/8</td>
<td>0/10</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>37 (30–52)</td>
<td>37 (20–49)</td>
</tr>
<tr>
<td>Body surface area (m$^2$)</td>
<td>1.7 (0.2)</td>
<td>1.7 (0.1)</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>78 (17)</td>
<td>78 (16)</td>
</tr>
<tr>
<td>Time end of surgery to extubation (min)</td>
<td>13.4 (5.3)</td>
<td>13.3 (3.5)</td>
</tr>
<tr>
<td>Rectal temperature in recovery room ($°C$)</td>
<td>36.5 (0.3)</td>
<td>36.4 (0.4)</td>
</tr>
</tbody>
</table>
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Fig. 2. Changes in $\dot{V}O_2$ (mean, SEM) in shivering (●) and non-shivering (△) patients in the placebo group and non-shivering patients in the clonidine group (●●). * Significant difference ($P < 0.05$) between shivering patients in the placebo group ($n = 5$) compared with non-shivering patients in the clonidine group ($n = 9$). † Significant difference ($P < 0.05$) between shivering and non-shivering patients in the placebo group.

Fig. 3. Changes in the scores (mean, SEM) for sedation and pain in the control (●) and clonidine (○) groups. Differences do not reach statistical significance ($P < 0.1$).

Fig. 4. Changes in mean values of systolic arterial pressure (SAP) and heart rate (HR) (mean, SEM) in the control (●) and clonidine (○) groups. Differences do not reach statistical significance ($P < 0.1$).

In this study we have observed that clonidine was associated with a reduction in the increase in $\dot{V}O_2$ and $\dot{V}CO_2$ observed commonly during recovery from anaesthesia. This result was associated with a decreased incidence in shivering, as documented previously [4].

Measurement of $\dot{V}O_2$, according to the Haldane equation, assumes that the amount of nitrogen is equal in both inhaled and exhaled gas. Excretion of anaesthetic gas, especially residual nitrous oxide, may therefore lead to an error in measurement of $\dot{V}O_2$ [6]. However, we began measurements at least 20 min after withdrawal of nitrous...
oxide when its concentration should be less than 5% of the concentration maintained during anaesthesia (50%)—that is, less than 2.5% [7]. In addition, if there was an error in $VO_2$ and $VCO_2$ measurements, it should be the same in the two groups of patients, so that a comparison between groups remains valid. Furthermore, measurements performed in healthy volunteers with the Canopy system and the Deltatrac metabolism monitor did not reveal any difference in $VO_2$ and $VCO_2$ measurements performed before, 20 min, 30 min and 40 min after inhalation of nitrous oxide.

There are conflicting data on the effect of clonidine on postoperative shivering. Flacke and colleagues reported that patients with coronary artery disease who had received clonidine before operation as premedication, and at the end of surgery shivered less commonly than patients in a control group [8]. After administration of clonidine in the recovery room, Quintin and colleagues also reported that the incidence of shivering was decreased [9]. In addition they observed that clonidine reduced the degree of hypertension and tachycardia observed during recovery in a control group and prevented the increase in $VO_2$ (calculated from measurements of cardiac output and arterial and mixed venous oxygen contents) [10]. However, it has been reported recently that clonidine failed to change postoperative shivering [11, 12]. Nevertheless, in both these studies calculated or measured $VO_2$ was less in patients who received clonidine, especially during the shivering periods, suggesting that the degree of shivering was reduced.

Goldfarb and colleagues also reported that i.v. clonidine induced a rapid decrease in $VO_2$ in postoperative patients [12]. Although shivering is described as visible phenomenon, subclinical shivering has been detected using a strain gauge or electromyographic recordings [13, 14]. Difficulties in quantitative analysis of shivering may explain, therefore, the observed discrepancies in these different studies.

In our study, the values of $VO_2$ and $VCO_2$ were about 40% greater in the control group at the beginning of measurements compared with those in the clonidine group, despite the same temperatures. As shivering is mainly responsible for the increase in $VO_2$ and $VCO_2$ during recovery from anaesthesia [2, 15], the effect of clonidine on $VO_2$ might be related to prevention of shivering. Indeed, values of $VO_2$ were comparable in non-shivering patients in both clonidine and placebo groups. Nevertheless, clonidine reduces sympathetic nervous system activity and plasma catecholamine concentrations [8, 16-18]. This might result in a decrease in whole body metabolism while the decrease in cardiac output related to clonidine [17, 18] leads to a decrease in myocardial oxygen consumption. These effects may combine in reducing the $VO_2$ and $VCO_2$ observed after administration of clonidine. Furthermore, the analgesic effect of clonidine observed previously in postoperative patients [19-21] might account partly for the reduction in $VO_2$, as Muneyuki and colleagues have demonstrated that reduction of pain in the postoperative period caused a 7-8% decrease in $VO_2$ [22].

REFERENCES
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