Studies in anaesthetized animals have shown decreases in cGMP within the central nervous system after halothane or isoflurane anaesthesia. However, in the present study, salivary cGMP increased during anaesthesia compared with concentrations immediately pre-induction. This may be partially explained by nitric oxide synthase activity or haemoglobin activity during anaesthesia. Both nitric oxide, produced by the action of nitric oxide synthase, and carbon monoxide, the product of haemoglobin activity, are potent activators of soluble guanylate cyclase.

The results of this study need to be extended to a larger study of various anaesthetic techniques to establish whether this is a common link for a mechanism of anaesthesia in humans. Also, the possible development of a 'real time' cGMP monitor is appealing and may allow an alternative technique for measuring depth of anaesthesia.

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References

Propofol and remifentanil are used for this purpose. However, the benefits, side-effects, and optimal dose of these drugs in such patients are unclear.

**Methods.** Sixty patients were included in a prospective, randomized, single blinded study. All patients received a deep cervical plexus block with 30 ml ropivacaine 0.75% and were randomized to receive either remifentanil 3 μg kg⁻¹ h⁻¹ or propofol 1 mg kg⁻¹ h⁻¹. The infusions were started after performing the regional block and were stopped at the end of surgery. Arterial pressure, ECG, ventilatory rate, and $P_{aCO_2}$ were measured continuously and recorded at predetermined times. Twenty-four hours after surgery, patient comfort, and satisfaction were also evaluated.

**Results.** In three patients, the infusion of remifentanil had to be stopped because of severe respiratory depression or bradycardia. No significant differences were found between the two groups in haemodynamic variables or sedative effects, but there was a significantly greater decrease in ventilatory frequency and increase in $P_{aCO_2}$ in the remifentanil group. The patient’s subjective impressions and pain control were excellent in both groups.

**Conclusion.** As a result of the higher incidence of adverse respiratory effects with remifentanil and similar sedative effects, propofol is preferable for sedation during cervical plexus block in elderly patients with comorbid disease at the dosage used.

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Propofol and remifentanil have been shown to be effective as adjuncts to regional anaesthesia in clinical trials. However, no study has compared the effects of these drugs in patients with coexisting morbidity undergoing cervical plexus block.

We hypothesized that remifentanil 3 μg kg⁻¹ h⁻¹ and propofol 1 mg kg⁻¹ h⁻¹ would be equal in sedative, haemodynamic and respiratory effects, and improved patient acceptability of the technique. In a prospective, randomized, single blinded, and controlled study, we compared these drugs in patients undergoing carotid endarterectomy using deep cervical plexus block.

**Methods and results**

Following approval by the institutional ethics committee and having obtained written informed consent, 60 patients (ASA class III–IV) undergoing elective carotid endarterectomy were included in the study. Exclusion criteria were repeated operation, emergency surgery, or allergy to one of the drugs used. Using a computer-generated list (MS Excel 7.0), patients were randomized into two groups, to receive propofol or remifentanil.

Before the placement of the cervical plexus block, patients were monitored by five-lead electrocardiography, invasive arterial pressure, ventilatory frequency, and pulse oximetry. Deep cervical plexus block was performed using the single bolus-technique described by Winnie and colleagues and a dose of 20 ml of ropivacaine 0.75%.

Three millilitres of ropivacaine 0.75% were also injected below the inferior border of the mandible, and 7 ml were used to infiltrate the area of the skin incision. This was followed immediately by the start of an infusion of propofol 1 mg kg⁻¹ h⁻¹ or remifentanil 3 μg kg⁻¹ h⁻¹. Preoperatively, and at fixed points (P1=skin incision; P2=1 min after; P3=cross-clamp the carotid; P4=10 min later; P5=open the cross-clamp of the carotid; and P6=end of surgery), mean arterial pressure, heart rate, ventilatory frequency, $P_{aCO_2}$, and sedative effect were noted. Only episodes of bradycardia not related to surgical stimulation were recorded. The effect of sedation was measured on a 5-point scale: (1) awake, (2) tired, (3) very tired, (4) asleep, but wakes up when called by name, or (5) only wakes up when the shoulder is shaken. At the end of surgery, the infusion was stopped and all patients were transferred to the postanaesthesia care unit. On the first postoperative day, the patients’ subjective impression of their pain control was recorded using a 10-point visual analogue scale (1=very good, 10=very bad).

Groups were compared using the Mann–Whitney U test. A $P$ value of 0.05 was considered to be significant. Calculations were performed on a personal computer, using a standard software package (Winstat™ 3.0, Kalmia, US).

Sixty patients (median age 74 yr, range 54–83 yr) were investigated. In three patients in the remifentanil group, complications were encountered. In two cases, a bradycardia (heart rate between 30 and 35 beats min⁻¹) was
detected a few minutes after starting the infusion. In one patient, sedation was excessive and respiratory depression (less than 6 bpm) occurred. The infusion of remifentanil was stopped in each instance and all patients recovered quickly, but were excluded from further evaluation.

After cross clamping of the carotid artery, one patient in the propofol group stopped breathing and lost consciousness. The patient’s trachea was intubated and general anaesthesia was instituted. Postoperatively, a cerebrovascular accident was diagnosed and the patient was excluded from further evaluation. Four patients in the propofol group (13.8%) and three patients in the remifentanil group (11.1%) required additional local anaesthetic (lidocaine 0.5%) around and within the carotid sheath.

Nitroglycerin 1–5 mg h⁻¹ to treat hypertension was used in eight patients (26.6%) in the propofol group and seven patients (25.9%) in the remifentanil group. Nausea and vomiting occurred in five patients (16.7%) in the propofol group and seven patients (25.9%) in the remifentanil group. At no point were any differences found between groups in the mean arterial pressure, heart rate, or SpO₂. There was no difference in sedative effects between groups. Mean scores were the same at each time point.

Ventilatory frequency was found to be significantly different between the groups at every time point (P<0.01) (Fig. 1).

The patient’s subjective impression of pain on a visual analogue scale was similar in both groups and showed good acceptance of the procedure (propofol group 1.67 (0.75); remifentanil group 1.77 (0.42)).

**Comment**

A large study, describing 1000 cervical plexus blocks for carotid endarterectomy, reported that 66% of patients required sedation during the operative period.³ We compared two procedures, using dosages of propofol or remifentanil proven to be safe and effective in our institution, for sedation of patients with significant comorbidity. We found that both drugs supplied sufficient sedation, resulting in an excellent acceptance rate by the patients. However, adverse effects were higher in the remifentanil group.

The requirement for additional sedation during carotid endarterectomy results from: inability of the patient to move his head during surgery, causing pain in the cervical spine; or surgical manipulation in the area of the carotid sheath or under the mandible. Additionally, some patients are anxious. Such discomfort can result in adverse cardiovascular events, which are undesirable, as haemodynamic and respiratory instability are associated with a poor outcome after such surgery.⁴

Propofol is well established for sedation, as is remifentanil during regional anaesthesia.¹ ⁵ ⁶ However, there is no concordance about the optimal doses of these drugs in such circumstances and no data are available concerning patients of ASA class III–IV, the predominant group of patients undergoing this type of surgery. Lauwers and colleagues¹ used propofol 3 mg kg⁻¹ h⁻¹ or remifentanil 6 µg kg⁻¹ h⁻¹ for sedation during regional anaesthesia, and reported considerable side effects in both groups. Respiratory depression was reported to be more frequent in the remifentanil group.

In another study, Lauwers and colleagues⁶ compared three different doses of remifentanil (2.4 vs 4.2 vs 6 µg kg⁻¹ h⁻¹) and found significant rates of respiratory depression, nausea, and sweating in all three groups. Using either propofol 4.5 mg kg⁻¹ min⁻¹ or remifentanil 6 µg kg⁻¹ h⁻¹, Smith and colleagues¹ noted a greater degree of sedation in patients receiving propofol, whereas patients from the remifentanil group had more marked respiratory depression.

Mingus and colleagues⁸ used higher doses of remifentanil 12 µg kg⁻¹ h⁻¹ and propofol 6 mg⁻¹ kg⁻¹ in patients undergoing orthopaedic and urological surgery. These doses were increased by 50% when patients expressed discomfort, or decreased by 50% in the case of hypoventilation or haemodynamic instability. Remifentanil proved to be more effective than propofol in minimizing pain, but was...
associated with more respiratory depression and short-term nausea. In our study, 26% of patients in the remifentanil group suffered from nausea and vomiting compared with 17% in the propofol group.

The results reported by Mingus,\textsuperscript{8} indicate that the remifentanil dose should be reduced to 6 $\mu$g kg$^{-1}$ h$^{-1}$ and to 3 $\mu$g kg$^{-1}$ h$^{-1}$ in elderly patients. However, our data suggest that in patients over 70 yr of age and classified as ASA III or IV, even a dose of 3 $\mu$g kg$^{-1}$ h$^{-1}$ can induce side effects. Thus, we believe that a further reduction in dosage is required. With a dose of propofol 1 mg kg$^{-1}$ h$^{-1}$, we found stable haemodynamics, mild sedation, and no respiratory depression. Using the lowest remifentanil dose (3 $\mu$g kg$^{-1}$ h$^{-1}$) recommended by Mingus and colleagues,\textsuperscript{8} resulted in stable haemodynamics and mild sedation, but respiratory depression was significantly higher than in the propofol group.

We suggest that when using remifentanil for sedation in ASA III–IV patients undergoing carotid endarterectomy, the initial dose should be decreased to 1.5–2 $\mu$g kg$^{-1}$ h$^{-1}$ to minimize cardiovascular and respiratory complications in these elderly patients with significant comorbidity. A stepwise adaptation of the remifentanil dosage as proposed by Servin and colleagues\textsuperscript{9} appears to be a promising alternative to a fixed dose regime. However, it remains to be determined whether a reduction in remifentanil dosage to avoid side effects leads to a loss of sedative and analgesic effects.

References