The purpose of the study was to compare the clinical activity of remifentanil or alfentanil under propofol sedation with regard to respiratory rate, sedation and recovery rate when used for outpatient endometrial biopsy. Patients were randomized to receive intravenously either bolus remifentanil 0.4 µg/kg and propofol 1 mg/kg in the remifentanil group (n = 30), or bolus alfentanil 20 µg/kg and propofol 1 mg/kg in the alfentanil group (n = 30). Patients were monitored for heart rate, systolic and diastolic arterial pressure, peripheral O₂ saturation (SpO₂), respiration rate, and Aldrete sedation score. Pulse oximetry was used to monitor heart rate and SpO₂ during endometrial biopsy. Apnoea was observed in five patients from the remifentanil group, and in three patients from the alfentanil group. The groups did not differ with regard to apnoea incidences. Times were recorded for orientation and Aldrete score > 8, and were similar between the two groups (13.20 ± 3.64 min and 14.0 ± 3.87 min in the remifentanil group, 14.7 ± 3.64 min and 15.9 ± 3.15 min in the alfentanil group, respectively). The sedative and analgesic combination of remifentanil-propofol does not offer any advantages compared with a combination of alfentanil-propofol with regards to respiration and recovery during sedation for outpatient endometrial biopsy.

**KEY WORDS: REMIFENTANIL; ALFENTANIL; HYPNOTICS; PROPOFOL; SEDATION; ENDOMETRIAL BIOPSY**

### Introduction

Short-acting drugs such as propofol, alfentanil and remifentanil have been given to provide sedation and analgesia for a variety of procedures. Remifentanil is a novel, esterase-metabolized opioid that is chemically related to the synthetic, µ-opioid receptor agonists. Until recently, alfentanil was a widely used synthetic opioid that is rapidly eliminated from the body due to its small volume of distribution; however, early clinical studies show that remifentanil is highly effective in providing profound intraoperative analgesia and faster recovery than alfentanil.

We aimed to compare the clinical efficacy of remifentanil or alfentanil with regard to respiration, sedation and post-sedation emergence under clinical conditions similar to those currently approved for propofol during outpatient endometrial biopsy.
Patients and methods

PATIENT SELECTION
Patients aged 35 years or more with American Society of Anaesthesiologists (ASA) physical status I – II who were undergoing elective endometrial biopsy were admitted to the study. They gave individual informed consent and the study was approved by the local ethics committee. Patients were randomized to either the remifentanil group (n = 30) or the alfentanil group (n = 30).

Excluded patients included those with systemic disorders or hypertension, chronic users of opioids, benzodiazepines, tricyclic antidepressants, anticonvulsants or clonidine, or patients who had consumed any of the above drugs within 12 h before surgery, or had been treated with erythromycin or cimetidine.

PROCEDURE
On arrival in the endometrial biopsy room and following patient orientation, catheters were placed intravenously. Patients were given 0.9% saline, 4 ml/kg intravenously. A pulse oximeter (BCI, Inc., Waukesha, WI 53188, USA) probe was attached. Blood pressure was measured non-invasively. Oxygen was administered at the rate of 2 l/min with nasal oxygen prongs. The numbering of syringes was blinded. Supplemental injection was repeated if sedation was inadequate, as defined by spontaneous moving. Patients in the remifentanil group were given bolus remifentanil intravenously 0.4 µg/kg slowly, followed by propofol 1 mg/kg intravenously for 30 s manually. Patients in the alfentanil group were given bolus alfentanil intravenously 20 µg/kg slowly, followed by propofol 1 mg/kg intravenously for 30 s manually.

The anaesthesiologist attempted to maintain an Aldrete sedation score of 2 or 3 during the curettage period; patients received intermittently a combination of propofol 10 mg intravenously and remifentanil 0.2 µg/kg or alfentanil 10 µg/kg, as required. Supplemental drug demands were noted. Sedation levels were evaluated at 2-min intervals. The number of excessive sedative patients (sedation score > 3) was noted. Apnoea was defined as the absence of respiratory effort over a 15-s period. The number of patients with apnoea was noted, and these patients were ventilated with a bag-mask. Time to orientation and time to Aldrete score > 8 were recorded during the recovery period. After the endometrial biopsy any adverse events, such as nausea, vomiting and shivering, were recorded.

STATISTICAL ANALYSIS
Results are presented as means ± SD. Power analysis revealed that a sample size of 30 patients for each group provided 80% power at $\alpha = 0.05$ to detect a difference of two in the number of changes required in the study. Data were analysed with Fisher's exact test and Student's $t$-test for unpaired data. Statistical significance was taken as $P < 0.05$.

Results
The two groups were similar with respect to age, weight, numbers, mean propofol dose and mean endometrial biopsy time (Table 1).

All patients awoke within 13 min after eye opening, and followed verbal instructions spontaneously. There was no need for intubations or the administration of naloxone. There were no statistical differences between the groups in orientation time and time to the Aldrete score reaching > 8 (Table 2). No significant differences were found between the two groups regarding either the number of patients with sedation level > 3 or the number experiencing apnoea (Table 3).

Similarly, there were no significant
TABLE 1: Patient demographics and characteristics

<table>
<thead>
<tr>
<th></th>
<th>Remifentanil group</th>
<th>Alfentanil group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (n)</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47.8 ± 7.79</td>
<td>45.2 ± 7.65</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.2 ± 12.8</td>
<td>68.6 ± 10.1</td>
</tr>
<tr>
<td>Endometrial biopsy time (min)</td>
<td>8.76 ± 1.83</td>
<td>8.20 ± 1.78</td>
</tr>
<tr>
<td>Total dose of propofol (mg)</td>
<td>79.3 ± 9.3</td>
<td>76.4 ± 11.0</td>
</tr>
</tbody>
</table>

Values are mean ± SD. All data not statistically different between the groups.

TABLE 2: Recovery properties

<table>
<thead>
<tr>
<th></th>
<th>Remifentanil group</th>
<th>Alfentanil group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to orientation (min)</td>
<td>13.2 ± 3.64</td>
<td>14.0 ± 3.87</td>
</tr>
<tr>
<td>Time to Aldrete score &gt; 8 (min)</td>
<td>14.7 ± 3.64</td>
<td>15.95 ± 3.15</td>
</tr>
</tbody>
</table>

Values are mean ± SD. All data not statistically different between the groups.

TABLE 3: Number of patients with bolus supplemental study drug demands and complications

<table>
<thead>
<tr>
<th></th>
<th>Remifentanil group</th>
<th>Alfentanil group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolus supplemental study drug demands</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Apnoea (measured over a 15-s period)</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Sedation level &gt; 3 (Aldrete score)</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Shivering</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

All data not statistically different between the groups.

differences in the number of patients administered bolus supplemental study drugs, which were administered to eight patients in the remifentanil group and 11 patients in the alfentanil group. There were also no differences between the two groups in the number of cases of vomiting, nausea and shivering (Table 3).
Discussion

The present study shows that similar sedation, apnoea and recovery times were achieved with both remifentanil and alfentanil. Remifentanil and alfentanil have been used for sedative regimens to achieve higher sedation levels and analgesia, and lower incidences of nausea and vomiting. Previous comparative studies have reported that remifentanil is approximately 40 times more potent than alfentanil; these studies have suggested 0.2 – 1 µg/kg bolus doses of remifentanil and 20 – 50 µg/kg of alfentanil. This comparison, however, has never been tested previously during outpatient endometrial biopsy. In the current study, we used a 1:40 dose ratio of remifentanil to alfentanil to achieve a similar level of analgesia; these doses are similar to those of previous studies. The manufacturers of remifentanil recommend that the loading dose should be given over a period of 30 s in an effort to limit respiratory depression. The recommended loading dose of remifentanil for monitored anaesthesia care is 0.5 – 1.0 µg/kg body weight; however, although patients may be awake, they can be apnoeic and need to be reminded to breathe. In our study, patients were given intravenous bolus injections of remifentanil 0.4 µg/kg or alfentanil 20 µg/kg slowly, followed by propofol 1 mg/kg in 30-s, manually administered, intermittent, intravenous bolus injections.

The most frequent adverse event in our study was apnoea. Sa Rego et al. reported higher patient comfort during extra-corporeal shock wave lithotripsy when remifentanil was administered by infusion. These patients, however, had greater desaturation (30% versus 0%) compared with those receiving intermittent boluses of remifentanil. Sa Rego et al suggest that remifentanil infusion must be carefully titrated to avoid excessive respiratory depression. White et al. have reported that short-acting drugs allow better titration of anaesthesia, and may therefore reduce the incidence of respiratory depression and permit a rapid recovery. Remifentanil or alfentanil were administered with an intermittent slow bolus technique in our study, and we observed apnoea in five patients (16%) from the remifentanil group and in three patients (10%) from the alfentanil group, but no differences with respect to desaturation or recovery were found between the two groups. Oxygen saturation was unaffected because of supplemental oxygen. Our results on respiratory rate depression are consistent with previous study results. Previous studies have shown that recovery from remifentanil-propofol anaesthesia was within 3 – 9 min, and from alfentanil-propofol anaesthesia was within 5 – 16 min. Several of these are not consistent with our study because our total doses of remifentanil and alfentanil were lower than previous studies.

In conclusion, these results demonstrate that intravenous slow bolus injections of remifentanil or alfentanil can be used safely during outpatient endometrial biopsy, although the use of this sedation strategy should be restricted to an experienced anaesthesiologist in a hospital setting.

References
Sedation for outpatient endometrial biopsy


