Sedative and analgesic practice in the intensive care unit: the results of a European survey

H. M. Soliman, C. Mélot and J.-L. Vincent*

1Department of Intensive Care, Erasme University Hospital, Free University of Brussels, Route de Lennik 808, B-1070 Brussels, Belgium

*Corresponding author

Sedation and analgesia are important aspects of patient care on the intensive care unit (ICU), yet relatively little information is available on common sedative and analgesic practice. We sought to assess international differences in the prescription of sedative and analgesic drugs in western European ICUs by means of a short, self-administered questionnaire. Six hundred and forty-seven intensive care physicians from 16 western European countries replied to the questionnaire. Midazolam was used as a sedative often or always by 63% of respondents and propofol by 35%. There were considerable international variations, with midazolam being preferred over propofol in France, Germany, the Netherlands, Norway and Austria. For analgesia, the drugs most commonly used were morphine (33%), fentanyl (33%) and sufentanil (24%). Morphine was preferred over fentanyl and sufentanil in Norway, UK and Ireland, Sweden, Switzerland, the Netherlands, and Spain and Portugal. Fentanyl was preferred in France, Germany and Italy. Sufentanil was preferred in Belgium and Luxemburg and in Austria. Multivariate analysis showed that the combination of midazolam with fentanyl was most often used in France; propofol with morphine in Sweden, the UK and Ireland, and Switzerland; midazolam with morphine in Norway; and propofol with sufentanil in Belgium and Luxemburg, Germany and Italy. The use of a sedation scale varied from 72% in the UK and Ireland to 18% in Austria. When used, the most common sedation scale was the Ramsay scale. This study demonstrates substantial international differences in sedative and analgesic practices in western European ICUs.

Br J Anaesth 2001; 87: 186–92

Keywords: analgesia; sedation; intensive care

Accepted for publication: January 16, 2001

Anxiety and pain are commonly encountered by intensive care unit (ICU) patients, and almost all critically ill patients, particularly those receiving mechanical ventilation, will receive either a sedative or analgesic agent; many will receive both. A wide variety of pharmacological agents are now available for sedation and analgesia and, while recommendations have been made regarding the ‘best’ sedative and analgesic regimes for ICU patients,1 practice varies widely between and within ICUs. The choice of agent can be based on many factors, including the relative needs for sedation and analgesia, the pharmacodynamics and pharmacokinetics of the drug in question, route and ease of administration, the tolerance profile and the cost. While many studies have been conducted comparing the effectiveness of various agents,2–12 there is relatively little published information on variations in sedative and analgesic drug use among units or across national and international boundaries.13–18

The aim of our study was to assess differences in the clinical use of sedative and analgesic drugs, alone or in combination, in western European ICUs.

Methods

A short questionnaire was sent by e-mail to all names on a database, obtained from the European Society of Intensive Care Medicine, Intensive Care Symposium activities and other academic meetings, of ICU doctors in 17 western European ICUs.

This article is accompanied by Editorial II.

© The Board of Management and Trustees of the British Journal of Anaesthesia 2001
European countries: Belgium, Luxemburg, France, Germany, Netherlands, UK, Ireland, Finland, Denmark, Switzerland, Spain, Portugal, Greece, Italy, Austria, Sweden and Norway. The short questionnaire (Table 1) asked seven questions about the clinical use of sedative and analgesic drugs in ICU patients. Of the 3639 e-mail addresses, 340 were found to be incorrect and the messages were returned.

The answers were collected on a computer database. Univariate statistical analysis consisted of $\chi^2$ tests or Fisher’s exact tests. Multivariate statistical analysis was also performed, using multiple correspondence analysis. The level of statistical significance was set at $P<0.05$.

### Results

We received 647 replies to the questionnaire (20% response rate) from 16 countries. For analysis, we pooled the answers from Luxemburg with those from Belgium, Portugal with Spain, and Ireland with the UK, because of the small number of responses (Table 2). Of the respondents, 49%, 35% and 16% were working in university, city and community hospitals, respectively.

The use of sedation in ventilated patients varied considerably between countries; 78% of respondents from the UK

### Table 1 Questionnaire used in study

<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
</table>
| 1. In your ICU, what percentage of mechanically ventilated patients require continuous i.v. sedation? | $\square <50\%$  
$\square 50\%$  
$\square 75\%$  
$\square 100\%$ |
| 2. In patients requiring a continuous infusion of sedative agents, how often do you use the following agents? | midazolam: $\square$ never  
$\square$ seldom  
$\square$ regularly  
$\square$ often  
$\square$ always  
propofol: $\square$ never  
$\square$ seldom  
$\square$ regularly  
$\square$ often  
$\square$ always  
other (please specify): $\square$ never  
$\square$ seldom  
$\square$ regularly  
$\square$ often  
$\square$ always |
| 3. What other intravenous sedative agents do you use regularly?          | haloperidol: $\square$ never  
$\square$ seldom  
$\square$ regularly  
$\square$ often  
$\square$ always  
other (please specify): $\square$ never  
$\square$ seldom  
$\square$ regularly  
$\square$ often  
$\square$ always |
| 4. Do you use a sedation score?                                         | $\square$ yes  
$\square$ no |
| 5. In patients requiring continuous infusion of analgesic agents, how often do you use the following agents? | morphine: $\square$ never  
$\square$ seldom  
$\square$ regularly  
$\square$ often  
$\square$ always  
fenfluramine: $\square$ never  
$\square$ seldom  
$\square$ regularly  
$\square$ often  
$\square$ always  
sufentanil: $\square$ never  
$\square$ seldom  
$\square$ regularly  
$\square$ often  
$\square$ always |
| 6. Type of ICU (several answers possible)                               | $\square$ medical  
$\square$ surgical  
$\square$ trauma  
$\square$ coronary  
$\square$ paediatric  
$\square$ burns |
| 7. Type of hospital (one answer)                                        | $\square$ university/academic  
$\square$ city  
$\square$ community |

### Table 2 Response rates according to country

<table>
<thead>
<tr>
<th>Country</th>
<th>Sent</th>
<th>Responses received (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>180</td>
<td>40 (22.2)</td>
</tr>
<tr>
<td>Belgium</td>
<td>528</td>
<td>67 (12.6)</td>
</tr>
<tr>
<td>Denmark</td>
<td>134</td>
<td>23 (17.1)</td>
</tr>
<tr>
<td>Finland</td>
<td>75</td>
<td>15 (20)</td>
</tr>
<tr>
<td>France</td>
<td>632</td>
<td>175 (27.6)</td>
</tr>
<tr>
<td>Germany</td>
<td>371</td>
<td>76 (20.4)</td>
</tr>
<tr>
<td>Greece</td>
<td>73</td>
<td>0</td>
</tr>
<tr>
<td>Ireland</td>
<td>19</td>
<td>2 (10.5)</td>
</tr>
<tr>
<td>Italy</td>
<td>215</td>
<td>44 (20.4)</td>
</tr>
<tr>
<td>Luxembourg</td>
<td>7</td>
<td>2 (28.5)</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>203</td>
<td>23 (11.3)</td>
</tr>
<tr>
<td>Norway</td>
<td>137</td>
<td>33 (24)</td>
</tr>
<tr>
<td>Portugal</td>
<td>127</td>
<td>5 (3.9)</td>
</tr>
<tr>
<td>Spain</td>
<td>141</td>
<td>12 (8.5)</td>
</tr>
<tr>
<td>Sweden</td>
<td>136</td>
<td>38 (27.9)</td>
</tr>
<tr>
<td>Switzerland</td>
<td>117</td>
<td>24 (20.5)</td>
</tr>
<tr>
<td>UK</td>
<td>524</td>
<td>68 (12.9)</td>
</tr>
</tbody>
</table>
and Ireland stated that >75% of their ventilated patients required continuous intravenous sedation while in Italy the figure was just 30%.

Sixty-three per cent of respondents said they used midazolam often or always in patients requiring sedation, and 35% used propofol (Table 3). Although midazolam was the most commonly used sedative drug in both medical and surgical units, the common (often or always) use of propofol was more frequent in surgical units than in medical units (34% and 12%, respectively; \(P<0.05\)); the reverse was true for midazolam (55% and 88%, respectively; \(P<0.05\)). There was a highly significant difference (\(P<0.01\)) in the use of midazolam and propofol between countries. Midazolam was often or always used by 85% of respondents in Norway, but only by 39% in Denmark, and propofol was often or always used by 65% of Italian respondents, but only by 3% of respondents from Norway (Figure 1). Midazolam was more commonly used than propofol in France, Germany, the Netherlands, Norway and Austria (\(P<0.05\)), and propofol appeared to be more commonly used than midazolam in Italy, and Belgium and Luxemburg, although this was not significant (Figure 1). Lorazepam was used often or always by only three (0.5%) respondents.

Thirty-three per cent of respondents stated that they used morphine often or always in patients requiring continuous intravenous analgesia, 33% said they used fentanyl and 24% sufentanil (Table 3), with significant differences among countries. The common (often or always) use of morphine varied from 88% in Norway to 3% in Germany, that of fentanyl from 58% in Italy to 0% in the Netherlands, and that of sufentanil from 52% in Belgium and Luxemburg to 0% in Switzerland. Morphine was used more commonly than the other agents in the UK and Ireland, Sweden, Norway, Switzerland, Spain and Portugal, and the Netherlands (\(P<0.05\)). Fentanyl was preferred over the other agents in France, Germany and Italy (\(P<0.05\)), and sufentanil was preferred in Belgium and Luxemburg, and Austria (\(P<0.05\)) (Figure 2). There was no significant difference in the use of analgesic drugs between different types of ICU.

Multivariate analysis showed that the combination of midazolam and fentanyl was most often used in France, and that the combination of propofol and morphine was most used in Sweden, the UK and Ireland, and Switzerland. The combination of midazolam with morphine was most often used in Norway. The combination of propofol and sufentanil was most often used in Belgium and Luxemburg, Germany, and Italy (Figure 3).

The use of a sedation scale varied widely (\(P<0.01\)) around a mean of 43% (Figure 4), with doctors from the UK and Ireland most frequently using a sedation scale (72%), and those in Austria using one least often (18%). When a

![Fig 1 Prevalence of frequent use of midazolam and propofol (often or always) for sedation according to country. *\(P<0.05\) between drugs for that country.](image)

![Table 3 Prevalence of frequent use (often or always) of sedative and analgesic drugs. *Used regularly or often.](table)

<table>
<thead>
<tr>
<th>Sedative drug</th>
<th>Number (%)</th>
<th>Analgesic drug</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td>408 (63)</td>
<td>Morphine</td>
<td>214 (33)</td>
</tr>
<tr>
<td>Propofol</td>
<td>229 (35)</td>
<td>Fentanyl</td>
<td>214 (33)</td>
</tr>
<tr>
<td>Haloperidol*</td>
<td>58 (9)</td>
<td>Sufentanil</td>
<td>153 (24)</td>
</tr>
<tr>
<td>Clonidine</td>
<td>12 (1.8)</td>
<td>Piritramide</td>
<td>5 (0.7)</td>
</tr>
<tr>
<td>Ketamine</td>
<td>8 (1.2)</td>
<td>Others</td>
<td>7 (1)</td>
</tr>
<tr>
<td>Flunitrazepam</td>
<td>6 (0.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Droperidol</td>
<td>5 (0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alfentanil</td>
<td>5 (0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorazepam</td>
<td>3 (0.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>2 (0.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methohexital</td>
<td>2 (0.3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
sedation scale was used, the Ramsay scale was employed most commonly (74% of cases).

Discussion

The ICU environment can appear hostile, even threatening, to patients; the noisy ICU environment, unfamiliar monitoring and support equipment, medical jargon, loss of day–night cycle and painful invasive procedures are associated with a high incidence of psychological problems and sleep deprivation. Sedation and analgesia are important to ensure patient comfort, from both psychological and physical points of view. The stress response can lead to profound changes in endocrine function, hypermetabolism, sodium and water retention, mobilization of substrates from energy stores and increased lipolysis. Pain can have many adverse consequences, including sympathetic overactivity with an increase in heart rate and myocardial oxygen consumption, increased respiratory rate and hypoxaemia, altered gastrointestinal motility, impaired urinary tract function, changes in blood viscosity, clotting time and

Fig 2 Prevalence of frequent use of morphine, fentanyl and sufentanil for analgesia according to country. *P<0.05 between drugs for that country.

Fig 3 Sedative and analgesic drug combinations in different countries.
platelet aggregation, diminished immune function and impaired wound healing.\textsuperscript{24,25} However, excessive sedation can have negative side-effects, including an increased risk of venous thrombosis, decreased intestinal motility, hypotension, reduced tissue oxygen extraction capabilities, prolonged ICU stay and increased costs.\textsuperscript{26-30} An acute withdrawal syndrome following prolonged use of sedative or analgesic drugs has also been reported in ICU patients.\textsuperscript{31} Ideally, administration of sedative and analgesic drugs should aim to keep the patient comfortable but easily aroused.\textsuperscript{32} Attitudes may have changed over time, as suggested by two enquiries in the UK: in 1981, Merriman\textsuperscript{33} reported that 67% of ICUs aimed to keep patients completely detached from the environment, whereas by 1987, Bion and Ledingham noted that 69% of respondents preferred patients sleepy but easily awakened.\textsuperscript{14}

In 1995, the Society of Critical Care Medicine (SCCM) published practice parameters for intravenous analgesia and sedation in the ICU.\textsuperscript{1} Evidence-based medicine recommendations regarding the ‘preferred’ agents were developed by a task force of more than 40 experts. Midazolam and propofol were preferred for short-term sedation, lorazepam for long-term sedation and haloperidol for treating delirium, while morphine and fentanyl were the preferred analgesic agents in critically ill patients.\textsuperscript{1} Despite such guidelines, there are large differences in the use of sedative and analgesic agents among units and across national and international boundaries.\textsuperscript{13-18,34} A survey of head nurses from 164 hospitals across the USA in 1991 found that 18 different sedative agents were used, with a preference for benzodiazepines and opiates.\textsuperscript{15} Also in the USA, Dasta and colleagues\textsuperscript{16} reported the use of 23 different agents for sedation and relief of anxiety and pain in their surgical ICU with extensive use of benzodiazepines (including, most commonly, lorazepam) and morphine. In our study, 22 different drugs were cited as being used often or always for sedation or analgesia, with midazolam, morphine and fentanyl generally being the preferred agents.

Benzodiazepines, e.g., diazepam, lorazepam and midazolam, are widely used as sedative agents in the ICU. Diazepam use has become less common as newer shorter-acting benzodiazepines have become available. Lorazepam is more potent than midazolam and, because of its low lipid solubility, crosses the blood–brain barrier more slowly, delaying its onset of action and prolonging the sedative effect.\textsuperscript{6,35} Hence, it is recommended for longer-term sedation while midazolam is preferred for short-term sedation.\textsuperscript{1} Propofol, another frequently used sedative agent, resembles midazolam in terms of pharmacological profile.\textsuperscript{35} Studies comparing midazolam and propofol have generally shown the two agents to be of similar efficacy and safety in sedating various groups of critically ill patients.\textsuperscript{3,5,9,36-37} Midazolam is, however, cheaper than propofol,\textsuperscript{9,12,38,39} which may account for the preferred use of midazolam seen in our study and others.\textsuperscript{17,18,40} Nevertheless, some would argue that propofol, when used as a sedative in mechanically ventilated patients, is associated with shorter weaning times and hence, while midazolam may be cheaper, the overall cost–benefit analysis taking into account duration of mechanical ventilation and ICU stay may in fact be better with propofol.\textsuperscript{2,8}

We also found great differences in the drugs most commonly used for analgesia, although morphine and fentanyl were most commonly prescribed, a finding supported by other groups.\textsuperscript{15,16,18,34,40} and in accord with the recommendations of the SCCM.\textsuperscript{1} Opioids, generally administered as a continuous intravenous infusion, remain the

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig4.png}
\caption{Prevalence of frequent use of sedation scale in each country.}
\end{figure}
mainstay of ICU analgesia. Morphine is the most widely used of the opioids, possibly again related to its lower cost, although the shorter-acting fentanyl and sufentanil are preferred by some.

Importantly, sedative and analgesic drugs are distinct agents, having separate, although complementary and sometimes synergistic, actions. Combined use of these drugs is common in the ICU patient; Watling and colleagues reported that 25% of patients received combination drug therapy, 46% of whom received a benzodiazepine–opioid combination. Magarey reported that, in Australia, the most common form of sedation was a benzodiazepine–opioid combination (used in 88% of ICUs), notably morphine with midazolam. In our study, the particular combination of drugs differed among countries, with, for example, midazolam and fentanyl preferred in France, but midazolam and morphine preferred in Norway.

While it was not the aim of the questionnaire, it is interesting to speculate on the reasons behind the differences in sedative and analgesic use seen among western European countries. The costs of drug therapy are certainly important and international differences in drug price may exist as a result of individual pricing policies, costs of transport and packing, and the cost of the mark-up added to the price of drugs by the importer and distributor. Several groups have reported lorazepam to be an effective sedative agent with lower costs than midazolam or propofol, and yet lorazepam was used often or always by only three of our respondents.

Differences in the timing of drug registration in various countries may account for certain preferences. As an example, the fact that midazolam has only recently been registered in Italy may explain why propofol was used more than midazolam in Italy, while the fact that sufentanil is less easily available in the UK may explain why morphine and fentanyl were used more than sufentanil in the UK. The primary speciality of the intensivist questioned may also influence drug choice; for example, anaesthetists may favour anaesthetic agents more than intensivists with a general medical background. While the design of our questionnaire did not allow us to investigate this aspect specifically, it is interesting to note that propofol was used more frequently on surgical than on medical units, perhaps related to its common use as an anaesthetic agent. It may also be preferred to facilitate earlier weaning and extubation. Communication with patients by verbal and non-verbal methods, such as touch by staff or relatives, is very important and depends on individual cultural, educational and socio-economic differences. This may decrease the need for sedation, although it may not significantly affect the choice of agent.

Both under- and over-sedation can have negative effects on the ICU patient, and in this population, particularly those who are mechanically ventilated, the level of sedation is often difficult to assess. Various sedation scales and scores have been developed in order to facilitate this process, and the use of a sedation scale has been shown to reduce the numbers of patients with excessive degrees of sedation. However, many units still rely on staff assessment of sedation rather than routinely employing any of the available scoring systems. Watling and colleagues reported that just 26% of the respondents in their survey of ICUs in the USA used a sedation scale, while Christensen and Thunodborg noted that only 16% of Danish ICUs used a sedation scoring system. In our study, we found that 43% of units used a scale, but this figure varied greatly among individual countries. As we report, the Ramsay scale is generally the most widely used sedation assessment system, probably chiefly because it is easy to apply, although it has never been scientifically tested for reliability or validity.

In conclusion, our enquiry has revealed substantial international differences in the clinical use of drugs for sedation and analgesia in western European countries, and in the use of sedation scales to monitor levels of sedation. While we acknowledge the inherent limitations of questionnaire surveys and accept that the response rate was relatively low, we received replies from a broad cross-section of ICUs and hospital types, and have no reason to believe the data obtained are not representative of the current situation in western Europe. Such information can encourage valuable discussion about the reasons behind the variations seen, and perhaps help in the development of sedation and analgesic protocols, which have been shown to improve outcome.

References


13 Merriman HM. The techniques used to sedate ventilated patients. A survey of methods used in 34 ICUs in Great Britain. Intensive Care Med 1981; 7: 217–24


34 Watling SM, Dasta JF, Seidl EC. Sedatives, analgesics, and paralytics in the ICU. Ann Pharmacother 1997; 31: 148–53


43 Park GR. Drugs used to make critically ill patients comfortable. Curr Opin Crit Care 1999; 5: 249–50

44 Vincent JL. Communication in the ICU. Intensive Care Med 1997; 23: 1093–8


