

## The Techniques Used to Sedate Ventilated Patients

A Survey of Methods Used in 34 ICUs in Great Britain\*

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**Abstract.** A survey of sedation techniques for ventilated patients was performed by visiting 34 Intensive Care Units in Great Britain and Northern Ireland. The opiates in frequent use were phenoperidine (21 units – 62% of units), papaveretum (11–32%) and morphine (9–26%). Many units used more than one opiate. Levorphanol, buprenorphine, pethidine, fentanyl and codeine were little used. Frequent use of diazepam was found in 22 units (64%), of lorazepam in 11 (32%) and of Althesin in four (12%). Other sedative drugs, droperidol, chlormethiazole, chlorpromazine and ketamine were used on an occasional basis. Continuous sedation using nitrous oxide was employed in nine (26%) of units – for more than 24 h in six (18%). All units used pancuronium – 31 (91%) used it frequently. Curare was in frequent use in five units (15%). There was wide variation in the way in which the drugs were used. A compromise between the ideal and the practicable method was common, depending more upon shortage of trained nursing staff than upon lack of funds for equipment or expensive drugs. The depth of sedation thought to be ideal depended on the state of the patient as well as the usual practice in the ICU – however a majority (23 = 67%) of units aimed to keep most patients well sedated and detached from the ICU environment. The use of very large doses of opiate to obtund the stress response was thought helpful in only six units (18%) and then in a minority of patients.

**Key words:** Intensive care units – Sedatives – Narcotics – Respiration, artificial

### Introduction

Patients are mechanically ventilated for a wide variety of reasons and their response to illness and its management in the intensive care unit is similarly variable. It is therefore hardly surprising that the amount and type of sedation is different between patients, and for the same patient as his illness changes.

A successful sedation regime has several requirements and these include; relief of anxiety, analgesia, reduction of patients' respiratory drive, safety and simplicity. These requirements call for ingenuity and care in the choice of sedation technique and many different techniques have evolved. Little has been documented although there are accounts of the use of individual drugs [1–3].

### Methods

This survey involved a series of visits to 34 of the 200–250 intensive care units in Great Britain and Northern Ireland to witness their methods of sedating patients and discuss related problems with the staff. At least half a day was spent in each ICU so that as full and accurate an impression as possible could be gained.

The units visited were chosen on the basis of a known interest in sedation techniques, ease of access and personal contacts. The geographical distribution of the units is listed at the end of the paper. A questionnaire tested in a 4-unit pilot study served as a basis for discussion and views were obtained from consultant and junior medical staff and from the nurses. From these discussions it was possible to build up a picture of the work load of each unit (and how this affected sedation techniques) and to see the solutions to various practical problems.

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**Table 1.** Types of ICU

Post cardiac surgery only	2
Post cardio/thoracic surgery and other patients	3
Post neurosurgery and other patients	6
Other patients	23
	34

**Table 2.** Who runs the ICU? (Consultants' speciality)

Anaesthetist	23
Anaesthetist + physician + surgeon	4
Anaesthetist + physician	2
Anaesthetist + surgeon	2
Clinical physiologist	2
Physician + surgeon	1

**Table 3.** Is there a member of junior medical staff on call solely for the unit?

No	12
Yes	22

Specialities of these junior staff

Anaesthetist	15
Physician + anaesthetist	2
Anaesthetist + surgeon	3
Anaesthetist + physician + surgeon	1
Physician	1

**Table 4.** Is there a protocol for method of sedation on unit?

Yes	2
- written	2
- unwritten (by mutual consent)	16
No	16

### The Units Visited

The 34 units were either teaching hospitals (24) or district general hospitals (10). Details of the administration and medical staffing may be seen in Tables 1-5.

From the lack of statistical evidence (evident from Table 5) it may be understood that it was not possible to quantify precisely the pattern of drug use which could only be described as "frequent", "sometimes" or "rarely". Personnel interviewed described their use of each drug as one of these three categories and a consensus view obtained.

## Results

### Aims of Sedation

The ideal depth of sedation and degree of detachment from the environment were discussed in each ICU. Although it was difficult to generalise, the following views were given.

**Table 5.** Are there unit statistics related to sedation?

Yes	1
No	33

**Table 6.** Sequences in which drugs are used

1st line	2nd line	3rd line	No. of units using sequence
B	-	-	15
O	B	R	11
O + B	R	-	8
O	-	-	6
O	R	B	5
O + R	B	-	4
O + R + B	-	-	4
O	B	-	3
O + B	-	-	3
O + N <sub>2</sub> O	-	-	2
O	R	-	1
O + Althesin	-	-	1
R	-	-	1
Entonox	-	-	1
O	B + R	-	1

B Benzodiazepine, O opiate, R relaxant, N<sub>2</sub>O nitrous oxide (continuous, not intermittent)

**Table 7.** Choice of opiate

	No. of preferences		
	Phenoperidine	Papaveretum	Morphine
Respiratory depression	19	5	5
Sedation	12	11	6
Analgesia	10	5	4
Predictable duration of action	2	-	-

A patient fully orientated with an ICU environment who received analgesic drugs solely for painful procedures was considered in an ideal state in only nine units. It was thought that only the less ill patients would tolerate this and the presence of a tracheostomy (rather than endotracheal) tube helped. The alternative, a patient completely detached from the environment who was woken only on occasions was thought best in 23 units. Nearly everyone considered this sedated state best for the very ill. A midway point "sedated to the point of no distress" was chosen by nine units. It can be seen that some units chose more than one aim.

Other factors in the unit were recognized to have an effect on the ideal depth of sedation. Noise levels [4] and the presence of windows [5] were among these. An aim of sedation was considered to be an unnatural distinction in one unit: "We aim to keep our patients alive". Other observations made were that it did not matter as patients forgot their time in ICU -

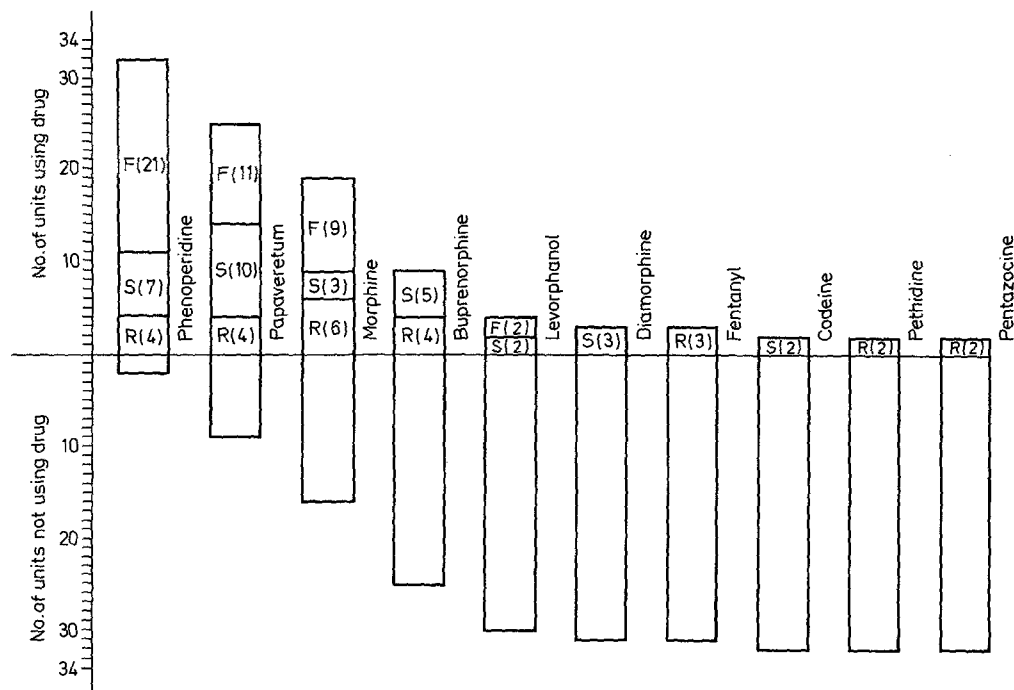


Fig. 1. Frequency of use of opiates and other analgesics. R = rarely, S = sometimes, F = frequently

although others dispute this [6, 7]. It was admitted that patients were sometimes sedated for the peace of mind of their attendants because it was easier to give a drug than interpret what a patient was trying to say.

*The Drugs Used*

Such was the wide variation in sedation techniques that information was obtained about the use of 21 different drugs. These are described as:

1. analgesics
2. benzodiazepines and other sedatives
3. other techniques including muscle relaxants

The frequency of use of these drugs is summarized in the bar-graphs in Figs. 1 – 4 and in Table 6.

*Choice of Opiate (Table 7)*

It was noticeable how advantage was taken of the differing properties of the opiates, although a common reason for preferring a drug was because “the unit was used to using it”.

Phenoperidine was chosen most commonly as an effective depressant of respiratory drive; its analgesia, sedation and predictable duration of action were secondary factors in the decision to use it. Papaveretum and morphine were chosen principally for sedative effect.

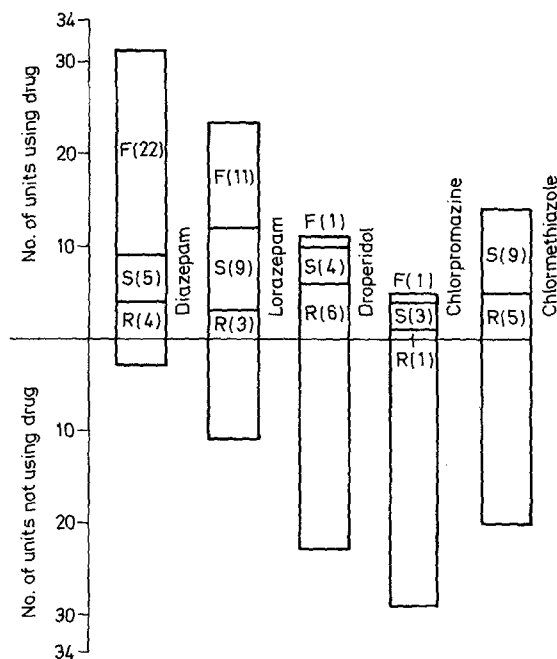


Fig. 2. Frequency of use of benzodiazepines and other sedatives

The timing of doses of opiates was almost universally “as needed” and an intravenous bolus of drug was used. Continuous infusions of opiate were very rarely used despite a widespread awareness of the advantages of such a system and it was only those using Althesin, chlormethiazole and lignocaine for sedation who routinely used a continuous infusion technique.

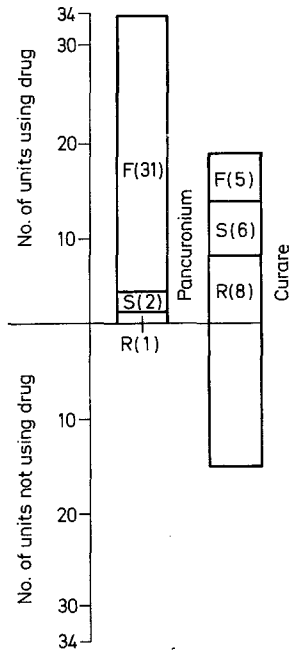


Fig. 3. Frequency of use of muscle relaxants

#### Muscle Relaxants (Fig. 3)

Pancuronium was the most popular muscle relaxant used as an adjuvant to the sedation technique. Those who preferred curare emphasized its advantages for hypertensive patients, for those with tetanus and for the less abrupt cessation of relaxation.

#### Ketamine

Intermittent doses of ketamine were used in four units before short painful procedures – for example change of tracheostomy tube or dressing. Infusions of ketamine had been tried in several units with the intention of using the analgesic and non-cardiac depressant properties of the drug. Despite efforts to attenuate the unwanted cardiovascular effects with various drugs [8], infusions of ketamine had been largely discontinued.

#### Althesin [9]

Use of Althesin was increasing. Four units used it frequently and reported no problems with use. It was given either as an undiluted drug in a syringe pump or in varying dilutions (usually 40%, e.g. 200 ml Althesin + 300 ml 5% dextrose) with the rate of infusion being judged by the patient's needs. Indications for the use of Althesin included:

1. Second line drug to supplement the effect of opiate in patients who need particularly effective sedation or to avoid awareness in patients receiving post-operative ventilation.
2. To sedate head injuries who need frequent clinical assessment and to sedate patients with chronic bronchitis during extubation.

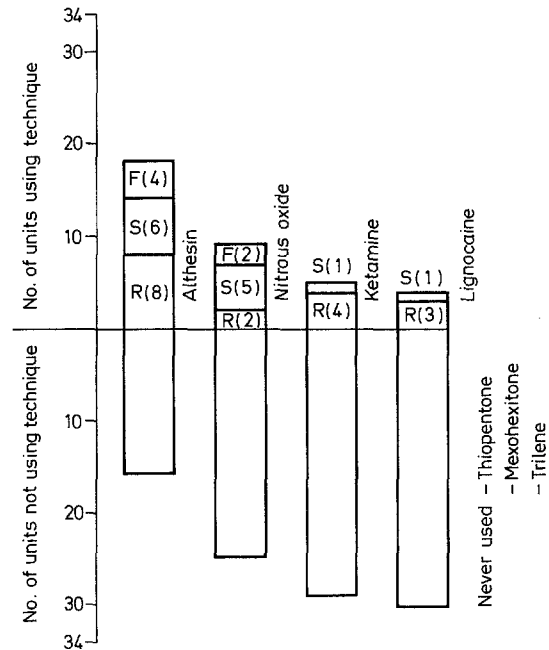


Fig. 4. Frequency of use of other techniques

#### Etomidate

This drug was not yet part of regular practice on any unit visited – infusions are on trial.

#### Lignocaine

Infusion of lignocaine (750 mg in 500 ml 5% dextrose) were used for sedation in only two units. Each 500 ml was given over 8 h to provide background sedation and was used frequently, being found of particular value in patients with extensive muscle trauma.

#### Thiopentone and Methohexitone Infusions [10]

These were not used for sedation on any units visited although thiopentone infusions were recognized as useful in the management of status epilepticus, head injuries and tetanus.

#### Nitrous Oxide and Entonox

Intermittent use of nitrous oxide occurred in 85 % of the units visited, most often to cover the pain of physiotherapy. Continuous use of nitrous oxide was employed in nine units. A further seven units visited would have used nitrous oxide had a supply been possible. Indications of the use of nitrous oxide included supplementation of opiates and muscle relaxants in post-operative patients and in patients not tolerant of other techniques, particularly young major trauma victims. Head injuries who needed frequent clinical assessment and patients with low cardiac output could also benefit from the use of nitrous oxide.

Continuous use of nitrous oxide via a ventilator depended upon the presence of a pipeline supply. Cylinders were considered too cumbersome.

The advantages of sedation with nitrous oxide was weighed against the risks of bone marrow depression [11, 12]. One unit used it for more than 36 h and six for more than 24 h. No clinical problem had arisen with prolonged use although several units used prophylactic vitamin B12 and folate supplements.

The avoidance of giving a hypoxic mixture led some units to use a gas mixture blender and in another the rotameters had been set such that the nitrous oxide would not come on until 2 l of oxygen per minute were already flowing.

#### *Local Blocks*

The excellent analgesia which can be produced by local blocks in particular epidural techniques with the use of a catheter were widely recognized, although only used by 12 units and then for only a minority of patients.

#### *Methods of Sedation for Particular Patient Problems*

Sedation forms but a small part of the management of particular patient problems, however most units found it needed to be modified under the following circumstances:

**1. Low Cardiac Output.** Patients with low cardiac output frequently need sedation during resuscitation, although it is recognized that smaller doses will be needed [14]. Seventeen units chose to use an opiate in a reduced dose – phenoperidine was the most popular – five units avoided opiates and merely controlled the patient with a reduced dose of pancuronium. Some units used Entonox as an alternative to either opiate or relaxant.

**2. Head Injuries.** A patient with a head injury who requires both mechanical ventilation and sedation needs a technique which permits ready assessment and effective control. The choice is dependent upon the type and facilities of the unit as well as on the patient's general condition. The disastrous effect on intracranial pressure of the movements of the inadequately settled patient are only too well known. In units with specialized diagnostic facilities e.g. a computer-assisted tomographic scan (CAT) and where there was expertise in the ventilator care of the postoperative neurosurgical patient, techniques differed markedly from those units where these services were not available.

In this latter group greater reliance had to be placed upon frequent clinical assessment and consequently little or no sedation was given. Pancuronium (or curare) was used in cases where there

were difficulties in achieving effective ventilation and diazepam was reserved for the control of fits. Opiates were used in a few units to treat the pain of any associated injuries.

In the six units with specialized facilities patients received an initial 48 h of ventilation after assessment including CAT scan. If sedation was needed diazepam was used, with pancuronium to control the patient. Thiopentone and Althesin infusions were used to reduce the cerebral oxygen demand (500 mg of Thiopentone over 5 h). Monitoring of intracranial pressure and cerebral function were used in assessment and to indicate the need for further doses of Thiopentone. Opiates were used frequently if there was evidence that the patient had a response to painful stimuli, while some used continuous nitrous oxide. Withdrawal of the drug to allow clinical assessment occurred at regular intervals.

**3. "Difficult to Settle".** Despite evidence of adequate pulmonary ventilation a minority of patients apparently needed large and frequent doses of sedative drugs in order to remain "settled" while receiving mechanical ventilation. Patients habituated to alcohol who were "difficult to settle" could be helped by a chlormethiazole infusion (14 units) or 5% intravenous ethanol. Intermittent mandatory ventilation was used in many centres to settle patients in preference to increasing drug doses.

**4. Prolonged Ventilation.** With prolonged drug administration there is a risk of drug accumulation [16] especially when drugs are not rapidly metabolised because of cardiovascular, hepatic or renal dysfunction.

While many patients do not require much sedation after their initial few days of acute illness, some presented a difficult problem for which each unit had its own solution. Lorazepam (6-hourly) was favoured in several units as being less cumulative than diazepam, and one unit had found particular success with a regime using alternate doses of buprenorphine and lorazepam every 3 h.

**5. Asthmatics.** Many units found it necessary to change their sedation regime for asthmatics. Morphine was avoided and pethidine or buprenorphine used as alternatives. Diazepam was often used. Lignocaine infusion (two units) and Lignocaine 1% topical spray down the endotracheal tube (one unit), Entonox and Halothane were valuable reserve methods.

**6. Bronchitics.** These patients often need minimal sedation. Opiates (morphine or phenoperidine) were favoured. Diazepam was used for these patients in four units and lorazepam in one.

7. *Night Sedation.* The establishment of a diurnal rhythm was considered helpful in 14 units. Those patients able to absorb fluids received nitrazepam or diazepam. Other drugs used for night sedation included lorazepam, buprenorphine, morphine, chlormethiazole, ethanol and Althesin.

*Are There Other Factors Apart from the State of the Patient Which Alter Sedation?*

1. *Shortage of Nursing Staff.* Although 26 units had no problems, five units were short of nursing staff day and night and a further three units had shortages at night. Many units commented that when there were fewer nurses the patients tended to receive more drugs (in particular muscle relaxants) as there was less time for the nurse to talk to the patient. The problem was known in most busy units at night. Only one unit particularly avoided muscle relaxants when short of nursing staff.

2. *Available Medical Staff.* There was no shortage of available medical staff in 31 units. Three units noticed difficulties in patient sedation when doctors were not available.

3. *Equipment.* Ventilators which could be adapted for the use of Intermittent Mandatory Ventilation were not available in three units. Piped nitrous oxide was needed in seven ICUs and piped air (to run ventilators) in five units. Infusion pumps were in short supply in five units and it was difficult to give continuous infusions for sedation. One unit felt they could sedate patients better if they had a CO<sub>2</sub> analyser to measure endtidal CO<sub>2</sub>.

4. *Lack of Space and Unsuitable Design of Unit.* A recognized problem in one unit, the patients being too close together and needing more sedation.

5. *Lack of Funds for More Expensive and Better Drugs.* This was not reported in any unit.

*Some Practical Problems Associated with Sedation Techniques*

1. *Thrombophlebitis.* This was not a problem in most units, as central venous lines were used for drug administration. A minority felt it unsafe to use central lines in this way. The drugs implicated in damaging peripheral veins were diazepam and Althesin. A diluent for diazepam (2 ml diazepam and 8 ml 9% ethanol in normal saline) had been found useful – as had the dilution of diazepam in Intralipid.

2. *Withdrawal of Opiate.* Ill patients requiring prolonged ventilation receive large, frequent doses of opiate and the pattern of opiate use is quite different

from that in general surgical wards. A fear that the patient will become habituated is present in the minds of many doctors and nurses and hence it was of interest to find out how frequently this problem occurs. Only four units had found any difficulties when opiate was stopped after a period of ventilation. However, how much distress was due to the withdrawal of the opiate and how much was due to the stress of weaning and the return to wakefulness was hard to judge.

No unit could recall a patient who had demanded opiate once weaned who was not in pain. The feeling was that although some physiological as well as psychological dependence may occur, its effects were short-lived and it did not affect the rate at which patients recovered. The many advantages of using opiates outweighed any risk of dependence. Chlormethiazole, diazepam or physeptone were found useful in some patients while opiate was being stopped. No problems were found if the opiate was used for pain only and stopped when no pain was present. A change from one opiate to another helped as tolerance developed more slowly. Several units felt that nursing staff could be encouraged to understand that patients would come to no harm if given frequent and adequate doses of opiate for pain.

3. *Dysphoria and Other Unwanted Psychological Effects Due to Sedative Drugs.* The most common causes of disorientation and dysphoria in ICU patients are the severity of the patient's illness and the unnatural environment of the unit [19]. Deprivation of stimuli and sleep must account for many psychological problems. Many of those questioned believed that too little sedation rather than too much was a cause of distress. There were anecdotal accounts of disorientation after the use of diazepam and lorazepam in elderly patients.

4. *Stress Ulcer Prophylaxis.* It was not possible to link the routine use of (or need for) either Cimetidine or antacids with any sedation technique.

5. *Does Sedation Need to be Changed Before Nasogastric Feeding can be Started?* 26 units would not change their sedation regime to aid intestinal absorption. Some emphasized the importance of intravenous feeding while others advocated the use of Metoclopramide. Of the minority who changed sedation, four units reduced opiate and four reduced muscle relaxant dose.

*Monitoring Depth of Sedation*

Clinical observation of the patient was the most usual method of judging when further increments of sedation were needed.

Plasma diazepam levels were measured in four units. It was recognized that patients could remain drowsy for up to one week after stopping diazepam [16] (some units tried to avoid this problem by limiting the total dose of diazepam given to each patient). Other measurement of level of consciousness (EEG or CFM) was not used (except in neurosurgical assessment). The autonomic response to pain – as may be measured by digital plethymography [20] was not used.

### *ICU Patients and the Stress Response*

The stress response, and the use of large doses of opiate to block the response to surgery are now well recognized [21–25]. It was of interest to find out if those working in ICUs thought that generous opiate sedation may help patients under their care.

The stress response was recognized in ICU patients in 28 units. In six units the phrase “stress response” was not understood despite an explanation and was interpreted as psychological problems with staff and patients. In the remainder the patient with weight loss, tachycardia, sepsis, stress ulcers and hypertension was a commonly recognizable problem.

Measurement of the response took the form of metabolic studies in nine units. Nitrogen balance, plasma proteins, 24-h urinary nitrogen and electrolyte balance were used as an index of the severity of illness and as a guide for intravenous fluid therapy. The measurement of hormone levels was performed as part of research projects in three centres. It was too early in these projects to determine a link between hormone levels and depth of sedation. The cellular response to the level of the hormone plays a part in determining the biochemical effects, and this link was difficult to assess.

The possible value of increased sedation in stressed ICU patients was acknowledged in six units and only for more ill patients. The remaining 23 units would treat their stressed patients with increased parenteral feeding and insulin/dextrose infusions. Stress ulcer prophylaxis and alpha and beta adrenergic blocking were considered important as was prompt treatment for any infection. The value of deep sedation in reducing oxygen consumption in severely ill patients was recognized and a few would use a thiopentone drip for this purpose. The majority of units did not feel that large doses of opiates had anything to offer and had a variety of reasons for their views. These were:

1. Problems with heavy sedation may outweigh the benefits
2. The case was not proved that ICU patients could be helped by heavy sedation as the situation in inten-

sive care is very much more complex; even though there was a case for blocking this stress response to surgery.

3. Sedation cannot remove the cause of continuing stress, for example, septicaemia can increase metabolic demand by 60% [26] and the addition of heavy sedation will not improve the metabolic state of these patients.
4. The stress response is a physiological response and is part of the body's natural adaptations and it should therefore not be blocked.
5. Patients secrete their own endorphines and therefore others may not be needed
6. There is no specific anti-stress drug
7. Local blocks may be just a useful in preventing catabolic states as large doses of opiates and are much less harmful [27]

### **Conclusions**

The wide variation in the drugs and techniques used to sedate patients receiving mechanical ventilation is an indication that the ideal drug or drug combination has not yet been found. Specific techniques have been found valuable for special patient problems. Patients with low cardiac output require reduced dosage of opiate or relaxant or may be made comfortable with nitrous oxide/oxygen alone. Head injured patients in hospitals with special neurological diagnostic facilities may receive sedation with diazepam and opiates and may also receive the benefits of thiopentone infusions. Those in hospitals with non-specialist diagnosis facilities use as few drugs as possible in order that physical signs may not be missed.

Patients habituated to alcohol could be helped to “settle” with ventilation with use of a chlormethiazole infusion. Prolonged ventilation requires a drug regime that is non-cumulative and lorazepam is particularly useful in this respect. Buprenorphine is similarly useful. Patients with respiratory disease (asthma or bronchitis) do not require a special sedation regime although the avoidance of drugs which cause histamine release (morphine) is helpful. Where the use of night sedation might benefit the patient – the orally administered drugs (e. g. diazepam) are best if absorption is possible.

The requirements for a successful sedation technique (anxiolytic, analgesic, respiratory depressant, simple and safe) are not always met. The use of a muscle relaxant alone or benzodazepine alone is inadequate for most patients. The use of nitrous oxide without the necessary safety devices (including anti-pollution) may be unsafe. Pipeline supplies would however increase the use of nitrous oxide. The use of IMV would alter the way in which certain patients are

sedated and reduce the amount of drug needed. Although continuous infusion techniques are less easily used without infusion pumps, there could be further use of this way of using drugs. A constant depth of analgesia and sedation could be maintained and the total dose of drug used could be reduced. The duration of action of drugs seems to play little part in their frequency of use and alternating drugs given as boluses could be used to give a smoother effect.

Further interest in monitoring the effects of drugs – in particular their effects on autonomic response to stimulus could lead to more effective use of sedation.

The degree of interest shown in sedation techniques mirrored the interest shown in the total care of the patients, and the progressive search for new, improved methods was a source of admiration and inspiration.

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