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Use of sedatives, analgesics and neuromuscular blocking agents in Danish ICUs 1996/97

A national survey

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Abstract *Objective:* To assess the use of sedatives, analgesics and neuromuscular blocking agents (NMBAs) in patients requiring mechanical ventilation in Danish Intensive Care Units (ICUs).

Design: Questionnaires were mailed in December 1996 to all Departments of Anaesthesiology listed in the Annual Directory of Danish Hospitals. The questionnaires asked about the use of sedatives, analgesics and NMBAs in patients on mechanical ventilation in the ICU.

Results: Forty-nine questionnaires were received from a possible 53 ICUs with ventilators (response rate 92.5%). Sedatives and analgesics were given to patients on mechanical ventilation at virtually all the ICUs surveyed (60% used the combination routinely).

The frequency of use was influenced by both the level of ventilatory support and the type of underlying disease.

Opioids, benzodiazepines and propofol were employed most commonly, in particular by continuous infusion. NMBAs were used in 65% of the ICUs surveyed in less than 20% of the total number of patients in the respective ICU. Overall 98% of the ICUs reported the occurrence of some kind of side effect secondary to the sedative treatment, but in most ICUs they were reported to occur in less than 20% of the patients.

Conclusion: Sedatives and analgesics are widely used in patients requiring mechanical ventilation in Danish ICUs. NMBAs are only used in a few patients. The frequency of use is correlated to the level of ventilatory support required and to the kind of respiratory disease

Key words National survey · Sedatives · Analgesics · Neuromuscular blocking agents · ICU

Introduction

Sedation and analgesia have been widely used throughout the history of Intensive Care Units (ICUs) and mechanical ventilation. The development of new drugs and progress in the methods of sedation have taken place and the number of clinical trials is growing. However, current practice is not known in detail as only a few reports have described the practice of sedation during the last two decades [1–6]. In order to be able to make a comparison with the practices described in the

literature and to establish the present level from which practice can be improved upon, we carried out a survey comprising the ICUs in Denmark. We found it of special interest to concentrate on topics such as 1) the preferred level of sedation, 2) the sedatives and analgesics most commonly used 3) extent of the use of NMBAs and 4) assessment of sedation carried out using sedation scores.

Materials and methods

A list of Danish hospitals with at least one consultant anaesthesiologist was compiled from the 1996 edition of the Directory of Danish Hospitals. Questionnaires were mailed in December 1996 to the consultants in charge. Respondents were asked to provide their name and responsibilities and the name of the hospital in order to send a new survey to the non-responders after 4 weeks. However, the identity of the responders were kept confidential.

The questionnaire consisted of seven parts, which focused on the following subjects:

Part 1: The number of beds in the ICU (defined as the maximum number of places for patients on mechanical ventilation), the kind of speciality which was responsible for the management of the ICU, the kind of specialities which admitted patients to the ICU, the use of standard protocols for sedation, weaning and/or handling of special categories of patients, the type of drugs used for abstinences, the use of sedation scoring systems, the use of a peripheral nerve stimulator, the use of supplemental sedation before certain procedures such as tracheal suction, the level of sedation estimated to be appropriate when mechanical ventilation using a FIO₂ of more than 0.5 was applied and when the patient was ready to be weaned from the ventilator. The following modified Ramsay scale [7] was used:

1. Patient anxious and agitated or restless or both.
2. Patient cooperative, orientated and tranquil.
3. Patient asleep – responds to commands and touch only.
4. Patient asleep – weakly responds to commands and touch.
5. No response to commands and touch. Reacts on pain stimulation.
6. No response.

Part 2: Interactions between the use of sedatives, analgesics and NMBAs and the modalities of mechanical ventilation.

Part 3: The administration of sedatives, analgesics and NMBAs in patients with adult respiratory distress syndrome (ARDS), chronic obstructive pulmonary disease (COPD), heart insufficiency and head traumas.

Part 4: The kind of sedatives used and the frequency of use in relation to the modality of ventilation.

Part 5: The kind of analgesics used and the frequency of use in relation to the modality of ventilation.

Part 6: The routes of administration of the drugs used.

Part 7: The type and frequency of side-effects observed in relation to sedatives, analgesics and NMBAs.

To estimate the frequency of the use of the drugs we adopted and included the following scale in the questionnaires: Never; occasionally (< 20% of patients); frequently (20 to 70% of patients); routinely (> 70% of patients) [1, 2].

Results

Fifty-three ICU departments with ventilators received a questionnaire. Forty-nine completed questionnaires were returned (response rate 92.5%). The four non-responders were distributed over the country and were of different sizes (2–10 beds). The answers covered 353 out of 383 ICU beds (92.2%). The mean number of beds was 7.2 (range 2–17). The answering rate for university hospitals was 94% and for other hospitals 92%.

Table 1 Frequency of use of sedation, analgesia and neuromuscular blocking agents (NMBAs) in relation to different modalities of ventilatory assistance (PC-CPPV pressure-controlled-continuous positive pressure ventilation, VC-CPPV volume-controlled-continuous positive pressure ventilation, Pt. CV patient-controlled ventilation (e.g. PSV pressure support ventilation, CPAP continuous positive airway pressure). No. total number of ICUs who had answered the question. Percents are calculated from this number)

	Patient frequency	Sedation		Analgesia		NMBAs	
		(n)	(%)	(n)	(%)	(n)	(%)
PC-CPPV No. = 47	Never	0	(0)	0	(0)	15	(32)
	< 20%	2	(4)	4	(9)	28	(60)
	20–70%	16	(34)	16	(34)	2	(4)
	> 70%	29	(62)	26	(57)	2	(4)
VC-CPPV No. = 48	Never	0	(0)	0	(0)	23	(48)
	< 20%	1	(2)	4	(9)	25	(52)
	20–70%	18	(38)	17	(35)	0	(0)
	> 70%	29	(60)	27	(56)	0	(0)
Pt. CV No.* = 46 No.** = 47	Never	2	(4)*	1	(2)**	0	(0)
	< 20%	27	(59)*	22	(47)**	0	(0)
	20–70%	16	(35)*	19	(40)**	0	(0)
	> 70%	1	(2)*	5	(11)**	0	(0)

The questionnaire was filled out by 40 consultants (82%) and by 9 senior registrars (18%).

The ICUs served the following specialities: internal medicine 92%, general surgery 88%, orthopaedic surgery 80%, gynecology – obstetrics 65%, pediatric 47%, thoracic surgery 12%, neuro-surgery 16% and other 20%. Only 8% of the ICUs served only one speciality (3 neurosurgery, 1 thoracic surgery). In 35 of 40 ICUs which had answered the question the ICU was managed by anaesthesiologists (88%).

Sixteen departments (33%) had written standard protocols for sedation. Special regimes were used for alcoholics in 12 departments (24%), for patients with renal failure in 7 departments (14%), for neurosurgical patients in 2 departments (4%) and for patients with COPD in 6 departments (12%).

Scoring systems for evaluation of the levels of sedation were used in only eight (16%) of the ICUs, who all used the Ramsay sedation score [7].

Thirty-eight (78%) of the ICUs aimed at obtaining a circadian rhythm; some by changing the activities at night and others by adding sedation for the night. Additional sedation was used at 25 (51%) of the ICUs before certain procedures were carried out (e.g. endotracheal suction). The preferred level of sedation according to the modified Ramsay sedation score [7] for patients needing ventilator treatment using a FIO₂ more than 0.5 was 3.1 (range 2–5) and for patients during weaning it was 2.1 (range 1.5–4).

Only three departments (6%) used a standard weaning regime. Abstinences were treated with phenobarbit-

Table 2 Frequency of use of sedation, analgesia and neuromuscular blocking agents (NMBAs) in relation to different causes of ventilatory treatment (ARDS adult respiratory distress syndrome, COPD chronic obstructive pulmonary disease. No. total number of ICUs who had answered the question. Percents are calculated from this number)

	Patient frequency	Sedation		Analgesia		NMBAs	
		n	(%)	n	(%)	n	(%)
ARDS No. = 44	Never	0	(0)	0	(0)	12	(27)
	< 20%	2	(5)	2	(5)	27	(62)
	20–70%	7	(16)	12	(27)	5	(11)
	> 70%	35	(79)	30	(68)	0	(0)
COPD No. = 46	Never	1	(2)	0	(0)	26	(57)
	< 20%	5	(11)	12	(26)	20	(43)
	20–70%	27	(59)	21	(46)	0	(0)
	> 70%	13	(28)	13	(28)	0	(0)
Heart insufficiency No. = 46	Never	1	(2)	0	(0)	31	(67)
	< 20%	7	(15)	5	(11)	15	(33)
	20–70%	21	(46)	22	(48)	0	(0)
	> 70%	17	(37)	19	(41)	0	(0)
Head trauma No. = 35	Never	0	(0)	0	(0)	13	(37)
	< 20%	2	(6)	2	(6)	17	(49)
	20–70%	8	(23)	6	(17)	3	(8)
	> 70%	25	(71)	27	(77)	2	(6)

al in 43 (88%) of the departments and with clomethiazol in 4 (8%).

Table 1 shows the use of sedatives, analgesics and NMBAs in relation to different modalities of mechanical ventilation. The use of sedatives and analgesics was independent of whether pressure-controlled – continuous positive pressure ventilation (PC-CPPV) or volume-controlled – continuous positive pressure ven-

tilation (VC-CPPV) was used. Less sedation and analgesia was used when patient-controlled ventilation (PtCV) was used. The use of sedatives decreased more than the use of analgesics with a decreasing level of ventilatory support. NMBAs were not used in 15 departments (32%) and they were used in less than 20% of the patients in 28 departments (60%). Only four (8%) used them for more than 20% of the patients. Forty-four percent of the departments using NMBAs applied peripheral nerve stimulators for monitoring the patients

Table 2 shows the frequency of the use of sedatives, analgesics and NMBAs in relation to different indications for ventilatory treatment. The most frequent use was in patients with ARDS and patients with head trauma. In Table 3 the frequency of the use of different groups of sedatives and analgesics in relation to different modalities of ventilatory assistance is shown. The sedatives used most often were benzodiazepines and propofol. Barbiturates, haloperidol and clomethiazol were rarely used. The analgesics used most often were opioids, paracetamol and local anaesthetics. NSAIDs were rarely used.

Table 4 shows the routes of administration. Both sedatives and analgesics were mainly given by continuous infusion or by intermittent i.v. injection without fixed intervals. NMBAs were mainly given by intermittent i.v. injections. For analgesia the preferred drugs were morphine (94%), fentanyl (76%) and sufentanyl (43%). For sedation midazolam (100%) was used slightly more frequently than propofol (92%) while diazepam was used more seldomly (24%). The preferred NMBAs were pancuronium (63%) and vecuronium (33%). A regional anaesthetic technique was used in 84% of the ICUs, mainly as epidural infusion. The pre-

Table 3 Frequency of use of different sedative groups and analgesics in relation to different modalities of ventilatory assistance (PC-CPPV pressure-controlled – continuous positive pressure ventilation, VC-CPPV volume-controlled – continuous positive pres-

sure ventilation, Pt. CV patient-controlled ventilation (e.g. PSV pressure support ventilation, CPAP continuous positive airway pressure), No. total number of ICUs which answered the question. Percents are calculated from this number)

	Patient frequency	Benzo-diazepines		Barbiturates		Propofol		Haloperidol		Clomethiazol		Opioids		NSAIDs		Paracetamol		Local anaesthetics	
		n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
PC-CPPV No. = 45	Never	0	(0)	20	(44)	11	(24)	36	(80)	38	(84)	0	(0)	15	(33)	3	(7)	8	(18)
	< 20%	3	(7)	20	(44)	21	(47)	9	(20)	7	(16)	0	(0)	24	(54)	9	(20)	20	(45)
	20–70%	20	(44)	4	(9)	10	(22)	0	(0)	0	(0)	22	(49)	6	(13)	22	(49)	15	(33)
	> 70%	22	(49)	1	(3)	3	(7)	0	(0)	0	(0)	23	(51)	0	(0)	11	(24)	2	(4)
VC-CPPV No. = 48	Never	0	(0)	21	(44)	10	(21)	39	(81)	41	(85)	0	(0)	18	(38)	3	(6)	8	(17)
	< 20%	3	(6)	24	(50)	21	(44)	8	(17)	7	(15)	0	(0)	22	(46)	10	(21)	24	(50)
	20–70%	22	(46)	2	(4)	14	(29)	1	(2)	0	(0)	25	(52)	8	(16)	22	(46)	15	(31)
	> 70%	23	(48)	1	(2)	3	(6)	0	(0)	0	(0)	23	(48)	0	(0)	13	(27)	1	(2)
Pt. CV No. = 49	Never	2	(4)	35	(71)	21	(43)	40	(82)	44	(90)	0	(0)	8	(37)	4	(8)	10	(20)
	< 20%	28	(57)	13	(27)	17	(35)	9	(18)	5	(10)	24	(49)	24	(49)	13	(27)	22	(45)
	20–70%	14	(29)	1	(2)	8	(16)	0	(0)	0	(0)	18	(37)	7	(14)	20	(41)	15	(31)
	> 70%	5	(10)	0	(0)	3	(6)	0	(0)	0	(0)	7	(14)	0	(0)	12	(24)	2	(4)

Table 4 Routes of administration of different sedatives, analgesics and NMBAs for patients needing mechanical ventilation (*NA* indicates not available for that method of administration. *n* number of ICUs using this route of administration. *No.* total number of ICUs using the drug. Percents are calculated from this number)

	Number of ICUs		Continuous infusion +/- i.v. bolus		Intermittent i.v. with fixed intervals		Intermittent i.v. without fixed intervals		Enteral route (oral or rectal)		Epidural		Subarachnoidal	
	No.	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)
Midazolam	49	(100)	43	(88)	11	(22)	22	(45)	1	(2)	NA	NA		
Diazepam	12	(24)	1	(8)	3	(25)	7	(58)	5	(42)	NA	NA		
Propofol	45	(92)	44	(98)	0	(0)	7	(16)	NA		NA		NA	
Ketamin	9	(18)	3	(33)	0	(0)	6	(67)	NA		0	(0)	0	(0)
Fentanyl	37	(76)	32	(86)	4	(11)	17	(46)	NA		6	(16)	1	(3)
Morphine	46	(94)	29	(63)	17	(37)	24	(52)	4	(9)	35	(76)	7	(15)
Alfentanil	8	(16)	3	(38)	1	(13)	6	(75)	NA		0	(0)	0	(0)
Sufentanyl	21	(43)	14	(67)	2	(10)	5	(24)	NA		13	(62)	0	(0)
Methadone	9	(18)	1	(11)	2	(22)	3	(33)	7	(78)	NA		NA	
Pancuronium	31	(63)	1	(3)	16	(52)	20	(65)	NA		NA		NA	
Vecuronium	16	(33)	1	(6)	4	(25)	15	(94)	NA		NA		NA	
Atracurium	6	(12)	0	(0)	2	(33)	5	(83)	NA		NA		NA	
Bupivacaine	35	(71)	NA		NA		NA		NA		35	(100)	6	(17)

Table 5 Assumed frequency of side effects in relation to the use of sedatives, analgesics and NMBAs (*n* number of ICUs reporting side effects. Percents are calculated from total answers (*tot. ans*) which differ from group to group)

	Patient frequency	Delayed emergence		Paradoxical agitation		Respiratory depression		Gastro-intestinal disorders		Tachyphylaxis		Myopathia		Tachycardia		Tolerance	
		<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)
Sedative drugs	Never	1	(2.2)	9	(20.9)	3	(7.5)	-	-	-	-	-	-	-	-	3	(7.7)
	< 20%	23	(50)	33	(76.8)	31	(77.5)	-	-	-	-	-	-	-	-	18	(46.2)
	20-70%	21	(46.5)	1	(2.3)	6	(15)	-	-	-	-	-	-	-	-	16	(41)
	> 70%	1	(2.2)	0	(0)	0	(0)	-	-	-	-	-	-	-	-	2	(5.1)
	tot. ans	46		43		40										39	
Analgesic drugs	Never	2	(4.3)	-	-	3	(6.4)	1	(2.2)	4	(10)	-	-	-	-	2	(5)
	< 20%	31	(67.4)	-	-	30	(63.8)	18	(39.1)	19	(47.5)	-	-	-	-	20	(50)
	20-70%	13	(28.3)	-	-	13	(27.7)	19	(41.3)	15	(37.5)	-	-	-	-	16	(40)
	> 70%	0	(0)	-	-	1	(2.1)	8	(17.4)	2	(5)	-	-	-	-	2	(5)
	tot. ans	46				47		46		40						40	
NMBAs	Never	24	(77.4)	-	-	-	-	22	(81.5)	-	-	22	(81.5)	11	(39.3)	-	-
	< 20%	6	(19.4)	-	-	-	-	3	(11.1)	-	-	5	(18.5)	17	(60.7)	-	-
	20-70%	1	(3.2)	-	-	-	-	2	(7.4)	-	-	0	(0)	0	(0)	-	-
	> 70%	0	(0)	-	-	-	-	0	(0)	-	-	0	(0)	0	(0)	-	-
	tot. ans	31						27				27		28			

ferred drugs, beside bupivacaine (100%), were morphine (76%) and sufentanyl (62%)

There were some differences in the use of sedatives, analgesics and NMBAs in relation to the type and size of hospital. The university hospitals used propofol, fentanyl, alfentanil, atracurium and methadone more often than the other hospitals. On the other hand, the smaller hospitals more often used diazepam, pancuronium, vecuronium and bupivacaine.

Finally, Table 5 shows the respondents assumed frequency of side effects related to the use of sedatives, an-

algesics and NMBAs. Overall side effects were assumed to occur by 98% of the ICUs for sedatives and analgesics and for NMBAs by 60%. For analgesics a patient frequency of more than 20% was reported concerning gastro-intestinal disorders, respiratory depression, delayed emergence and tolerance. For sedatives this frequency was reported for delayed emergence and tolerance.

Discussion

This Danish survey was carried out to assess the current use of sedatives, analgesics and NMBAs administered to patients undergoing mechanical ventilation. The results are based on the estimates of current drug utilization offered by consultants in charge and senior registrars with close affiliation to the ICUs. With an answering rate of 92.5%, representing roughly 92% of ICU beds in Denmark, equally distributed over the country, the results probably give a good estimate of the current use of sedatives, analgesics and NMBAs in Denmark in the period 1996–97.

All the ICUs represented in this survey used a combination of sedatives and analgesics, frequently a combination of benzodiazepines and opioids, in the treatment of patients who needed mechanical ventilation. The use was independent of the ventilation modus (PC-CPPV or VC-CPPV), but decreased when assisted ventilation was applied (PtCV). NMBAs were used slightly more often (Table 1) when PC-CPPV was used than when VC-CPPV was used, probably because, in Denmark, PC-CPPV is preferred more often when the patient is more critically ill. The use of sedatives, analgesics and NMBAs were also influenced by the kind of disease. Thus the use was greatest for patients with ARDS and head traumas. NMBAs were virtually never used for patients with COPD and heart insufficiency. Previous surveys in Europe [1, 3] and USA [2] have also reported that sedating drugs were widely used during ventilatory treatment in the ICUs, but in these surveys the frequency of NMBA use was greater.

The level of sedation considered optimal has altered significantly through the years from deep sedation towards a painfree comfortable patient, who has periods of sleep, but who also rouses to a comprehending awareness spontaneously or on command [3]. From the answers on the preferred level of sedation, we found that the Danish practice aimed at complying with this “new” level of sedation and, in addition, tried to obtain a circadian rhythm by changing the sedation level during the day and at night.

Compared to other countries [1–4] the Danish ICUs used similar sedatives and analgesics, but propofol, midazolam and fentanyl were used more often. In Denmark the intravenous route of administration of sedatives and analgesics is preferred as is continuous infusion, as compared to the intermittent i.v. injections used in USA [2]. The use of diazepam and haloperidol was lower. The former was used in 78% of the ICUs in USA compared to only 24% of the Danish ICUs. Haloperidol was used in 60% of the ICUs in USA compared to only 44% in Denmark and only for fewer than 20% of the patients. These differences may be due to the different period of registration and may reflect the introduction of newer drugs, such as midazolam and propo-

fol, and the use of newer medical equipment, such as infusion pumps.

The Danish results as regards the type of NMBAs used were comparable to those found in the USA survey [2], but the frequency of use was lower. On the other hand, a national survey from USA concerning the use of muscle relaxants [8] concluded that the most used NMBA was vecuronium, which was used by 52%, and pancuronium, which was used by 28%. In our survey 63% used pancuronium and 33% vecuronium.

It has been shown that prolonged neuromuscular blockade may occur after long-term vecuronium administration [9]. A consensus report [10] recommends pancuronium as the best NMBA for the most critically ill patients and vecuronium as the preferred NMBA for those patients with cardiac disease or hemodynamic instability in whom tachycardia may be deleterious. There is a clear consensus among experts to recommend peripheral nerve stimulation to guide sustained neuromuscular blockade in the ICU [10]. Despite this, only 34% in the USA survey [8] and 44% in the present survey used a peripheral nerve stimulator. The indications for use of NMBAs in the USA survey was facilitation of mechanical ventilation (89%), increased intracranial pressure (35%), high oxygen consumption (25%) and agitation or combativeness in spite of sedation (23%). These indications correlated well with the results from this survey, where the most frequent use was in patients with ARDS or head traumas.

The results concerning side effects resemble those of Pelosi [1], but in his study the overall frequency was about 10% lower. In his study there was no graduation of patient frequency in relation to the side effects. We think that the more detailed Danish study, though based on assumptions of the respondents, gives a truer picture of the occurrence of side effects.

This Danish study have many similarities with the study of Pelosi who surveyed 10 ICUs (nine in Europe and one in USA) [1]. There were similarities with regard to the frequency of use of sedation, analgesia and NMBAs in relation to different types of ventilatory assistance and different causes of respiratory failure. In the Pelosi survey the preferred sedatives and analgesics were benzodiazepines and opioids, too.

Only few of the Danish ICUs used objective and subjective assessment of sedation. This may be the reason for the estimated relatively high frequency of side effects. All the departments using subjective assessment used the Ramsay score, which was created nearly 25 years ago. Over the years the Ramsay sedation scale, sometimes with modifications, has become the standard method for assessing and comparing the efficacy of sedating drugs in the ICU. However, many critically ill patients in the everyday life of the ICU are difficult to assess on the Ramsay scale. The patients may be restless or agitated (level 1) at the same time as they are respon-

sive only to a light physical, or a loud auditory, stimulus (level 4–5). This may be an explanation of why the Ramsay scale is not used more often. Today ICUs need new clinical measures to assess the efficacy of sedating drugs during mechanical ventilation [11].

We reached the following conclusions:

1. Sedatives and analgesics are widely used in the treatment of patients who require mechanical ventilation for respiratory failure in Denmark. NMBA's are used, but to a small extent.
2. The use of sedatives and analgesics correlated to both the level of ventilatory support and to the indication for ventilatory support
3. The preferred sedative drugs were midazolam and propofol given by continuous infusion
4. The preferred analgesics were morphine, fentanyl and sufentanyl, in that order, mainly given as continuous infusions.
5. Very few ICUs used assessment of the level of sedation, analgesia and neuromuscular blockade, thus risking unnecessary sedation and side effects.

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