Changed Patterns in Dutch Palliative Sedation Practices After the Introduction of a National Guideline

Jeroen G. J. Hasselaar, MSc; Stans C. A. H. H. V. M. Verhagen, MD, PhD; André P. Wolff, MD, PhD; Yvonne Engels, PhD; Ben J. P. Crul, MD, PhD; Kris C. P. Vissers, MD, PhD, FIPP

Background: Continuous sedation, contrary to euthanasia, has been increasingly accepted among medical professionals worldwide. In the Netherlands, a national guideline for continuous palliative sedation has been developed to contribute to the quality of palliative sedation practice. The present follow-up study investigated whether the practice of continuous sedation has changed after the introduction of this guideline.

Methods: This study compared the practice of continuous sedation before and after the introduction of the guideline on December 7, 2005. A baseline measurement was performed between February 1, 2003, and May 1, 2005, with an enrollment of 492 physicians (medical specialists, general practitioners, and nursing home physicians). From January 1 to June 30, 2007, after the introduction of a national guideline for palliative sedation, a follow-up study was performed with the respondents of the baseline study. Physicians were asked to report on their last case of deep and continuous sedation in the past 12 months.

Results: This study reports the results of the follow-up study and compares them to the results of the baseline study. The response rate was 69.3% (n=341). Of these physicians, 160 reported a last case of continuous sedation in both the baseline and the follow-up studies. Physicians reported a significant increase in patient involvement in decision making, from 72.3% to 82.2%. Pain remained the most often reported reason to start sedation, whereas exhaustion as a reason for sedation increased. The use of benzodiazepines increased from 69.9% to 90.4%. In the first and second measurements, symptom-directed treatment during sedation was applied in 56% to 58% of the cases. In the second period, there was more often an explicit decision to not give artificial hydration during sedation (78.8% vs 56.3%). Of the physicians, 34.2% were convinced that sedation shortened the life of the patient because of dehydration.

Conclusions: After the introduction of the guideline, physicians reported that changes in palliative sedation practice conform to the recommendations of this guideline. For example, benzodiazepines were used for sedation more frequently than before and patient involvement in the decision-making process improved. Possible effects of dehydration and the large variation in symptom-directed treatment during sedation deserve careful attention.

Arch Intern Med. 2009;169(5):430-437

Author Affiliations:
Department of Anaesthesiology, Pain, and Palliative Medicine, Radboud University Nijmegen Medical Center, Nijmegen, the Netherlands.

PALLIATIVE SEDATION involves the use of sedative medication to relieve intolerable and refractory distress by a reduction in the patient's consciousness.[1] Refractory distress indicates that the symptoms are unbearable for the patient but cannot be alleviated quickly enough by more conventional treatment methods without unacceptable adverse effects. The practice of palliative sedation, in particular its continuation until death, has raised much debate about its proper use in end-of-life care. The advantage of palliative sedation is that it provides an easy resolution of severe discomfort and refractory symptoms. In addition, the time delay between the start of the sedation and the eventual death of the patient permits reassessment of treatment options.[2]

For editorial comment see page 429

However, some have argued that continuous deep sedation until death (to be known hereafter as continuous sedation), particularly without the administration of artificial hydration, may easily slip into slow euthanasia,[3] whereas others consider continuous sedation a middle ground between the polarized views of the proponents and opponents of euthanasia.[4,5] In fact, there appeared to be large differences between euthanasia practices and palliative sedation practices.[6] For many

medical professionals, palliative sedation has become an acceptable medical practice, contrary to that of euthanasia.[7-9] Recent figures showed an increase in the use of continuous sedation in the Netherlands between 2001 and 2005.[10]

In the Netherlands, continuous sedation is mainly applied within 3 medical disciplines: general practitioners, medical specialists, and nursing home physicians.[11] However, these disciplines demonstrated considerable problems in medication administration, symptom management, and guideline compliance.[12] In 2005, drawing from previous local guidelines, the Royal Dutch Medical Association (RDMA) published a national guideline for palliative sedation.[13] This guideline sought to define palliative sedation (including continuous sedation), to set the rules for indications and contraindications, and to give recommendations for medication and practical procedures. The RDMA guideline restricts the application of continuous sedation to patients who experience refractory symptoms and who are expected to die within 1 or 2 weeks. Also, this guideline regarded palliative sedation as common medical practice as laid down in the Dutch Medical Treatment Act.

Although several local clinical guidelines for palliative sedation have been proposed in the literature,[14,15] the RDMA guideline is, to our knowledge, the first and only one that is mandatory for all physicians within a country. This presents the possibility of uncovering whether the practice of continuous sedation changed after the introduction of the RDMA guideline. Therefore, the aim of this study is to compare the practice of continuous sedation before and after the introduction of the RDMA guideline for palliative sedation.

METHODS

From February 1, 2003, to June 30, 2007, a cohort study regarding the practice of continuous sedation was performed in a sample of physicians. Before the introduction of the RDMA guideline, between February 1, 2003, and May 1, 2005, 1464 physicians were approached with a structured questionnaire about continuous sedation. The sample included all pulmonologists and geriatric specialists registered in the Netherlands and all the general practitioners, nursing home physicians, and internal medicine specialists (including medical oncologists) registered in the southeastern part of the Netherlands.

Besides asking the respondent's general opinions about the differences between continuous sedation and euthanasia, the questionnaire asked whether the physician had had experience with the application of continuous sedation during the past 12 months and, if so, the questionnaire asked him or her to describe the characteristics of the most recent patient. This method enabled comparison between the practices of physicians pairwise (1 case from period 1 vs 1 case from period 2). Further details about the methods and the results of the baseline study have been published elsewhere.[11,12] From January 1 to June 30, 2007, 1 year after the launch of the RDMA guideline, all responding medical specialists, general practitioners, and nursing home physicians (n=492) of the baseline measurement were invited for a follow-up study. Again, they were asked to report details about their last case of continuous sedation in the past 12 months. After 1 month, nonresponders received a reminder by mail. After 2 months, the remaining nonresponders were contacted by telephone. In the instruction for the questionnaire (in both periods), a definition of continuous sedation was provided which pointed to sedation with the intent of its continuation until the death of the patient. The time constraint of the past 12 months was chosen to restrict recall bias and to ensure that the second measurement would not consist of cases from before the introduction of the RDMA guideline.

Topics regarding artificial hydration and patient prognosis before sedation appeared to be important in the RDMA guideline and have therefore received more attention in the follow-up measurement. The main topics of the guideline that were addressed in this study are listed in **Table 1**. In order to achieve the aim of this study, the conceptual distinction between palliative sedation and euthanasia was approached via 3 measurable variables: (1) the proportion of physicians who regarded euthanasia as being equivalent to continuous sedation, (2) the number of patients who formulated a request for euthanasia in advance of continuous sedation, and (3) the proportion of physicians who reported that continuous sedation shortened the life of the patients who received it. Physicians were able to report the following symptoms: physical pain (mostly due to progressive disease), dyspnea, anxiety, delirium, nausea, vomiting, exhaustion, existential distress, perceived loss of dignity, and other. This study defined exhaustion as "a serious weakening and loss of energy," based on Webster's online dictionary.[16] Following Dutch guidelines for palliative care and the international literature, the RDMA guideline recommends continuation of symptom-directed treatment during sedation. On the basis of RDMA guidelines on palliative care and supported by the literature. This recommendation was translated into measurable variables as follows: (1) for severe pain or dyspnea, morphine is primarily indicated, except perhaps when delirium is also present; (2) for delirium, antipsychotic medications are primarily indicated; and (3) for the purpose of sedation, a benzodiazepine should be added.[17-19] Physicians were asked to estimate whether life-shortening effects due to dehydration had occurred ("yes," "no," or "don't know"). Data were analyzed using SPSS statistical software, version 14.0 (SPSS Inc, Chicago, Illinois). Frequencies were used to compare the results of both measurements. Wilcoxon signed rank and McNemar tests were used to identify statistically significant differences between the 2 periods. The χ^2 test was used for some specific calculations in the 2007 sample. A Kruskal-Wallis test was used to calculate patient survival rate in the 2007 sample. An α of .05 was used to test statistical significance.

RESULTS

Of the 492 physicians eligible for inclusion, 341 responded to the follow-up questionnaire (response rate, 69.3%) (**Figure**). The final cohort of physicians who completed questionnaires from both periods consisted of 116 medical specialists, 170 general practitioners, and 55 nursing home physicians. The mean age of the responding 341 physicians was 49 years (2007), and 64.6% were men. In 2007, 48.3% of the physicians had ever taken a course in palliative care, a rate which was significantly higher than the rate of the baseline measurement (36.0%; **Table 2**). The reported frequency of the application of end-of-life care in the past year, continuous sedation in particular, did not significantly differ between the 2 periods. Data showed that, compared with the first episode, physicians in 2007 more often regarded continuous sedation as a natural way of dying, whereas different medication and different legal status were increasingly seen as important differences between continuous sedation and euthanasia (Table 2). The number of physicians who regarded continuous sedation equal to euthanasia remained small (5 physicians in the first and 9 in the second period).

Table 1. Presumed Changes in Dutch Practice Regarding the Royal Dutch Medical Association Guideline for Palliative Sedation

Guideline Recommendation	Research Variable	Expected Direction of Change
The indication is a refractory symptom with a mostly somatic nature.	Presence of somatic (vs nonsomatic) symptoms as an indication for palliative sedation	Increase
Patient should be involved in decision making before sedation as much as possible.	Patient involvement in decision making for palliative sedation	Increase
Symptom management should be continued during sedation.	Use of morphine in case of physical pain and/or dyspnea plus use of antipsychotic medication in case of delirium	Increase
Benzodiazepine should be used as a sedative.	Use of midazolam, clonazepam, and diazepam	Increase
Morphine should not be used as a sedative.	Use of morphine without benzodiazepine	Decrease
Artificial hydration during sedation is not recommended.	No. of physicians who decided to forsake artificial hydration	Increase
Sedation should not be used as slow euthanasia.	a. No. of patients who formulated a request for euthanasia before sedation b. No. of physicians who regarded euthanasia as equivalent to palliative sedation c. No. of physicians who associated their sedation with life shortening caused by dehydration (this portion included only in 2007)	Decrease
Patient life-expectancy prognosis should not exceed 1 or 2 weeks before the start of sedation.	Patient prognosis: <1 week, 1-2 weeks, >2 weeks	NA: only asked in 2007
Patients with oral intake should explicitly refuse artificial hydration. In other cases, artificial fluids are regarded as medically futile.	a. Oral intake before sedation: yes, ≥0.5 L/d; yes, <0.5 L/d; no b. Percentage of patients with oral intake with whom artificial hydration was discussed	NA: only asked in 2007

Abbreviation: NA, not applicable.

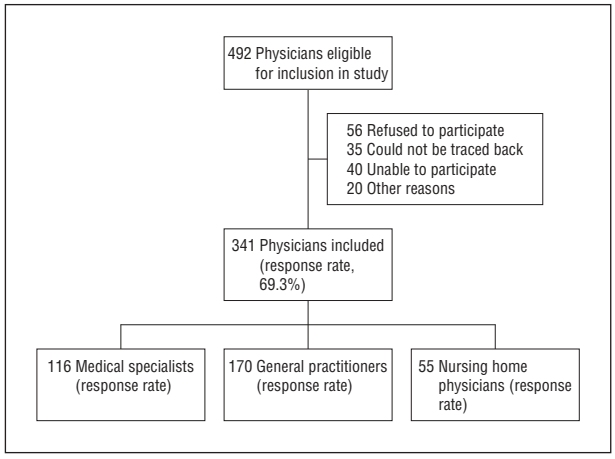

Figure. Flowchart of physicians throughout the study.

Of all the physicians, 160 reported a last case of continuous sedation in the past 12 months in both the baseline study and the follow-up study (**Table 3**). This sample consisted of medical specialists (62 [38.8%]), general practitioners (67 [41.9%]), and nursing home physicians (31 [19.4%]). In 2007, sedated patients had the following diseases: cancer (65.4%), chronic obstructive pulmonary disease (11.9%), pulmonary disease (8.2%), heart failure (9.4%), and other diseases (18.2%). Detailed analysis showed large differences in the presence of oncologic diseases in patients treated by medical specialists (64.5%), general practitioners (84.8%), and nursing home physicians (25.8%) ($P<.001$; χ^2 test). Also, in 2007, 92 of 153 (60.1%) of the physicians who sedated 1 or more patients reported always using a guideline of some sort. This percentage has more than doubled compared with the first episode (Table 2). In 2007, 78.1% of the physicians who applied continuous sedation reported being familiar with the RDMA guideline, although percentages differed significantly among medical specialists (83.9%), general practitioners (67.2%), and nursing home physicians (90.3%) ($P=.01$; χ^2 test).

DECISION MAKING REGARDING SEDATION

According to the reporting physicians, patient involvement in decision making regarding continuous sedation increased significantly between both periods from 72.3% to 82.2% ($P<.001$) (Table 3). In particular, the proportion of physicians who discussed sedation with patients some time in advance of sedation increased from 40.1% in the first period to 49.3% in the second period, whereas the proportion of physicians that did not discuss sedation with the patients who would receive it decreased from 27.6% to 17.8%. Regarding the reasons for initiating continuous sedation, physical pain and dyspnea were most often reported during both periods (Table 3). However, pain was the single reason for sedation in 6 (3.8%) of the patients in the first period and 2 (1.3%) of the patients in the second period ($P=.28$). Exhaustion increased significantly as an indication for continuous sedation, from 31.4% to 56.0% (Table 3). Nevertheless, the occurrence of nonphysical distress without the concomitant presence of physical symptoms remained comparable between both periods (Table 3). Finally, patient requests for euthanasia before sedation occurred significantly less often in 2007 (6.3%) compared with the first period (14.5%) ($P=.01$; Table 3). Detailed analysis showed a decrease in arousable patients from 45.5% to 25.8% in the practices of general practitioners ($P=.048$; Wilcoxon signed rank test).

SYMPTOM MANAGEMENT AND SEDATION

In accordance with the guideline, benzodiazepines were more often prescribed for continuous sedation after the introduction of the guideline than before (69.9% and 90.4%, respectively) ($P<.001$) (Table 3). The use of midazolam increased from 52.2% to 79.2% of the cases, whereas the use of diazepam decreased from 20.8% to 6.9% ($P<.001$ for both drugs). A similar use of benzodiazepine combined with morphine was prescribed before (51.9%) and after the introduction of the guideline (83[51.9%]), whereas the use of benzodiazepine without morphine increased after the introduction of the guideline (from 30 [18.8%] to 58 [36.3%]) ($P<.001$; McNemar test). In addition, the use of morphine without a benzodiazepine medication decreased (from 23.1% to 8.8%) ($P<.001$; McNemar test). Also, the overall use of morphine in continuous sedation practice diminished significantly from 75.5% in the first period to 62.9% during the second period (Table 3). However, in total, the application of symptom-directed treatment remained comparable during both periods (55.6% in the first period and 58.1% in the second period) (McNemar test; $P=.72$) (**Table 4**).

SEDATION AND HYDRATION

Regarding artificial hydration, 56.3% of the physicians explicitly decided to forsake artificial hydration during the first period compared with 78.8% in 2007 ($P<.001$) (Table 3). The median survival time of patients did not change: it was 2 days during the first period and the second period ($P=.67$; Wilcoxon signed rank test). In the second period (2007), more details were explored concerning decisions about continuation of hydration and its potential influence on survival (data not shown). An oral intake of half a liter per day or more before sedation occurred in 37 (23.1%) of the 160 patients in 2007. All these patients had been involved in decision making for continuous sedation (data missing for 5 patients). During this decision-making process, the issue of hydration was discussed with the patient in 11 cases, discussed with his or her representatives in 9 cases, and not discussed at all in 12 cases. In total, 37 patients (23.1%) received artificial hydration before sedation, which was not continued during sedation in the majority of patients (n=27), mostly after discussion with the patient (n=10) or his or her family (n=12). Of these 37 patients, 34 were treated by a medical specialist. Of all 160 physicians, 48 (34.3%) were convinced that life was shortened by dehydration during sedation (data regarding 20 physicians was missing). Physicians who were convinced that sedation shortened life or who said they did not know reported a longer survival time for their patients compared with physicians who were convinced that sedation did not shorten life (a median survival of 3 days for the first 2 categories and 1 day for the latter) ($P<.001$; Kruskal-Wallis test). Also in 2007, patient prognosis of life expectancy before the start of sedation was less than 1 week in 99 cases (61.9%), 1 to 2 weeks in 49 cases (30.6%), and more than 2 weeks in 11 cases (6.9%). No differences among medical specialists, general practitioners, or nursing home physicians were found.

Table 2. Physician Experience With Continuous Sedation: Development Between 2 Episodes

Experience	No. (%) of Physicians: Before Guideline (n=341)	No. (%) of Physicians: After Guideline (n=341)	*P* Value
Active as palliative care consultant[a]	17 (5.1)	22 (6.6)	.30
Took a course in palliative care[b]	119 (36.0)	160 (48.3)	<.001
Experience with end-of-life care in past year[c]			
0 Occasions	29 (8.7)	37 (10.9)	.23
1-5 Occasions	151 (45.1)	159 (46.6)	
6-10 Occasions	64 (19.1)	65 (19.1)	
11-20 Occasions	60 (17.9)	44 (12.9)	
21-50 Occasions	23 (6.9)	27 (7.9)	
>50 Occasions	8 (2.4)	8 (2.4)	
Experience with continuous sedation in past year[d]			
0 Occasions	124 (37.1)	118 (35.3)	.60
1-5 Occasions	163 (48.8)	183 (54.8)	
6-10 Occasions	33 (9.9)	20 (6.0)	
11-20 Occasions	10 (3.0)	7 (2.1)	
21-50 Occasions	3 (0.9)	3 (0.9)	
>50 Occasions	1 (0.3)	3 (0.9)	
Reported opinions about the difference between continuous sedation and euthanasia (more answers possible)[e]	5 (1.4)	9 (3.1)	.39
No difference	5 (1.4)	9 (3.1)	.39
Sedation not aimed at patient death	248 (84.1)	232 (78.6)	.07
During sedation, the patient dies a natural death	157 (53.2)	179 (60.7)	.04
Sedation is symptom control	207 (70.2)	220 (74.6)	.20
Medication differs	154 (52.2)	200 (67.8)	<.001
Decision-making procedure differs	152 (51.5)	172 (58.3)	.09
Legal status differs	175 (59.3)	216 (73.2)	<.001
Physician is used to following a guideline for continuous sedation[f]			
No	72 (47.1)	16 (10.5)	<.001
Sometimes	43 (28.1)	45 (29.4)	
Yes	38 (24.8)	92 (60.1)	

[a] Missing: n=8; McNemar test.
[b] Missing: n=10; McNemar test.
[c] Missing: n=7; Wilcoxon signed rank test; median, 1 to 5 occasions in both periods.
[d] Missing: n=7; Wilcoxon signed rank test; median, 1 to 5 occasions in both periods.
[e] Missing: n=46; McNemar test.
[f] Missing: n=7; Wilcoxon signed rank test (only reported by physicians who sedated 1 or more patients in both periods, n=160).

COMMENT

Recommendations of the RDMA guideline (Table 1) were increasingly applied in daily practice after the introduction of the guideline: most physicians distinguished continuous sedation from euthanasia, the number of patient requests for euthanasia before sedation decreased, patient involvement in decision making

Table 3. Characteristics of Patients Who Receive Continuous Sedation: Development Between 2 Time Periods[a]

Characteristics	No. (%) of Patients: Before Guideline (n=160)	No. (%) of Patients: After Guideline (n=160)	*P* Value
Patient sex, male[b]	74 (48.7)	79 (52.0)	.63
Patient age, y[c]			
≤40	6 (3.8)	3 (1.9)	.44
41-60	20 (12.8)	30 (19.2)	
61-80	82 (52.6)	80 (51.3)	
≥81	48 (30.8)	43 (27.6)	
Patient involvement in decision making regarding continuous sedation[d]			
Patient not consulted before start of continuous sedation	42 (27.6)	27 (17.8)	.008
Patient consulted shortly before continuous sedation	49 (32.2)	50 (32.9)	
Patient consulted for some time before continuous sedation	61 (40.1)	75 (49.3)	
Presence of a (refused) request for euthanasia before sedation[e]			
Yes, request from patient	23 (14.5)	10 (6.3)	.01
Indication for continuous sedation, more than 1 answer possible[e]			
Pain	86 (54.1)	89 (56.0)	.81
Dyspnea	80 (50.3)	93 (58.5)	.12
Anxiety	71 (44.7)	73 (45.9)	.91
Delirium	34 (21.4)	34 (21.4)	>.99
Vomiting	9 (5.7)	17 (10.7)	.13
Nausea	12 (7.5)	22 (13.8)	.09
Exhaustion	50 (31.4)	89 (56.0)	<.001
Existential pain	29 (18.2)	41 (25.8)	.08
Perceived loss of dignity	32 (20.1)	43 (27.0)	.11
Nonphysical distress as an indication for continuous sedation[f]			
Involvement of nonphysical distress as an indication	111 (69.4)	130 (81.3)	.01
Continuous sedation without presence of physical symptoms	18 (11.3)	15 (9.4)	.70
Medication, more than 1 answer possible[e]			
Midazolam	83 (52.2)	126 (79.2)	<.001
Diazepam	33 (20.8)	11 (6.9)	<.001
Clonazepam	1 (0.6)	1 (0.6)	>.99
Morphine	120 (75.5)	100 (62.9)	.008
Chlorpromazine	0 (0)	0 (0)	.50
Haloperidol	31 (19.5)	42 (26.4)	.15
Methotrimeprazine	6 (3.8)	6 (3.8)	>.99
Promethazine hydrochloride	5 (3.1)	0 (0)	.06
Ketamine hydrochloride	1 (0.6)	1 (0.6)	>.99
Use of benzodiazepines for continuous sedation (perhaps in combination)[g]	109 (69.9)	141 (90.4)	<.001
Use of morphine and fentanyl without benzodiazepine[g]	37 (23.1)	14 (8.8)	<.001
Depth of continuous sedation[h]			
Patient could be aroused	73 (47.1)	62 (40.0)	.31
Patient could not be aroused, intact reflexes	76 (49.0)	89 (57.4)	
Patient could not be aroused, threat of obstruction, threat of hypoxia	6 (3.9)	4 (2.6)	
Artificial hydration[i] forsaken	90 (56.3)	126 (78.8)	<.001

[a] A total of 160 physicians were able to report a patient case of continuous sedation during the past 12 months in both the baseline and follow-up studies. Physicians who did not report a last case or who reported a last case in only 1 of both periods were excluded.
[b] Missing: n=8; McNemar test.
[c] Missing: n=4; Wilcoxon signed rank test; median, 61 to 80 years for both periods.
[d] Missing: n=8; Wilcoxon signed rank test; median, "yes, for a brief period" for both periods.
[e] Missing: n=1; McNemar test.
[f] Nonphysical distress is defined as distress from sources of anxiety, exhaustion, existential distress, or perceived loss of dignity. Physical distress is defined as distress from somatic symptoms such as pain, dyspnea, delirium, nausea, or vomiting without the concomitant presence of nonphysical distress (McNemar test).
[g] Missing: n=4; McNemar test.
[h] Missing: n=5; Wilcoxon signed rank test.
[i] McNemar test.

increased significantly, the use of benzodiazepine improved largely, the use of morphine alone for sedation decreased, and artificial hydration was increasingly forsaken. The systematic use of a guideline was reported significantly more often after the introduction of the RDMA guideline. Despite the recommendations of the guideline, this study also showed a large variety in symptom-directed treatment during sedation. In addition, exhaustion was more often reported as an indication of continuous sedation after the introduction of the guideline. Approximately one-third of the physicians were convinced that life shortening due to dehydration occurred during sedation. In our cohort of physicians, the frequency of continuous sedation was stable between the 2 periods studied, whereas changes in median patient survival were not found.

Table 4. Medication for Symptom Management During Sedation

Indication for Sedation	Recommended Medication[a]		Before Guideline Medication Applied? (n=160)		After Guideline Medication Applied? (n=160)	
	For Sedation	For Symptom Management	Yes	No	Yes	No
Delirium with or without pain or dyspnea	Benzodiazepine	Antipsychotic medication with or without morphine	14	20	14	20
Pain or dyspnea without delirium	Benzodiazepine	Morphine	57	44[b]	64	45[c]
Other symptoms	Benzodiazepine	NA	18	7	15	1
Total, No. (%)			**89** (55.6)	**71** (44.4)	**91** (56.9)	**67** (41.9)

Abbreviation: NA, not applicable.
[a]Antipsychotic medications included chlorpromazine, haloperidol, methotrimeprazine, and promethazine; benzodiazepine medications included midazolam, clonazepam, and diazepam.
[b]Twenty-four patients were sedated with morphine only; 6 with a benzodiazepine medication only.
[c]Eleven patients were sedated with morphine only; 18 with a benzodiazepine medication only.

REGARDING PALLIATIVE SEDATION AND DECISION MAKING

Patient involvement in decision making increased mostly because of earlier involvement of the patient, an option recommended by the latest World Health Organization definition on palliative care.[20] The fact that sedation can be carried out without explicit patient consent has been a cause of concern.[2] Therefore, it is important to note that, in the follow-up measurement, palliative sedation was initiated significantly less often without patient involvement in the decision-making process. Exhaustion as a reason for starting continuous sedation was more often reported in the second period. Exhaustion can be caused not only by the deterioration due to terminal disease, but also by the complex social interaction between patient and relatives, as well as by fear of the future. It may have not only a somatic dimension but also a psychoexistential dimension.[21] The latter dimension can make the refractory nature of exhaustion difficult to assess, whereas these patients are not necessarily in their last phase of life.[21,22] Multidisciplinary assessment of the patient is therefore recommended, at least regarding cases in which exhaustion is an important reason for the discomfort of the patient. Finally, although physical pain is often presented as a reason for starting continuous sedation, it is seldom the only reason to start sedation. This statement is confirmed in international literature.[23-25]

SEDATION IN A CONTEXT OF SYMPTOM MANAGEMENT

Regarding the increased use of benzodiazepines in palliative sedation, this positive trend has also been experienced in Italy, where no national guideline exists.[26] Therefore, some of the improvements could also be explained by increased expertise on the part of physicians with continuous sedation, based on other sources besides just the guideline. However, the increased use of benzodiazepine for sedation does not automatically imply adequate symptom management during sedation. In determining the purpose of continuous sedation to be patient comfort, the aim should be to reduce patient discomfort maximally and patient consciousness minimally. In this regard, the wide variety in types of symptom-directed treatment during sedation is problematic. Many physicians in our study remained reluctant to use opioid medications for pain or dyspnea during sedation. Nevertheless, extensive evidence indicates that hesitancy in supplying morphine for these symptoms is not in the interest of the patient in pain.[27-29] Moreover, it seems that palliative sedation and symptom-directed treatment are often regarded as opposites rather than supplements. In this regard, the trend toward deeper levels of sedation, as perceived in this study for general practitioners, needs further exploration. Therefore, it should be further investigated whether symptom-directed treatment in end-of-life care can be improved, via such options as opioid rotation and consultation of a palliative care specialist.[30] In addition, the possibility of reassessment of the depth of sedation in relation to the refractory nature of symptoms should be considered. For this reason, the place of intermittent and/or light sedation as a quality indicator in the pathway toward continuous sedation deserves extensive research.

SEDATION AND HYDRATION

The practice of continuous sedation seems to be complicated by the fact that approximately one-third of the physicians in our study associate it with life-shortening effects from dehydration, mostly when sedation occurs for a longer period. However, it should not be concluded that this finding reduces continuous palliative sedation to a kind of slow euthanasia in principle. First, in dying patients with limited or absent oral intake before sedation—most of the patients according to this study—a process of dehydration is not at all initiated by sedation, but only continued or accepted during sedation. Whether these results are acceptable exceeds the discussion of palliative sedation as such and points to the more general discussion about the acceptability of withdrawing artificial hydration in dying patients. At the least, palliative sedation can be applied in tandem with artificial hydration. Second, approximately a quarter of the patients had substantial oral intake before sedation. In these patients, continuous sedation without artificial hydration can be regarded as a direct cause of de-

hydration. However, even in these cases, it may be doubtful whether patients will eventually die of dehydration during a *limited* time of continuous sedation because the median survival of patients after the start of sedation is only 2 days.[31] The most relevant factor of the application of artificial hydration during palliative sedation concerns the effects of artificial hydration on the comfort of the sedated patient. The RDMA guideline does not recommend artificial hydration during sedation because parenteral hydration increases the risk of edema and incontinence. However, some other guidelines have formulated a more conservative position at this point.[14] More research about the effects of hydration on the comfort of sedated patients is therefore recommended. In conclusion, the physician's estimation of life-shortening effects caused by dehydration during palliative sedation needs to be taken seriously, but one should be extremely hesitant to interpret this as a moral deficit of palliative sedation practice itself. The RDMA guideline has recommended that, when patients have considerable oral intake before the start of continuous sedation, physicians should explicitly discuss the issue of artificial hydration before the start of continuous sedation or physicians should only offer intermittent sedation. This can be improved in daily practice considering our finding that approximately two-thirds of all patients with considerable oral intake, although involved in decision making for palliative sedation, were not explicitly informed about the possible implications of withholding hydration. In addition, it should be further investigated whether considerable oral intake counts as a contraindication for palliative sedation because it can be a sign that patient death is not imminent.

The advantages of our study design are that the total group of respondents in the baseline measurement is large, whereas the follow-up study had been performed in the same group of physicians. The study method of the last case registration has been used more often in research concerning medical decision making at the end of life,[6] but it has some weaknesses. Its results should be interpreted with caution because physicians may have had recall bias or may have neglected to mention difficult aspects of their cases. But, for the study of practices and their regulatory guidelines from a broad quality-of-care perspective, it seems suitable to approach those who directly carry out these practices. Because of the specific political background of end-of-life care in the Netherlands, generalization of the results to other countries may be limited. Nevertheless, palliative sedation is an acceptable practice in many countries and, therefore, the approach of regulating the practice via a specific guideline may be of interest for many countries.[32] Our study did not confirm the trend of an increased frequency of palliative sedation practice, which may be owing to the fact that the methods of this study had not been aimed at unraveling the frequency of use of continuous sedation in the total RDMA population of physicians. Regarding the aforementioned issues surrounding the appropriateness of symptom management during continuous sedation, the topic of hydration, and the place of exhaustion as a refractory symptom, it would be advisable that the guideline be more explicit about the assessment of refractory symptoms and the continuation of symptom-directed treatment. Further implementation of the guideline may be stimulated by a multidisciplinary expert consultation[12] in advance of sedation, or by an accreditation that limits the application of sedation to professionals with proven expertise. Further research should include prospective patient-based research and also concentrate on optimal symptom management before and during sedation, on the nature of refractory symptoms, and on the use of continuous sedation in patients with oral intake.

In conclusion, van der Heide et al[33] showed that euthanasia in the Netherlands was to some extent replaced by palliative sedation between 2001 and 2005. It has been debated whether the high burden on the physician to perform euthanasia has contributed to this shift.[34] However, our study also suggests another explanation: the finding that patients were more actively involved in the decision-making process for palliative sedation, whereas they formulated fewers requests for euthanasia during this process, may point to a more straightforward patient preference for palliative sedation at the end of life (Table 3). This important topic deserves further investigation. Our study showed a change in the practice of continuous sedation toward the recommendations of the RDMA guideline. Nevertheless, issues concerning the proper indication and application of continuous sedation still deserve more attention and implementation.

Accepted for Publication: April 8, 2007.
Correspondence: Jeroen G. J. Hasselaar, MSc, Department of Anaesthesiology, Pain, and Palliative Medicine, Radboud University Nijmegen Medical Center, Postbus 9101, 6500 HB Nijmegen, the Netherlands (j.hasselaar@anes.umcn.nl).
Author Contributions: Mr Hasselaar had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Hasselaar, Verhagen, Crul, and Vissers. *Acquisition of data:* Hasselaar. *Analysis and interpretation of data:* Hasselaar, Verhagen, Engels, Crul, Vissers, and Wolff. *Drafting of the manuscript:* Hasselaar. *Critical revision of the manuscript for important intellectual content:* Hasselaar, Verhagen, Wolff, Engels, Crul, and Vissers. *Statistical analysis:* Hasselaar. *Administrative, technical, and material support:* Hasselaar and Wolff. *Study supervision:* Verhagen, Crul, and Vissers.
Financial Disclosure: None reported.
Additional Contributions: M. Schmitz, MA, and C. Van der Welle, BSc, helped with administrative support.

REFERENCES

1. Morita T, Tsuneto S, Shima Y. Proposed definitions for terminal sedation. *Lancet*. 2001;358(9278):335-336.
2. Quill TE, Lo B, Brock DW. Palliative options of last resort: a comparison of voluntarily stopping eating and drinking, terminal sedation, physician-assisted suicide, and voluntary active euthanasia. *JAMA*. 1997;278(23):2099-2104.
3. Orentlicher D. The Supreme Court and physician-assisted suicide—rejecting assisted suicide but embracing euthanasia. *N Engl J Med*. 1997;337(17):1236-1239.
4. Tannsjö T, ed. *Terminal Sedation: Euthanasia in Disguise?* Dordrecht, the Netherlands: Kluwer Academic Publishers; 2004.
5. Seymour JE, Janssens R, Broeckaert B. Relieving suffering at the end of life: prac-

titioners' perspectives on palliative sedation from three European countries. *Soc Sci Med*. 2007;64(8):1679-1691.
6. Rietjens JA, van Delden JJ, van der Heide A, et al. Terminal sedation and euthanasia: a comparison of clinical practices. *Arch Intern Med*. 2006;166(7):749-753.
7. Müller-Busch HC, Oduncu FS, Woskanjan S, Klaschik E. Attitudes on euthanasia, physician-assisted suicide and terminal sedation: a survey of the members of the German Association for Palliative Medicine. *Med Health Care Philos*. 2004;7(3):333-339.
8. Morita T, Akechi T, Sugawara Y, Chihara S, Uchitomi Y. Practices and attitudes of Japanese oncologists and palliative care physicians concerning terminal sedation: a nationwide survey. *J Clin Oncol*. 2002;20(3):758-764.
9. Sykes N, Thorns A. Sedative use in the last week of life and the implications for end-of-life decision making. *Arch Intern Med*. 2003;163(3):341-344.
10. Rietjens J, Delden JV, Onwuteaka-Philipsen B, Buiting H, Maas PV, Heide AV. Continuous deep sedation for patients nearing death in the Netherlands: descriptive study. *BMJ*. 2008;336(7648):810-813.
11. Hasselaar GJ, Reuzel RP, Van den Muijsenbergh ME, et al. Dealing with delicate issues in continuous deep sedation: varying practices among Dutch medical specialists, general practitioners, and nursing home physicians. *Arch Intern Med*. 2008;168(5):537-543.
12. Hasselaar JG, Reuzel RP, Verhagen SC, de Graeff A, Vissers KC, Crul BJ. Improving prescription in palliative sedation: compliance with Dutch guidelines. *Arch Intern Med*. 2007;167(11):1166-1171.
13. Guideline for palliative sedation. Royal Dutch Medical Association (RDMA) Web site. http://knmg.artsennet.nl/uri/?uri=AMGATE_6059_100_TICH_R193567276369746. Accessed March 2, 2008.
14. Morita T, Bito S, Kurihara Y, Uchitomi Y. Development of a clinical guideline for palliative sedation therapy using the Delphi method. *J Palliat Med*. 2005;8(4):716-729.
15. Braun TC, Hagen NA, Clark T. Development of a clinical practice guideline for palliative sedation. *J Palliat Med*. 2003;6(3):345-350.
16. Webster's Online Dictionary Web site. http://www.websters-online-dictionary.org/. Accessed March 20, 2008.
17. Hesselman GM, Krol RJA, Kuyper MB, Verhagen EH, Vollaard EJ, De Graeff A, eds. *Palliatieve Zorg: Richtlijnen Voor de Praktijk*. Utrecht, the Netherlands: Vereniging van Intergrale Kankercentra; 2006.
18. Jennings AL, Davies AN, Higgins JP, Gibbs JS, Broadley KE. A systematic review of the use of opioids in the management of dyspnoea. *Thorax*. 2002;57(11):939-944.
19. Vella-Brincat J, Macleod AD. Haloperidol in palliative care. *Palliat Med*. 2004;18(3):195-201.
20. Definition of palliative care. World Health Organization Web site. http://www.who.int/cancer/palliative/en/. Accessed October 11, 2007.
21. Murata H, Morita T; Japanese Task Force. Conceptualization of psycho-existential suffering by the Japanese Task Force: the first step of a nationwide project. *Palliat Support Care*. 2006;4(3):279-285.
22. Morita T. Palliative sedation to relieve psycho-existential suffering of terminally ill cancer patients. *J Pain Symptom Manage*. 2004;28(5):445-450.
23. de Graeff A, Dean M. Palliative sedation therapy in the last weeks of life: a literature review and recommendations for standards. *J Palliat Med*. 2007;10(1):67-85.
24. Morita T, Chinone Y, Ikenaga M, et al; Japan Pain, Palliative Medicine, Rehabilitation, and Psycho-Oncology Study Group. Ethical validity of palliative sedation therapy: a multicenter, prospective, observational study conducted on specialized palliative care units in Japan. *J Pain Symptom Manage*. 2005;30(4):308-319.
25. Fainsinger RL, Waller A, Bercovici M, et al. A multicentre international study of sedation for uncontrolled symptoms in terminally ill patients. *Palliat Med*. 2000;14(4):257-265.
26. Bulli F, Miccinesi G, Biancalani E, et al. Continuous deep sedation in home palliative care units: case studies in the Florence area in 2000 and in 2003-2004. *Minerva Anestesiol*. 2007;73(5):291-298.
27. Abernethy AP, Currow DC, Frith P, Fazekas BS, McHugh A, Bui C. Randomised, double blind, placebo controlled crossover trial of sustained release morphine for the management of refractory dyspnea. *BMJ*. 2003;327(7414):523-528.
28. Rich BA. A legacy of silence: bioethics and the culture of pain. *J Med Humanit*. 1997;18(4):233-259.
29. Fohr SA. The double effect of pain medication: separating myth from reality. *J Palliat Med*. 1998;1(4):315-328.
30. Foley K. A 44-year-old woman with severe pain at the end of life. *JAMA*. 1999;281(20):1937-1945.
31. Verkerk M, van Wijlick E, Legemaate J, de Graeff A. A national guideline for palliative sedation in the Netherlands. *J Pain Symptom Manage*. 2007;34(6):666-670.
32. Quill TE. Physician assisted death in vulnerable populations. *BMJ*. 2007;335(7621):625-626.
33. van der Heide A, Onwuteaka-Philipsen BD, Rurup ML, et al. End-of-life practices in the Netherlands under the Euthanasia Act. *N Engl J Med*. 2007;356(19):1957-1965.
34. van Marwijk H, Haverkate I, van Royen P, The AM. Impact of euthanasia on primary care physicians in the Netherlands. *Palliat Med*. 2007;21(7):609-614.