

Original Article

Continuous Deep Sedation: Physicians' Experiences in Six European Countries

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Abstract

Continuous deep sedation (CDS) is sometimes used to treat refractory symptoms in terminally ill patients. The aim of this paper was to estimate the frequency and characteristics of CDS in six European countries: Belgium, Denmark, Italy, The Netherlands, Sweden, and Switzerland. Deaths reported to death registries were sampled and the reporting doctors received a mailed questionnaire about the medical decision making that preceded the death of the patient. The total number of deaths studied was 20,480. The response rate ranged between 44% (Italy) and 75% (The Netherlands). Of all deaths, CDS was applied in 2.5% in Denmark and up to 8.5% in Italy. Of all patients receiving CDS, 35% (Italy) and up to 64% (Denmark and The Netherlands) did not receive artificial nutrition or hydration. Patients who received CDS were more often male, younger than 80 years old, more likely to have had cancer, and died more often in a hospital compared to nonsudden deaths without CDS. The high variability of frequency and characteristics of CDS in the studied European countries points out the importance of medical education and scientific debate on this issue. J Pain Symptom Manage 2006;31:122–129. © 2006 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.

Key Words

Sedation, palliative care, medical end-of-life decisions

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Introduction

Severe symptoms, sometimes defined as “refractory,” have high prevalence during the last days of life among terminal cancer and other diseases.^{1–3} In such cases, sedation is an accepted procedure in palliative care.⁴ In general, deep sedation is to be used only temporarily;⁵ nonetheless, continuous deep sedation (CDS) may be the only means to control symptoms.⁶

It is already known that sedatives are rather frequently used to treat severely suffering patients nearing death. Within palliative care settings, incidence estimates of the use of sedatives range from 15% to more than 60%.^{7–13} Furthermore, a survey among palliative care specialists in North America and the United Kingdom showed that 77% of the respondents had at one time applied deep sedation in patients close to death¹⁴ and a study from Japan showed that 64%–70% of a sample of palliative care physicians and oncologists reported having used some form of deep sedation for severe physical distress.¹⁵ However, these estimates are difficult to compare due to differences in the settings studied and the definitions used. CDS without administering artificial nutrition/hydration is, by some authors, considered as a special kind of sedation (“terminal sedation”) due to the intended or foreseen life-shortening effect.^{16,17}

To gain more insight into the practice of CDS, more information on characteristics of sedated patients would be helpful. Previous studies reported that important indications for the use of sedatives in patients nearing death are intractable pain, dyspnea, delirium, agitation, and severe psychological symptoms such as anxiety and existential distress.^{7,10–12,14,18,19} A nationwide Dutch study found that half of the cases of terminal sedation were performed by clinical specialists; 30% of the patients receiving terminal sedation were 80 years of age or older, and 54% were concerned patients with cancer.¹⁸ However, further detailed and reliable information about characteristics of patients who receive CDS is needed because most studies were performed in a specific setting or focused on specific groups of patients.

In a recent death-certificate study about end-of-life decision making in six European

countries (EURELD),²⁰ physicians were also asked about the use of CDS. In this paper, we present comparable population-based estimates for Belgium (Flanders), Denmark, Italy (four areas), The Netherlands, Sweden, and Switzerland (German-speaking part) regarding the use of CDS—with and without the administration of artificial nutrition and hydration (ANH)—and to describe the characteristics of patients receiving CDS.

Methods

Design

In every participating country or region, random samples of death certificates of people aged 1 year or older (Italy, 18 or older) were obtained from death registries. The sampling period varied from 3 to 6 months. All deaths arose between June, 2001 and February, 2002. In all countries (apart from Switzerland), all deaths reported during the sampling period were stratified for the likelihood that death had been preceded by an end-of-life decision. Based on the cause of death, all deaths were assigned to one of three (Belgium, Denmark, Italy, and Sweden) or five (The Netherlands) strata. Sampling fractions were higher for strata in which the cause of death made an end-of-life decision more likely. Stratification was applied to enhance the efficiency and to yield smaller confidence intervals around estimates. Details have been described elsewhere.²⁰ In all countries, the data collection procedure precluded identification of any of the doctors or patients. A clearinghouse, usually a notary’s office, was interposed in each participating country. No envelope that contained a returned questionnaire reached the researchers before all identifying information had been removed from the data set using a separate code system. An application to the Research Ethics Committee (REC) was required in all countries except in Denmark (where questionnaire research only has to be assessed by an REC if it is part of a project involving biomedical research), in Switzerland (cantonal authority for data security confirmed anonymity of the data used in the study), and in The Netherlands (where the Royal Dutch Medical Association and the Health Inspectorate approved of the study).²¹

Questionnaire

For all sampled cases, the attending physicians were asked if death had occurred suddenly and unexpectedly. If cases were reported to have been nonsudden, the attending doctors were asked to fill out a four-page written questionnaire about the medical decision making that had preceded the death involved. The penultimate item in the questionnaire dealt with CDS: "Did the patient receive drugs, such as barbiturates or benzodiazepines, to keep him/her continuously in deep sedation or coma until death?" Answering options were "Yes, and artificial nutrition and hydration were not given"; "Yes, and artificial nutrition or hydration were given"; and "No." This question was asked for all nonsudden deaths, except in The Netherlands, where, due to a routing difference, the question was asked only if an end-of-life decision preceded death.

Statistical Analyses

If applicable, results were corrected for stratification by giving all cases a weight that is the reverse of the sampling fraction within the stratum they were assigned to. To allow the results to be representative of all deaths in the studied period, an additional weight was calculated from age, gender, cause of death, and place of death-specific response rates. Absolute frequencies and weighted percentages on total studied deaths were reported. The prevalence of CDS was compared for different classes of gender, age, cause of death, and place of death. To calculate estimates for all countries together, an additional country-specific weighting factor (the inverse of the weighted number of deaths studied in each country) was applied. The statistical significance of differences in CDS prevalence was estimated by means of Pearson Chi-squared statistic corrected for the survey design.²² A logistic regression was fitted to the data to determine the independent association of each characteristic of deaths with CDS. The model considered nonsudden deaths without CDS as controls. Likelihood ratio tests were used to test statistical interactions. All the statistical analyses were made using the "svy commands" of the statistical package STATA, release 8.²³

Results

A questionnaire was sufficiently filled out and returned for 20,480 deaths. These data were included in the study. Response percentage ranged from 59% to 75%, except for Italy (44%).

Table 1 shows that Italy and Belgium reported the highest percentages of CDS: 8.5% and 8.2% of all deaths, respectively, were preceded by the use of CDS. Denmark and Sweden reported the lowest frequencies: 2.5% and 3.2%, respectively. Switzerland was somewhat in-between (4.8% of all deaths). The prevalence of CDS while ANH were withdrawn or withheld varied less between countries (range 1.6%–3.2%, Denmark and Belgium, respectively). Of all sedated patients, 35%–64% did not receive artificial nutrition or hydration (Italy and Denmark/The Netherlands, respectively).

Table 2 shows characteristics of deaths in which CDS was applied. Cancer was the cause of death with the highest prevalence of CDS in all countries. In all countries, CDS was less frequently applied in patients older than 80 years old and more frequently in hospitals.

In a multivariate analysis that considered all countries together, each characteristic of the patients was independently associated to CDS (Table 3). The probability of receiving CDS was increased in males by 17%, in patients dying from cancer by 15%, in patients 65–79 years old by 91%, in patients younger than 65 years old by 134%, and in patients dying in the hospital by 63%. Statistically significant ($P < 0.01$) interactions were found between age and cause of death (effects of age and hospital were reduced in patients dying of cancer).

Discussion

Our study has, for the first time, enabled an international estimation to be carried out on the incidence of the use of drugs to keep patients in CDS in a large sample of nonselected patients from six European countries. CDS is practiced in all countries, in hospitals, as well as in other settings of care for cancer patients as well as for other kinds of patients.

The finding that CDS is a frequently applied practice is in line with other studies conducted

Table 2
 Characteristics of Deaths in Cases of CDS in Six European Countries

	Belgium		Denmark		Italy		The Netherlands ^a		Sweden		Switzerland		All countries	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Gender														
Male	133	9.2	48	3.1	170	9.4	159	5.8	62	3.6	80	4.8	652	6.0
Female	105	7.1	36	1.9	141	7.6	177	5.5	61	2.7	80	4.7	600	4.9
P-value ^b	0.059		0.046		0.103		0.665		0.121		0.866		0.001	
Age (years)														
<65	67	11.4	26	4.4	72	14.0	98	6.7	31	6.2	32	5.4	326	3.8
65–79	113	11.6	35	2.4	133	10.1	137	7.6	56	4.5	53	5.4	527	7.0
80+	58	4.7	23	1.8	107	6.3	101	3.7	36	1.7	75	4.2	400	7.7
P-value ^b	<0.001		0.006		<0.001		<0.001		<0.001		0.271		<0.001	
Cause of death ^c														
Cardiovascular dis.	36	7.5	12	2.2	29	4.6	28	2.9	26	2.0	30	2.5	161	3.5
Malignant dis.	127	9.9	55	4.0	260	16.3	155	6.6	79	5.0	74	9.0	750	8.7
Respiratory dis.	25	8.8	6	2.9	3	2.9	26	6.1	3	2.5	10	3.5	73	4.7
Nervous system dis.	16	7.2	6	2.6	8	14.8	25	4.4	1	2.9	23	6.4	79	5.6
Other/unknown	34	7.4	7	0.9	13	4.5	102	7.5	15	3.5	23	3.4	194	4.6
P-value ^b	0.4781		0.019		<0.001		<0.001		0.002		<0.001		<0.001	
Place of death														
Hospital	160	13.2	36	2.9	138	8.3	107	7.7	83	5.0	92	7.4	616	7.7
Other ^d	78	3.2	50	2.2	175	8.8	229	4.7	39	1.6	68	3.2	639	3.9
P-value ^b	<0.001		0.267		0.652		<0.001		<0.001		<0.001		<0.001	

Frequencies of CDS and weighted percentages of CDS on total studied deaths.

^aDue to a routing difference, Dutch data refer only to deep sedation until death, which occurred together with another end-of-life decision.

^bP-value of Pearson Chi-squared statistic (corrected for the survey design). Significance of difference in CDS prevalence among the categories of the characteristics (gender, age, cause of death, place of death) of deaths.

^cCerebrovascular disease is included in cardiovascular diseases for Italy and Sweden and in diseases of the nervous system for Belgium, Denmark, The Netherlands, and Switzerland.

^d“Other” places of death include both home and institution.

Table 3
Determinants of CDS in Six European Countries

	RR	95% CI
Gender		
Male	1.17	1.02–1.34
Female	1	
Age (years)		
<65	2.34	1.93–2.85
65–79	1.91	1.62–2.25
80+	1	
Cause of death		
Malignant diseases	1.15	1.00–1.33
Other diseases	1	
Place of death		
Hospital	1.63	1.43–1.86
Other ^a	1	

Logistic regression, nonsudden deaths only, all countries together.
^a“Other” places of death include both home and institution.
 RR = relative risk.

forgoing ANH.¹⁸ In medical and ethical discussions, it is debated whether forgoing ANH in deeply sedated patients shortens life, and if so, whether this should be considered as acceptable medical practice. The issue is controversial, also because forgoing ANH can sometimes be clinically indicated in imminently dying patients,⁵ and because sedation in terminally ill cancer patients has not been proved to be substantially influential on the duration of residual survival.²⁶ However, when the patients’ estimated life expectancy is more than a week, forgoing artificial nutrition or hydration in deeply sedated patients has been indicated as a possible marker of an intention to hasten death.^{16,27}

CDS is clinically indicated for imminently dying patients with severe symptoms refractory to conventional palliative treatments. It is not surprising that it was more often performed in cancer patients and in hospital settings, where there are more dying patients with the worst clinical conditions. The Italian exception (CDS more often in nonhospital settings) may be motivated by the rather high diffusion of domiciliary palliative care in the areas participating to the EURELD study. It is more difficult to find an explanation for the higher frequency of male patients among sedated patients. As far as the younger age of sedated patients is concerned, this result confirms other observations reported in the literature¹⁸ and was more prevalent in our data among non-cancer patients.

Our study has some limitations. We cannot exclude the possibility that nonresponse has to some extent biased our result, especially for Italy. Further, our results probably cannot be extrapolated to other than the regions studied in Belgium, Switzerland, and Italy. Although our definition of CDS was quite strict, excluding the secondary, intermittent, and mild sedation, we did not ask for the specific intention of the reported sedation, for the specific drugs used, or for the presence of refractory symptoms.

To conclude, the substantial practice of CDS in and outside hospitals and the cross-national differences point out the importance of further scientific debate and medical education on these medical procedures. Developing and implementing practice guidelines could contribute to assure high quality of this practice, and its appropriate use (i.e., after having considered all the other options and mainly the present palliative treatments available). Further studies will be necessary to describe the costs and benefits of CDS in terms of quality of dying.

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Appendix

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