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"Palliative Syringe Driver"? A Mixed-Methods Study in Different Hospital Departments on Continuous Infusions of Sedatives and/or Opioids in End-of-Life Care

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Objectives: Continuous infusions of sedatives and/or opioids (continuous infusions) are frequently used in end-of-life care. Available data indicate challenges in nonspecialist palliative care settings. We aimed to assess the use of continuous infusions during the last week of life in different hospital departments.

Methods: In a sequential mixed-methods design, a retrospective cohort study was followed by consecutive qualitative interviews in 5 German hospital departments. Medical records of 517 patients who died from January 2015 to December 2017 were used, and 25 interviews with physicians and nurses were conducted. Recorded sedatives were those recommended in guidelines for "palliative sedation": benzodiazepines, levomepromazine, haloperidol (≥5 mg/d), and propofol. Exploratory statistical analysis (R 3.6.1.) and framework analysis of interviews (MAXQDA 2018.2) were performed.

Results: During the last week of life, 359 of 517 deceased patients (69%) received continuous infusions. Some interviewees reported that continuous infusions are a kind of standard procedure for "palliative" patients. According to our interviewees' views, equating palliative care with continuous infusion therapy, insufficient experience regarding symptom control, and fewer care needs may contribute to this approach. In addition, interviewees reported that continuous infusions may be seen as an "overall-concept" for multiple symptoms. Medical record review demonstrated lack of a documented indication for 80 of 359 patients (22%). Some nurses experienced concerns or hesitations among physicians regarding the prescription of continuous infusions.

Conclusions: Continuous infusions seem to be common practice. Lack of documented indications and concerns regarding the handling and perception of a "standard procedure" in these highly individual care situations emphasize the need for further exploration and support to ensure high quality of care.

Key Words: continuous infusions, sedatives, opioids, palliative care, mixed-methods, hospital

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BACKGROUND

Dying patients may suffer from symptoms such as pain, dyspnea, or agitation.[1] Opioids and sedatives are crucial for controlling these symptoms.[2–4] Because oral intake often becomes difficult at the end of life, alternative routes of administration are needed. Several studies on medication at the end of life in general hospital departments suggest that drugs are frequently administered via continuous infusion in these circumstances.[2,4,5] Used correctly, continuous infusions are an appropriate and effective measure for symptom control.[6] However, some reports, predominantly from the United Kingdom, raised concerns regarding misuse of continuous infusions in end-of-life care in general hospital departments.[7,8] This includes inadequate documentation, prescription without adequate indication, use of inappropriately high doses, and withholding of medication due to the fear of hastening death.[5,9–11] Moreover, existing literature indicates various challenges such as drug incompatibilities, difficulties with calculation of doses, and technical problems, for example, disconnection.[9,11,12] Errors in handling continuous infusions can result in serious adverse patient outcomes and pose a risk for patient safety, including life-shortening effects.[12] However, empirical data on the handling of continuous infusions at the end of life in general hospital departments are still scarce, in particular internationally. To our knowledge, articles report results of small single-center studies, focus on specific components such as drug compatibilities, or reflect expert opinions.[3,13–20]

Therefore, this study aims to assess the current clinical practice of continuous infusions of sedatives and opioids within the last week of life in general hospital departments and explore health care professionals' respective experiences.

METHODS

Continuous infusions of sedatives and/or opioids are called "continuous infusions" in the following.

Design, Setting, and Participants

In an explanatory sequential mixed-methods design,[21] a multicenter retrospective cohort study was followed by semistructured qualitative interviews. Five hospital departments of 2 hospitals (university and teaching hospital) participated in the study: hematology/oncology (n = 2), geriatrics, gynecology, and neurology. For the retrospective cohort study, patients who died in the participating departments between January 2015 and December 2017 were included. Inclusion criteria for the qualitative interviews were experience in caring for dying patients and sufficient German language skills. Recruitment took place via contact persons at the participating centers. In cases of acceptance, an appointment for a face-to-face interview was made by email or telephone. Information on nonparticipation was not collected. Purposeful sampling balancing for age, sex, profession, and work experience was intended. We followed the COREQ checklist for the qualitative phase and the STROBE checklist for the quantitative phase to

ensure methodological rigor.[22,23] For details, see Supplement Table 1, http://links.lww.com/JPS/A437. The study was approved by the Research Ethics Committee of the Medical Faculty at Ludwig-Maximilians-University Munich (reference number 17-792).

Data Collection

Retrospective Cohort Study

Two researchers (B.G., S.M.) and 2 research assistants extracted data from the electronic and paper medical records using an Excel-based data extraction tool, which had been piloted on 23 records. Data extraction was guided by a detailed instruction sheet, and 2 researchers jointly extracted data for randomly selected 20% of all records to ensure accuracy. We defined "sedatives" as drugs recommended by guidelines for "palliative sedation": benzodiazepines, levomepromazine, haloperidol ≥5 mg/d (as lower doses are unlikely to be sedating), and propofol.[24–28] Data on the use of sedating drugs (sedatives and opioids) in the last week of life were collected: doses per day, indication, and routes of administration. In addition, demographic and clinical data were extracted, including age, sex, cause of death, support by specialist palliative care service, and use of the word "palliative" or synonyms (e.g., "palliative situation," "symptom-orientated approach"). Total daily dose was defined as the actually administered total dose within 24 hours, taking into account the time treatment was started and any dose changes. An exception was the day of death, for which the total daily dose was defined as the dose prescribed for the full day.

Semistructured Interviews

The approach was used to allow for flexibility and in-depth discussion of a complex topic, while ensuring consistency between interviews. The interview guide (Supplement File 2, http://links.lww.com/JPS/A438) was informed by the literature and the quantitative results, and was piloted in 2 interviews. It covered 4 main topics: understanding of palliative care and end of life, indications for the prescription of sedating drugs, experience with different forms of sedation, and perceived need for change and/or support in handling sedating drugs. Interviewees gave their written informed consent. Two researchers (B.G., S.M.) conducted the interviews in interviewees' workplaces between May 2019 and September 2019. Parallel to the interviews, the research team constantly discussed whether new and important themes emerged. Interviews were conducted until achieving data saturation. Interviews were audiorecorded and transcribed verbatim. Data on sociodemographic and professional background of the interviewees were collected by a questionnaire.

Initially, both researchers were unexperienced in qualitative research and therefore thoroughly trained and supervised by an experienced qualitative researcher (E.S.) as well as by external training. Because of the preceding retrospective chart review, B.G. and S.M. had insights into the practice of administration of sedative drugs in the participating hospital departments. There were no previous relationships between interviewers and interviewees. In advance to the interview, interviewees were informed about the interviewer's educational background and occupational status.

Analysis

Quantitative data were used to describe the clinical practice, and qualitative data to explore experiences as perceived by health care professionals. For data analysis and interpretation, both phases were integrated with equal weight. Qualitative results were used to explain quantitative results, or the results were compared with each other.

Retrospective Cohort Study

We performed descriptive statistics and bivariate analysis using R version 3.6.1. If medical records were missing entirely, we excluded the patients from the analysis. For missing information within the records, we excluded the respective values from the analysis. Medians, interquartile range (IQR), and ranges were used to describe drug doses, excluding values of 0. Doses of opioids were converted to the parenteral morphine equivalent dose (MED) according to published guidelines.[29,30] To evaluate differences between patients with and without continuous infusions as well as differences between hospital departments, we conducted t tests or Mann-Whitney U tests for continuous data and χ^2 tests for categorical data. α Level was set at 0.05. Because of the study's exploratory nature, we did not adjust for multiple testing.

Semistructured Interviews

We thematically analyzed the qualitative interviews by the framework approach using MAXQDA version 2018.2.[31] After familiarization with part of the interview material, we constructed an initial analytical framework, with categories derived both inductively and deductively (close collaboration of S.M. and B.G., with support of E.S.). The analytical framework was continuously refined during the indexing of all interviews. At the end of the indexing process, no new themes emerged.[32] The analytical framework consisted of 8 categories with 0 to 9 subcategories, respectively. We summarized and charted the indexed data into a matrix. Analysis and interpretation were based on the charted data. Continuous infusions of sedatives and/or opioids emerged as an important theme within the category "other." We developed a thematic sheet for this theme, consisting of 10 thematic columns: (1) choice of drugs, (2) procedure, (3) frequency of continuous infusions, (4) evaluation of the handling, (5) indications, (6) cooperation, (7) involvement of the specialist palliative care team, (8) challenges, (9) need for support, and (10) evaluation of the patient.

We used several strategies to ensure rigor and trustworthiness. We discussed the interview guide with qualitative expert groups both at the university and at the university hospital. To ensure consistency of analysis, 2 researchers (S.M., B.G.) independently indexed 16% of the transcripts and summarized a subset of the indexed data. Disagreements were discussed, partly involving a third researcher (E.S.), until consensus was reached. Because of anonymization, transcripts could not be returned to participants. The interviewers, however, continuously confirmed accounts during the interview to guarantee correct understanding. Moreover, we conducted a workshop and final conference for health care professionals, including interview participants, where they could provide feedback on the findings. Constant exchange within the project team and weekly discussion workshops with experienced researchers at the department ensured rigor and integrity of the analysis. Quotations were translated by a Language Support Service and checked for equivalent meaning by the team.

RESULTS

Between January 2015 and December 2017, 530 patients died in the hospital departments. Thirteen patients were excluded from the analysis because of missing medical records. The median age of the remaining 517 decedents was 77 years, 51% were female, and the most frequent cause of death was malignant diseases (52%). All hospital departments had access to a specialist palliative care service, and in 52% of the cases, such a service was involved (Table 1). Qualitative interviews were conducted with 13 nurses and 12 physicians. The majority of participating nurses was between 40 and 59 years old (61.5%), and most physicians were between 30 and 49 years old (83%). Sixteen of the interviewees were

TABLE 1. Comparison of Sociodemographic and Clinical Characteristics of Patients With and Without Continuous Infusions of Sedatives and/or Opioids Within the Last 7 Days of Life

	Total Group	Continuous Infusions of Sedatives and/or Opioids		
	All (n = 517)	Yes (n = 359)	No (n = 158)	*P*
Age, y				0.089
Median (IQR; range)	77 (65–85; 22–105)	77 (64.5–84; 22–105)	79 (69.3–85; 24–99)	
Mean (SD)	74.3 (13.9)	73.7 (14.2)	75.9 (12.9)	
Sex, n (%)				0.215
Female	265 (51)	191 (53)	74 (47)	
Department, n (%)*				**<0.001**
Hematology/oncology I	190 (37)	147 (77)*	43 (23)*	
Hematology/oncology II	58 (11)	30 (52)*	28 (48)*	
Neurology	168 (33)	128 (76)*	40 (24)*	
Geriatrics	83 (16)	42 (51)*	41 (49)*	
Gynecology	18 (3)	12 (67)*	6 (33)*	
Cause of death, n (%)				
Malignant disease	270 (52)	195 (54)	75 (48)	**<0.001**
Neurological + neurovascular disease†	156 (30)	123 (34)	33 (21)	**<0.001**
Cardiovascular disease	31 (6)	11 (3)	20 (13)	0.129
Respiratory disease	14 (3)	8 (2)	6 (4)	0.635
Other	45 (9)	22 (6)	23 (15)	‡
Missing	n = 1	n = 0	n = 1	
Support by specialist palliative care team, n (%)				**<0.001**
Yes	248 (48)	214 (60)	34 (22)	
Labeled palliative§, n (%)				**<0.001**
Yes	281 (54)	229 (64)	52 (33)	

The figures are column numbers and percentages, with one exception: For department, row percentages are reported. Percentages are reported in "valid percent," that is, based on the number of patients for whom data for the respective variable were available.

Figures in bold denote statistically significant differences between patients with and without use of sedatives with "continuous effect."

*For department, row percentages are reported.

†Including intracranial hemorrhage stroke and dementia.

‡Test for difference judged as not clinically important.

§Includes palliative therapy/treatment/measures/status/situation, palliation, symptom-oriented/symptom control/symptom based therapy/treatment/measures, limitation of therapy, change of treatment goal (from curative to palliative).

female (11 nurses, 5 physicians), the median number of years of professional experience was 12.0 with a range from 1.0 to 38.0 years (nurses, 17.0 [range, 3.5–35.0]; physicians, 7.3 [range, 1.0–38.0]), and 16 interviewees (8 nurses, 8 physicians) stated experience in palliative care (training in palliative care or work experience on a palliative care unit).

Prevalence and Characteristics of Continuous Infusions

Of the 517 deceased patients, 359 (69%) received a continuous infusion on at least 1 day during the last week of life. Of the 359 patients, 222 (62%) received both sedatives and opioids, 130 (36%) received only opioids, and 7 (2%) received only sedatives. The proportion of patients receiving any kind of continuous infusion increased from 6 days before death until the day of death (Fig. 1). Of the 229 patients with sedatives, 226 (99%) received midazolam, 11 (5%) received levomepromazine, 8 (4%) received haloperidol, and 1 (0.4%) received propofol. Opioids comprised morphine for 283 of 352 (80%), hydromorphone for 64 (18%), and piritramid for 21 (6%) patients. Most interviewees emphasized that, although there are common drug combinations for continuous infusions (primarily morphine and midazolam), drugs and doses are individually adapted according to the patient's symptoms. The physician's experience was mentioned as an important factor for the choice of drugs (Table 2 (1)). Figures 2 and 3 show the total daily dose of midazolam and opioids, respectively. The median total daily dose of midazolam varied between 6.9 mg (IQR, 4.1–10.0 mg; range, 0.8–26.5 mg) 6 days before death and 10.0 mg (IQR, 5.0–21.5 mg; range, 0.9–144.0 mg) on the day of death. The median MED varied between 12.0 mg (IQR, 16.3–21.8 mg; range, 1.0–50.4 mg) 6 days before death and 17.1 mg (IQR, 10.0–28.3 mg; range, 0.5–272.0 mg) on the day of death. Nearly all interviewees stated to start with low doses and titrate until the patient is symptom-free. A start with high doses is only seen as an adequate measure in case of extreme symptom burden. Some interviewees experience challenges in finding the right dose because it is very individual, and feel uncertainties concerning hastening of death.

Most frequent indications for prescribing a continuous infusion were pain (57%), agitation (43%), dyspnea (37%), and anxiety (31%; multiple indications possible). No indication was recorded for 22% of the patients with continuous infusions. A possible explanation may be the reported challenge to differentiate symptoms at the end of life. Combined continuous infusions are then used as an overall concept for patients with multiple symptoms (Table 2 (2)).

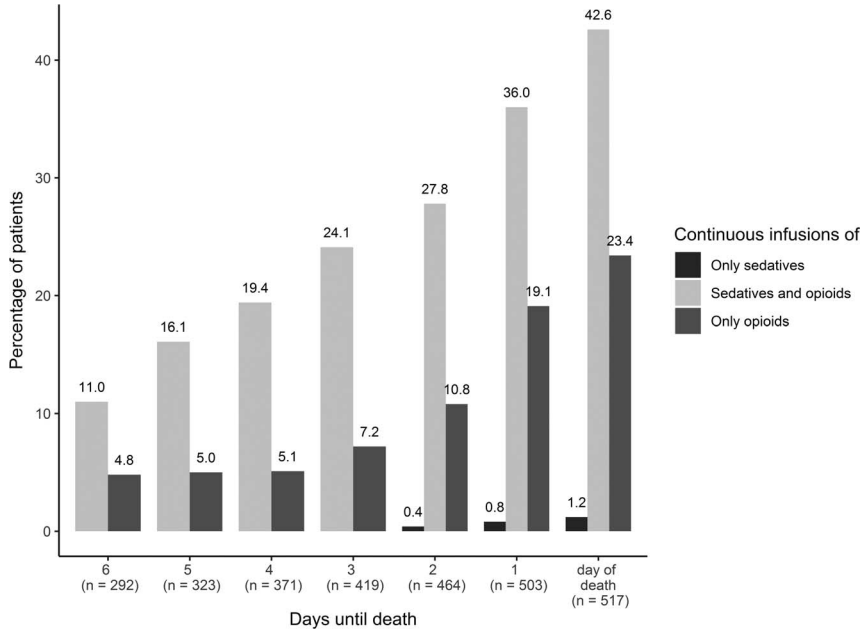

FIGURE 1. Percentage of patients* receiving continuous infusions of sedatives, opioids, or sedatives and opioids. *In relation to the total number of patients who were cared for in the 5 analyzed departments on the respective days. These numbers are given in brackets beneath the respective days.

Interviewees of all departments reported that they usually administer continuous infusions of opioids first and add continuous infusions of sedatives in the course of the treatment only if necessary. However, for 153 of 222 patients (69%) who received both sedatives and opioids, these continuous infusions were started on the same day (combined continuous infusion) and continued until the day of death. Interviewees stated to generally administer prn (as needed) doses before starting a continuous infusion. According to the medical records, 73 of 153 (48%) of the subgroup of patients with combined continuous infusions received a prn dose of opioids and 54 of 153 (35%) a prn dose of sedatives before or on the starting day of the combined continuous infusion.

Association of the Label Palliative and the Start of Continuous Infusions

Many interviewees reported to start continuous infusions only in cases of a substantial level of suffering and only in situations when other attempts of symptom control have failed (Table 2 (3)). However, data indicate an association of the label palliative and the start of continuous infusions. Medical records showed that the term palliative was significantly more often documented in the records of patients with continuous infusions ($P < 0.001$). The documented day of transition to a palliative concept was also the starting day of the continuous infusions in 66% (59 of 89 cases for which

TABLE 2. Quotes of the Healthcare Professionals Regarding Continuous Infusions of Sedatives and/or Opioids at the End of Life in General Palliative Care

Prevalence and characteristics of continuous infusions

(1) The physician's experience as an important factor for the choice of drugs

Nurse 7:

"But how this combined syringe driver is put together is still arranged by our doctors on a very individual basis. […] Sometimes there is a doctor who has to be trained for the first time and maybe there is already someone who has been here for one and a half years, that makes a huge difference."

(2) Combined continuous infusions as an overall concept for patients with multiple symptoms

Nurse 1:

"But in 99% of the cases, it always comes down to administering continuous sedation including symptom control, i.e. something against nausea with something to go with it […] even if they no longer report nausea, but it is still given because it can happen and, simultaneously, something against pain. It is always so difficult when someone is restless because they are not relaxed or in pain, then the sedation is increased without considering the pain, which is why the standard plan for a dying patient is actually always continuous sedation and pain medication."

Association of the label palliative and the start of continuous infusions

(3) Continuous infusions only in cases of a substantial level of suffering, and only in situations, when other attempts of symptom control have failed

Nurse 4:

"Well, the patient says he is in pain and needs something. And all the other medicines are not enough. […] then we simply give it as an infusion, as a continuous infusion, and make sure that it can be adjusted well. Or they say they are afraid or yes, the symptoms are so unbearable that they can't manage any other way."

(Continued next page)

TABLE 2. *(Continued)*

(4) Continuous infusions as standard procedure for palliative patients

a. Physician 1:

"[…] there are standards for everything and also for our patients who are palliative, we have this standard combined syringe driver. And you just give this, this and that and then it's good. […] Well, we often kind of say here: 'Uh, palliative – combined syringe driver'"

b. Physician 3:

I: "And can you perhaps remember a case where there was no syringe driver?"

B: "Well, no, I can't really think of any. Well, it's a standard, you have to say, such a morphine syringe driver."

c. Nurse 6

I: "Can you explain what you mean by the classic sedation syringe driver?"

B: "Oh, yes, at least that's what we do here on the ward when we notice that patients are nearing the end of their lives and are very agitated, we put on a syringe driver with morphine in it and then midazolam, for example […] Exactly, that's the standard syringe driver for us."

(5) Physicians sometimes postpone the start because of fears to hasten death

a. Nurse 2

"Well, we see that it is now becoming difficult, so to speak, many older nurses, thank God we have many nurses with many years of experience, who then really repeatedly point it out and say, yes, but in the late shift, I think she is alone with 20 people or only has one pupil, the patient is not well, something has to be done. Then our doctors first of all defend themselves a bit, 'No, we don't want to kill her', and when a palliative physician is called in, then everything is a bit smoother and then they also agree and then it can be implemented. […] That's a bit of a borderline here, where they say, we can't add a morphine syringe drive yet, because the patient could die."

b. Nurse 4

"Yes, I think it's also the case that many doctors don't dare to put on a syringe driver, or say, 'OK, this is where we're headed'. Or we nurses come back and say, hey, listen, he's in respiratory distress or he's in pain, we need something now. Then every now and then a dose of morphine is administered. But only as a single medication."

(6) Factors that might lead to inappropriate use of continuous infusions

- Limited experience and knowledge with symptom control at the end of life: equating the application of continuous infusions with palliative care, lack of knowledge of other symptom control measures
- prospect of fewer care needs of sedated patients
- assumption of a near death might strengthen this trigger

a. Nurse 1

"But what should perhaps be done more and should also be schooled more are the purely palliative methods, i.e. all these combined syringe drivers, because I think they have a more resounding success with the patients […]."

b. Physician 4

"And if you know specific dosages or indications for the use of certain sedating medications, which do not require IV morphine syringe driver, and the patient is tired and only sleeps. But they can cause a slight symptom relief, so to speak. I think that would definitely help."

c. Physician 1

"And yes, I would like us to be a bit more detailed or to divide it up a little more into smaller parts. There should be other options besides midazolam or whatever, depending on the form of application."

d. Physician 2

"I think that one of the arguments is that you increase the medication quickly. When you say: 'The patient is palliative anyway,' in inverted commas […] And in my experience, in some wards, let's say, with a dose increase or the start of double sedation or pain therapy in higher doses, this happens more quickly than in wards that perhaps have a palliative care unit which perhaps has more experience with these drugs or can titrate them better or perhaps also has more time to visit the patient regularly. […] So maybe there is also a bit of a bias that many are more generous with morphine, dormicum [midazolam], because it certainly makes care easier or the doctor's interaction with the patient simpler."

e. Nurse 5

"So, we often have combined syringe drivers. […] The bottom line is that [in the palliative situation] you can no longer break anything."

Cooperation

(7) Involvement of the specialized palliative care team

a. Nurse 5

"Well, the rule is that we wait until the palliative team arrives and then we wait to hear what they say. So, it's not really ordered by a general physician. And the nurses are not allowed to order it on their own. Yes."

b. Physician 3

"It is not the case that we administer midazolam or something like that to the patients. Well, it's really only in consultation with the palliative care doctors, as a syringe driver or something, which we then also prescribe. We don't actually do that on our own."

c. Nurse 3

"The only thing that sometimes causes difficulties is that the palliative side sometimes prescribes other medications that are not so convenient for us on the normal ward. So, that's how it is, they work a lot with mixed combined syringe drivers in the palliative wards […] And if conditions change there, then there is also the time and the staff […] And that is then always reprocessed in palliative medicine. That is a bit difficult for us to handle. So we prefer to work with individual infusions […] and can then, for example, administer boluses individually."

the date of transition to a palliative approach was documented). Moreover, continuous infusions were labeled as "palliative syringe driver" in 5 cases. The interviews revealed that continuous infusions may be seen as a kind of standard procedure when recognizing that the final days of life of a patient have begun. Some interviewees reported that nearly all patients with the label palliative receive a continuous infusion (Table 2 (4)). According to the interviews, most patients need continuous infusions at the end of life, as they are usually symptomatic. However, we determined factors that might contribute to an inappropriate standard use of continuous infusions. First, interviewees reported limited experience and knowledge regarding symptom control at the end of life. Some interviewees seemed to wrongly equate the application of continuous infusions with palliative care (Table 2 (6a)), others were not aware of alternative measures for symptom control (Table 2 (6b/c)). Second, the prospect of fewer care needs of sedated patients

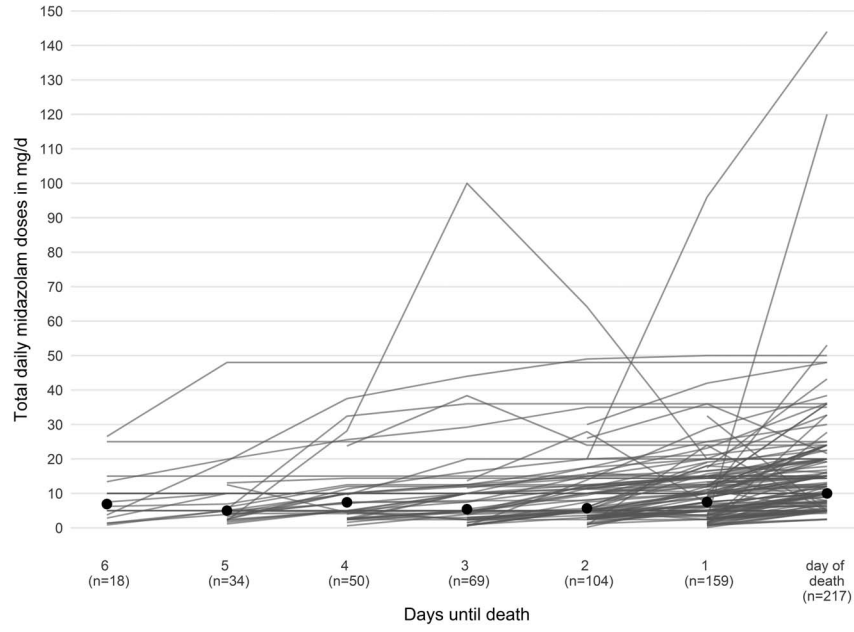

FIGURE 2. Individual total daily midazolam doses in the last week of life. Black dots: median.

may prompt professionals to start continuous infusions earlier and in higher doses than necessary (Table 2 (6d)). Some interviewees assumed that the assumption of a near death might strengthen these triggers (Table 2 (6d/e)).

On the one hand, the association of the label palliative and continuous infusions poses the risk of using continuous infusions by default for every palliative patient. Accordingly, some physicians stated that they would prefer a more differentiated and individual approach, that is, using other measures of symptom control before starting continuous infusions (Table 2 (6c)). In contrast to the presumption of administering continuous infusions by default, some nurses criticized that physicians sometimes postpone the start because of fears to hasten death (Table 2 (5)). Our data indicate that the label palliative may serve as a kind of justification for administration of continuous infusions, whereas in situations not yet labeled as palliative, fears to hasten death may preclude use of this measure.

Cooperation

Both nurses and physicians considered specialist palliative care as an important support for adequate practice. Many interviewees stated to involve the specialist palliative care team for nearly all patients at the end of life, and some acknowledged that continuous infusions are only prescribed and administered after consultation with the specialist palliative care service (Table 2 (7a/b)). Medical

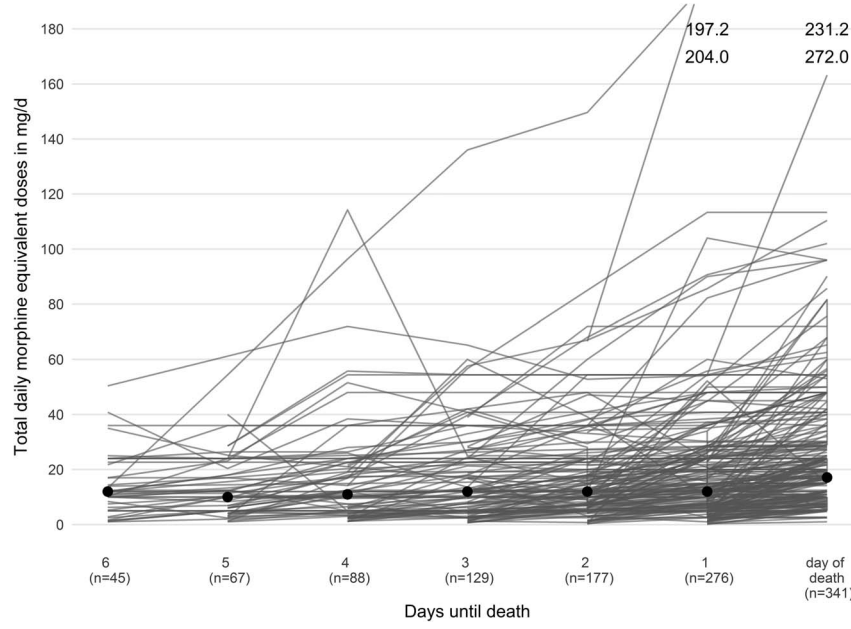

FIGURE 3. Individual total daily MEDs in the last week of life. Black dots: median. Doses >180 mg/d are depicted at the top of the figure, giving their exact values in numbers.

records revealed that involvement of the specialist palliative care team differs highly between hospital departments: 19.1% of all decedents in geriatrics, 60.9% in neurology, 62.6% in hematology/oncology I, 80% in hematology/oncology II, and 100% in gynecology. The only perceived challenges were some technical aspects of the specialist palliative care teams' recommendations, which can be difficult to implement in general settings (Table 2 (7c)). Although the drug prescription is the physicians' responsibility, nurses suggest the initiation of continuous infusions in many cases, according to the interviewees. Physicians regarded good cooperation with experienced nurses as crucial for end-of-life care, and nurses as well as physicians emphasized discussion within the team as an important requirement for starting continuous infusions. However, some nurses criticized that their opinion is not sufficiently considered. They described resistance or hesitations of the physicians when nurses suggest starting continuous infusions (Table 2 (5)).

DISCUSSION

To our knowledge, this is the first mixed-methods study assessing the practice of continuous infusions at the end of life and exploring experiences of health care professionals in different general hospital departments. The data demonstrated that continuous infusions are frequently used in this setting, nearly 70% of the deceased patients received a continuous infusion in the last seven days of life. Analysis of the documented practice and of experiences indicated areas for quality improvement and need for support.

Administration of continuous infusions at the end of life seems to be dependent not only on patients' symptoms but also on the label palliative. Some physicians do not prescribe continuous infusions before the transition to a palliative concept is documented and only with support of specialist palliative care because of fears to hasten death. The results are consistent with previous findings that health care professionals wrongly associate continuous infusions with imminent death.[9,33] The possible requirement of the label palliative or waiting for specialist palliative care support can lead to avoidance or postponement of continuous infusions, resulting in harm due to inadequate symptom control. In addition, avoiding to start continuous infusions without specialist palliative care support may hinder health care professionals to build up own experiences. In contrast, our data regarding the association between the label palliative and continuous infusions also demonstrate the risk of using continuous infusions by default for every palliative patient. This problem has also been identified by a previous smaller study in general palliative care, and various recommendations emphasize to avoid starting continuous infusions as a matter of routine at the end of life.[1,5,34] Symptom control should be adjusted as needed for the individual, and sedation should only be considered after exploiting other measures of symptom control.[1,24,34,35] Equating combined continuous infusions with palliative care by our interviewees and documentation of the term "palliative syringe driver" in the medical records demonstrate that there are deviations from these best practice recommendations. Another aspect that might lead to the application of continuous infusions by default is insufficient knowledge of symptom control measures other than continuous infusions. The results confirm the need for competencies regarding end-of-life care for nurses and physicians in general palliative care settings.[36–38] Moreover, as one interviewee assumed, the argument "palliative anyway" might prompt professionals to start continuous infusions at the end of life earlier and in higher doses than necessary. Professionals might neglect possible harm by continuous infusions in "palliative patients" and solely perceive them as an easy and effective symptom control measure. In addition, continuous infusions may be used to reduce effort of care and communication with the patient, which has also been reported by Costello et al[9]: "Syringe drivers reduce the need for professional contact." Lack of time and the fast pace of the acute hospital setting have been identified as contributing factors for suboptimal end-of-life care.[36,39,40] It is therefore questionable to what extent existing guideline recommendations for the specialist setting regarding frequent assessments of symptoms and adjusting the medication accordingly are applicable to the general care setting.[41] Finally, the indication for the continuous infusions was missing in the medical records of 1 in 5 patients in our sample. Potentially because of challenges to differentiate symptoms from each other, continuous infusions may be used as a "belt and braces approach" to cover a wide range of symptoms. However, guidelines advise to have a clear rationale for continuous infusions and to avoid a standard procedure for every patient.[1,34,41]

STRENGTHS AND LIMITATIONS

The main strength of the study is its mixed-methods design across different hospital departments and including nurses' and physicians' experiences. The design allowed us to compare and explain qualitative and quantitative results, and we gained a detailed and comprehensive picture of the practice. Moreover, the use of the framework approach as a systematic tool for qualitative data analyses, which produces highly structured outputs, facilitated a holistic overview of the entire data.

The study results must be considered in the context of the following limitations, which have partly been discussed in the previous publication regarding the quantitative phase.[42] To gain a realistic picture of everyday practice, we chose a retrospective design. However, some data have been recorded incompletely, for example, the route of continuous administration (subcutaneous or intravenous) or symptoms. Although we included different specialties, generalization is precluded because of data collection from a limited number of centers in only one geographical region, all having access to specialist palliative care services, which is not the case in many hospitals. We intended purposive sampling for the qualitative interviews. Because of difficult recruitment, inexperienced health care professionals were underrepresented. Insecurities and perceived challenges of entrants may therefore not be taken into account. The time interval between patients' death, included in the quantitative phase, and conduct of interviews was between 17 and 56 months. Changes in staff, structures, or procedures may have occurred during this period. However, at the time of quantitative data collection (mid- to end-2018), we could only access medical records of decedents who died up to December 2017, and we had to extend the period for inclusion of decedents until January 2015 to include enough cases to analyze the whole spectrum of different types of sedation. Qualitative interviews could only start once first analyses of the quantitative data had been done, as these informed the interview guide.

CONCLUSIONS

Two main problems seem to be associated with the use of continuous infusions in general palliative care, which may result in harm to patients. First, hesitations to use continuous infusions before a patient is labeled as palliative may cause unnecessary delay in relieving suffering. Second, the association between the label palliative and continuous infusions may result in their use by default without individual assessment of needs and adequate indication. Using the label palliative solely for patients in the dying phase and equating continuous infusion therapy with palliative care are not in accordance with the palliative care aspiration of holistic care and early integration. Numerous studies have

indicated suboptimal quality of end-of-life care in general hospital departments, which has led to the development of recommendations and programs in recent years.[43] The present study underlines the need to include symptom control with continuous infusions in recommendations and provides crucial information for further developments.

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