

**Brief Report**

# Palliative Sedation in Advanced Cancer Patients Followed at Home: A Retrospective Analysis

Sebastiano Mercadante, MD, Giampiero Porzio, MD, Alessandro Valle, MD, Flavio Fusco, MD, Federica Aielli, MD, Claudio Adile, MD, and Alessandra Casuccio, BS, on behalf of the Home Care—Italy Group (HOCAI) *Pain Relief and Palliative Care Unit (S.M., C.A.), La Maddalena Cancer Center, Palermo; Palliative Medicine (S.M.), Department of Anesthesia & Intensive Care and Department of Experimental Biomedicine and Clinical Neuroscience (A.C.), University of Palermo, Palermo; Home Care Program (G.P., F.A.), L'Aquila per la vita, L'Aquila; Home Care Program (A.V.), Fondazione FARO, Torino; and Home Care Program (F.F.), ASL 3 Genovese, Genova, Italy*

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**Abstract**

**Context.** Data regarding palliative sedation at home in dying patients are lacking.

**Objectives.** To describe the frequency, indication, and modality of palliative sedation (PS) in patients followed at home.

**Methods.** A retrospective analysis of home care cancer patients was performed. Patients who received PS before dying were selected and information about epidemiologic characteristics, indications, duration, drugs, and outcomes was collected.

**Results.** Of 370 medical charts of patients who died at home, 49 patients received PS before dying. PS was proposed by the team, relatives, or both in 63.3%, 4.1%, and 32.6% of cases, respectively. Delirium alone or in combination with other symptoms was the most frequent indication to begin PS. Midazolam was the most frequently used drug to initiate PS (98%), at a mean dose of 28.1 mg/day, in combination with parenteral morphine (84.7%) at a mean dose of 25.4 mg/day. At the time of death, midazolam was administered in 98% of patients (mean dose 22.3 mg/day), combined with parenteral morphine in 87.8% of patients (mean dose 28.1 mg/day). Satisfaction for physicians and principal caregivers after PS was good in 46 and 48 cases, respectively.

**Conclusion.** PS at home seems to be a feasible treatment option among selected patients and makes a potentially important contribution to improving care for those who choose to die at home. *J Pain Symptom Manage* 2012;43:1126–1130. © 2012 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.

**Key Words**

*Palliative sedation, end of life, palliative care, home care*

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*Address correspondence to:* Sebastiano Mercadante, MD, Pain Relief and Palliative Care Unit, La Maddalena Cancer Center, Via San Lorenzo 312,

Palermo 90146, Italy. E-mail: [terapiadeldolore@lamaddalenanet.it](mailto:terapiadeldolore@lamaddalenanet.it) or [03sebelle@gmail.com](mailto:03sebelle@gmail.com)

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## Introduction

Some terminally ill patients with cancer near the end of life may experience intolerable suffering refractory to targeted palliative therapies. The home setting has been reported to be preferred by most patients and relatives and seems to be the favorite place of death.<sup>1</sup> Admission to hospital or staying at home in this period depends on many different factors, including resource availability and personal preference, other than clinical needs.<sup>2</sup> It is likely that hospitalized patients tend to have a greater symptom burden than those who remain at home. Home care may offer a better environment, limiting the occurrence of disorientation and delirium.<sup>3</sup> However, a distressing death may be of concern for the family. Palliative sedation (PS) is a common procedure in palliative care that has caught the attention of several authors and investigation groups in the last years. According to recent definitions, PS is the use of a nonopioid sedative medication to relieve intolerable suffering in the last days of life.<sup>4,5</sup> PS is considered to be an effective treatment modality for refractory symptoms when aggressive efforts fail to provide relief in terminally ill patients with cancer.<sup>6</sup>

Although in one study the frequency of PS at home was higher than that reported in hospital (36% vs. 21%), only 36% of patients who were followed by the palliative care team died at home.<sup>7</sup> In another study of advanced cancer patients followed at home, more patients were sedated when moved to hospital than when remaining at home (32% vs. 23%).<sup>8</sup> In a systematic review of PS at home, only six papers reported data regarding patients who were sedated at home. However, data reporting indications, mean duration, and drug used for PS were not available or clearly outlined, and no a priori definition of PS was adopted.<sup>9</sup>

The Home Care—Italy Group recently has been established with the intent to report the information on cancer patients followed at home, given the paucity of existing data in this setting. The aim of this multicenter study was to retrospectively analyze the frequency, the indications, and the modalities of PS at home, in a consecutive sample of patients followed by three home care units in Italy.

## Patients and Methods

The study was conducted in three home palliative care units (HPCUs). The activities of these groups in three areas of Italy have been described elsewhere. The three palliative home care programs that participated in the study provide similar levels of assistance, with visits ranging between two to three per week for physicians and three to seven per week for nurses, in addition to providing on-call visits in case of need.<sup>10</sup>

The medical charts of all consecutive patients who received assistance from an HCPU in a six-month period were reviewed. Patients who died at home during this period were included in the study. A physician was trained to collect and enter data into a standardized data sheet. From the medical chart review, all patients who were administered “specific sedatives to relieve intolerable suffering from refractory symptoms by reducing a patient’s level of consciousness with nonopioid sedative medication in the last days of life” were selected and considered as patients receiving PS.<sup>9</sup> The characteristics of this group of patients were analyzed, as well as the indications to start PS, the duration, and the drugs and their doses used at the beginning of PS and at the time of death. Involvement of relatives in the decision-making process also was retrieved from the charts when available, and whether physicians and relatives were satisfied with the efficacy and the purpose of the treatment.

## Statistical Analysis

Collected data were analyzed using SPSS Software v.14.0 (SPSS, Inc., Chicago, IL). Descriptive summaries for all measures are reported as means and standard deviations (SD) for numeric variables, and as percentages for categorical variables. Statistical analysis of quantitative data, including descriptive statistics, was performed for all items. The Chi-squared test was used to make comparisons with respect to categorical variables, and Fisher’s exact test was used if sample size criteria were not met for Chi-squared approximation. The paired samples Student’s *t*-test was used to compare mean doses at the different intervals. The one-way analysis of variance was used for parametric analysis. All *P*-values were two-sided and *P*-values less than 0.05 were considered to indicate statistical significance.

## Results

The medical charts of 370 consecutive patients who died at home were examined. Forty-nine patients (13.2%) received PS before dying, according to the definition stated in the Methods. Thirty-three patients were male. The mean age was 72.3 (SD  $\pm$  12) years, and the primary diagnoses in rank order were gastrointestinal cancer ( $n=13$ ), lung cancer ( $n=12$ ), genitourinary cancer ( $n=10$ ), and other ( $n=14$ ).

Age and gender did not influence the parameters examined. PS was proposed by the team, relatives, or both in 63.3%, 4.1%, and 32.6% of cases, respectively. No differences in survival between patients who were sedated and those not sedated were found ( $P=0.98$ ). The mean survival in sedated and not sedated patients was 38 and 35 days, respectively. No relationship between relatives' involvement and specific symptoms requiring PS was found ( $P=0.975$ ). In two cases, PS was requested by the patients themselves (4.1%). PS was never discontinued for any reason. Duration of PS was 86 (SD  $\pm$  242) hours. Delirium alone or in combination with other symptoms was the most frequent indication to begin PS. The symptoms that prompted PS initiation are listed in Table 1.

Opioids (parenteral morphine) were started in 41 patients (84.7%) at mean doses of 25.4 mg/day (SD  $\pm$  19.6). Most patients already were receiving opioids for pain management and were continued or converted to the parenteral route. Nineteen of 21 patients with dyspnea were given opioids. No differences in use and doses of opioids were found when compared with patients who received PS and

did not have dyspnea ( $P=0.781$ ). Midazolam was started in 48 patients (98%) at mean doses of 28.1 mg/day (SD  $\pm$  2.08). Haloperidol was started in seven patients (14.3%) at mean doses of 2.8 mg.

At time of death, parenteral morphine was administered in 43 patients (87.8%) in mean doses of 28.1 mg/day (SD  $\pm$  20.8), and midazolam was administered in 48 patients (98%) at mean doses of 22.3 mg/day (SD  $\pm$  12.5). No differences between starting and final doses of both drugs were found ( $P=0.374$ ). Neuroleptics, including chlorpromazine and promethazine, were given in two and four patients, respectively.

The level of satisfaction for physicians and principal caregivers after PS was good in 46 and 48 cases, respectively. In no cases were relatives unsatisfied with the treatment, and only in one case did the physician consider PS unsatisfactory. In two cases, this information was unavailable from the chart review.

## Discussion

Results from this retrospective analysis of data regarding patients who were sedated at home before dying provide interesting information. Each HCPU used the same definition for PS. PS was found to be an effective method to relieve terminal suffering in the last days of a dying patient, especially for relatives who considered PS effective and were satisfied with the treatment. The need to begin PS was carefully explained, as evidenced in the clinical notes, and in about one-third of cases, the decision was made by the patient's relatives.

Data gathered from this study indicate a frequency of PS of 13.2%, which is lower than that found in a previous study of how cancer patients die at home (35%). This finding could be attributed to the different time periods examined and the number of units included in the survey, and the use of a different definition of PS.<sup>10</sup> Different frequencies of PS performed at home have been reported in the literature.<sup>9</sup> The large variability observed in the use of PS among centers suggests a lack of appropriate criteria adopted for definition of PS. For example, in a multi-center Italian study, the ranges varied between

Table 1  
Indications to Start PS

Reasons to Start PS	Frequency	Percentage
Delirium	26	53.1
Delirium/pain	1	2
Delirium/dyspnea	7	14.3
Dyspnea	10	20.4
Dyspnea/O	1	2
Pain	1	2
Pain/dyspnea	2	4.1
Pain/dyspnea/psychological distress	1	2
Total	49	100

PS = palliative sedation; O = other.

0% and 60%. It is likely that this implies a lack of consensus on definition of PS among the centers involved.<sup>11</sup> The frequency found in the present study also seems to be lower than the 20%–50% rate reported by hospital-based palliative care units or hospice,<sup>12–15</sup> with the highest rate in acute care units.<sup>16</sup> It is likely that hospitalized patients tend to have a greater symptom burden than those who remain at home or patients are admitted to hospital as an emergency because of the development of refractory symptoms close to death.<sup>7,8</sup> Finally, the different environment at home could potentially influence the decision to start PS; factors include lack of a continuous bedside presence, family cooperation, time for planning, and decision making in case of an emergency.<sup>9</sup>

The principal symptom to be relieved with PS was delirium; alone or in combination with other symptoms, it was the indication for PS in about 70% of patients. This confirms recent data in the home care setting<sup>3,7,17</sup> and in a pioneer study,<sup>8</sup> and is similar to data reported in a palliative care unit population.<sup>16</sup> Dyspnea was the second most frequent reason to start PS (about 43% of patients). Similar to other studies, delirium and dyspnea combined were also a most frequent indication for PS.<sup>3,17</sup> Dyspnea (52%), pain (49%), and delirium (17%) in different combinations were more frequently reported in a pioneer study as an indication for PS,<sup>8</sup> whereas in two other Italian studies, percentages were not reported.<sup>11,18</sup> Pain seems to be a relatively infrequent indication for PS, reflecting other recent experiences;<sup>3,7</sup> this differs from the early study, where drowsiness was not clearly distinguished from PS,<sup>8</sup> and a more recent study performed in Israel, where uncontrolled pain was deemed to require PS at the end of life in more than half of patients followed at home.<sup>17</sup> It is likely that an unclear definition of PS, including, for example, the use of opioids for sedating patients for pain relief, biased these data. This is confirmed by the use of increasing doses of opioids, given alone, to achieve PS.<sup>17</sup> In the present study, doses of opioids remained relatively stable, as did doses of midazolam. Morphine, converted to the parenteral route, was, in most cases, a continuation of the previous treatment for pain.

Midazolam was the drug most frequently used to begin and maintain PS for almost all

patients. This drug preference also was reported in another retrospective analysis of patients who died at home.<sup>3</sup> Similarly, doses of midazolam did not change significantly until death; this differs from data found in patients followed on an acute care unit.<sup>16</sup> It is likely that patients admitted in such units may have more intense distressing symptoms or may be receiving large amounts of other drugs prescribed previously. However, doses of midazolam were lower than those reported (about 60–100 mg/day) in a similar retrospective study performed in a single institution in Spain.<sup>3</sup>

Duration of sedation was in the range of previous experience (more than 72 hours) when compared with previous experiences at home where duration of PS largely varied, ranging from one day or less to 13 days, with an average duration of two to three days.<sup>9</sup>

No differences in survival were evident between patients who received PS and patients who did not undergo this treatment. This was similar to the results reported in other studies performed at home,<sup>3,7,18</sup> confirming that both the aim and the effect of PS do not result in shortening survival when used to relieve refractory symptoms.<sup>15</sup>

Finally, both physicians and relatives were satisfied with the treatment, and in many cases, relatives asked to start PS before a team member could propose it, suggesting that the decision was shared to a great degree with the team members and an agreement was clearly achieved before starting PS. In a web-based structured questionnaire, PS was considered insufficiently effective by 42% of home care nurses. However, these data expressed just an opinion rather than raw data.<sup>19</sup>

Informed consent was obtained from patients or relatives after an agreement among staff members was achieved.<sup>7</sup> Verbal informed consent to initiate PS was received directly from patients deemed to be competent or from their immediate family member.<sup>17</sup> However, in a large Italian study, 62% of the sedated patients at home had not been informed, and data regarding relatives were unavailable.<sup>18</sup> More awareness of prognosis was found in patients who were sedated before death, and the decision to start sedation was made with the patient in 45% of cases.<sup>3</sup> In previous experiences at home, no formal evaluation and outcomes of

PS have been reported.<sup>9</sup> Marked and good improvement in symptom control was achieved in 61% and 17% of patients, respectively.<sup>17</sup>

Data gathered from this study have the obvious limitations as a result of its retrospective nature. However, the data set was simple and the standardized checklist minimized data missed, as demonstrated by data retrieved and available for analysis.

PS appears to be a feasible treatment at home. This treatment was considered safe and effective by both team members and relatives, who shared the decision to relieve intractable symptoms at the end of life and achieve a peaceful death for the patient.

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