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Opioid consumption by cancer patients in an in-patient hospice — a retrospective study

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Abstract

Introduction. Opioids are essential in relieving moderate to severe pain in patients in palliative care. This study aimed to assess daily opioid consumption in cancer patients hospitalized in an in-patient hospice from admission to the end of their stay.

Material and methods. This retrospective, single-center study was performed in a Hospice in Olsztyn. The total amount of daily opioid intake was studied at three time points: on the second, seventh day, and penultimate days of patients' stay in the stationary hospice. The doses of various opioids were converted to an equivalent dose of oral morphine in milligrams [morphine equivalent daily dose (MEDD)].

Results. Forty-two percent of patients started their stay at the stationary hospice without opioid drugs. There was a significant difference in MEDD between the second day (53.31 mg) and penultimate day (80.96 mg) of stay for 72 patients (we excluded patients, who had lived fewer than 4 days) ($p < 0.001$). Among the 60 patients (excluding patients who lived fewer than 8 days) MEDD increased from the second (44.47 mg) to the seventh day (68.02 mg) ($p < 0.01$), and then the dose slightly decreased on the penultimate day of their stay (63.15 mg) ($p = 0.04$). In the case of patients who started hospitalization without opioids, MEDD on the seventh day was 14.29 mg ($p < 0.01$) and 28.57 mg on the penultimate day ($p < 0.001$). A significant negative linear correlation between MEDD and age was shown.

Conclusions. Opioid consumption increased during patients' stay at in-patient hospice. Younger patients needed higher doses of opioids.

Keywords: opioid consumption, hospice, cancer patients, morphine equivalent daily dose

Introduction

Pain management is a crucial aspect of palliative care, and opioids are the primary drugs in relieving moderate to severe pain [1–4]. However, it appears that pain is often inadequately controlled, especially in terminally ill patients [5–7]. Therefore, understand-

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ing opioid consumption patterns in hospice patients is critical not only to provide effective pain control but also to optimize the use of healthcare resources. Rising rates of opioid abuse worldwide have led to the implementation of policies to decrease opioid prescriptions. There is evidence that policy can affect opioid prescribing rates outside palliative care, but there is limited evidence to suggest how policy affects opioid prescribing in hospices [8]. Opioid use among patients dying of cancer in the United States has declined substantially from 2007 to 2017 and rising numbers of pain-related emergency department visits suggest that near-the-end-of-life cancer pain management may be worsening [9].

Previous studies have explored various aspects of opioid use in palliative care, including patient characteristics that may influence consumption [10–12]. However, a detailed retrospective analysis of opioid use, in terms of daily consumption and variations over time, particularly in hospice patients, remains less explored. These gaps in knowledge pose a challenge to healthcare providers who are responsible for meeting patient needs and properly allocating resources.

This study aimed to assess daily opioid consumption among cancer patients hospitalized in an in-patient hospice from admission to the end of their stay.

Material and methods

Study design and setting

The study included a group of consecutive 100 hospice patients hospitalized from 1 January 2022 in a Hospice in Olsztyn. A list of 100 cancer patients was generated from the hospital system. The study assessed individual patients' opioid consumption during their stay in the stationary hospice. The total amount of opioid intake was studied, taking into account treatment of baseline pain and breakthrough pain. The doses of various opioids were converted to an equivalent dose of oral morphine in milligrams [morphine equivalent daily dose (MEDD)] [13]. The doses of daily opioid use were measured at three time points: on the second, seventh, and penultimate days of these patients' stay in the stationary hospice.

Demographic data (age, sex), type of cancer, and length of stay in the in-patient hospice were collected to identify the factors that could have influenced MEDD.

Nine patients were excluded from the analysis because they started hospitalization before 1 January 2022. Among the remaining 91 cancer patients, 2 patients, who had died on the first day of hospitalization, were excluded from the analysis. Eighty-nine patients, who stayed in the stationary hospice for at least 2 days were included in the analysis of MEDD on the second day of stay. Seventy-two patients, who stayed in the stationary hospice for at least 4 days were included in the comparative analysis of MEDD on the second and penultimate day. The analysis of MEDD at all 3 time points (second, seventh, and penultimate day) was conducted on a group of 60 patients, who stayed in the stationary hospice for at least 8 days (Fig. 1). Eighty-five patients (93%) of 91 analyzed cases died in the hospice.

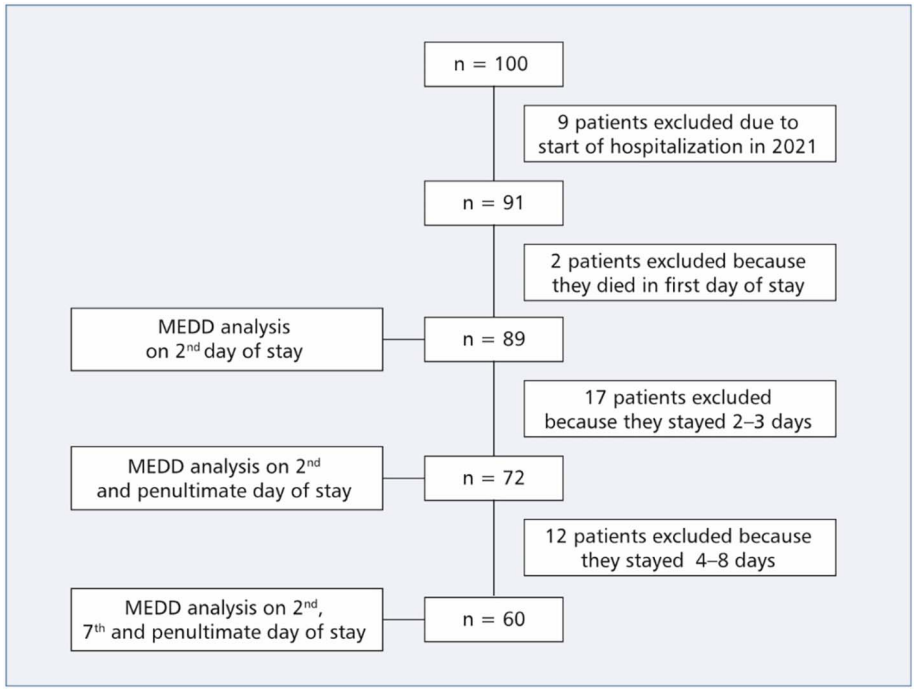

Figure 1. Flowchart of first 100 inpatients in a Hospice in Olsztyn in 2022; MEDD — morphine equivalent daily dose

Statistical analysis

The data were presented as means and standard deviations for continuous variables and as frequencies, and percentages for categorical variables. The normality of data distribution was tested using the Shapiro-Wilk test. The daily opioid consumption (MEDD) on the second, seventh, and penultimate days of patients' stay at the hospice was compared using the Wilcoxon pair test (for 2 time points) or Friedman test, with posthoc pairwise comparisons performed using the Durbin-Conover test (for 3 time points). The correlation between total daily opioid consumption on the penultimate day and patients' age and length of stay in the stationary hospice were examined using the Spearman rank correlation coefficient. The differences in total daily opioid consumption on the penultimate day according to type of cancer and sex were determined using the Kruskal-Wallis test and Mann-Whitney U test, respectively. A p-value < 0.05 was considered to be significant. Statistical analyses were performed using R software and the 'ggstatsplot' approach [14].

Results

Patient characteristics

Patients age ranged from 49 to 96 years (mean 72 years). There were 57% women and 43% men. The mean length of stay in the hospice was 28 days. Patients undergoing palliative care were diagnosed with various cancers, mostly lower digestive system cancer (15.7%), upper digestive system cancer (13.5%), lung cancer (12.4%), gynecological cancer (10.1%), head and neck cancer (10.1%), breast cancer (9%), and unknown primary site cancer (7.9%) (Tab. 1).

Table 1. Characteristics of patients who stayed at the in-patient hospice for at least 2 days

	n = 89	
	Mean	**SD**
Age [years]	72	± 10.7
Stay at the in-patient hospice [days]	28	± 55.8
	n	**[%]**
Sex		
Male	38	42.7
Female	51	57.3
Cancer		
Lower digestive system	14	15.7
Upper digestive system	12	13.5
Lung	11	12.4
Gynecological	9	10.1
Head and neck	9	10.1
Breast	8	9.0
Unknown primary site	7	7.9
Prostate	5	5.6
Urinary system except for prostate	4	4.5
Brain	4	4.5
Other	6	6.7

SD — standard deviation

Table 2. Initial doses of morphine equivalent daily dose (MEDD)

Initial MEDD [mg]	n = 89	[%]
0	37	42
< 30	12	13
30–60	18	20
> 60	22	25

Opioid consumption analysis

The total daily consumption of opioid drugs, converted into oral morphine equivalent dose (MEDD) was calculated.

The mean MEDD on the second day of stay at the in-patient hospice determined for 89 patients was 50.97 ± 71.14 mg. Thirty-seven patients (42%) started in-patient hospice stay without any opioids. Among 52 patients, who were under opioid treatment, 22 patients (42%) received MEDD above 60 mg (Tab. 2).

A total of 72 patients were included in the MEDD analysis on the second and penultimate days of their stay in the hospice. Changes in MEDD were assessed, and it was found that MEDD significantly increased from the second day (mean 53.31 ± 75.78 mg) to the penultimate day (mean 80.96 ± 109.54 mg) (p < 0.001) (Fig. 2). Of 72 patients who stayed in the stationary hospice for at least 4 days, 31 patients (43%) had no opioids at the start. On the penultimate day of stay in the stationary hospice, no opioid use was reported among 16 individuals (22% of all 72 analyzed patients and 52% of 31 patients without opioid consumption at the start). Four of 41 patients who received opioids on the second day (10%) received additional doses of opioids, while only 3 of 57 patients received opioids on the penultimate day (5%).

A comparative analysis of MEDD in 60 patients was conducted across three time points: the second, seventh day, and penultimate days of the stay in the in-patient hospice. There was a significant difference in daily opioid consumption (p < 0.001). Post-hoc analysis using the Durbin-Conover test showed significant differences in opioid consumption between all the time points. On the second day of stay, among 60 patients who were in the stationary hospice for more than 8 days, the mean MEDD was 44.47 ± 65.15 mg, on the seventh day 68.02 ± 103.17 mg, and on the penultimate day 63.15 ± 69.80 mg (Fig. 3A).

Among the 60 analyzed patients, 28 individuals (47%) started hospitalization in the inpatient hospice without any opioid drugs. Opioid consumption significantly increased over time in this subgroup (p < 0.001). On the seventh day of their

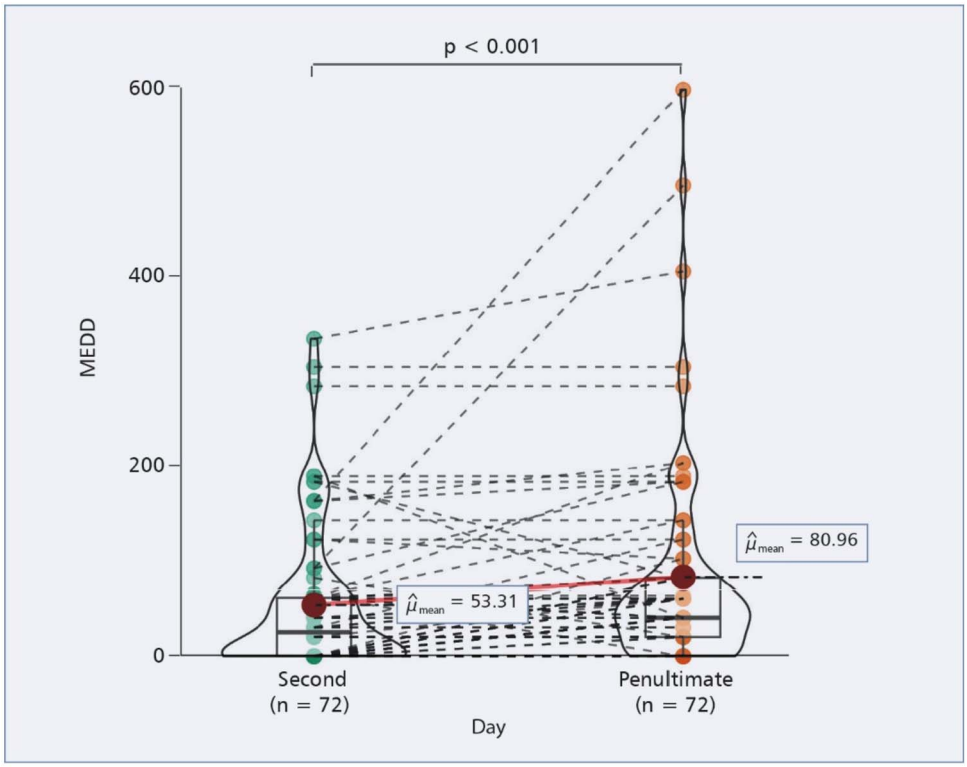

Figure 2. Changes in morphine equivalent daily dose (MEDD) during the stay at the in-patient hospice (2nd *vs.* penultimate day)

stay in the in-patient hospice, the mean MEDD was 14.29 ± 22.84 mg ($p < 0.01$), and on the penultimate day of their stay, the mean MEDD was 28.57 ± 31.94 mg ($p < 0.001$) (Fig. 3B). Half of these patients (14 patients) received opioids to the end of their hospitalization.

Among the 60 analyzed patients, 32 patients (53%) received opioids from the time of admission. In this subgroup, there were no significant differences between time points ($p = 0.09$). The mean MEDD on the second day of their stay was 83.38 ± 68.76 mg, and it increased to 115.03 ± 122.13 mg on the seventh day. A decrease in MEDD was then observed on the penultimate day, with a mean of 93.41 ± 79.75 mg (Fig. 3C).

Twelve patients (38%) at the start of hospitalization received > 60 mg MEDD. There were no significant differences over time ($p = 0.97$). On the second day of their stay, the mean MEDD was 149.83 ± 71.81 mg on the seventh day 166.25 ± 125.75 mg, and on the penultimate day 140.75 ± 103.41 mg (Fig. 3D).

Correlations between MEDD on the penultimate day due to age, length of stay, sex, and type of cancer

A significant negative linear correlation between MEDD calculated on the penultimate day of stay in the stationary hospice and age was observed ($p < 0.01$) (Fig. 4). There were no significant differences in MEDD on the penultimate day of stay due to cancer type, sex, and length of stay at the hospice ($p > 0.05$) (Tab. 3).

Discussion

The majority of cancer patients in the present study were receiving opioids during their stay in the stationary hospice. Fifty-eight percent of patients obtained opioids at the start of hospitalization in the stationary hospice and 78% of patients on the penultimate day of stay in the stationary hospice, i.e. on the day before death. Some patients in palliative care need opioid pain management [4, 15]. Opioids are among the most commonly prescribed medications, and 60% of patients with cancer receive opioid analgesia [16]. Gerlach et al. [17] demonstrated that 63.3% of hospice patients from 554 022 analyzed individuals were prescribed opioids in the United States in the years 2014–2016. Compared to other hospice principal diagnoses, cancer patients were significantly more likely to receive opioids [17]. The results of the present study showed that cancer patients begin their in-patient hospice stay on a relatively low dose of opioid drugs — mean MEDD for all investigated individuals was 50.97 mg. Only 25% of patients required MEDD above 60 mg and as many as 42% of patients did not require opioid pain management. However, opioid consumption by patients hospitalized

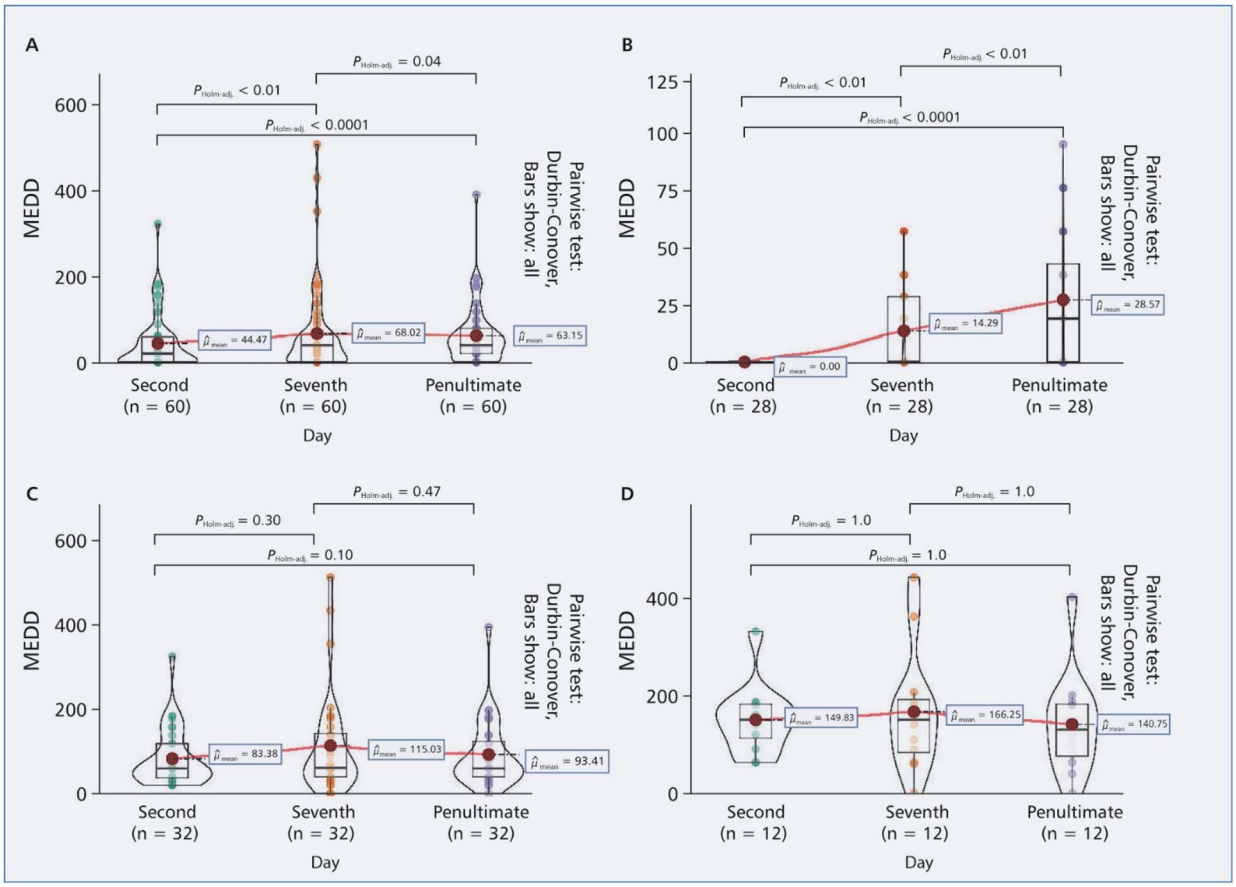

Figure 3. Changes in morphine equivalent daily dose (MEDD) at the in-patient hospice (2nd *vs.* 7th vs. penultimate day); **A.** Group of 60 patients, who had MEDD analysis on the 2nd, 7th, and penultimate days; **B.** Group of 28 patients (from 60 patients), who had initial MEDD = 0; **C.** Group of 32 patients (from 60 patients), who had MEDD > 0; **D.** Group of 12 patients (from 60 patients), who had MEDD > 60

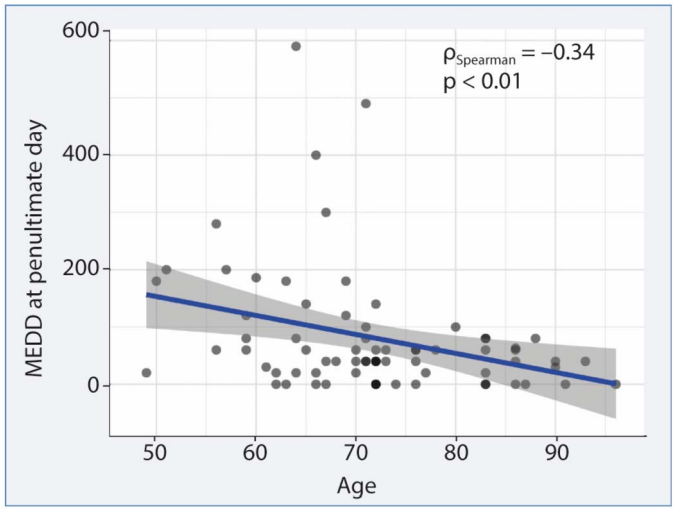

Figure 4. Correlation between morphine equivalent daily dose (MEDD) on the penultimate day and age (n = 72)

at the in-patient hospice increased significantly during their stay. However, 22% of cancer patients did not require opioid treatment until the end of their in-patient hospice stay. This applies to half of those who did not take any opioid drugs at the beginning. Evaluation of interviews with hospice staff in the United States found that opioids were prescribed to 92% of all hospice patients within the last week of life [18].

Table 3. Correlations between morphine equivalent daily dose (MEDD) on the penultimate day and length of stay at the in-patient hospice, sex, and type of cancer (n = 72)

	n = 72		
	MEDD at penultimate day [mg]		p-value
Stay at the in-patient hospice	r = 0.03		> 0.05
	Mean	**SD**	
Sex			0.40
Male	82.2	± 99.8	
Female	80.1	± 117.2	
Cancer			0.43
Lower digestive system	52.5	± 55.1	
Upper digestive system	143.3	± 179.7	
Lung	82.5	± 98.8	
Gynecological	178.0	± 243.1	
Head and neck	114.3	± 104.1	
Breast	40.0	± 68.3	
Unknown primary site	82.5	± 39.0	

r — correlation coefficient; SD — standard deviation

This study identified a trend in opioid dose use in the in-patient hospice setting. This pattern is characterized by a significant increase in MEDD from the second to seventh day ($p < 0.01$), and then holding the dose constant with a tendency to decrease ($p = 0.04$) on the penultimate day of the patient's stay. In an analysis of older hospice patients in the United States, opioid prevalence increased in the patients staying in the hospice for > 7 days [17]. In the present study, it seems that the opioid dose set after one week of the patient's stay in the stationary hospice was already optimal and was not increased until the end of the stay, and even slightly decreased on the penultimate day of stay, which was generally the patients' penultimate day of life. Pain treatment at the stationary hospice seems to have been effective, as only 4 of 41 patients who had received opioids on the second day (10%) were administered additional doses of opioids. On the penultimate day of the stay in the hospice, only 5% of patients who had received opioids needed an extra dose of an opioid drug.

Half of the patients who did not receive opioids at the start of their stay finally had to get opioid pain management. For patients who did not have opioids at the beginning, the consumption of opioids was systematically increasing and on the penultimate day, MEDD was significantly higher than on day 7. It could suggest that these patients needed opioid treatment earlier. There are probably some barriers to using opioid pain management: opioidophobia, fear of using morphine and its side effects from patients and physicians, and systemic and regulatory barriers [5].

The presence study showed a significant negative correlation between MEDD calculated on the penultimate day of stay and age. Vigano et al. [10] also observed that elderly patients require a lower dose of opioids on the second day ($p = 0.007$). Patients over 75 years of age required 27–71 mg of parenteral morphine per day less than younger patients, experiencing similar levels of pain [10]. Bercovitch et al. [11] investigated 453 palliative cancer patients who received morphine for pain relief and noted that there was a negative association with age ($p = 0.01$). The elderly may have a higher threshold for pain [10]. Elderly patients may require smaller doses of opioids because they achieve better analgesia from them [19] and due to higher levels of morphine and its metabolites and longer duration of opioid analgesia [20]. In a Polish study conducted by Życzkowska et al. [12], the authors noted that in patients under 60 years old, the difference between the daily dose of opioids on the last and first days of hospitalization was the highest.

Another observation in current study was the lack of a significant correlation between the duration of patients' stay in the in-patient hospice and their total daily opioid consumption. This differs from the study by Hardy et al. [21], where a positive correlation was reported.

Our study showed no significant discrepancy in total daily opioid consumption between men and women. This is consistent with other research suggesting that sex may not significantly affect pain management requirements in hospice care [10, 22]. However, some authors have observed correlations with sex. Male patients in a study by Bercovitch et al. [11] required slightly higher dosages than female patients. In the study by Życzkowska et al. [12], women under the age of 60 years had a significantly higher MEDD than men, except for the start of hospitalization.

In terms of tumor types, this study showed the highest MEDD in patients with gynecological cancers, upper digestive system cancers, and head and neck cancers, and the lowest MEDD in patients with breast cancer. However, we did not analyze whether our patients had bone metastases and patients with bone metastases often require a higher dose of pain medication. In a study by Bercovitch et al. [11], patients with metastases to bone and with spinal diseases needed higher morphine doses.

Limitations

However, our study has some limitations. It was a retrospective and single-center study. The number of analyzed patients was relatively small. Some other factors that might affect opioid consumption, such as previous oncological treatment, general health condition, comorbidities, and pain localization and severity, were not been studied.

Conclusions

Not all cancer patients during hospitalization in in-patient hospices need opioid pain management. In

our study, opioid consumption increased during our patients' stay. However, in the case of patients who started their stay in the stationary hospice with opioids, dose escalation was not significant. In the case of patients, who had no opioid drugs at the start, the dose increased significantly, both on the seventh and penultimate days of stay at the in-patient hospice. Younger patients needed higher doses of opioids.

Article Information and Declarations

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics statement

The study was conducted according to the criteria set by the Declaration of Helsinki.

Author contributions

B.Kędziora: investigation, data analysis, and interpretation, writing — original draft; J.T.: investigation, writing — original draft; B.Komsta: data collection; K.O.: methodology, data analysis, and interpretation, writing — original draft and review and editing; M.R.: conceptualization, methodology, writing — original draft and review and editing.

All authors read and approved the final version of the manuscript.

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None.

Conflict of interest

The authors declare no conflict of interests

Supplementary material

None.

References

1. Sinha A, Deshwal H, Vashisht R. End-of-Life Evaluation and Management of Pain. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. 2023, indexed in Pubmed: 33760512.
2. Rucińska M. Podstawowe zasady leczenia bólu u chorych na nowotwory – aktualne wytyczne. Onkologia po Dyplomie. 2021; 18(5): 21–25.
3. Swarm RA, Paice JA, Anghelescu DL, et al. BCPS. Adult Cancer Pain, Version 3.2019, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2019; 17(8): 977–1007, doi: 10.6004/jnccn.2019.0038, indexed in Pubmed: 31390582.
4. Caraceni A, Hanks G, Kaasa S, et al. European Palliative Care Research Collaborative (EPCRC), European Association for Palliative Care (EAPC). Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC. Lancet Oncol. 2012; 13(2): e58–e68, doi: 10.1016/S1470-2045(12)70040-2, indexed in Pubmed: 22300860.
5. Scarborough BM, Smith CB. Optimal pain management for patients with cancer in the modern era. CA Cancer J Clin. 2018; 68(3): 182–196, doi: 10.3322/caac.21453, indexed in Pubmed: 29603142.
6. Kwon JH. Overcoming barriers in cancer pain management. J Clin Oncol. 2014; 32(16): 1727–1733, doi: 10.1200/JCO.2013.52.4827, indexed in Pubmed: 24799490.
7. Apolone G, Corli O, Caraceni A, et al. Cancer Pain Outcome Research Study Group (CPOR SG) Investigators. Pattern and quality of care of cancer pain management. Results from the Cancer Pain Outcome Research Study Group. Br J Cancer. 2009; 100(10): 1566–1574, doi: 10.1038/sj.bjc.6605053, indexed in Pubmed: 19401688.
8. Borders JR, Letvak S, Amirehsani KA, et al. Opioid epidemic and prescribing in hospice and palliative care: a review of the literature. Int J Palliat Nurs. 2021; 27(5): 255–261, doi: 10.12968/ijpn.2021.27.5.255, indexed in Pubmed: 34292770.
9. Enzinger AC, Ghosh K, Keating NL, et al. US Trends in Opioid Access Among Patients With Poor Prognosis Cancer Near the End-of-Life. J Clin Oncol. 2021; 39(26): 2948–2958, doi: 10.1200/JCO.21.00476, indexed in Pubmed: 34292766.
10. Viganó A, Bruera E, Suarez-Almazor ME. Age, pain intensity, and opioid dose in patients with advanced cancer. Cancer. 1998; 83(6): 1244–1250, indexed in Pubmed: 9740092.
11. Bercovitch M, Waller A, Adunsky A. High dose morphine use in the hospice setting. A database survey of patient characteristics and effect on life expectancy. Cancer. 1999; 86(5): 871–877, doi: 10.1002/(sici)1097-0142(19990901)86:5<871::aid-cncr25>3.0.co;2-l, indexed in Pubmed: 10463988.
12. Życzkowska J, Grądalski T, Kleja J, et al. Age influence on opioid consumption in terminally ill digestive cancer patients. Palliat Med Pract. 2013; 7(2): 50–54.
13. Perkins R, Fudin J, Gudin J. Opioid calculator. Practical pain management. Published 2018. https://opioidcalculator.practicalpainmanagement.com.
14. Patil I. Visualizations with statistical details: The 'ggstatsplot' approach. Journal of Open Source Software. 2021; 6(61): 3167, doi: 10.21105/joss.03167.
15. Ventafridda V, Tamburini M, Caraceni A, et al. A validation study of the WHO method for cancer pain relief. Cancer. 1987; 59(4): 850–856, doi: 10.1002/1097-0142(19870215)59:4<850::aid-cncr2820590432>3.0.co;2-1, indexed in Pubmed: 3802043.
16. Sera L, McPherson ML, Holmes HM. Commonly prescribed medications in a population of hospice patients. Am J Hosp Palliat Care. 2014; 31(2): 126–131, doi: 10.1177/1049909113476132, indexed in Pubmed: 23408370.
17. Gerlach LB, Kales HC, Kim HM, et al. Prevalence of psychotropic and opioid prescribing among hospice beneficiaries in the United States, 2014-2016. J Am Geriatr Soc. 2021; 69(6): 1479–1489, doi: 10.1111/jgs.17085, indexed in Pubmed: 33683703.
18. Lau DT, Dwyer LL, Shega JW, et al. Medications That Older Adults in Hospice Care in the United States Take, 2007. J Am Geriatr Soc. 2015; 63(11): 2282–2289, doi: 10.1111/jgs.13795, indexed in Pubmed: 26531894.
19. Bellville JW, Forrest WH, Miller E, et al. Influence of age on pain relief from analgesics. A study of postoperative patients. JAMA. 1971; 217(13): 1835–1841, indexed in Pubmed: 5109724.
20. McQuay HJ, Carroll D, Faura CC, et al. Oral morphine in cancer pain: influences on morphine and metabolite concentration. Clin Pharmacol Ther. 1990; 48(3): 236–244, doi: 10.1038/clpt.1990.145, indexed in Pubmed: 2401122.
21. Hardy N, Zeba F, Ovalle A, et al. Association of prescription opioid use on mortality and hospital length of stay in the intensive care unit. PLoS One. 2021; 16(4): e0250320, doi: 10.1371/journal.pone.0250320, indexed in Pubmed: 33886667.
22. Mercadante S, Casuccio A, Fulfaro F. The course of symptom frequency and intensity in advanced cancer patients followed at home. J Pain Symptom Manage. 2000; 20(2): 104–112, doi: 10.1016/s0885-3924(00)00160-3, indexed in Pubmed: 10989248.