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Neuropsychiatric Symptoms and Use of Psychotropics in the Last Week of Life in Patients with Advanced Cancer

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Abstract: *Neuropsychiatric symptoms such as delirium, anxiety, depression, and agitation are prevalent among cancer patients at the end of life, significantly impacting quality of life for both patients and caregivers. Despite their clinical importance, these symptoms are often underrecognised and undertreated. This study aims to assess the frequency of neuropsychiatric symptoms and use of psychotropics in the last week of life in patients with advanced cancer. We conducted a retrospective review of medical records from adult cancer patients who died between January 1, 2024 and September 31, 2024, at Hospice Casa Sperantei and County Emergency Hospital of Brasov, Romania. Data collected included demographic information, documented neuropsychiatric symptoms, and psychotropic prescriptions in the last week of life. Descriptive statistics and subgroup analyses were used to assess symptom prevalence and prescribing trends. Among 305 patients included in the analysis, 70 (23%) had delirium, 55 (18%) had confusion, and 50 (16.4%) had insomnia. The main risk factors for delirium were nausea and constipation. The most used psychotropics in the last week of life were Haloperidol, Midazolam, and Lorazepam, but the patterns of prescribing varied by care setting. These findings highlight the need for improved recognition and management of psychiatric symptoms in palliative care, as well as the development of evidence-based prescribing guidelines to support appropriate and effective psychotropic use in this vulnerable population.*

Keywords: *advanced cancer; last week of life; delirium; confusion; insomnia; psychotropics.*

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1. Introduction

In the last week of life, patients with advanced cancer suffer from a range of severe problems (Kobayakawa et al., 2017). These may include pain, fatigue, delirium, dyspnea, confusion, seizures, nausea, vomiting, insomnia, drowsiness and others (Azhar & Hui, 2022). During the dying phase, certain symptoms may be misdiagnosed and inadequately managed, often escalating in severity as patients near death (Hui et al., 2019; Perez-Cruz et al., 2014). These aspects are highly problematic because they compromise the quality of life and are associated with a greater burden among caregivers (Bernard et al., 2017).

Among the neuropsychiatric symptoms, terminal delirium is the most common, affecting approximately 85% to 88% of patients during the final week of life (Grassi et al., 2015; Ijaopo et al., 2023). From these patients, almost 50–70% have hyperactive or mixed delirium, which is marked by agitation and commonly accompanied by hallucinations, delusions, and hypervigilance. Agitation can range from restlessness to aggressive behaviour, which might compromise the safety of patients, caregivers, and healthcare professionals (Hui, Cheng, & Paiva, 2024). Despite its high prevalence, delirium is frequently misdiagnosed and may be confused with conditions such as depression, anxiety, insomnia, dementia, or psychosis (de la Cruz et al., 2015). The presence of delirium decreased survival of patients with advanced cancer (Corli et al., 2021), and symptom management became challenging (Azhar & Hui, 2022). In the last days of life, the cause of terminal delirium is multifactorial and irreversible (Jennes et al., 2024), and the goals of treatment are palliation of symptoms and offering comfort to patients (Hui, Cheng, & Paiva, 2024).

To manage neuropsychiatric symptoms in patients with advanced cancer in the last week of life, clinicians must be able to diagnose them, assess the potential underlying factors appropriately and understand the benefits and risks of the pharmacological and nonpharmacological interventions (Breitbart, Alici, & Nelson, 2008). These aspects raise significant challenges for patients during the dying process, particularly for those experiencing hypoactive delirium, characterised by a reduced level of consciousness and difficulties in communication (Azhar & Hui, 2022).

The present study aimed to assess the frequency of neuropsychiatric symptoms and use of psychotropics in the last week of life in patients with advanced cancer.

2. Materials and Methods

Study design

This is a retrospective, multicenter study conducted in four clinical settings: an inpatient palliative care unit, a home-care service, an oncology ward and an intensive care unit.

Settings

The oncology ward and intensive care unit are from County Emergency Hospital of Brasov, Romania. Inpatients' palliative care unit and home care service are from Hospice Casa Sperantei, Brasov, Romania.

Data collected

Sociodemographic data such as age, gender, marital status, and place of care, as well as clinical information including diagnosis, presence of metastases, comorbidities, and use of psychotropic medications, were extracted from the patients' medical records.

For the inpatients' palliative care unit and home care service, we collected data on neuropsychiatric symptoms by reviewing standardised medical records routinely used across palliative care settings at the national level. These records, such as the General Clinical Observation Sheet for Palliative Care, include structured sections for documenting patient symptoms, treatments, and clinical

observations. These forms allowed us to retrospectively extract relevant information on symptoms such as delirium, confusion and insomnia recorded by healthcare professionals during the dying phase.

For the oncology ward and intensive care unit, data on neuropsychiatric symptoms were collected retrospectively from patients' medical records. As there was no single standardised assessment tool applied across all cases, symptom information was extracted from different sources within the medical records, such as progress notes, observation sheets, and symptom checklists.

Data were collected by a single researcher using a structured data extraction tool. The tool was designed to integrate relevant information about neuropsychiatric symptoms and psychotropic medication. This approach aimed to standardise data collection and ensure consistency across cases.

Study population

The study population included all patients with cancer who died at Hospice Casa Sperantei, Brasov, Romania and County Emergency Hospital of Brasov, Romania, between January and September 2024 (N-305). The inclusion criteria were patients over 18 years of age, diagnosed with advanced-stage cancer, and who died in one of the medical settings above. There were excluded patients who died within the first 24 hours of admission in one of the medical settings.

Ethical Considerations

The study protocol was approved by the Ethics Committee of the Hospice Casa Sperantei (08 / 31.10. 2024) and County Emergency Hospital (10327/18.06.2024).

Statistical Analysis

Data analysis was conducted using SPSS Statistics 20. In the descriptive analysis, qualitative variables are reported as frequencies and percentages, while quantitative variables are presented as means and standard deviations. The sociodemographic and clinical characteristics of patients with and without delirium were compared using the chi-square test, with p-values < 0.05 considered statistically significant. Cases with missing values were excluded listwise in all relevant analyses.

3. Results

Between January and September 2024, 160 (52.6%) patients died in home care service, 89 (29.1%) in an inpatient palliative care unit, 49 (16%) in an oncology ward and 7 (2.3%) in an intensive care unit. The median age of the whole sample was 70.29 (19–99) years, and 50.2% were male. The most common primary cancer sites were digestive (35%), lung (16.1%), genitourinary (16%), head and neck (9.5%), breast (9.5%), bladder, skin, kidney, bones and haematological. Over 77% of patients had metastases, and over 75% had different comorbidities (Table 1).

Prevalence of neuropsychiatric symptoms

From all 305 patients, 70 (23%) had delirium, 55 (18%) had confusion, and 50 (16.4%) had insomnia. The prevalence of neuropsychiatric symptoms differed depending on the care setting. The highest rates of delirium (47%), confusion (45%), and insomnia (62%) were reported among patients receiving home care services.

Table 1. Sociodemographic and clinical characteristics of patients in relation to place of care

Category	All N/%	Inpatients PC Unit	Home Care	Oncology	Intensive Care Unit
Number of patients	305	89	161	49	7
Age (average, min, max)	70.29	71.53 (89-89)	71.15 (19-99)	65.9(43-80)	65.5 (53-74)
Gender					
Male	154 (50.2)	46	76	27	5
Female	152 (49.8)	43	85	22	2
Diagnostic					
Head &Neck	40 (9.5)	5	27	7	2
Digestive	107 (35)	32	59	13	3
Lung	49 (16.1)	13	23	12	1
Breast	29 (9.5)	11	14	4	0
Female genital tumours	30 (9.8)	7	14	8	1
Male genital tumours	19 (6.2)	6	12	1	0
Bladder tumours	10 (3.2)	7	3	0	0
Melanoma	6 (1.9)	1	4	1	0
Kidney tumours	7 (2.3)	3	1	3	0
Bones	1 (0.3)	0	1	0	0
Hematologic	7 (2.3)	4	3	0	0
Comorbidities					
Yes	229 (74.8)	68	118	38	5
No	76 (25.2)	21	42	11	2
Metastases					
Yes	237 (77.7)	67	120	44	6
No	68 (22.3)	22	41	4	1
Neuropsychiatric symptoms					
Delirium	70 (23)	28	33	8	1
Confusion	55 (18)	20	26	9	0
Insomnia	50 (16.5)	10	31	6	3

Confusion (61%) and delirium (56%) were more frequently observed in patients aged over 71 compared to younger age groups. However, no significant differences were found in the occurrence of delirium, confusion, or insomnia based on gender, age, comorbidities, or the presence of metastases.

Correlation between delirium and other symptoms

Related to other symptoms that appear in the last week of life, the presence of nausea ($p < 0.005$) and constipation ($p < 0.002$) were significantly correlated with the presence of delirium (Table 2). No significant differences were observed in the prevalence of other symptoms, such as pain, fatigue, dyspnea, drowsiness, confusion, and insomnia, between patients with and without delirium.

Table 2. Prevalence of end-of-life symptoms according to the presence of delirium

Symptoms	All patients	Presence of delirium (%)		P value
	N (305)/%	YES (N 70)	NO (N235)	
Pain	295 (97)	66 (85.7)	229 (97.4)	0.192
Fatigue	247 (81)	51 (73.8)	196 (83.4)	0.048
Dyspnea	85 (27.8)	22(31.4)	63(19.4)	0.449
Nausea	113 (37)	16 (22.8)	97 (41.3)	0.005
Death rattle	57 (18.7)	10 (14.3)	47 (20)	0.282
Constipation	191 (62.6)	33 (47.2)	158 (67.2)	0.002
Bleeding	49 (16.1)	8 (11.4)	41 (17.4)	0.229
Insomnia	50 (16.4)	12 (16.4)	38 (16.2)	0.847
Drowsiness	90 (29.5)	15 (21.4)	75(32)	0.091
Confusion	55 (18.1)	18(25.7)	52 (22.2)	0.057
Differences between the two groups were tested using chi-square test				

Use of psychotropic medications

Out of 305 patients, 195 (64%) required psychotropic medications. With seven days before death, the most used drugs were Haloperidol and Lorazepam. On the last day of life, the use of Midazolam increased from 56 patients to 79, and the use of Lorazepam decreased from 76 to 52 patients. Among the psychotropics, Haloperidol showed the greatest increase in average dose from 1.91 mg seven days before death to 2.75mg in the last day of life (Figure 1).

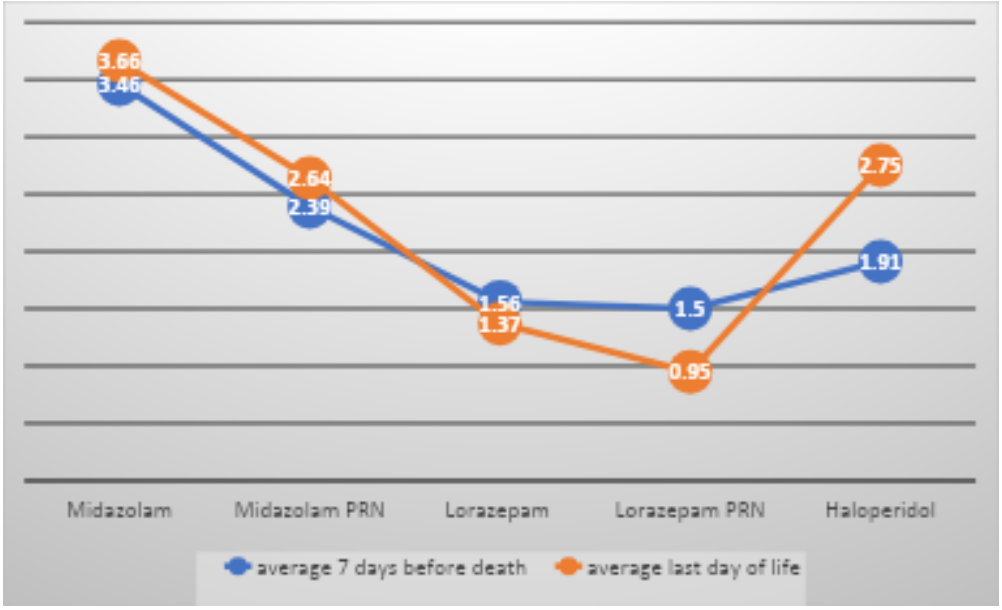

Figure 1. Average doses per drug - 7 days before death and the last day of life

For the management of delirium, the most used drugs were Haloperidol (40%) and Midazolam (37%), followed by Lorazepam (10%). In a few cases, Midazolam was combined with Haloperidol (8.5%), while Levomepromazine was used less frequently (4.5%). In 33% of patients, psychotropic dosages needed to be increased; in 1%, the dosage was reduced; and in 66%, the same dosage was maintained throughout care.

The use of psychotropic medications varied across care settings. In the inpatient palliative care unit, Midazolam was the most commonly used (64%). In-home care services, Haloperidol (40%) and Lorazepam (38%) were the most frequently administered. In the oncology ward, Haloperidol was used in 70% of cases, while in the intensive care unit, all patients received Midazolam.

4. Discussion

This study found that neuropsychiatric symptoms such as delirium, confusion, and insomnia were highly prevalent in the dying phase of patients with cancer, with delirium being the most common.

Identifying neuropsychiatric symptoms for dying patients may be challenging even for most experienced palliative care specialists (Hui, Cheng, & Paiva, 2024). The incidence of patients with delirium in our study was lower (about 23%), compared with other studies (Hosie et al., 2017; Watt et al., 2019). Our data indicate that delirium is misdiagnosed, especially in the case of hypoactive delirium. Possible causes are the limited prognosis that makes it inappropriate to investigate different causes of delirium (Bush, Tierney, & Lawlor, 2017), low level of consciousness and patients` inability to communicate (Azhar & Hui, 2022). However, additional psychiatric expertise can improve symptom recognition and guide treatment planning during the dying phase by offering specialised assessments and ensuring comprehensive care (McCrone & Henderson, 2025). Furthermore, clinicians need ongoing education to improve care of patients in the dying phase (Brajtman, Higuchi, & Murray, 2009; Mitrea et al., 2023; Sutherland et al., 2020).

The aetiology of delirium in the last week of life is multifactorial (Guo et al., 2021). This study shows that symptoms as constipation and nausea are highly correlated with delirium. The neuropsychiatric framework related to terminal delirium encompasses understanding both the neurobiological mechanisms of delirium in patients with cancer and the differential diagnoses that must be considered (Kim et al., 2013).

In our study, neuropsychiatric symptoms were most prevalent in the home care service. In this setting, the family caregivers have an important role in identifying the symptoms, management and advocating for patients (Finucane et al., 2017). On the other hand, these roles are a burden for family members and can lead to psychological distress, including anxiety and depression (Kobayakawa et al., 2017). An important aspect is to educate family caregivers about the various manifestations of these symptoms (Uchida et al., 2019), the process of the dying phase and goals of care (Mori et al., 2023).

Patients who experience neuropsychiatric symptoms in the dying phase need pharmacologic interventions (Azhar & Hui, 2022). In our study, the most frequently used psychotropics in the last week of life were Haloperidol, Midazolam, and Lorazepam. The average Haloperidol dose on the last day of life was 2.75 mg, which is comparable to the 2.1 mg reported in Crawford's study (Crawford et al., 2013). This study showed that psychotropic prescribing practices vary across different care settings. For the intensive care unit and palliative care unit, Midazolam was the drug of choice, while Haloperidol was used more frequently in the oncology ward and the home care. Variability often arises because clinical guidelines differ across various healthcare settings. According to Gerlach et al. (2021), while psychotropic medications may be frequently used in palliative care, the limited studies on their effectiveness complicate clinical decision-making and lead to different prescribing practices. On the other hand, clinicians with more experience in palliative care may be more confident in using psychotropics to manage symptoms, while others may be more cautious.

Ethical considerations regarding patients with neuropsychiatric symptoms during the dying phase focus on balancing the principles of autonomy, beneficence, and non-maleficence, especially when the patient's capacity to make decisions is impaired. Symptoms such as delirium or confusion can hinder the ability to ascertain a patient's wishes and may lead to considerable suffering (Beauchamp & Childress, 2019). In cases where all other treatments have proven ineffective and the patient's symptoms result in intolerable distress, the option of palliative sedation must be carefully contemplated (Surges et al., 2024). The involvement of the patient's family and the interdisciplinary care team is crucial in navigating these ethical complexities (Akdeniz, Yardımcı, & Kavukcu, 2021).

5. Strengths and limitations

This study has some limitations. First, the use of retrospective data collection may limit the accuracy and completeness of symptom reporting, as it relies on existing documentation rather than standardised, prospective assessments. The second limitation is that the unequal distribution of patients across the four study groups may have influenced the reliability of prevalence estimates and also limited the generalisability of findings. This is likely because the patients in our study were in their final week of life, with most passing away at home. One strength of this study is the inclusion of multiple care settings, which enables meaningful comparisons of clinical practices and symptom prevalence across different environments. Another strength of this study is its focus on neuropsychiatric symptoms and the use of psychotropic drugs in cancer patients during their final week of life.

6. Conclusions

This study identified several critical factors relevant to patients with cancer who experience neuropsychiatric symptoms in their final week of life. Clinicians should be vigilant about the potential misdiagnosis of hypoactive and hyperactive delirium. Notably, symptoms such as nausea and constipation show a significant correlation with delirium, particularly in cancer patients nearing the end of life. Additionally, a considerable number of patients exhibiting neuropsychiatric symptoms are cared for at home. Recognising and managing these symptoms poses significant challenges for family caregivers, including emotional strain and differing perceptions of the symptoms. These challenges can greatly affect the well-being of both caregivers and patients, highlighting the necessity for comprehensive support focused on education, resources, and tailored interventions.

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