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ORIGINAL ARTICLE

Cancer pain management in an oncological ward in a comprehensive cancer center with an established palliative care unit

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Abstract

Background This survey was performed to draw information on pain prevalence, intensity, and management from a sample of patients who were admitted to an oncologic center where a palliative care unit (PCU) has been established for 13 years.

Methods Cross-sectional survey in an oncological department performed 1 day per month for six consecutive months.

Results Of the 385 patients, 69.1, 19.2, 8.6, and 3.1 % had no pain, mild, moderate, and severe pain, respectively. Inpatients and patients with a low Karnofsky score showed higher levels of pain intensity ($p < 0.0005$). One hundred twenty-eight patients with pain or receiving analgesics were analyzed for pain management index (PMI). Only a minority of patients had negative PMI score, which was statistically associated with inpatient admission ($p = 0.011$). Fifty of these 128 patients had breakthrough pain (BTP), and all of them were receiving some medication for BTP.

Conclusion It is likely that the presence of PCU team providing consultation, advices, and cultural pressure, other than offering admissions for difficult cases had a positive impact on the use of analgesics, as compared with previous similar surveys performed in oncological setting, where a PCU was unavailable. This information confirms the need of the presence of a PCU in a high volume oncological department.

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Introduction

Pain is a common symptom experienced by cancer patients with wide variations according to the primary diagnosis and disease stage, the prevalence of pain being more than 70 % in advanced stages [28]. Despite available treatments and the development of effective guidelines for the management of cancer pain, proven effective in the majority of subjects [15, 27], a large proportion of cancer patients remain undertreated due to barriers related to health care resources, patient, and family [10, 16]. However, misconceptions about opioids,

insufficient education of healthcare professionals, and restrictive regulation in some countries for many years have been the main cause of the lack of application of simple guidelines of the World Health Organization for cancer pain relief [6, 12]. Barriers to adequate cancer pain management include unnecessarily strict rules and regulations, lack of economic means and insufficient resources, patients', relatives', and medical professionals' negative perceptions about controlled drugs limiting their rational use [6, 8, 14]. Despite legislative impediments have been overcome, however, opioid consumption in Italy is ranked among the lowest in Europe [12, 13, 17]. Data regarding Italy still remain discouraging despite the large availability of drugs. In a national cross-sectional survey of patients representative of the cancer population referring to the majority of oncologic centers distributed in the different regions, strong opioids were used only in about 53 % of patients in the presence of severe pain [18]. Similar results have been reported more recently in a mixed oncologic and palliative care population [1]. It is likely that a better integration between oncologic wards and palliative/supportive care, as assumed by the European Society of Medical Oncology, may produce better outcomes than those reported so far.

The aim of this institutional cross-sectional no controlled study was to draw information on pain prevalence, intensity, and management in patients admitted as outpatient or inpatient oncologic unit in a department where a long tradition of palliative care exists, able to provide consultations, continuous educational programs and, when necessary, admission to an acute palliative care unit for pain and symptom management.

Patients and methods

This survey was performed in an oncological unit of a cancer center where a palliative care unit has been established 13-years ago, concomitantly to the oncological ward, with the intent to provide supportive care to oncological patients referred by internal oncologists or other hospitals in Sicily, a region of about six million of inhabitants. Agreement with oncological staff was achieved, but neither ward nurses nor physicians were involved in the research. A special form containing easy questions was prepared, and the interview was performed by an external team which was trained in an investigator meeting to gather this kind of information. The study was approved by the ethical committee of the University of Palermo, and patients' informed consent was achieved.

The survey took place on a randomly established day, excluding weekends of each month for six consecutive months, according to a cross-sectional design. All patients attending the day hospital (DH) or admitted to the

oncological ward as inpatients in the planned day of the month were surveyed. Inclusion criteria were age more than 18 years and diagnosis of cancer. Exclusion criteria were a level of cognitive failure impeding the interview or inability to complete the questionnaire and evaluation tools, no consent to give an interview, or patients previously already interviewed.

The following data were collected: Karnofsky status, duration of disease, administration of chemotherapy in the last 30 days, the presence of chronic pain that is persisting more than 12 h per day, and breakthrough pain (BTP), defined by a peak of pain clearly distinguishable by persistent pain.

The Edmonton system assessment scale (ESAS) was used for measuring intensity of physical and psychological symptoms on a numerical scale from 0 to 10, including pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, shortness of breath, well-being, and others [3, 24]. Prescriptions of analgesics for persistent pain and BTP medications were also collected.

Pain intensity was stratified for categories, according to validated cutoff points to define mild, moderate, and severe pain [24]. Pain management index (PMI) was calculated to make a historical comparison with previous other epidemiological studies [1, 5, 9, 25], where this tool was used as a surrogate of appropriateness of pain management.

Statistical analysis

Data were collected and analyzed by the SPSS software 14.0 version (SPSS, Inc., Chicago, Ill, USA) and the Epi Info software version 3.2.2. (Centers for Disease Control and Prevention). Statistical analysis of quantitative and qualitative data, included descriptive statistics, was performed for all the items. Frequency analysis was performed with chi-square test. The univariate and multivariate between group one-way analysis of variance and Kruskal–Wallis statistic test were used for parametric and nonparametric differences analysis between quantitative and qualitative variables, respectively. All *p* values were two-sided and *p* values less than 0.05 were considered to indicate statistical significance.

Results

Three hundred eighty-five patients, aged 24–83 years (mean 61.6; SD±12.4), were interviewed. One hundred sixty patients were males (41.6 %). The most frequent cancer diagnoses were in a rank order: breast 122 (31.7 %), colon–rectum 80 (20.8 %), lung 60 (15.6 %), urogenital 56 (14.5 %), pancreas 23 (6 %), liver 12 (3.1 %), head and neck 11 (2.9 %), and others 21 (5.4 %).

The mean duration of disease was 25 months (SD±35). Three hundred six patients were admitted as DH (79.5 %) and

79 were inpatients (20.5 %). Three hundred thirty-one patients had been receiving chemotherapy in the last month (86 %). The mean Karnofsky status was 77.2 (SD±17.5), with 229 patients having a value of >70. Karnofsky status was associated with younger age ($p=0.0005$), DH admission ($p=0.0005$), previous surgery ($p=0.003$), ongoing chemotherapy ($p=0.001$), less previous admission to palliative care unit (PCU) ($p=0.0005$), less persistent pain ($p=0.0005$), and less background pain intensity ($p=0.0005$). No differences were found in gender ($p=0.668$) and primary tumor ($p=0.323$).

Pain prevalence

Characteristics of patients stratified for pain intensity are listed in Table 1.

Of the 385 screened patients, 266 patients (69.1 %) had no pain, 74 (19.2 %) had mild pain intensity, 33 patients (8.6 %) had moderate pain [5, 6], and 12 patients (3.1 %) had severe pain intensity ($\geq 7-10$). There was no relationship between the four pain groups and age ($p=0.900$), gender ($p=0.882$), type of admission ($p=0.220$), previous surgery ($p=0.112$), and ongoing chemotherapy ($p=0.174$). Inpatients and patients with a low Karnofsky score showed higher levels of pain intensity ($p<0.0005$ and $p<0.0005$, respectively) (Table 2).

Pain management

Two hundred fifty-eight, 21, 80, and 26 patients were not receiving analgesics but were receiving non-opioid drugs,

weak opioids or low doses of strong opioids, and strong opioids, respectively. Data on patients stratified for pain intensity categories are shown in Table 1.

Pain management index

The values of PMI of 128 patients who had different pain levels or were taking analgesics are reported in Table 3. Only a minority of patients had a negative PMI, almost with a minimal value (-1). There was no relationship between PMI and age ($p=0.898$), gender ($p=0.716$), diagnosis ($p=0.798$), ongoing chemotherapy ($p=0.618$), Karnofsky score ($p=0.174$), previous surgery ($p=0.099$), or opioid doses expressed as oral morphine equivalents ($p=0.838$). There was a relationship between PMI and kind of admission (inpatients having more negative scores, $p=0.011$). General data regarding the calculation of PMI are reported in Table 4. Only 33 (25 %) patients had negative scores, most of them having a score of -1.

ESAS

The mean ESAS was 24.5 (SD±12.8). ESAS was not related to gender ($p=0.540$), surgery ($p=0.092$), ongoing chemotherapy ($p=0.238$), diagnosis ($p=0.510$), persistent pain ($p=0.880$), pain intensity categories ($p=0.388$), analgesic classes ($p=0.136$), opioid dose ($p=0.613$), and PMI ($p=0.865$). Inpatients had higher ESAS than DH patients ($p=0.002$) as well as older patients ($p=0.046$), while patients with higher Karnofsky score had lower ESAS ($p=0.002$).

Table 1 Characteristics of patients. Data are expressed as a mean (SD) and percentages

No. of patients	385
Age, mean	61.6 (SD±12.4)
M/F	160/225 (41.6–58.4 %)
Karnofsky status	77.2 (SD±17.5)
Outpatient/inpatient	306/79 (79.5–20.5 %)
Previous surgery, Y/N	178/207 (46.2–53.8 %)
CT (last month), Y/N	331/54 (86–14 %)
Persistent pain, Y/N	119/266 (30.9–69.1 %)
Patients with BTP	50/119 (42 %)
No. of BTP episodes/day	2.5 (SD±1.6)
Diagnosis	
Breast	122 (31.7 %)
Colon–rectum	80 (20.8 %)
Lung	60 (15.6 %)
Urogenital	56 (14.5 %)
Pancreas	23 (6 %)
Liver	12 (3.1 %)
Head and neck	11 (2.9 %)
Others	21 (5.4 %)

Breakthrough pain

Fifty of 128 patients reporting pain or receiving analgesic drugs had a mean of 2.5 (SD±1.6) BTP episodes. All 50 patients were prescribed a BTP medication in a rank order: oral transmucosal fentanyl 11 patients, ketorolac 9 patients, oral morphine 6 patients, intravenous morphine 5 patients, fentanyl buccal tablet 4 patients, nasal pectin fentanyl 3 patients, intranasal fentanyl 2 patients, subcutaneous morphine 2 patients, codeine–paracetamol 2 patients, paracetamol 2 patients, tramadol 2 patients, sublingual fentanyl 1 patient, and oxycodone 1 patient.

Discussion

Findings of this survey show that in a cancer center with a long tradition of palliative care, patients receive an acceptable pain management. The population recruited in this study was representative of the real world of a daily oncological activity. Most of them were receiving active treatment, had a DH admission, and a relatively high performance status. As

Table 2 Number of patients with pain intensity categories and different classes of analgesics

Pain intensity categories	0	1–4	5–6	7–10	Total
No analgesics	257	1	0	0	258
Non-opioid analgesics	0	13	8	0	21
II step drugs	7	49	15	9	80
III step drugs	2	11	10	3	26
Total	266	74	33	12	385

expected, a poor Karnofsky status was correlated with persistent pain and higher pain intensity.

Of patients with pain problems, most subjects had a positive or neutral PMI, with only 1/4 of patients having negative score, mainly the minimal negative score of -1 . Of interest, the majority of patients had positive PMI scores, which means that the level of management was relatively adequate to the pain intensity reported by patients. PMI was used as an anchor to compare the present data with previous experience reported in the last years, which used this parameter to provide an indirect evidence of poor pain management. In the pioneer study using PMI, 60 % of patients with moderate to severe pain were not prescribed with analgesics appropriate to their level of pain [9]. PMI is a not perfect tool, and criticisms have been reported about the meaning of PMI [18]. The achievement or not of an adequate analgesia cannot be considered by using as a parameter the drug class and the pain level, according to the PMI which was originally constructed to measure the health care provider's response to a patient's pain, even including drugs prescribed but not administered. For example, any patient treated with strong opioids should be considered as adequately treated in spite of a severe pain state, regardless of the dosage (score 0). As a consequence, PMI should only generally indicate inadequate orders for analgesic drugs or undermedication. This is confirmed by the finding that more than half of patients receiving strong opioids had uncontrolled pain [9].

Nevertheless, PMI has been repeatedly reported as giving exhaustive proof of its validity and this tool was used as an anchor of comparison with previous similar studies. Thus, we used this tool as a surrogate to make a historical comparison with existing literature on cancer pain management in

oncologic wards conducted in Italy. Patients with non-small cell lung cancer undergoing three different protocols of chemotherapy, 82 % of patients had negative PMI scores and were considered poorly managed, according to the class drug–pain intensity ratio [11]. In another Italian survey performed in hospitalized patients, analgesic prescription was found to be inadequate in 43 % of cases [5]. In a large survey performed in Italy about the prevalence of pain and its treatment of a cancer population referring to the majority of oncologic centers, it has been found that about 85 % of patients had their pain uncontrolled, despite receiving opioids [18]. Of interest, PMI scores were found negative in a relevant number of patients even mixing oncologic patients with a palliative care population, which should potentially receive a better pain management [1]. These percentages, by using the same parameter, have been found to be sensibly lower in this study performed in a similar setting, with the only existing difference being a consolidated system of educational activities, research, consultation, cultural pressure, and if needed, available beds in a PCU established in 1999, and actively collaborating with the oncologic ward since the beginning [19]. In a tertiary oncological hospital in Italy with the longest tradition on palliative care and pain management, 31 % of patients with pain were not receiving analgesics, poor pain relief was observed in about 43 % of patients, and 20 % of patients had uncontrolled pain [26].

To confirm this observation, BTP, which is an indirect signal of attention to details by treating oncologists, appears to be managed carefully. All patients having BTP were prescribed a medication as needed. Of interest, this data is of paramount importance if compared with attitudes of treating physicians about BTP recorded even in Italian

Table 3 Distribution of patents according to the pain intensity categories (mean values \pm SD) and some variables (previous admission in a palliative care unit (PCU/no PCU), kind of admission (day hospital

(DH) or inpatients (IN)), operated or not (SURG/no SURG), or ongoing chemotherapy (CH/no CH)

Pain intensity	No. of patients	PCU/no PCU	DH/IN	SURG/no SURG	CH/no CH
0	266	11/254	218/48	134/5	234/32
1–4 (2.9 \pm 0.8)	74	8/64	57/17	24/2	63/11
5–6 (5.3 \pm 0.6)	33	7/26	23/10	15/3	25/8
7–10 (7.3 \pm 0.7)	12	5/7	8/4	5/0	9/3
Total	385	382	385	188	385

Table 4 PMI distribution in patients with pain or receiving analgesics, according to some variables (previous admission in a palliative care unit (PCU/no PCU), kind of admission (day hospital (DH) or inpatients (IN)), operated or not (SURG/no SURG), or ongoing chemotherapy (CH /no CH))

	Total	PCU/no PCU	DH/IN	SURG/no SURG	CT/no CT
-3	0				
-2	3	1/2	3/0	0/3	3/0
-1	30	7/23	18/12	9/21	23/7
0	34	5/29	21/13	10/24	27/7
1	20	4/16	16/4	10/10	16/4
2	39	3/36	36/3	18/21	35/4
3	2	2/0	2/0	2/0	2/0
Total	128	22/106	96/32	49/79	106/22

hospices [20]. Different classes of drugs were prescribed according to the analgesics used as around the clock medication. It is likely that patients receiving non-opioids (I step drugs) or II step drugs were prescribed non-opioids or II step drugs for BTP, given that the minimal dose strengths of any of the commercially available rapid onset opioids (transmucosal fentanyl, fentanyl buccal tablets, sublingual fentanyl, or nasal fentanyl) are recommended to be used in patients tolerant to 60 mg of oral morphine equivalents (Table 5) [21].

The symptom burden was measured with ESAS, which is a valid, reliable, and feasible instrument for physical symptom assessment in routine “palliative care” clinical practice with a potentially different responsiveness in different situations or care settings [24]. ESAS data confirm that the symptom burden is correlated with inpatient admission, age, and poor Karnofsky status, as an indirect sign of advanced disease. Symptom assessment is of paramount importance in selecting more complex situations, for a possible consultation with a palliative–supportive team to allow the right integration among specialists. Unfortunately, such tools are often used for research purpose only rather than for routine activity. At the moment, after this research, this tool is going to be introduced even in the nursing sheet of the oncologic wards in our center, other than the standard assessment performed in the palliative care unit for years.

The limitations of this study are inherent to the uncontrolled nature of this study. However, as mentioned above, to make some comparison, tools like PMI were used. Based on this parameter, data of this survey are quite different from previous data presented by most oncologic units in Italy and the only distinction relies on the presence of supportive/care unit, deeply rooted in the entire department for 15 years [23].

In conclusion, the management of pain in patients admitted to an oncological unit with a long tradition of cooperation and simultaneous care with a PCU is acceptable, in comparison with previous experienced reported in oncologic wards where a PCU was unavailable. These data suggest that palliative care physicians may positively influence the cultural barriers existing among oncologists about the use of analgesics, particularly opioids, and should work earlier in any oncological department, rather than limiting their activity to end of life issues in hospices or home care [2]. Their role appears to be prominent in all the phases of disease. The reason for a low opioid consumption in Italy, recently denounced by a senator of the Italian Parliament, particularly sensible to cancer patients' problems [13] is not based on drug unavailability, as dramatically reported by ESMO [6, 7], but relays on a low level of knowledge also existing among specialists in palliative care [1, 20], dealing preferably with end of life issues. Regrettably, a recent law in Italy has confined palliative care to hospice and home care, which

Table 5 PMI and use of the different classes of analgesics

PMI	Total	No analgesic	I step drugs	II step drugs	III step drugs
-3	0	0	0	0	0
-2	3	0	3	0	0
-1	30	0	4	25	1
0	34	1	4	13	16
1	20	0	10	6	4
2	39	0	0	36	3
3	2	0	0	0	2
Total	128	1	21	80	26

means in the Italian reality, about 20 days before death [17, 22]. This is in evident contrast with the definition of World Health Organization, “Palliative care is...applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy”. It has been suggested by experts to spread palliative care in other settings, other than traditional home care and hospice, to intercept oncologic patients in their disease trajectory early; for example, in high volume oncologic departments [23], rather than restricting the action area only in the last weeks of life [4], providing advice, resolving the most difficult cases, and creating a favorable environment for the culture of pain management.

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