Impact of early access to a palliative/supportive care intervention on pain management in patients with cancer

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Background: No study has so far addressed whether differences do exist in the management of cancer pain between patients receiving usual care by primary specialists and those receiving early palliative/supportive intervention.

Patients and methods: A multicentre cross-sectional study in 32 Italian Hospitals has included 1450 patients, receiving analgesic therapy for cancer pain: 602 with access to primary specialist alone (standard care, SC) and 848 with early access to a palliative/supportive care (ePSC) team, concomitant with primary oncology care.

Results: Statistically significant differences in the analgesic drug administration according to care model have been evident: non-opioids were more frequently used in SC (9.5 % versus 2 %; P < 0.001), while strong opioids in ePSC group (80 % versus 63 %; P < 0.001). The number of patients with severe pain was lower in ePSC compared with SC (31 % versus 17 %; P < 0.001). Results of multivariate analysis have shown that ePSC integrated with primary oncologic care (relative risk 0.69; 95% confidence interval 0.48–0.99; P = 0.045) was an independent factor associated with a 31% reduced risk of suffering from severe pain.

Conclusions: An ePSC team provides the most effective standard of analgesic therapy for cancer pain. A randomized clinical trial is needed to confirm these findings.

Key words: analgesic therapy, pain supportive care, palliative care

Introduction

Almost half of cancer patients still receive inappropriate care for pain despite many guidelines have been published during the last decades and much efforts have been made in the last few years to implement educational programs, especially in oncology units [1–6]. The ECAD-O (Epidemiologia Clinico-Assistenziale del Dolore in Ospedale / Clinical-Caring Epidemiology of Pain in Hospital) group has been established to activate a surveillance on pain management, as part of a routine care, by creating a multicentre network of hospitals and a multidisciplinary working group in Italy. Specifically, a survey has been carried out in order to evaluate which analgesic therapy is administered in hospital to pain control and to investigate the perception of pain control both from patients and health care professionals [7]. The first results of this ECAD-O survey have shown that cancer pain remains one of the main causes of analgesic therapy administration both in oncology and in non-oncology wards, but that oncology wards provide the most adequate standard of analgesic treatment for cancer-related pain [8].

A recent USA trial has shown that newly diagnosed non-small-cell lung cancer patients assigned to receive early palliative care integrated with standard care had a better quality of life than did patients assigned to standard oncologic care alone [9]. Of interest, in the Oncology and Palliative Care Unit of Local Health Unit in Modena, included in the ECAD-O study, an interdisciplinary working group had been established since 2006, integrating primary oncologist specialists with a palliative/supportive care team.

Thus, it might be worth investigating the possible impact of early integrating palliative and supportive care (ePSC) to standard oncologic care (SC) on pain management in cancer patients in routine clinical practice. Specifically, a comparison was made between a sample of cancer patients followed in a setting of ePSC with a sample of cancer patients managed in a setting of SC, according to analgesic therapy and pain intensity.
patients and methods
study design and setting
The ECAD-O survey, promoting as a hospital pharmaco-surveillance activity, was a cross-sectional study, originally conducted in 2007–2008 in six index days over 1 year in 48 Italian hospitals, to identify patients treated with analgesic therapy [7, 8]. A multidisciplinary working group, made up of physicians, nurses and pharmacists, has been established in each hospital to collect information on patients treated with analgesic therapy according to the usual practice. The local multidisciplinary working groups continued the survey in some hospitals, until 2010. This project has been authorized by the Local Health Authority and by the Local Ethical Committee. For each patient included in the study, data have been obtained according to Italian law about privacy (D.Lgs. 196/2003), so that all patients have been included anonymously to the central data analysis.

For the present analysis, only cancer patients, observed in 32 Italian hospitals (medicine and oncology wards), were considered. In 3 years (2007–2010), 1450 cancer patients were identified. Among these, 602 patients were treated in accordance with standard clinical practice, and specifically they met the primary specialists, who took care of all the primary disease assessment and management as well as the supportive/palliative care needs. Hence, they were included in SC group. Eight hundred and forty-eight patients included in ePSC group were observed in the Oncology and Palliative Care Unit of Local Health Unit in Modena, where ECAD-O survey was performed and where an integrating approach of ePSC had been established. Specifically, patients of ePSC group meet the PSC team soon after the cancer diagnosis, generally within 2–3 weeks since diagnosis. The PSC team consists of a specially trained team of professionals, committed to provide care and support in inpatient and outpatient settings, being the latter possible through a collaborative network with a team of general practitioners. The PSC team, including two physicians, two nurses, one psychologist and some volunteers, has been created in January 2006 to provide comprehensive symptom management and psychosocial, spiritual and emotional support to cancer patients and their families, from the time of diagnosis onward, according to general guidelines, to ensure an uniform and reproducible intervention. Although the specific care provided by the PSC team depends on individual patient and family needs, these guidelines include evaluation and management of the following symptoms: pain, gastrointestinal symptoms (anorexia and weight loss, nausea and vomiting, constipation and diarrhea), fatigue, sleep and mood disturbances (anxiety and depression). The PSC team also provides assistance with treatment choice, assistance of patients and family caregivers in coping with a life-threatening illness and has also recently launched a program of psychological support for patients’ relatives and friends after death. The PSC team followed each patient on a regular basis, in conjunction with the primary oncologist, at the regularly scheduled visits or chemoradiotherapy sessions, every 3–4 weeks. Patients; symptom evaluation was routinely assessed by Numerical Rating scale [10], Edmonton Symptom Assessment Scale [11] and Hospital Anxiety Depression Scale [12]. The PSC team and the primary oncologists attended weekly meetings to discuss active patient issues to ensure a reproducible team approach to the patients’ care.

data collection
Information regarding patients and wards has been collected using standardized forms. For each patient involved in the survey, demographics (age and gender), clinical treatment (type of pain, primary cancer and presence of metastasis) and analgesic treatment (schedule of analgesic treatment, type of analgesic drug prescribed and administered in the last 24 h, route of administration, dosage and adjuvant treatment modality) have been obtained from medical records.

Patients have been interviewed by a pharmacist—not directly involved in patients’ care—concerning their perception of pain control and their pain intensity at interview and the worst intensity of pain perceived during the previous 24 h. Pain intensity has been estimated by using a four-level Verbal Rating Scale scored as 0 points = no pain, 1 point = mild pain, 2 points = moderate pain and 3 points = severe pain.

statistical analysis
Descriptive statistics (means and standard deviations) and absolute frequencies and percentages were generated for study variables. Differences between study groups in demographic, clinical and therapeutic characteristics were assessed with the use of Pearson’s χ² test and for categorical variables and Mann–Whitney U test for continuous variables. Overall Pearson’s χ² tests were done to evaluate the difference in the distribution of patients according to analgesic therapy (categorized as non-opioids, weak opioids and strong opioids according to WHO analgesic ladder) [5] and pain intensity in the last 24 h. If results of these tests showed that the differences of patients distribution among two groups (ePSC and SC) were statistically significant (P value < 0.05), post hoc contrasts using the Hochberg method have been done in order to test the equality of proportions in each category of the above-mentioned variables. The P values presented have been adjusted so that values of < 0.05 indicate statistical significance.

In order to account for the multilevel nature of the data (patients clustered within wards) and to simultaneously control possible confounding effects of the different variables, a multiple multilevel log-binomial model (hierarchical models) was used [13, 14], to identify independent characteristics associated with the prevalence of severe pain in the last 24 h before the interview. The covariates tested were gender, age, metastatic disease and analgesic therapy as level-1 variables related to baseline patient characteristics, wards and care model as level-2 variables related to care setting characteristics. Results are expressed as relative risk (RRs) with their 95 % confidence intervals (95 % CI). All the analyses were performed by using SAS Statistical Package Release 9.2 (SAS Institute, Cary, NC). A P value < 0.05 was considered as being statistically significant.

results
A total of 1450 cancer patients were included in the study: 848 in ePSC and 602 in SC approach. The two groups show statistically significant differences according to gender (P = 0.010) and metastatic disease (P < 0.001), but none by age (Table 1). Moreover, while in ePSC group all patients were recruited from oncological wards, in SC group, 43 % of patients derived from non-oncological wards (internal medicine). When considering the administration schedule of analgesic treatment, almost all patients (over 90 %) were treated around the clock. Of note, the percentage of patients receiving analgesics as needed was greater in SC group than in ePSC (4 % versus 0.1 %). The type of analgesic therapy in the two care settings has been analyzed and significant differences in the distribution of patients were found (P < 0.001). In particular, as reported in Table 2, non-opioid and weak opioid drugs have been administered more frequently in SC than in ePSC group (non-opioids: 9.5 % versus 2 %, P < 0.001; weak opioids: 27 % vs. 18 %, P < 0.001), while strong opioids were used more frequently in the ePSC model (80 % versus 63 %, P < 0.001).

The distribution of patients treated with strong opioids differed, by type of the drug administered, between SC group
Table 1. Characteristics of study sample by care model

<table>
<thead>
<tr>
<th></th>
<th>SC (N = 378)</th>
<th>ePSC (N = 675)</th>
<th>P value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD), years</td>
<td>64.7 (13.8)</td>
<td>65.2 (9.1)</td>
<td>0.14</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>313 (52.0)</td>
<td>499 (58.8)</td>
<td>0.010</td>
</tr>
<tr>
<td>Female</td>
<td>289 (48.0)</td>
<td>349 (41.2)</td>
<td></td>
</tr>
<tr>
<td>Metastatic disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>427 (70.9)</td>
<td>753 (88.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No</td>
<td>169 (28.1)</td>
<td>95 (11.2)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>602 (100.0)</td>
<td>848 (100.0)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Chi-square test comparing frequencies between SC group and ePSC group.

Table 2. Analgesic therapy by care model

<table>
<thead>
<tr>
<th>Analgesic therapy</th>
<th>SC (N = 602)</th>
<th>ePSC (N = 848)</th>
<th>P value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-opioids</td>
<td>57 (9.5)</td>
<td>17 (2.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weak opioids</td>
<td>167 (27.7)</td>
<td>156 (18.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Strong opioids</td>
<td>378 (62.8)</td>
<td>675 (79.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

\(^a\) P values are for the between-group comparisons of the proportion of patients receiving one kind of analgesic therapy and the proportion of remaining patients, calculated using Pearson’s \(\chi^2\) test (post hoc contrasts: \(P\) values adjusted using Hochberg method).

and ePSC group (Table 3). In particular, the use of transdermal fentanyl was sixfold higher in SC than in ePSC group (41 \% versus 7 \%, \(P < 0.001\)), while the use of morphine (54 \% versus 25 \%, \(P < 0.001\)) and oxycodone (34 \% versus 20 \%, \(P < 0.001\)) was about twofold higher in ePSC than in SC group.

The intensity of pain, during the last 24 h before the interview, has also been compared in the two care models. As reported in Table 4, the percentage of patients with no pain was much higher in ePSC than in SC group (27 \% versus 17 \%, \(P < 0.001\)). Similarly, the percentage of patients with mild pain was higher in ePSC than in SC group (33 \% versus 24 \%, \(P < 0.001\)). On the contrary, the percentage of patients with moderate or severe pain was higher in SC than in ePSC group. Of note, the percentage of patients with severe pain, an issue in management of cancer patient, was about twofold higher in SC than in ePSC model (31 \% versus 17 \%, \(P < 0.001\)).

Therefore, it was worthwhile exploring the specific contribution of ePSC in the pain management by evaluating whether ePSC was associated with a decreased risk of severe pain (Table 5). Results from univariate analysis showed that ePSC, age and gender (men) were associated with a lower prevalence of severe pain. No significant differences were found for other variables (wards, analgesic therapy and metastatic disease). Results from multivariate analysis, by using the multilevel log-binomial model, showed that care model and gender were the only factors that continued to be independently associated with a decrease of severe pain prevalence. Particularly, ePSC group was associated with 31 \% reduced risk of severe pain (RR 0.69; 95 \% CI 0.48–0.99; \(P = 0.045\)), adjusted for other confounders including age, gender, metastatic disease, analgesic therapy and wards.

Table 3. Type of Strong opioids by care model

<table>
<thead>
<tr>
<th>Strong opioids</th>
<th>SC (N = 378)</th>
<th>ePSC (N = 675)</th>
<th>P value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>95 (25.1)</td>
<td>362 (53.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>76 (20.1)</td>
<td>231 (34.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>154 (40.8)</td>
<td>45 (6.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other</td>
<td>53 (14.0)</td>
<td>37 (5.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

\(^a\) P values are for the between-group comparisons of the proportion of patients receiving one kind of strong opioid and the proportion of remaining patients, calculated using Pearson’s \(\chi^2\) test (post hoc contrasts: \(P\) values adjusted using Hochberg method).

discussion

Palliative care is ‘... an approach that improves the quality of life of patients and their families, facing the problem associated with life-threatening illness, through the prevention and relief of suffering, by means of early identification and impeccable assessment and treatment of pain and other ...’ physical symptoms and by providing psychosocial and spiritual care and assistance in communication, complex decision making and transition of care [15]. Although being now a recognized specialty in many countries, palliative medicine has largely focused on end-of-life care, because of existing barriers to early palliative care access, limiting the number of patients referred to these programs and especially delaying their referral in the trajectory of illness. The effectiveness of early palliative care interventions has recently been emphasized by a randomized controlled trial that compared the usual care provided to advanced non-small-cell lung cancer patients with usual care combined with access to a specialist palliative care team [9]. The results of this trial showed that patients with access to the team had reduced depression, improved quality of life and a 3-month survival advantage. However, these results have not addressed whether the early and structured access to a

Table 4. Pain intensity during the previous 24 h by care model

<table>
<thead>
<tr>
<th>Pain 24 h</th>
<th>SC (N = 602)</th>
<th>ePSC (N = 848)</th>
<th>P value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain</td>
<td>102 (16.9)</td>
<td>230 (27.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mild</td>
<td>143 (23.7)</td>
<td>279 (32.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate</td>
<td>168 (27.9)</td>
<td>192 (22.6)</td>
<td>0.022</td>
</tr>
<tr>
<td>Severe</td>
<td>189 (31.4)</td>
<td>147 (17.3)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

\(^a\) P values are for the between-group comparisons of the proportion of patients with specific pain intensity and the proportion of remaining patients, calculated using Pearson’s \(\chi^2\) test (post hoc contrasts: \(P\) values adjusted using Hochberg method).

ePSC, early palliative/supportive care; SC, standard care.
palliative care team had an influence on issues related to cancer pain management [9].

We took advantage of data collected within the ECAD-O study to provide the first comparative description of cancer pain management between two different care models: ePSC versus SC. In particular, ePSC was identified in the Oncology and Palliative Care Unit of the Modena Hospital, where a program of simultaneous care based on integrating early supportive/palliative care with primary oncology care was adopted. The SC approach was identified as routine clinical practice in the hospitals included in the ECAD-O study, where the issues of pain management in cancer patients were exclusively referred to primary specialists alone.

Our results showed that in the choice of analgesic strategy, the main recommendations provided by international guidelines were more strictly followed in integrated care model than in routine approach. According to these recommendations and Cochrane systematic review, the gold standard in moderate–severe cancer pain management continues to be oral formulations and specifically oral morphine [15–17]. Our results showed that the use of non-opioid analgesics and weak opioids was more common in the SC group, while, conversely, strong opioids were more frequently employed in ePSC group. Moreover, among the strong opioids, oral formulations (morphine and oxycodone) were more frequently used in ePSC group, and in particular oral morphine was the most widely used strong opioid. In SC group transdermal formulations were more often used, in particular TTS fentanyl.

Clearly, the most striking finding from our study is that the risk of severe pain is remarkably reduced when an integrated care model is used compared with a model of routine care based on primary specialist alone. However, it is clear that the control rate of cancer pain needs to be improved: despite an integrated care model is adopted an unacceptable high percentage (17 %) of patients still suffering with severe intensity. Thus, both pharmacological (such as therapy for breakthrough cancer pain) and non-pharmacological (such as psychosocial and spiritual) interventions should be considered and become the object of extensive research in the near future to address this issue [18].

In summary, our data confirm the feasibility of ePSC to hospital oncology practice and suggest a more positive impact of such an integrated care model on cancer pain management, compared with the routine care model. Due to the observational nature of the study, a randomized controlled trial is warranted to confirm and better substantiate these findings.

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disclosure

The authors declare no conflicts of interest.

references

Health-related quality of life in recurrent platinum-sensitive ovarian cancer—results from the CALYPSO trial

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Background: In the CALYPSO trial, carboplatin–pegylated liposomal doxorubicin (CD) demonstrated superior therapeutic index versus carboplatin–paclitaxel (CP) in patients with recurrent ovarian cancer. This paper reports the health-related quality of life (HRQoL) findings.

Materials and methods: HRQoL was measured with the EORTC QoL-QC30 questionnaire and OV28 ovarian cancer module. Mean change scores from baseline in HRQoL subscales (five functional scales and global health status) in each arm and the proportion of patients improved or worsened were calculated every 3 months until 12 months.

Results: Compliance was 90% at baseline and 76%, 64%, 57% at 3, 6, and 9 months, respectively. Baseline HRQoL showed already impaired global scores (mean 62/100) and considerable symptom burden (90% of patients reporting nonzero scores). Global QoL and abdominal symptom scores improved over time in both arms; at 6 months, 36% of patients met criteria for improved symptoms. Treatment with CD resulted in less peripheral neuropathy (9.8 versus 24.2), fewer other chemotherapy side-effects (9.5 versus 16.2), and less impact on body image (3.8 versus 10.4) versus CP (all P < 0.02) at 6 months.

Conclusions: These patient-reported outcomes confirm the overall lower toxicity of CD versus CP. The improved disease-related outcomes achieved with CD were not at the expense of QoL.

Key words: carboplatin, paclitaxel, pegylated liposomal doxorubicin, platinum sensitive, recurrent ovarian cancer, quality of life

introduction

The management of recurrent ovarian cancer (ROC) is an ongoing topic of clinical research designed to guide practice. For patients with ovarian cancer who initially present with advanced disease, standard therapy includes a combination of maximal cytoreductive surgery with subsequent chemotherapy [1]. However, despite high response rates to this initial management, many patients experience relapse. Such patients are not curable, hence, the goals of therapy for disease recurrence focus on improving both length of life and quality of life (QoL) [2].