End-of-life palliative chemotherapy: Where do we stand?

Amrallah A. Mohammed a,b,*, Abdullah S. Al-Zahrani a, Hafez M. Ghanem a, Mian U. Farooq c, Amr M. El Saify a, Hani M. EL-Khatib a

a Oncology Center, King Abdullah Medical City-Holy Capital, Saudi Arabia
b Medical Oncology Department, Faculty of Medicine, Zagazig University, Egypt
c Strategic Planning Department, King Abdullah Medical City-Holy Capital, Saudi Arabia

Received 18 January 2015; revised 1 February 2015; accepted 3 February 2015
Available online 25 February 2015

Keywords
End of life;
Palliative chemotherapy;
Futile chemotherapy

Abstract
Background: This study evaluates the use of palliative chemotherapy (PCT) and possible associated factors at the end of life.
Method: The study includes all advanced non hematological cancer patients who died in the King Abdullah Medical City during the period from January 2011 to April 2014. Demographic and disease features were registered.
Results: 420 patients were included in the study, median age 62 years (range 17–108); 52% female and 48% male. 87.4% of patients were Saudis and 12.6% non Saudis. 124 (29.5%) patients received PCT at the last month before death (LM-PCT): 21.8%, 22.6% and 55.6% within one, two and four weeks of death, respectively. Place of death (critical care vs. regular ward) and mode of admission (ER vs. OPD vs. Transferred) had a strong association with LM-PCT (p < 0.0001, V = 0.35) and (p < 0.0001, V = 0.43), respectively. There was a gradual increase in the number of patients receiving LM-PCT from January 2011 to April 2014; 15.3%, 28.2%, 37.1% and 19.4%, respectively.
Conclusion: In our center; at the end of life, there is a gradual increase in the number of patients receiving chemotherapy which significantly increased cancer patients’ odds without clear predictive factors associated with its use, which calls into question the benefits of PCT in terminally ill cancer patients.

© 2015 The Authors. Production and hosting by Elsevier B.V. on behalf of National Cancer Institute, Cairo University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Chemotherapy for metastatic solid tumors such as lung, breast, colon, or prostate cancer rarely if ever cures patients. The indication for such chemotherapy is to improve disease-free or overall survival, relieve symptoms, and improve the
quality of life. Palliative chemotherapy (PCT) accounts for most of the work of everyday oncology given the rarity of curable disease, it may even shorten a patient’s life [1].

Many studies demonstrated that PCT given in the last month of life (LM-PCT) is increasing and treatment frequencies from 9% to 43% have been reported [2,3]. LM-PCT was recognized by The American Society of Clinical Oncology to be one of the top-five practices that could improve patients’ care and reduce costs, if stopped.

More than 20% of patients receiving Medicare who had metastatic cancer started chemotherapy treatment in the 2 weeks before death [4], with no clear predictive factors associated with this use [5,6]. On the other hand, some studies have shown that ceasing aggressive cancer treatments earlier by introducing palliative care can increase the survival time and quality of life in patients with lung cancer [7].

As we were interested in how to adjust the use of futile chemotherapy in terminal patients, this pushed us to investigate the current practice in the King Abdullah Medical City (KAMC); Saudi Arabia, to determine the proportion of patients with metastatic cancer who ever received PCT and the proportion of those who received chemotherapy within 2 and 4 weeks of death and to evaluate if there are any predictive factors to start PCT at the end of life. A secondary aim was to identify the potential drawback of ongoing PCT in the last month of life.

Materials and methods

The current retrospective cohort design included 429 advanced cancer patients who died in the KAMC during the period from January 2011 to April 2014.

PCT was defined as chemotherapy treatment with noncurative intent. The eligibility criteria were; pathological diagnosis of cancer, evidence of advanced disease and death during hospitalization at KAMC.

We recorded the demographic data of patients, including gender, age at time of death, cancer diagnosis, nationality (classified as Saudi or non-Saudi), and place of death [8]. The data collected from patient charts and from the electronic medical records of the Medica Plus Oncology Management System. Patients were excluded if the cancer diagnosis was a hematological malignancy, if they were not seen by the medical oncology service or if they were treated with adjuvant or curative intent.

Identified patients were divided in two groups: one group had received PCT in the last month of life (LM group) (which is subdivided into patients that received chemotherapy within one, 2 and 4 weeks of death) and the other group that had not received PCT in the last month of life (only supportive care).

Statistical analysis

Data were analyzed using SPSS Version 15.0. The outcome variables were the starting of PCT and continuation within the last one, 2 and 4 weeks of life. The influence of demographic features and cancer characters were determined using the chi-square test. P value of <0.05 denoted statistical significance.

Results

During the study period, a total of 429 patients died with cancer in KAMC, 9 patients were excluded due to incomplete data. The median age was 62 years (range 17–108); 52% female and 48% male. 87.4% of patients were Saudis and 12.6% non Saudis.

The following solid tumors types were represented: gastrointestinal cancer 54 (20.0%), colorectal cancer 61 (14.5%), lung cancer 56 (13.3%), breast cancer 54 (12.9%), genitourinary 41 (9.8), HCC 32 (7.7%), biliary tract 23 (5.5%), head and neck 21 (5.0%), cancer unknown 20 (4.6%), gall bladder carcinoma 10 (2.4%), sarcoma 8 (1.9%), CNS cancer 3 (0.7%), and miscellaneous 7 (1.7%).

Among the included patients, 124 (29.5%) received LM-PCT and 296 (70.5%) were treated with best supportive care alone. The patients that received LM-PCT were subjected to intensive medical care in the form of frequent admission to the hospital through ER (80.6%), and about half of those patients died in critical care (49.2%) compared to 33.6% and 15.9% in non PCT.

Chi-square test for independence revealed that LM-PCT had a strong association with place of death and mode of admission. However, no association was found with age, gender, tumor type and nationality (Table 1).

Of the 124 patients received LM-PCT, 63% were below 65 years old. Gender was nearly divided equally between males and females.

Among the patients received LM-PCT, 27 patients received PCT in the last one week of life, 28 patients in the last 2 weeks of life and 69 patients in the last 4 weeks of life. This represents 21.8%, 22.6% and 55.6% of patients who received LM-PCT (n = 124) respectively, and 6.4%, 6.7% and 16.4%, among the total number of deaths (n = 420), respectively. The distribution as regards each separate year was illustrated in Table 2, and Fig. 1.

Discussion

The availability of new chemotherapeutic agents has caused a subsequent increase in the length of time patients are receiving chemotherapy. It is not easy to identify the role of end of life chemotherapy. While the use of chemotherapy and its tolerability are increasing, balancing the risks and benefits of such a treatment is getting more complex. Ultimately, it may involve judgments about the use or restraint of use of costly resources despite little chance of benefit [8]. Deciding when to discontinue chemotherapy is often challenging, however, given limited data on whether chemotherapy is helpful or harmful in the final months of life.

This study to my knowledge is the first to describe the pattern of PCT utilization and continuation until the end of life in King Saudi Arabia. This study revealed that, among the patients with advanced cancer; 29.5% received LM-PCT. Multiple studies reported the increase of PCT practice. In Italy, within 30 days of death, 23% of patients with incurable cancer received PCT [6]. This was within the range of previous published results, 18–33% [9–11].

Among the identified patients who had been received PCT, 21.8% was commenced in the last week, 22.6% in the last
2 weeks and 55.6% in the last 4 weeks of life, compared with 8% in the Australian population and 18.5% in the North America population in the last 2 weeks of life [12].

During the study period, we observed a progressive increase in the number of LM-PCT; 19 patients (15.3%) in 2011, 35 patients (28.2%) in 2012, 46 patients (37.1%) in 2013 and 24 patients (19.4%) in first 4 months of 2014 (till April 2014).

The possible explanations to account for the higher rate and progressive increase in futile chemotherapy in our country include, limited access to hospice and palliative care services for all patients, the new era of using targeted therapy as longer- term maintenance treatment could be one of the justifications for patients receiving therapy nearer to the time of death. Moreover, our patients who received PCT were less likely to acknowledge that they were terminally ill and may not find it easy to accept their condition, in addition to some emotional and religious factors; the oncologist may find it hard to deliver this information to the patients or their caregivers, which is in agreement with other studies; On 95 consecutive patients receiving PCT, prognosis was discussed by only 39% of medical oncologists [13], and in other studies, about one third of patients and families reported, they did not believe in the concept of PCT [14,15].

In the present study, more than half (63%) of the patients with metastatic disease started LM-PCT; with age <60 years old which matches with many other studies [16–18], however, some studies show that the performance status is the most important issue for treatment results, not the age which is not evaluated in our study [19–21].

Also, patients received LM-PCT were subjected to intensive medical care in the form of frequent admission to the hospital through ER (80.6%), and about half of those patients died in critical care (49.2%) compared to 33.6% and 15.9% in non PCT, which is statistically significant. However, no association was found between age, gender, type of tumor or nationality and starting PCT. These results are consistent with studies

### Table 1  Patients characteristics in LM.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>LM-PCT status N; 420</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not received PCT N; 296 (70.5%)</td>
<td>Received PCT N; 124 (29.5%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td>160 (67.2%)</td>
<td>78 (32.8%)</td>
</tr>
<tr>
<td>≥65</td>
<td>136 (74.7%)</td>
<td>46 (25.3%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>141 (70.1%)</td>
<td>60 (29.9%)</td>
</tr>
<tr>
<td>Female</td>
<td>153 (70.5%)</td>
<td>64 (29.5%)</td>
</tr>
<tr>
<td>Nationality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saudi</td>
<td>259 (70.6%)</td>
<td>108 (29.4%)</td>
</tr>
<tr>
<td>Non Saudi</td>
<td>37 (69.8%)</td>
<td>16 (30.2%)</td>
</tr>
<tr>
<td>Mode of admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ER&lt;br&gt;</td>
<td>99 (49.7%)</td>
<td>100 (50.3%)</td>
</tr>
<tr>
<td>OPD&lt;br&gt;</td>
<td>186 (89%)</td>
<td>23 (11%)</td>
</tr>
<tr>
<td>Transferred</td>
<td>10 (90.9%)</td>
<td>1 (9.1%)</td>
</tr>
<tr>
<td>Place of death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Critical care; ICU, CCU, ER</td>
<td>47 (43.5%)</td>
<td>61 (56.5%)</td>
</tr>
<tr>
<td>Regular ward</td>
<td>249 (79.8%)</td>
<td>63 (20.2%)</td>
</tr>
</tbody>
</table>

Chi-square test for independence revealed that LM-PCT had strong association with place of death, i.e., critical care wards vs. regular wards and mode of admission, i.e., ER, OPD and direct transferred from other health care facilities ($\chi^2 (1df, N = 420) = 50.8$, $p < 0.0001$, $\phi = 0.35$) and ($\chi^2 (2df, N = 419) = 77.6$, $p < 0.0001$, $V = 0.43$), respectively. However, no association was found with age, i.e., <65 and ≥65 ($\chi^2 (1df, N = 420) = 2.8$, $p = 0.09$); gender, i.e., male and female ($\chi^2 (1df, N = 420) = 0.006$, $p = 0.93$); tumor type ($\chi^2 (1df, N = 420)$, $p = 0.3$) and nationality, i.e., Saudis and non Saudis ($\chi^2 (1df, N = 420) = 0.007$, $p = 0.94$).

* $P$, value ≤0.05 significant.

b ER; emergency room.
c OPD; outpatient department.
d ICU; intensive care unit.
e CCU; cardiac care unit.

### Table 2  Pattern of LM-PCT during the study period.

<table>
<thead>
<tr>
<th>Duration (days before death)</th>
<th>No. of patients died</th>
<th>Total/%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2011</td>
<td>2012</td>
</tr>
<tr>
<td>0–7</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>8–14</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>15–30</td>
<td>8</td>
<td>19</td>
</tr>
<tr>
<td>Total/%</td>
<td>19 (15.3%)</td>
<td>35 (28.2%)</td>
</tr>
</tbody>
</table>

* Palliative chemotherapy in the last month.

** Till April 2014.
done by Earle et al. [4] and Nappa et al. [22]. Similarly, Write et al. demonstrated that in terminal cancer patients who received chemotherapy in the last months of their lives are less likely to die where they want and are more likely to experience painful, aggressive procedures. These patients saw no survival benefits from end-of-life chemotherapy but they faced higher rates of cardiopulmonary resuscitation, mechanical ventilation, or both, during their last week of life (14% vs. 2%). Also more died in ICU (11% vs. 2%) [23].

Whether these unfavorable outcomes were a result of disease progression or caused by the last cycle of PCT cannot be concluded in this study.

It is not a regional observation, it is found in many studies from multiple countries revealing that patients with cancer preferred aggressive treatment even with major adverse effects for doubtful benefit [24].

Limitations

The use of one month as cut off may be questioned. But this time frame of has been used in other published studies [6,7,9,11,12,23,25-28]. Retrospective studies most always are criticized as the completeness of data often is suboptimal and depends totally on medical documentation without matched controls beside the limited information about patients that died outside the hospital. Data on performance status could not be reviewed in medical records which is an important factor in PCT selection.

Conclusion & recommendation

Our data demonstrated an increased use of chemotherapy near or at the time of death without apparent guidelines for its use. We are in need to better assessment of each patient’s prognostic factors at the time of chemotherapy. Also oncologists should note the availability of hospice and palliatives from the beginning, as part of routine good care of the seriously ill patient and must improve their skills in helping patients think clearly about the appropriateness of PCT.

Ethical consideration

Ethical approval to conduct the study was taken from the IRB review committee before the commencement of the study.

Conflict of interest

The authors certify that is no potential or actual conflict of interest related to this research.

References

Palliative chemotherapy at end-of-life


