

Utilization of systemic palliative chemotherapy at the end of life: a local experience

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Abstract

Objective: To evaluate attitude towards using systemic chemotherapy near the end of life for cancer patients.

Methods: This retrospective study comprised data of all patients who died with cancer at the Medical Oncology Department of the National Oncology Centre, Muscat, Oman, from January 2009 to December 2011. The records were retrieved from the electronic patient record system of ALSHIFA, Royal Hospital. Demographic data, chemotherapy at end of life, performance status, 'do not resuscitate' status, hospitalisation, and chemotherapy toxicity were analysed.

Results: The mean age of the 261 patients in the study was 52.3 ± 14.52 years. Ninety-two (35%) patients did not receive chemotherapy in the last 3 months of their lives. Chemotherapy administered at end of life was 169 (65%), 126 (48%), and 75 (29%) in last 3 months, one month and 2 weeks of life. Those who received more than 3 lines of chemotherapy were 66 (36%).

Conclusions: The end-of-life use of chemotherapy should always be carefully discussed. The patient's right to information should be honoured. The transition from active to best supportive care should be carefully guided.

Keywords: End of life care, Chemotherapy at EOL, Palliative care, Royal Hospital Oman, NOC Oman. (JPMA 64: 863; 2014)

Introduction

A large proportion of patients eventually expire, despite substantial advances in the treatment of cancer.¹ The issues these patients face near the end of life (EOL) are similar, regardless of cancer type.² The preference of cancer treatment at EOL has become increasingly complex due to more treatment options available, higher expectation with newer therapies, less toxic and more tolerable treatments, and the option of best supportive care (BSC). It has an unprecedented impact on patient, family, caregivers and health economics.³⁻⁷ Which treatment modality to opt for is essentially a patient's prerogative, yet the treating physician has a persuasive influence to make a justifiable choice.⁷⁻⁹ Appropriateness of chemotherapy use in the late-stage disease is a key question.⁴ Better palliative care and supportive resources influence the probability of chemotherapy treatment at EOL.⁵ Despite less toxic agents the costs and quality of life (QOL) are of immense concerns. Preceding studies showed that patients accept a minor probability of chemotherapy benefit, even with associated profound toxicity.⁶ On the other hand, physicians often struggle to initiate discussions about shifting treatment objectives to palliative care.⁷ Chemotherapy is

administered in last 2 weeks to up to 34% patients. As an increasing trend, more than 20% of patients with metastatic cancer are put on a new chemotherapy regimen in the last 2 weeks of life.^{2,3,8} There is no arbitration line to justify an active chemotherapy.³ A selected chemotherapy regimen should ideally have an anticipated response rate above 20%, and a median survival advantage in weeks to months. Any response rate greater than 3.3% is expected to increase survival advantage by one week.³

A patient's perception and belief that survival is worth 6 months obviously makes him opt for aggressive treatment over BSC. This will not actually translate in survival advantage and often lead to more morbidities and healthcare burden.³ Patients gradually transform from optimism to realism. Obtaining honest prognostic information is not easy and about one-third of patients on palliative treatment believe it to be with curative intent.³ Discussion with families on this subject is not easy, and they might shop around to get the treatment of their own choice unjustifiably. The issue is further complicated in developing world with patient's ignorance of disease, his education, perceptions, family issues, social taboos, and beliefs. Physicians can never predict the course of disease, or death; nor can they always communicate effectively.³ Treating physicians are often overoptimistic and overestimate survival by at least 30%. The choice of treatment being advocated is

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also influenced by its accessibility.³

Decision making is not a straightforward process either for patients or treating physicians. The available studies in the last 20 years indicate that cancer patients often don't agree with physicians in treatment choices.³ Patients like to be fighters and there are often do-something, do-anything scenarios.² They opt for aggressive therapy despite a marginal objective benefit and expected profound toxicity. Physicians can still influence the decision, if the information is presented to the patients objectively.³ There is a great variability in physicians approach based on perceptions, style, institutional guidelines, organisational practices, and financial incentives. The prescription of carboplatin was increased by 17% with a \$33 increase in reimbursement in USA.² Patients want their physicians to be realistic, available, interactive, and responsive to their reservations.³ The choice of patients vary widely, and it is unclear how realistic information (prognosis, options, consequences) and decision aid (DA) tools, influence the therapy. The patient and physician are always under pressure to maintain hope and believe in positive outcome.^{3,9} Most patients make a confident initial decision on first consultation (74% chemotherapy, 10% observation, and 7% BSC only). Most patients in current time need detailed information and desire to be a part of decision making.⁹ This may not be the case in developing cultures where about one-third don't understand the information provided due to physician-patient communication issues, information overload, anxiety and denial. DA tools can enhance understanding, and realistic expectations from palliative chemotherapy for appropriate decisions and justifiable use of resources at EOL.⁹

The availability of new chemotherapeutic agents has lengthened the treatment timeline and increased the likelihood of receiving chemotherapy near EOL.¹⁰ Undoubtedly, selected use of chemotherapy towards EOL may be justified, but we need to convince patients and care providers to reduce its use when it doesn't contribute to quality of care and standard of practice. It is difficult to determine when the life of a patient with advanced disease will actually end. Expected survival, response rate and toxicity are crucial tools for decision making. The National Cancer Policy Board USA has defined poor quality care as when "the practices of known effectiveness are being under-utilised, practices of known ineffectiveness are being over-utilised, and when services of equivocal effectiveness are being utilised in accordance with provider rather than patient

preferences".² The well-known examples are overuse of chemotherapy very near death, high rate of emergency room/intensive care unit (ER/ICU) and in-patient care, and underuse of hospice.²

National Oncology Centre (NOC), Muscat, Sultanate of Oman, is the prime oncology care facility in the country. According to the National Cancer Registry, new cancer cases in the years 2008, 2009, and 2010 were 901, and 921 and 945 respectively. Palliative care programme is yet to be fully established as a speciality, and active cancer management, palliative care, and EOL care are all provided by the same primary caregiver oncologist. The objective of this study was to evaluate the attitude towards using systemic chemotherapy near the EOL for cancer patients treated at the institution, and to compare the practices with published data.

Patients and Methods

This retrospective study comprised data of all patients who died with cancer at the Medical Oncology Department of the National Oncology Centre, Muscat, Oman, from January 2009 to December 2011. The records were retrieved from the electronic patient record system of ALSHIFA, Royal Hospital. Information collected for each patient which included age at time of death, gender, nationality, address, cancer type, number of lines of chemotherapy used, interval between last chemotherapy session and time of death, number of hospital admissions in the last 3 months of life, duration of hospitalisation in the last 3 months of life, chemotherapy-related toxicity grade III and IV, Performance Status (PS) during the last chemotherapy session, and 'do not resuscitate' (DNR) status.

Microsoft Office Excel 2007 was used for data collection and analysis.

Approval for the study was obtained by the institutional Medical Ethics and Scientific Research Committee.

Results

There were 261 patients in the study and their mortality, age, gender, location and cancer types were noted (Table-1). Overall, 75 (29%) patients had received chemotherapy in the last 2 weeks of life, 126 (48%) in the last one month, 169 (65%) in the last 3 months, and 92 (35%) didn't receive chemotherapy in the last 3 months of life (Table-2). Mean hospital admission in the last 3 months of life were 2.2 ± 1.28 (range: 1-6), and mean hospital stay was 19.8 ± 18.85 days (range: 1-85 days). Most of our patients 236 (90%) were coded Do Not Resuscitate (DNR).

Table-1: Demographic data (N=261).

Number of Cases	261	
Mean Age	52.3±14.52 years (range 14 - 90 years)	
Gender	Male 124 (47.4%)	Female 137 (52.6%)
Location	Muscat 121 (46.4%)	Outside Muscat 140 (53.6%)
Nationality	Omani 244 (94.3%)	Expatriates 17 (6.5%)
Mortality	2009 90 (34%)	
	2010 80 (31%)	
	2011 91 (35%)	
Tumour Site	Breast 53 (20.3%)	
	Lung 27 (10.3%)	
	Gastrointestinal Tract 27 (10.3%)	
	Lymphoma 24 (9.2%)	
	Colorectal Cancer 21 (8%)	
	Pancreato-biliary 21 (8%)	
	Gynaecological Cancers 18 (6.9%)	
	Sarcoma 17 (6.8%)	
	Urological tumours 16 (6.1%)	
	Head and Neck 14 (5.3%)	
	Unknown primary tumours 10 (3.8%)	
	Brain, Thymoma, HCC, Mesothelioma, Pheochromocytoma 13 (Less than 1.5%)	

Table-2: Chemotherapy at the End of Life (EOL) N=261.

Chemotherapy Administered at EOL	Number	Percentage %
No Chemotherapy in Last 3 Months of Life	92	35%
Patients Who never Received Chemotherapy	51	55%
Patients Who decided to Stop Chemotherapy	41	45%
Chemotherapy Administered in Last 3 Months of Life	169	65%
Chemotherapy Administered in Last 1 Month of Life	126	48%
Chemotherapy Administered in Last 2 Weeks of Life	75	29%

EOL: End of Life.

Of the 169 patients who had received chemotherapy in the last 3 months of life, 51 (30%) received one line, 52 (31%) received two lines and 66 (36%) received three or more lines of chemotherapy (Table 3). Forty-four (26%) patients were in Performance Status (PS) 1 or 2 on the World Health Organisation (WHO) Scale, and 125 (74%) were in PS3 or 4. Thirty-seven (22%) patients had grade III/IV chemotherapy related toxicity. Thirty-six (21%) received chemotherapy as per recommendation from abroad and/or on choice by the patients or their families.

Of the 75 patients who received chemotherapy in the last 2 weeks of life, 29 (38.6%) received it as 1st line, 16 (21.4%) as 2nd line, 13 (17.4%) as 3rd line, 11 (14.6%) as 4th line, 3 (4%) as 5th line and 3 (4%) received chemotherapy as 6th line. Two (2.5%) patients were PS1, 22 (29%) were PS2, 32

Table-3: Chemotherapy Administered in Last 3 Months of Life (N=169).

Lines of Chemotherapy Used	One Line of Chemotherapy	51	30%
	Two Lines of Chemotherapy	52	31%
	Three or More Than 3 Lines of Chemotherapy	66	36%
Performance Status as per WHO Scale	PS 1-2	44	26%
	PS 3-4	125	74%

WHO: World Health Organisation.

(43%) were PS3, and 19 (25.5%) were PS4. Seventeen (23%) patients received chemotherapy as per recommendation from abroad and as per the discretion of the patients or their families.

Of the 92 patients who didn't receive chemotherapy in the last 3 months of life, 51 (55%) didn't receive chemotherapy at any time, 41 (45%) stopped chemotherapy before 3 months of death mostly on the joint concerted decision between physician and family. A good number of patients did not have a realistic diagnosis known, nor were well aware of the prognostic information.

Discussion

Choices of cancer therapy at EOL are becoming increasingly complex. These are often aggressive and need to be a bilateral, well-informed, and consensual process.^{3,8} Aggressiveness of EOL care could be defined as the occurrence of at least one of the following indicators: last dose of chemotherapy received within 14 days of death; more than one emergency department visit within 30 days of death; more than one hospitalisation within 30 days of death; or at least one intensive care unit (ICU) admission within 30 days of death.^{11,12} Use of chemotherapy is increasing (29.5%), chemotherapy more frequently administered near EOL (18.5% in last 2 weeks), last regimen often started in last 30 days, frequent ER visits (9.2%), with frequent hospital admissions (9.1%), prolonged hospital admissions, and ICU admissions as 9.4%.^{2,8}

Chemotherapy remains the mainstay of cancer treatment, is increasingly available, and is better tolerated. Its institution at pre-terminal or terminal phase of disease involves a realistic judgment, a focus on goals of care, and a pragmatic outcome assessment balancing perspectives of the patient and treating oncologist. Appropriately timed cessation of chemotherapy is integral to patient's QOL.¹⁴ Using indicators for quality of EOL services, a study concluded that continuation of ongoing treatments very near death was aggressive care and less than 10% of

patients should receive chemotherapy in the last 14 days of life.¹⁴ There is no substantial evidence of increased efficacy or better overall OS with newer molecules at EOL.²

Chemotherapy use near EOL varies widely, indicating diverse trends. A study reported that the only predictor for continuing chemotherapy in the last 4 weeks of life was clinical oncologist.¹⁴ Data from 10 US community practices showed that chemotherapy was given within 30 days of death for 43% of patients with lung cancer and within 14 days for 20%.¹⁵ One study found in 17 Korean hospitals, 47.8% of patients received chemotherapy in last 6 months of life, and 30.9% in the last 30 days.¹⁶ In Canada, palliative chemotherapy was given in the last 2 weeks for 2.4%-9.3% of patients.¹⁷ In a study among 204 850 Taiwanese patients, rates of continued chemotherapy in the last month of life were 17.3%-21.0%.¹ A UK study found that during a 6-month period, of those receiving chemotherapy, 8% died within 30 days of last chemotherapy.¹⁸ In Sweden, 23% of patients received chemotherapy in the last month of life.¹⁹

In our study, 29% received chemotherapy in the last 2 weeks of life. This could be explained by insistence from patient's families, often unjustified recommendations from overseas oncologists (23%), despite counselling, and despite most of patients (90%) coded as DNR. The practice of physicians in private sector is often governed by financial benefits, and is beyond any moral/ethical/legal accountability. The non-availability of palliative care programme as an alternative option is another reason. Expensive chemotherapeutic drugs and targeted agents are often prescribed near EOL as forced decisions. The cost of managing chemotherapy induced toxicities (22% of patients received chemotherapy in the last 3 months of life) and costs of hospitalisation (mean hospital stay: 19.8 days) should always be considered. No major changes in the trend of using chemotherapy in last 2 weeks of life and mortality were noted in the study.

An Italian study found that for patients living in areas where palliative care services were not available, 52% received chemotherapy in the last 3 months, 15% in the last month, and 10-14% in the last 2 weeks of life. In contrast, of the patients living in the territory served by palliative care units or a hospice, none received chemotherapy in the last 2 weeks of life, and 37% received it in the last 3 months of life.² The study concluded that the availability of palliative care services can influence the interval between last chemotherapy

administration and death.⁴

A Canadian study showed that patients were more likely to receive aggressive EOL care if they were men, were younger, lived in rural regions, had a higher level of comorbidity, or had breast, lung or haematologic malignancies.¹³ Aggressiveness of active oncology care seems to be increasing in Canada, but is still lower than USA (increments multiple ER visits - 10.5%, ICU admissions - 5.4%, chemotherapy institution - 2.9%), with 22.4% having had at least one incident experienced.¹³ There is expected 1% increment in these indicators annually. EOL in Taiwan was found very aggressive in high grade high stage malignant disease, where care is given in high resource and well equipped centres by oncologists.¹¹

To decide cessation of chemotherapy and its timing is arbitrary, difficult, and with no clear "stopping rules".² Doctors may be not accurate in predicting a prognosis or death.² Discussion about death and supportive care is an arduous subject, especially when patients and/or family desire to continue aggressive therapy. Healthcare providers are likely to be reimbursed more for prescribing chemotherapy than for engaging in long conversations about EOL concerns.³ Information about prognosis and treatment efficacy seems to be important, yet almost one-third of patients misunderstand it.⁹ One-third of metastatic lung cancer patients thought they are receiving therapy with curative intent,²⁰ and 35% believed their palliative radiation was curative.²¹ Those treated in non-teaching hospitals received more chemotherapy and were less likely to receive opiates as optimal pain management.¹¹

Integration of palliative care early in the course of disease for incurable malignancies is a feasible and efficacious approach for improving QOL and extending survival.²² In a randomised controlled trial of 151 patients with newly diagnosed metastatic non-small-cell lung carcinoma (NSCLC), median survival was longer among patients receiving early palliative care (11.6 vs. 8.9 months). Fewer patients in the early palliative care group received aggressive EOL care (33% vs. 54%).²³ Analysis of data from 8 US hospitals with established palliative care programmes proved it to be very cost-effective.²⁴

The question, "To give or not to give chemotherapy near the EOL" remains unanswered. Further studies are required to elucidate the idyllic application of palliative chemotherapy and the correct time to say "Enough is enough". Palliative care services can offer great help to patients, families and oncologists in this scenario.

Palliative care and oncology clinicians should be logical partners in patient care with advanced life-threatening cancer, where communication is of paramount importance. Decision making in advanced cancer is complex in every possible dimension.¹¹ The dynamics of decision making is intricate. Decision often changes, and with time patient becomes less and less confident in decision making. Most patients in current time need detailed information as a part of decision making.⁹ This may not be true in the developing world. About 1/3 don't understand the information due to physician-patient communication issues, information overload, anxiety and denial. This understanding-misunderstanding leads to polarised management decisions.⁹

Cancer incidence and related mortality are expected to increase, emphasising the need for quality of care at EOL.¹³ Induction of palliative care as a feasible and efficacious strategy from the outset, soon after diagnosis, has a positive impact on quality of life, mood, and survival.²² The early palliative care alleviates toxicity symptoms, often allowing more justifiable chemotherapy. It facilitates smooth transition from active care to EOL BSC.²² Continuation of chemotherapy near EOL with minimal benefit and profound toxicity delays transition to BSC/hospice care, increases depression, anxiety and complicated bereavement issues.²² American Society of Clinical Oncology (ASCO) quality care initiative has described key indicators at EOL as no chemotherapy in the last 2 weeks of life, early referral to BSC/hospice, and hospice care of more than a week before death. Some patients were found to receive up to 9 lines of chemotherapy before death. Early transition to palliative care reduces this risk of continuing non-beneficial toxic chemotherapy, without compromising survival.²² Oral chemotherapy may, however, be considered as an option. There are issue of quality care, health economics, emotional burden, and failed expectations. These issues vary in intensity based on patients demographics (age, gender, educational status, marital status, co-morbidity, having dependent children), disease characteristics (lung, liver, pancreas; higher stage, performance status), patient's preferences, local health practices, and regional healthcare guidelines.^{12,25} All these issues influence and will shape future oncology practice and patient's trust.²⁵

Honouring patient's values and choice for care at EOL is an ethical obligation and a patient's right.²⁵ The patients who recognise their terminal illness (83%) will prefer a symptom directed management. About 17% still want

life-prolonging therapy with poor QOL and distress, and actually don't survive longer.²⁵ Patients' choice for treatment²⁵ has to be based on realistic expectations. About 1/3 patients discuss their wishes, but much lower in this part of the world.²⁵ Treating physician should encourage, initiate, and engage patients in EOL care discussions. The patients who go through such a discussion are less stressed and more comfortable.²⁵

Conclusion

Patient's right to information access is often denied intentionally by family, and by physician as a forced decision in the developing world. This has detrimental effect in oncology practice in terms of patient involvement, his perceptions, his confidence, and satisfaction in treatment and treating physicians.

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