

Impact of Early Palliative Care on Quality of Life of Patients with Advanced Stage of Carcinoma Cervix: A Prospective Observational Study

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Abstract :

Background: Palliative care aims to relieve suffering in all stages of disease. We studied the effect of introducing palliative care early at diagnosis on patient reported outcome among patients of carcinoma cervix.

Methodology: We assigned patients with advanced stage of carcinoma cervix to receive either early palliative care integration or standard oncologic care alone. Quality of life and overall health were assessed at baseline, 12 weeks and at 20 weeks with use of European Organisation for Research & Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C-30 scale and EORTC QLQ Cx-24 scale. We studied the secondary outcomes related to emergency hospital visits, compliance to treatment and End of life interventions. **Results:** The difference in score of EORTC C-30 and EORTC QLQ Cx-24 scales amongst groups was statistically significant at 12 weeks ($P < 0.05$). Group P patients had 100% compliance for treatment, as compared to patients from Group C, as 6 patients left treatment before conclusion. The difference in scores of Group P and Group C, for all EORTC C-30 and EORTC QLQ Cx-24 questions at 20 weeks were not statistically significant ($P > 0.05$).

Conclusion: Among patients with advanced stage of carcinoma cervix, early palliative care led to significant improvement in quality of life, overall health, emergency hospital visits, and admission at end of life.

Key words: Carcinoma of Cervix, Palliative Care

Introduction :

Early detection is the key point for the victory against cancer. There are many awareness activities and screening camps organised for early diagnosis of carcinoma cervix in women. But, because of lack of knowledge and sincerity towards the health, in developing countries, 80% of women present with advanced stage of carcinoma cervix.⁽¹⁾ Palliative care aims to relieve suffering in all stages of disease, starting from breaking the news of diagnosis of cancer. Palliative care interventions help patients to improve willpower and relieve treatment related pain, & suffering even during the treatment. Palliative Care visits motivate them to continue the treatment even with its troublesome side effects like nausea, pain,

malaise, etc. Thus, palliative care improves the compliance towards the treatment whether palliative or curative or adjuvant. Along with any cancer treatment, role of palliative care is un-separable.

Palliative care, with its focus on management of symptoms, psychological support, and assistance with decision making, helps to improve the quality of care and reduce the use of medical services.^(2,3) Usually, palliative care is preferred to be delivered late in the course of disease to patients who are hospitalised in specialised inpatient units or as a consultative service for patients with uncontrolled symptoms.^(4,5) To have meaningful effect on patients' quality of life and end of life care, palliative care services must be provided earlier in the course of disease.⁽⁶⁾ As the disease advances, patients' care by palliative medicine team lessens the burden to treating physician, surgeon, gynaecologist or radiotherapist.

Early studies show that patients who received early palliative care in the ambulatory setting, as compared with patients who received standard oncology care, had better quality of life and less aggressive end of life care.⁽⁷⁾ Several randomised trials have shown that simultaneous

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delivery of palliative and oncology care in the outpatient setting improves patient-reported outcomes.⁽⁸⁾ In patients with advanced cancer and a limited life expectancy, both telephone-based and in-person Palliative Care interventions led to improved Quality Of Life (QOL), reduced symptom burden, and greater satisfaction with care.⁽⁹⁻¹¹⁾

Aims and Objectives:

The aim of our study was to compare the effect of early palliative care integrated with standard oncology care and that of standard oncology care alone in patients with advanced stage of carcinoma cervix, on patient reported outcomes, e.g. overall quality of life and overall health of patients.

It was aimed to note the secondary outcomes like frequency of emergency hospital visits, compliance to CT (chemotherapy) and RT (radiotherapy), compliance to palliative care, interventions at End of Life like admissions to hospital for requirement of oxygenation or ventilation, survivor period and place of death, i.e. Home or Hospital or Hospice.

The aim of this research has been to improve symptom burden and quality of life in these patients with high morbidity and incurable disease.

Methodology:

This study included 50 patients reported at the outpatient onco-gynaecology clinic during the month of August 2015 to March 2017. They were randomly divided into two groups.

Group P, in which patients were invited by their clinician to enroll in this study by explaining the role of palliative medicine during her treatment period. These patients were newly diagnosed and received early palliative care beginning from the day of first visit, on confirmation of diagnosis. Palliative Care was integrated with standard oncological treatment and care in these patients. They were attended by palliative medicine team at least once a month. They were attended on phone whenever it was required.

Group C, in which patients were registered for study as control group and received only standard oncological treatment and care without integration of palliative medicine team.

All patients, from both groups, received either CT or RT or concurrent CT and RT, as part of standard oncology care. Patients with ECOG (eastern cooperative oncology group) performance status score 0, 1, or 2 and the ability to respond questions were included in the study.

Quality of life and other symptoms denoting overall health and disease related symptoms were assessed at baseline, at 12 weeks and at 20 weeks with use of translated version of EORTC QLQ C-30 scale and EORTC QLQ Cx-24 scale, which we translated in local languages, i.e., Gujarati and Hindi for better understanding of our patients. EORTC QLQ C-30 scale was used to assess health related quality of life which included all the dimensions like physical, functional, emotional and social wellbeing of patients. In addition, cervical cancer subscale EORTC QLQ Cx-24 was used to assess symptoms related to carcinoma of cervix.

The primary observations were, change in the Quality of the life of patients by observing the change from base line to twelve weeks. According to EORTC C-30 score questionnaire number 1 to 28 and EORTC QLQCx-24 score questionnaire (except question number 39 and 54), higher the score indicated poor results. According to EORTC C-30 score questionnaire number 29 and 30, and EORTC QLQ-CX24 score questionnaire number 39 and 54, higher the score indicated better health related quality of life. At the end of twelve weeks, assessment was done and after that we provided palliative care to all the patients till end of life. The secondary outcomes noted were frequency of emergency hospital visits, compliance to CT and RT, compliance to palliative care, interventions at End of Life like, oxygenation, ventilation, or ICU (intensive care unit) admission, survivor period and place where patient died weather at home or hospital or hospice.

Patients, who were lost to follow up, were excluded from the study and we enrolled new patients to complete the required study sample size. Statistical analyses were performed with Graph pad Quick calcs: t test calculator, scientific software, using Chi square categorical data, with the use of unpaired t test as intermediate value in calculation. The two tailed P value is derived to find statistical significance by conventional criteria.

Table 1: General characteristic of study participants

Variables	Group P	Group C
Age (M±SD) in years	49.84 ± 9.79	49.80 ± 9.68
Weight (M±SD)	49.16 ± 5.56	48.28 ± 6.88
Gender	Female	Female
Marital status		
Married	15	16
Single	2	3
Divorced or separated	3	3
Widowed	5	3
Number of patients with stage III B	18	19
Number of patients with stage IV	7	6
ECOG Score		
ECOG Score 0	8	6
1	13	14
2	4	5
Initial anticancer therapy		
Number of patients only on CT	4	3
Number of patients only on RT	4	6

Results:

All 50 patients from both the groups had no significant difference in demographic characteristics. Average age of patients in Group P was 49.84 ± 9.79 (M±SD) and Group C was 49.80±9.68. Number of patients living with spouse were 15 in group P and 16 in group C, rest were single, divorced or widowed (Table 1). 18 patients in Group P and 19 patients in Group C presented with stage III B and rest with stage IV of carcinoma of cervix (Table 1). In both the groups ECOG scores were comparable (Table 1). In Group P, 4 patients received RT alone, 4 patients received CT alone and 17 patients received combination RT and CT. In Group C, 6 patients received RT alone, 3 patients received CT alone and 16 patients received combination of RT and CT (Table 1).

Palliative care visits: Numbers of hospital visits in Group P were 3 within 12 weeks, which were planned follow ups. 90% of patients of Group C had average 4 emergency hospital visits, ranging from 3 to 6 within twelve weeks, primarily to address the management of symptoms (Table 5).

Quality of life: The baseline score of EORTC C-30 and EORTC QLQ Cx-24 scales was comparable ($P>0.05$) in both the groups (Table 2).

At 12 weeks, in Group P patients, Scores of EORTC C-30 questions 1 to 28 and EORTC QLQ Cx-24 questions 31 to 53 (except question 39& 54) decreased from baseline and Scores of EORTC C-30 questions 29 & 30 and EORTC QLQ Cx-24 question 39 & 54 increased from baseline (Table 3). In group C patients, in whom, standard care was taken by onco

Table 2: Bivariate analysis of quality of life outcomes at baseline

Variable	Group P N=25	Group C N=25	Difference between Group P and Group C (95% CI)	P Value	Standard error of difference
EORTC QLQ C-30 question number 1 to 28	2.249 ± 0.221	2.266 ± 0.210	0.01712	0.7807	0.061
EORTC QLQ C-30 question number 29	3.08 ± 0.70	3.16 ± 0.62	0.08	0.6723	0.188
EORTC QLQ C-30 question number 30	2.60 ± 0.50	2.72 ± 0.68	0.12	0.4799	0.169
EORTC QLQ Cx-24 question number 31 to 53 (except 39)	2.137 ± 0.074	2.121 ± 0.091	0.01632	0.4930	0.024
EORTC QLQ Cx-24 question number 39 & 54	1.280 ± 0.325	1.380 ± 0.389	0.100	0.3294	0.101

Table 3: Bivariate analysis of quality of life outcomes at 12 weeks

Variable	Group P N=25	Group C N=25	Difference between Group P and Group C (95% CI)	P Value	Standard error of difference
EORTC QLQ C-30 question number 1 to 28	1.935 ± 0.111	2.255 ± 0.162	0.031996	0.0001	0.039
EORTC QLQ C-30 question number 29	3.88 ± 0.78	3.56 ± 0.51	0.32	0.0921	0.186
EORTC QLQ C-30 question number 30	3.88 ± 0.73	2.64 ± 0.57	1.24	0.0001	0.164
EORTC QLQ Cx-24 question number 31 to 53 (except 39)	1.608 ± 0.068	1.859 ± 0.086	0.025112	0.0001	0.022
EORTC QLQ Cx-24 question number 39 & 54	1.780 ± 0.693	1.420 ± 0.373	0.36	0.0267	0.157

Table 4: Bivariate analysis of quality of life outcomes at 20 weeks

Variable	Group P N=25	Group C N=25	Difference between Group P and Group C (95% CI)	P Value	Standard error of difference
EORTC QLQ C-30 question number 1 to 28	1.906 ± 0.096	1.952 ± 0.069	0.04576	0.0610	0.024
EORTC QLQ C-30 question number 29	4.00 ± 0.58	3.92 ± 0.57	0.08	0.6247	0.162
EORTC QLQ C-30 question number 30	4.08 ± 0.49	4.00 ± 0.50	0.08	0.5717	0.140
EORTC QLQ Cx-24 question number 31 to 53 (except 39)	1.548 ± 0.050	1.573 ± 0.536	0.02532	0.0929	0.015
EORTC QLQ Cx-24 question number 39 & 54	1.820 ± 0.720	1.780 ± 0.663	0.040	0.4685	0.196

Table 5: Hospital visits, Hospital admission & EOL

Variables	Group P	Group C
Number of patients completed CT	21	15
Number of patients completed RT	21	17
Number of patients compliant to Palliative care visits	25	21
Emergency Hospital visits within 12 weeks	0	4

gynaecologist, average score of these scales didn't decrease or increased at 12 weeks (Table 3). The difference was statistically significant for all the question in both the groups ($P < 0.05$).

As all the patients from Group C were under palliative care after 12 weeks, there was improvement in scores of all questions in Group C at 20 weeks (Table 4). That's why, the difference in scores of Group P and Group C, for all EORTC C-30 and EORTC QLQ Cx-24 questions at 20 weeks were not statistically significant ($P > 0.05$).

3 patients from group C left Chemotherapy and Radiotherapy before conclusion. 2 patients from group C assigned to receive only RT left treatment after 11 and 17 fractions of external RT. 1 patient left chemotherapy after 3 cycles only because of lack of proper counselling and completed with intervention of palliative team after 12 weeks. All the patients from group P concluded their planned standard oncology treatment with palliative support (Table 5).

Out of 50 patients, 37 patients died after average 15 months ranging from 6 months to 23 months. 13 patients enrolled in later months are still alive and have coped well with their illness.

Out of these 37 patients, only 5 patients admitted to hospital at end of their life. 2 of them took discharge on request and died at home next week. Rest 3 required oxygen for breathing discomfort and they had choice to be under hospital care and died with dignity at hospital without any intervention or ventilatory support after few days stay. 1 of them took discharge once but came to hospital again after a week with complain of dyspnoea.

Discussion:

The World Health Organization and American Society of Clinical Oncology have recommended early integration of specialist palliative care in patients with cancer.^(8,12) Growing evidence supports a new role of palliative care specialists in the patients with advanced cancer.⁽¹³⁾ The literature has reported the results of early palliative care in patients of advanced carcinoma of lung,⁽¹⁴⁾ advanced stage of non colorectal GI (Gastro Intestinal) cancer,⁽⁷⁾ metastatic Non-Small-Cell Lung Cancer,⁽⁶⁾ in patients of advanced cancer,⁽¹⁰⁾ and End of Life experience of patients and caregivers.⁽¹⁵⁾

Carcinoma cervix is number one cancer in India.⁽¹⁶⁾ Patients report to healthcare facility in late stage. Hence; it was decided to provide early palliative care to these patients and report its outcome, when compared with patients receiving routine oncology care only. Nipp R D, E I-Jawahri A and colleagues⁽¹⁷⁾ found in their study that Male patients with lung cancer assigned to early palliative care reported better quality of life but the effect of early palliative care on this outcome was not significant for female patients. In our study conducted on 50 female patients, it is significant. We identified new benefit of the integrated palliative care model in improving patients' ability to cope with their prognosis, and enhancing their communication about end of life care preference with clinician.

The outcome measures following palliative care interventions are Quality of Life, patient health outcome, symptom control and End of life interventions. Many questionnaires are in practice to measure these outcomes. EORTC QLQ C-30 have

been developed by European Organization for Research and Treatment of Cancer QOL group of professionals and has been studied widely. We used translated version of EORTC QLQ-30 and EORTC -24 to assess health related QOL and Cervical cancer related symptom assessment respectively. There was significant improvement in overall health related QOL at the end of 12 weeks, in all patients who received Palliative care immediately after diagnosis. Similarly there was significant improvement in symptoms. According to Bakitas M, Layons KD,⁽⁹⁾ longer follow up might be needed to fully assess the effect of the early palliative care model on patient reported outcome. There was significant improvement in Cervical cancer related symptoms in patients receiving early palliative care compared to patients receiving standard oncology care, at 12 weeks. There is moderate evidence to support the role of early specialist palliative care intervention in improvement of symptoms, survival, and health-related communication.^(18,19)

After 12 weeks, all females received palliative care and EORTC QLQ-30 and EORTC C-24 were evaluated at 20 weeks. There was improvement in score, though not significant, in patients receiving palliative care very late during the course of their disease. Jennifer S. Temel, Joseph A.⁽⁶⁾ Greer studied early palliative care for patients with metastatic non-small cell lung cancer and found that early integration of palliative care with standard oncology care resulted in survival that was prolonged by approximately 2 months and clinically meaningful improvement in quality of life and mood. They also included greater documentation of resuscitation preference and less aggressive care at the end of life. Diane st Germain, R N, M S of NCI's division of cancer prevention said in her blog that, it is important to determine the impact of early palliative care in additional types of cancer. Joseph A Greer⁽⁷⁾ also suggested to investigators to explore the role of targeted palliative care interventions to address the specialised needs of specific cancer population with particular attention to appropriate timing for palliative care integration. Accordingly we decided to study on advanced carcinoma of cervix and found it effective as in GI cancer patients of Greer and team. A possible explanation for these findings is that patients with GI cancer spent more time in the hospital than did patients with lung cancer, which may have affected their quality of life.

Whereas symptom management is a core component of palliative care, providing patients with the skills they need to cope with and communicate about their life threatening illness is another essential element of palliative care for patients with advanced cancer. Limitation of our study was that, patients and clinicians were not blinded to group assignment. We conducted the trial at a single institution, which may limit the generalizability of the results of other care settings and clinical population. Because the sample lacked diversity with respect to race and ethnic group, we were unable to assess the effect of these important factors on study outcomes. Although we used randomized, controlled design, both the patients and the clinicians were aware of the study assignment.

We could not keep the patients from control group, out of our care as we assessed them at 12 weeks and found poor quality of life and poor symptom management. As we included all the patients in palliative care couldn't compare quality and management at End of life. Our trial had low rate of loss to follow up (plus we excluded those few patients) and high rate of participants who completed the study assignment (good compliance to palliative care). Finally, the trial was adequately powered to detect changes in both quality of life and overall health of patients and we are prospectively collecting data on end of life care for further presentation.

This study shows the effect of palliative care when it is integrated early in the course of disease in the patients of advanced carcinoma cervix. The results from this trial add to the growing literature on the benefits of integrating palliative care service in the course of disease for patients with advance cancer.

Conclusion:

Early integration of palliative care for patients with advanced stage of carcinoma cervix is a clinically meaningful and feasible care model that has significant effects on quality of life, overall health, emergency hospital visits, and admission at end of life.

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