Palliative Radiotherapy In Advanced Cancer Of The Cervix

B Rai, D Khosla, F Patel, M Arora, S Sharma

Citation

B Rai, D Khosla, F Patel, M Arora, S Sharma. *Palliative Radiotherapy In Advanced Cancer Of The Cervix*. The Internet Journal of Pain, Symptom Control and Palliative Care. 2012 Volume 9 Number 1.

Abstract

Aim: To assess the role of high dose palliative pelvic radiotherapy in patients with locally advanced/metastatic cancer of the cervix not suitable for radical treatment.Method: Seventy two patients with carcinoma of the cervix receiving palliative radiotherapy to the pelvis from January 2006-December 2010 were included in this study. Patients were treated with parallel-opposed pelvic portals with megavoltage radiation monthly up to a maximum of three fractions. The dose per fraction was 8Gy. The patients were assessed for relief of bleeding, vaginal discharge, pain, response and toxicity.Results: The mean age at presentation was 55 years and the mean duration of symptoms was 10 months. A control in vaginal bleeding was observed in 95% patients receiving three fractions. Sixty-six percent patients receiving three fractions had relief from vaginal discharge. Fifty eight percent patients had 100% pain relief after the third fraction. No grade 3-4 acute or late toxicity was observed in evaluable patients on follow up.Conclusion: 8Gy per fraction in two to three monthly fractions is an effective schedule for palliation in patients with advanced cancer of the cervix not suitable for radical radiation.

INTRODUCTION

Cancer of the cervix is one of the commonest malignancies in Indian women and is the leading cause of cancer mortality in India accounting for 23.3% of all cancer deaths (1).The high prevalence and burden of cervical cancer in India is attributed to lack of awareness, lack of access to health services, social inhibitions and poor socio-economic status. As a result many of our patients present to us late in advance stages of disease. Though standard curative treatment for cancer cervix is external radiation with concurrent chemotherapy followed by brachytherapy, many of these patients are not potentially curative in view of advanced and metastatic disease. Moreover, poor general condition, financial and logistical constraints make it further difficult for these patients to undergo prolonged treatment. Also acute treatment related toxicity with conventional fractionated regimens along with the co-existing problems only adds on to the patient's misery. Thus these patients with advanced local and/or metastatic disease are best suited for palliative radiotherapy where aim of treatment is symptom control and improvement of quality of life. A single or limited number of high dose fractions have been used by various centres in palliative radiotherapy of cancer cervix. Monthly palliative radiotherapy has been used in various studies in patients with advanced loco regional disease and has been found to be an effective schedule in terms of patient tolerance and symptom control (2-6). However, this treatment is recommended in only those patients in whom the life expectancy is less than one year (4).At our institute, we use a dose of 8Gy to the pelvis in 1-3 fractions at monthly intervals for patients with advanced or metastatic disease in whom life expectancy is less than one year. We present our experience of using this fractionation schedule in palliative radiotherapy in cancer cervix.

MATERIAL AND METHODS

A total of 72 patients received patients with carcinoma cervix in who palliative radiotherapy was delivered to the pelvis from January 2006-December 2010 were included in this prospective study. The inclusion criteria were as follows:

The demographic profile of patients is shown in table-1. The patients received treatment with local pelvic external radiotherapy with parallel opposed anterior-posterior field fields. The superior border of the radiation field was kept at junction of L4-L5 vertebral bodies and the inferior border was kept at the inferior border of the obturator foramina. The lateral borders were kept at 2 cm lateral to the pelvic brim. A dose 8 Gy was prescribed at mid plane delivered in a single fraction. The patients were treated with megavoltage radiation. All the patients were registered with the palliative clinic and were started on appropriate analgesics and

supportive care. The patients were reassessed at monthly intervals. A maximum of three fractions of 8 Gy each were delivered at monthly intervals. The patients were initially followed up every month for the first six months and were thereafter followed up every two months. The patients were assessed for relief of bleeding, vaginal discharge, pain, response and toxicity. Subjective assessment of clinical response was done according to the percentage relief in symptoms; i.e. (No response, 25%, 50%, 75% and 100%).Acute and late toxicity was graded according to the RTOG criteria.

RESULTS

Seventy-two patients with locally advanced or metastatic cancer cervix receiving palliative radiation to the pelvis were evaluated. The mean age at presentation was 55 years and the mean duration of symptoms was 10 months. The mean Karnofsky performance score was 60 and average haemoglobin was 9.1 gm%. Thirty seven (51.4%) patients had advanced loco regional disease and 35 (48.6%) had metastatic disease at presentation. Nine patients had frozen pelvis and four patients presented in uraemia.Thirty five patients had para-aortic lymph node metastasis at presentation and 35 patients had distant metastasis. The sites of metastasis were lung, liver and supraclavicular lymph nodes.

SOCIO-ECONOMIC STATUS

The socio-economic factors assessed were the education status, employment, income and marital status. Forty four (61% patients were completely illiterate) and only 3 (4.2%) patients were educated to secondary levels and higher. Sixty two (86%) patients were housewives and 10 (13.9%) patients had blue-collar jobs. None of the patients had a white-collar job. Fifty three (76%) patients were below poverty line and rest of the 17(23.6%) belonged to economically weaker section. Majority of the patients were married and 19 patients were widowed.

PATIENT COMPLIANCE AND TREATMENT

All 72 patients received the first fraction of radiation. Forty six of 72 patients received the second fraction of radiation. Of the 26 who did not receive second fraction of radiation, 15 patients were lost to follow up and 11 patients either had disease progression or no clinical response of disease. Thirty eight patients received the third fraction (table-2). No further RT was planned after 3 fractions.

RELIEF OF SYMPTOMS

Symptom relief was documented in all available patients after completion of each fraction of radiation.There was steady increase in percentage of patients relieved from bleeding from each fraction. A similar trend was observed for discharge and pain also. After 1 st fraction of radiation, out of 57 evaluable patients 11 patients (19%) had complete relief from bleeding. After the 2 nd fraction, out of 41 evaluable patients 22 patients (54%) had complete relief and after 3 rd fraction, out of 38 evaluable patients, 36 patients (95%) had complete relief from vaginal bleeding. In evaluable patients, complete relief in vaginal discharge after 1 st, 2 nd and 3 rd fraction was seen in 7 (12%), 17 (41%) and 25 (66%) patients respectively.

A complete pain relief after 2 nd fraction was observed in 10 (24%) patients and after 3 rd fraction was observed in22 (58%) patients. More than 50% pain relief was observed in forty five of 57 (79%) after the first fraction and in 41 (100%) after the second fraction. Thirty six of 41 evaluable patients (87.8%) patients had more than75% pain relief after the second fraction of radiation. All patients required analgesics before starting radiation. Thirty seven patients required step-1 analgesics, 31 patients required step-2 analgesics and four patients were started on oral morphine 10 mg 4 hourly for control of cancer pain. In patients on step-3 analgesics two patients were lost to follow up after the first fraction of radiation. In one patient, oral morphine was continued till the second fraction of radiation after which she was lost to follow up. The second patient had a good response to pain after the first fraction and was switched over to WHO step-I analgesics. There was complete relief from pain after the second fraction of radiation and she did not require further analgesics.

TOXICITY

All patients tolerated treatment well and acute toxicities were well controlled with symptomatic medical management. After the first fraction of radiation 8 patients developed grade I/II vomiting, 6 patients developed grade I/II diarrhea. Of the patients who received second fraction of radiation 5 patients developed grade I/II vomiting and 7 developed grade 1 diarrhea. After the third fraction only 2 patients developed grade II vomiting and 5 developed grade I diarrhea. No grade 3 acute toxicity was observed. Data available on late toxicity was very sparse. Of the patients on whom the data was available, 4 patients developed subcutaneous fibrosis of anterior abdominal wall and 2 patients developed radiation proctitis and bleeding per

rectum which was managed conservatively.

DISEASE RESPONSE AND SURVIVAL

After 1 st fraction, 42 out of 57 evaluable patients had a partial response, 14 had stable disease and 3 patients had clinical disease progression. After 2 nd fraction, 33 out of 41 evaluable patients had a partial response while 7 patients had stable disease and one patient had clinical progression of disease. Out of 38 patients who received all the three fractions, 29 patients had partial response 8 patients had stable disease and one patient had progressive disease. The median survival in our patients was 9 months. There were 25 patients who survived for 6-12 months and 10 survived for more than a year. Only one patient was alive at 20 months follow up.

Figure 1

Table 1: Demographic profile

Age (years)	Mean	55 (30-90)
Duration of symptoms (months)	Mean	10 (1-36)
KPS	Mean	60
Anemia	No of patients (%)	54 (75%)
	Mean Hb	8.4 (5.5-11.4 g/dl)
Stage	III B IV A IV B	11 (15.3%) 26 (36.1%) 35 (48.6%)

Figure 2

Table 2: Patient compliance and treatment

Dose	No of patients	Percentage	Absconded	No further RT planned
8 Gy x 1	72	100%	15	11
8 Gy x 2	46	64%	5	3
8 Gy x 3	38	53%	0	All

DISCUSSION

Many of our patients with cancer cervix present to us in advanced stage in a poor general condition with a limited life expectancy and are thus not suitable for curative radiotherapy Moreover, various patient factors and logistic factors like availability of resources, time for radiotherapy, patients' age and patients' household income need to be considered in such patients in whom palliation of symptoms is the main goal of treatment (7,8). In our study besides loco regionally advanced and or metastatic disease, we also tried to evaluate other patient related factors that were present in our patients. Nearly 2/3rd of our patients were illiterate and all but two patients belonged to the economically weaker section or were below the poverty line. Majority of the patients were housewives or widowed and were financially dependent. Thus, potential benefit and burden to the patient along with ethical principles and available clinical evidence need to be kept in mind when planning treatment for such patients. Also effective palliation should ideally have a lasting effect on patients' symptoms with minimal complications and should be inexpensive.

Radiotherapy is an ideally suited inexpensive modality used in palliative treatment. High dose per fraction in single or multiple fractions have been used in various centres in palliative radiotherapy of carcinoma cervix (4-6).As compared to protracted fractionation schedules, single or short fractionation schedules have been found to be as effective in symptom control in incurable cancers particularly in metastatic bone and brain lesions (9,10).However, though no randomized control trials for palliative radiation in gynaecological malignancies have so far been performed, trials in hypo fractionated palliative radiotherapy in lung and bladder cancers have been found to be as effective as protracted regimens in palliation of related symptoms (11,12). In a summary of 14 RCT's for the treatment of haemoptysis in patients with advanced lung cancer, 19 different dose fractionation regimes ranging from 10 Gy in one fraction to 60 Gy in 20 fractions over 6 weeks were compared. The authors concluded that hypo fractionation with one or two fractions were as effective as multiple fractions in the palliation of symptoms (11). In a similar randomized control trial in patients with advanced cancer of the bladder, palliative treatment with 35 Gy in ten fractions was compared to 21 Gy in three fractions. No difference in overall symptomatic improvement (50% and 53%) and in bladder and bowel related symptoms were reported. The survival was similar between the two arms (12).

In palliative radiation of pelvic malignancies, the first study reported from M.D Anderson Hospital found that 1000 cGy in a one to three fractions was effective in palliation of symptoms of vaginal bleeding, weight loss, pelvic pain, and edema in patients with advanced gynaecological malignancies. The authors reported 100% relief of bleeding and 63% relief of pain after three fractions of radiation (5).Retrospective studies using single fraction palliative pelvic radiotherapy in one to three fractions in advanced

cervical cancer have reported 50%-100% partial or complete relief of symptoms of bleeding, discharge and pain (2-4).

At our institute, we follow a protocol of using 8Gy per fraction in one to three fractions at monthly intervals for palliative radiotherapy to pelvis in patients with advanced cancer cervix. In the present series a complete relief in vaginal bleeding was observed in 54% patients after the second fraction and in 95% patients after the second fraction. A similar dose-response trend has been reported by Mishra et al where a 100% response to bleeding was observed after the third fraction of radiation.

In our study, a complete relief in vaginal discharge was observed in 66% patients after the third fraction. Highly variable results have been reported in the literature varying from 15%-100% in the complete relief of vaginal discharge (6, 13). Onsrud et al reported a relief from vaginal discharge in 36.4% receiving palliative radiation of 10Gy in one to three fractions in patients with cancer cervix. However, majority of patients 23 out of 28 patients with cancer cervix received two fractions of radiation. Only one out of 28 patients with cancer cervix received the third fraction. A complete relief in vaginal discharge was reported in 49% patients by Mishra et al. They observed that a dose response relationship for the relief of discharge was apparent only up to the second fraction (13).

However, in our study a progressive increase in relief from discharge was observed with increasing dose.

All patients in our study had some degree of pain requiring analgesic support. Nearly 50% of patients were started on step-2 and step-3 analgesics and more than 50% pain relief was observed in 100% patients after the second radiation fraction. A complete relief in pain was observed only in 58% patients after the second fraction. None of the patients required step-3 analgesics after the third fraction. Since the patients were on oral analgesics also, it is difficult to ascertain the pain relief occurring with radiation alone. Nevertheless, a steady increase in response to pain was observed in patients receiving three fractions. Boulware et al (5) reported pain relief in nearly 45% patients receiving a single fraction of 10Gy whereas in a study by Onsrud et al (6), none of the six patients receiving palliative pelvic radiotherapy had relief of pain. Mishra et al (13) reported complete relief of pain in 33% patients. Increased relief to pain in our study could be attributed to the concurrent use of analgesics which was not reported in any of these studies.

Acute grade 1-2 toxicity of nausea, vomiting and diarrhoea occurred in 10-12% patients receiving radiation. Though the data on late toxicity was very sparse, 4 patients developed subcutaneous fibrosis of the anterior abdominal wall and two patients complained of bleeding per rectum which was symptomatically managed by the use of stool softeners. Our fractionated schedule was well tolerated in all patients. In a study by Onsrud et al, 5 out of 53 patients who received two 10-Gy fractions developed late complications .Grade3 or 4 complications occurred in three (6%) patients, of which one patient had bowel perforation, one patient developed haemorrhagic cystitis and one patient developed bowel perforation and vesico vaginal fistula (6). All the three patients were more than 80 years of age and the complications occurred after 9 months of radiation. The lower rate of complications in our study could be because firstly, we used a lower dose of 8Gy instead of 10 Gy per fraction, only two patients in our study were above the age of 80 yrs and they did not come for follow up after the second fraction and a longer follow up is required for assessment of late complications. Though, none of the patients in our study had a complete response, the survival in our patients was comparable to the series reported by other authors.

In a systematic review on palliative radiotherapy for cervical carcinoma, the authors suggested that palliative radiation schemes that provide an optimal degree and duration of symptom relief while creating minimal burden to the patient and health care system were required. In this context, fewer fractions with less time at the hospital were preferable over multiple daily fractions (14). In our study, the schedule of 8Gy per fraction in two to three monthly fractions resulted effective palliation in patients with advanced cancer of the cervix not suitable for radical radiation. It was well tolerated with minimal toxicity and financial burden to the patient. However, well controlled randomized trials with quality of life endpoints are desirable to validate the same.

References

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM. GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 10 [Internet].Lyon, France: International Agency for Research on Cancer; 2010. Available from: http://globocan.iarc.fr, accessed on 29/05/2012.
2. Hodson DJ, Krepart GV. Once-monthly radiotherapy for the palliation of the pelvic gynaecological malignancy. Gyncol Oncol 1983;16:122-6.
3. Chafe W, Fowler WC, Currie JL, Dasvis ML, Walton LA, Montana G.Single fraction palliative pelvic radiotherapy in gynaecological malignancy;1000 rads. Am J Obst Gynecol 1984;148:701-5.

4. Hall JS, Rosenman JG, Varia MA, Fowler WC,Walton LA, Currie JL. 1000 cGy single dose palliation for advanced carcinoma of cervix or endometrium. Int J Radiat Oncol Bios Phys 1986;12:1947-50.
5. Boulware RJ, Caderao JB, Declos L, Warton JT, Peters LJ. Whole pelvis megavoltage irradiation with single dose of 1000 rad to pallite advanced gynaecologic cancers. Int J Rad Oncol Biol Phys 1979;5:333-8
6. Onsrud M, Hagen B, Strickert T. 10Gy single fraction irradiation for palliation and life prolongation in patients with cancer of the cervix and corpus uteri. Gynecol Oncol 2001;82:167-71
7. Coia L, Hanks G, Martz K, et al. Practice patterns of palliative care for the United States 1984-1983. Int J Radiat Oncol Biol Phys 1988; 14:1261-1269.
8. Lievens Y, Kesteloot K, Rijnders A, et al. Differences in palliative radiotherapy within Western European countries. Radiother Oncol 2000; 56:297-303.
9. Sze WM, Shelly MD, Held I, et al. Palliation of metastatic bone pain: single fraction versus multifraction radiotherapy-A systematic review of randomised trials. Clin Oncol 2003; 15:345-352.
10. Haie-Meder C, Pellae-Cosset B, Laplanche A, et al. Results of a randomized clinical trial comparing two radiation schedules in the palliative treatment of brain metastases. Radiother Oncol 1993; 26: 111-116.
11. Lester JF, MacBeth F, Toy E, et al. Palliative radiotherapy regimens for non small cell lung cancer. Cochrane Database Syst Rev 2006;4.
12. Duchesne GM, Bolger JJ, Griffiths GO T, et al. A randomized trial of hypofractionated schedules of palliative radiotherapy in the management of bladder carcinoma: results of medical research council trial BA09. Int J Radiat Oncol Biol Phys 2000;47:379–88.
13. Mishra SK, Laskar S, Muckaden MA, et al. Monthly palliative pelvic radiotherapy in advanced carcinoma of uterine cervix. J Cancer Res Ther 2005;1:208–12.
14. Lonkhuijzen LV, Thomas G. Palliative radiotherapy for cervical carcinoma, a systematic review. Radiother Oncol 2011;98:287–291.

Author Information

Bhavana Rai, M.D; dipNB Radiotherapy
Assistant Professor, Department of Radiotherapy and Oncology, Regional Cancer Centre, Postgraduate Institute of Medical Education and Research

Divya Khosla, M.D Radiotherapy
Senior Resident, Department of Radiotherapy and Oncology, Regional Cancer Centre, Postgraduate Institute of Medical Education and Research

Firuza.D. Patel, M.D Radiotherapy
Professor, Department of Radiotherapy and Oncology, Regional Cancer Centre, Postgraduate Institute of Medical Education and Research

Mini Arora, MBBS
Department of Radiotherapy and Oncology, Regional Cancer Centre, Postgraduate Institute of Medical Education and Research

Suresh C Sharma
Professor and Head, Department of Radiotherapy and Oncology, Regional Cancer Centre, Postgraduate Institute of Medical Education and Research