ORIGINAL RESEARCH PAPER

Radiotherapy

A STUDY ON PALLIATIVE HYPO- FRACTIONED RADIOTHERAPY IN CARCINOMA CERVIX IN MULTIPLE CLINICAL CONDITIONS

KEY WORDS: Cervix uteri, Carcinoma, Palliation, Hypo fractionation, Radiotherapy

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ABSTRACT

Aim: The study aims to apply the palliative hypo fractionated radiotherapy in cervical cancer patients to get rid of the pain, bleeding and obstructive symptoms.

Materials and Methods- Between January 2011 to December 2014, 95 patients of cervical cancers, underwent palliative hypo fractionated radiotherapy (RT). Both primary and metastatic regional lymph nodes were treated with 2D-RT technique. Median radiation dose was 30 Gy, 3 Gy daily fraction was delivered. Five out of total patients were excluded from study, due to acute intestinal obstruction and the remaining 90 patients were reviewed.

Results: Most common presenting symptom were bleeding and pelvic pain. Total follow up period was 15.6 months (range,5.5 to 22 months) and median survival time was 7.8 months (range, 4 to 24 months).The overall response rates were 90.8% and 65.6% for vaginal bleeding control and pelvic pain control, respectively. 45 patients (50%) patients did not have any acute side effects and 42 (46.66%) patients showed low grade toxicity(1,2),and only 3(3.33%) patients exhibited high grade(3,4) gastrointestinal toxicity which were treated satisfactorily. Late side effects occurred in 12 (13.3%) patients; only of grade 1 or 2.

Conclusion: Short-course palliative Radiotherapy is well tolerated, less time consuming and effective for relieving the major symptoms of uterine cervical cancer.

INTRODUCTION

The major cause of advanced cervical cancer in India is mainly due to poor sex organs hygiene maintenance (main reason for HPV infection), [1] illiteracy, low socio-economic status and lack of participation of general population in screening agendas.

Cervical cancer patients are treated with Radiotherapy (RT), Chemotherapy and Surgery, depending upon the stages. But Radiotherapy is the main modality of cure, alone or along with concurrent chemotherapy, performed with both radical and palliative intents for patients with cervical cancer. Use of Radical therapy is not wise for patients with poor performance status, in locally advanced and in metastatic stage. Under such conditions and in elderly patients with co morbidities (even in a curable disease status) palliative Radiotherapy is an appropriate option. Other causes of not to apply the Radical treatment are, acute toxicities and financial burden of long stay. Main discomforts of patients like pain and bleeding are relieved, thus quality of life is improved with palliative intent [2].

The Radiation Therapy Oncology Group (RTOG) 7905 trial and others studies proved that palliative EBRT in the form of large fraction size (range 6-10Gy) single or multiple dose on whole pelvis, control the bleeding and pain well, but late toxicities is a big issue, particularly the GI toxicity. [3], [4], [5] and [6]. Further in a prospective study conducted by RTOG, a dose of 3.7 Gy (two fractions per day) total 14.8 Gy monthly upto 3 months , but failed due to grade 3 toxicities [7].

Considering these high grade toxicities due to large fraction size, other palliative plans like 30 Gy in 10 fractions and 20 Gy in 5 fractions are commonly applied nowadays [8]. However, limited studies are available to describe the clinical benefit of small palliative fraction size.We used a schedule of 30 Gy in 10 fractions daily 3 Gy.The main aim of our study is to analyze the efficiency of short-course hypo fractionated RT to get rid of the symptoms due to cancer cervix for the palliation of uterine cervical cancer.

PATIENTS POPULATION

From January 2011 to December 2014, 95 patients of squamous cell carcinoma cervix were enrolled for palliative Radiotherapy. Five patients were excluded from study, due to acute intestinal obstruction. So remaining 90 patients were reviewed. The studied cervical cancer cases were staged clinically with revised FIGO 2009 staging system. Initial workup included pelvic and abdominal computed tomography (CT) or magnetic resonance imaging (MRI), cystoscopy, proctoscopy, positron emission tomography, endoscopic examination, and biochemistry analysis. [9].

PATIENT CHARACTERISTICS

Table 1, show the patient characteristics .The median age of patients is 65 years (range, 65 to 85 years). The Eastern Cooperative Oncology Group performance status is 1 (35 patients), 2 (40 patients), and 3 (15 patients), respectively. There were 4 reasons to do palliative treatment: extensive disease (43), age ≥75, morbidity (20) and refusal to radical treatment due to long stay (17). Almost 50% patients (45) suffered from vaginal bleeding and 50% patients (45) suffered from all symptoms including vaginal bleeding, pelvic pain and vaginal discharge. Anemia due to vaginal bleeding, treated successfully.

TABLE – 1
THE PATIENT CHARACTERISTICS

Characteristics	No of Patients
Age (Yr),median (range)	65(65-85)
ECOG Performance status	
1	35
2	40
3	15
Stage	
IIIA	25

IIIB	32
IVA	18
IVB	15

RADIOTHERAPY CHARACTERISTICS

Patients are treated with external beam RT. 2D-RT to deliver a dose of 30Gy in 3 Gy daily fractions for 5 fractions per week with 4-MV photon [10]. Total follow up period is 15.6 months (range, 5.5 to 22 months) interval was 1.5 to 2 months for the first 6 months, and 2.5 to 3 months after 6 months and median survival time is 7.8 months (range, 4 to 24 months). Treatment outcomes are palliation of symptoms and complications due to Radiotherapy.

TOXICITY EVALUATION

Symptoms and toxicities are graded and charted from the start of treatment till last analysis. The haemostatic effect is defined as nil to negligible vaginal bleeding, without medical intervention. Intensity of pain graded by the visual analogue scale (VAS). Radiation toxicities are measured with help of Common Terminology Criteria for Adverse Events ver.4.

Median pre treatment hemoglobin level was 7gm/dl (range 4.5-9) and median pretreatment VAS pain intensity was 8(range 6-10).

RESULTS

Total median follow-up time, survival time, and treatment period were 15.6 months (range, 5.5 to 22 months), 7.8 months (range, 4 to 24 months) and 8 days (range 6-10 days) respectively. Cessation of vaginal bleeding and pelvic pain was relieved in 95% of the patients (85patients). Most of the patients achieved control on vaginal bleeding in 3-5 days. Re irradiation was applied to five patients who suffered from relapse of vaginal bleeding during follow –up, with a total dose of 20 Gy in 5 fractions. Fifty four (60%) patients received either reduced dose or discontinued the analgesic.

All patients received planned Radiation at proper time and also no reduction in prescribed doses. 45 patients (50%) patients did not have any acute side effects and 42(46.66%) patients showed low grade and only 3(3.33%) patients exhibited high grade gastrointestinal toxicity which were treated satisfactorily. Late side effects occurred in 12 (13.3%) patients; only of grade 1 or 2. Table 2, shows the results of treatment-induced acute and late toxicities.

TABLE – 2
THE RESULTS OF TREATMENT-INDUCED ACUTE AND LATE TOXICITIES.

Toxicity	Grade1	Grade2	Grade3	Grade4
Acute Toxicity				
Diarrhoea	10	8	3	
Vomiting	6	5	-	
Pain abdomen	7	6	-	
Late toxicities				
Acute intestinal obstruction	2	3	-	
Constipation	4	2	-	
Urinary frequency	2	-	-	

Treatment induced toxicities.

DISCUSSION AND CONCLUSION

In many situations palliative RT remains better option for symptom control as compared to Radical RT in uterine cervical cancer .With Palliative treatment symptom control achieved in short duration and with less toxicity (with hemostatic RT). Multiple tumor sites have been successfully treated with RT [4], [5], [10], and [11]. Table 3, described the results in the literature, the dose of RT for hemostatic treatment of carcinoma of the uterine cervix.

For the palliation of gynecological cancers, many short course RT schemes have been described. In these regimens doses were 30 Gy /10 #, 3.7 Gy twice daily in 4 #, 8 Gy/1# single dose. Large dose per fraction produces excessive effect on healthy tissues. Previous studies of these large doses per fraction had only scanty data and irregular follow up; so long term endpoints are not significant. Fistula formation and high rate (12-24%) of late complications also of grade 3-4. [5], [12], [13]

EFFICACY AND TOXICITY DATA

The reported treatment induced acute toxicity rate is between 10% to 44% in large dose per fraction. In our study GI and genitourinary tracts toxicity is comparable with the previously reported results. Late complication rate. (0% vs. 6%-12%) [14], [15].

Using the linear-quadratic model, total dose of 30 Gy in 10 fractions corresponds to approximately 39 to 52.5 Gy in 2 Gy fractions [16]. Control of symptoms of vaginal bleeding and pelvic pain are outstanding i.e. 90% and 60% respectively. Acute gastrointestinal toxicity (grade3) is observed in only3 patients (3.3360%), which were managed conservatively. In follow up period late complications are observed but not severe. The main indication of palliative RT is control of vaginal bleeding and in these cases admission in hospital is indicated, when need for vaginal packing and blood transfusions.

Most of the patients in our study are of poor performance status and of old age, so close follow up was not possible. Median duration of follow up was of 15.6 months; therefore late complications could not be measured.

In conclusion, in short period this palliative 2D-RT regimen for uterine cervix cancer patients is very feasible for symptom palliation as well as tolerable treatment related toxicity.

TABLE – 3
THE RESULTS OF TREATMENT-INDUCED ACUTE AND LATE TOXICITIES.

References	Radiation dose per #/ no. of #	No of Patients	Treatment outcome %	Toxicity %
Boulware et.al	10Gy/#1	86	bleeding (45) Pain (40)	Acute (9.3)
	10Gy/#2, 3-4week int. .	55	bleeding (85) Pain (59)	Late(17.3)
Hodson and krepart	10Gy/#3,3 -4week int.	14	bleeding(100) Pain (100)	Late(14.3)
Spanos et.al	3.7Gy/#4, 48hr,2-4 int.	61	bleeding (76) Pain 31)	Acute(3) Late (7)
Choan et al	3Gy /10#	53	Bleeding(100) Complete response (88 %)	
Present Study	3Gy /10#	90	bleeding (90) Pain (80)	Acute(3) late

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