International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Sujindra E et al. Int J Reprod Contracept Obstet Gynecol. 2016 Oct;5(10):3572-3575
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20163447

Research Article

Radiation versus paclitaxel chemo radiation in the treatment of locally advanced carcinoma of cervix

Elamurugan Sujindra[1]*, Latla Chaturvedula[2]

[1]Department of Obstetrics and Gynaecology, Indira Gandhi Medical College and Research Institute, Puducherry, India
[2]Department of Obstetrics and Gynecology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

Received: 21 August 2016
Accepted: 16 September 2016

***Correspondence:**
Dr. Sujindra Elamurugan,
E-mail: sujindra@rediffmail.com

ABSTRACT

Background: Cervical cancer is the most common malignancy among women. Incomplete local control and the appearance of distant disease herald poor survival. Concurrent chemo radiation is recently developing as the preferred modality of treatment. The objective of this study was to compare the effectiveness of concurrent Paclitaxel chemo radiation to that of only radiation in treatment of patients with locally advanced squamous cell cervical cancer.
Methods: The study was carried out at JIPMER, Puducherry from October 2005 to October 2010. There were two groups with 25 patients each. Group 1 received only radiation - 4860 cGy EBRT daily in five fractions per week for a total of 27 fractions followed by HDR brachytherapy. Group 2 received 50 mg/m^2 of Paclitaxel on all Mondays followed by concurrent radiotherapy. Patients were assessed at 6 months and 1 year after completion of treatment. In October 2010 they were all examined to calculate four year survival and disease free survival rate.
Results: A total of 48 patients were analyzed. Complete response rate was 56% in group 1 and 72% in group 2. At the end of four years survival and disease free survival rate in group 1 was 57.9% and 31.6% and in group 2 was 57.1% and 33.3% respectively.
Conclusions: Concurrent chemo radiation with Paclitaxel gives promising results and is more effective method than treatment with only radiation.

Keywords: Radiation, Chemo radiation, Paclitaxel, Locally advanced, Carcinoma cervix

INTRODUCTION

Cervical cancer is the second most frequent cancer among women worldwide and accounts for 80% of all malignancies among women in developing countries.[1] It is the most frequent cause of death from cancer in Indian women.[2]

Advanced stages of cancer cervix is not amenable for surgical treatment. Radiation treatment has been the sole definitive treatment available for this category of patients.[3] However, radiotherapy is limited by the high dose required to treat large tumors. Efforts to overcome this problem have included use of heavy-particle radiotherapy, the use of different radiation-fractionation schedules, and the concurrent use of hyperthermia or chemotherapy.[4] Chemotherapy and radiotherapy have been found to have a synergistic effect.[4] Of the chemotherapeutic agents, Paclitaxel has been used in combination with radiation for the treatment of carcinoma cervix. Further there are very, few studies validating the superiority of such a combination to radiotherapy alone. Hence, we chose to study and compare the effectiveness of Paclitaxel chemo radiation with radiation alone, in the treatment of patients with locally advanced squamous cell carcinoma of cervix.

METHODS

The study was conducted in Jawaharlal Institute of post graduate medical education and research, Puducherry. There were two groups in the study: group I received only radiation and group II patients who received weekly Paclitaxel with radiation. The sample size was 25 in each group.

Prior approval was obtained from the Institutional Ethics Committee. Women presenting to the gynecology out-patient facility of our institute with locally advanced carcinoma of cervix (FIGO stages IIB to IIIB) were recruited for the study. The patients were randomized in blocks of five and allotted to the alternate groups. Patients of age > 65years, patients with associated cardiac, hepatic, and renal disease, with evidence of hydronephrosis or concurrent invasive malignancy were excluded from the study. Patients unreliable to follow-up and those with previous history of hysterectomy, pelvic radiotherapy or chemotherapy for treatment of cancer cervix were also excluded from the study.

Prior to treatment a detailed history was taken from all patients; all patients underwent thorough clinical examination and baseline investigations including hemogram, liver and renal function tests, chest x-ray, ultrasound of abdomen and pelvis for kidney, ureter and bladder and cervical biopsy. Cystoscopy and proctoscopy were done when warranted.

Group 1 received only radiation of 4860 cGy external beam therapy to the whole pelvis which was administered daily in five fractions per week at approximately 180 cGy per fraction for a total of 27 fractions (5 weeks) through one anterior and two posterior oblique beams starting on Monday. The radiation dose distribution in shown in Figure 1. Following external beam radiation, the patients were assessed and treated with two intracavitary applications (HDR - Iridium 192) placed 7-10 days apart for a total of approximately 7500 cGy effective dose to point A.

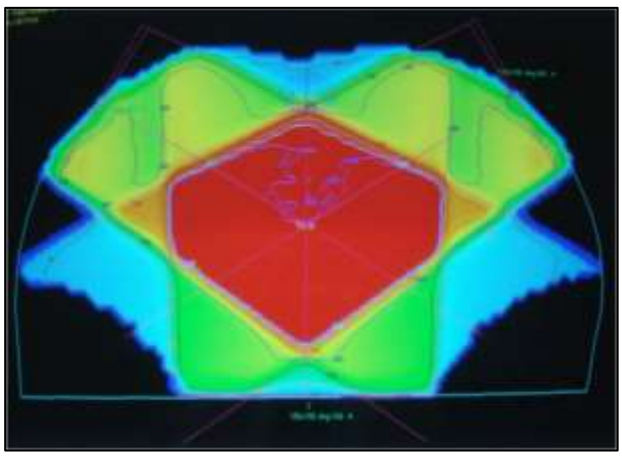

Figure 1: Radiation dose distribution.

Group 2 received 50 mg/m^2 of Paclitaxel (Max. single dose - 75 mg) on all Mondays followed by concurrent radiotherapy as mentioned above. They also received premedication with dexamethasone, ondansetrone and ranitidine. After treatment, the patients were followed up regularly. Outcome at 6 months, one year and at four years was analyzed.

Patients were assessed at follow up with Pap smear. Cervical biopsy was taken for histopathological examination when residual tumor was present. During follow up the response was assessed in terms of residual growth, residual disease and no growth. Residual growth was defined as any visible growth which was proven by biopsy. Residual disease was defined as no visible growth but presence of induration or thickening of the cervix and biopsy was normal. No growth was taken as a clinically normal cervix. If patients presented with secondary's it was also registered during follow up.

RESULTS

A total of 50 patients with locally advanced carcinoma cervix were enrolled to this study with 25 patients under each arm. 50.67% of the patients were in the age group 36-55 years. Almost all patients belonged to low socio-economic group.

Patients with locally advanced carcinoma of cervix FIGO stage IIB-IIIB were enrolled in the study. There were 26 and 24 patients in IIB and IIIB respectively.

After completion of the entire treatment patients were followed up regularly. Outcome at 6 months, one year and at four years was analysed.

At 6 months follow up in group 1, 14 patients had no growth, 9 patients had residual disease and 2 patients had residual growth. Similarly in group 2, 16 patients had no growth, no patients had residual disease and 7 patients had residual growth. There were 2 patients with secondary's in this group. Analysis carried out comparing the results at 6 months follow up were significant (Table 1).

At one year follow up after completion of treatment; only 23 patients could be followed up as two patients in the group which received concurrent Paclitaxel chemo radiation died of secondary's to bone. The rest 48 were analysed. In group1, there were 1, 10, and 14 patients with residual growth, residual disease and no growth respectively. In group 2, residual growth, residual disease and no growth were found in 4, 1 and 18 patients respectively. The difference in outcome at one year follow up was also statistically significant (Table 2).

The overall outcome of the study was computed at the end of one year. Based on the outcome patients were grouped into four categories viz. complete response, partial response, no response or progressive disease. The

results are shown in Table 3. Analysis of the outcome at the end of one year was statistically significant.

After four years, all patients were contacted through post and were asked to come for evaluation and documentation of disease status. The maximum months of follow up were 52 months. The average months of follow up were 48.2 months. In group one. 11 patients could be traced. 8 were dead and 6 were lost to follow up. Of these 11 patients who were examined 6 patients were free of disease and 5 had had recurrent disease and had received palliative radiation. Excluding the 6 patients who were lost to follow up, the four year survival rate was 57.9% and four year disease free survival rate was 31.6% in group 1. In group two, 12 patients could be traced. 9 were dead and 4 were lost to follow up. Of these 12 patients who were examined 7 patients were free of disease and 5 had had recurrent disease and had received palliative radiation. Excluding the 4 patients who were lost to follow up, the four year survival rate was 57.1% and four year disease free survival rate was 33.3% in group 2.

Table 1: Results at 6 months follow up.

Group	Result				Total	p-value*
	Secondary's	Residual growth	Residual disease	No growth		
RT	0	2	9	14	25	0.003
T+RT	2	7	0	16	25	

*Significant p-value is <0.05; RT- Radiation; T- Paclitaxel.

Table 2: Results at 1 year follow up.

Group	Result				Total	p-value*
	Secondary's	Residual growth	Residual disease	No growth		
RT	0	1	10	14	25	0.009
T+RT	2	4	1	18	25	

*Significant p-value is <0.05; RT- Radiation; T- Paclitaxel.

Table 3: Overall outcome at the end of one year.

Group	Result				Total	p-value*
	Progressive	No response	Partial response	Complete response		
RT	0	1	10	14	25	0.009
T+RT	2	4	1	18	25	

*Significant p-value is <0.05; RT- Radiation; T- Paclitaxel.

DISCUSSION

In patients who have bulky cervical cancer, residual disease is a problem within the irradiated volume. As cervical cancer has a low potential for distant metastasis, a majority of these women die of uncontrolled local disease or its complications. It is obvious that enhanced local control might improve disease-free survival.[5-8] In order to improve the loco-regional control; chemotherapy can be incorporated along with the conventional radiation. Concurrent chemo radiation is one of the newer modality of treatment which has shown promising results in various studies. Chemotherapy potentiates the effect of radiation. It increases the sensitivity of the tumor to radiation.

Recently many investigators have started using concurrent chemo radiation in the treatment of cervical cancer. They have used a different combination of chemotherapeutic drugs. Significant response was achieved in many studies. In 2005, Terauchi et al showed that Paclitaxel was very effective in treatment of relapsed cervical cancer.[9]

At 6 months follow up it was found that the response rate in group 1 was same as that at 3 months. In group 2 complete response rate was 64%. 28% patients had no response. Progressive disease was found in 8% of cases.

Though some patients had residual disease at 6 months, the response rate at one year was good. This is because the doubling time of squamous cell carcinoma is on an average 170 days and hence some clones of cells still remain alive at the end of treatment till there lifespan. This is the reason for the delayed response.

In 2005, in a study by Tinker et al, they showed a 40% response rate when paclitaxel with carboplatin was used in recurrent cervical cancer.[10] Also, in 2005, in a study by Roa et al, they showed 80% progressive free survival in stage IB2-IVA using paclitaxel with carboplatin.[11] In 2007, in a study by Lee et al, the authors used paclitaxel and carboplatin and showed 70% complete response rate in all stages of cervical cancer.[12] In our study, it was found that at one year follow up the complete response rate was 56% in group 1 and 72% in group 2. secondary's in the group that received paclitaxel developed in patients with stage IIIB disease. This could be due to poor individual response of tumor to chemo radiation.

CONCLUSION

Concurrent chemo radiation with Paclitaxel proved to be safe with significant increase in response rate at 6 months but failed to produce consistent long term results on further follow up when compared with only radiation. Larger studies are recommended to establish the difference.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Mohar A, Frias-Mendivil M. Epidemiology of cervical cancer. Cancer Invest. 2000;18:584-90.
2. Gonzalez AD, Cetina L, Mariscal I, Garza J. Modern management of locally advanced cervical carcinoma. Cancer Treat Rev. 2003;29:389-99.
3. Singh TT, Singh IY, Sharma DT, Singh NRK. Role of chemo radiation in advanced cervical cancer. Indian J Canc. 2003;40:101-7.
4. Rose PG, Bundy BN, Watkins EB, Thigpen JT, Deppe G, Maiman MA, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. N Engl J Med. 1999;340:1144-53.
5. Jampolis S, Andras EJ, Fletcher GH. Analysis of sites and causes of failure of irradiation in invasive squamous cell carcinoma of the intact uterine cervix. Radiology. 1975;115:681-95.
6. Perez CA, Camel HM, Kuske RR, Kao MS, Galakatos A, Hederman MA, et al. Radiation therapy alone in the treatment of carcinoma of the uterine cervix: a 20 years' experience. Gynecol Oncol. 1986;23:127-40.
7. Rotman MZ. Chemo irradiation: a new initiative in cancer treatment: 1991 RSNA annual oration in radiation oncology. Radiology. 1992;184:319-27.
8. Thomas G, Dembo A, Fyles A, Gadalla T, Beale F, Bean H, et al. Concurrent chemoradiation in advanced cervical cancer. Gynecol Oncol. 1980;38:446-51.
9. Terauchi F, Nagashima T, Kobayashi Y, Yamamoto Y, Moritake T, Seiki T, et al. A pilot study for weekly paclitaxel administration for patients with relapsed cervical cancer after heavy medication. Gan To Kagaku Ryoho. 2005;32:641-4.
10. Tinker AV, Bhagat K, Swenerton KD, Hoskins PJ. Carboplatin and Paclitaxel for advanced and recurrent cervical cancinoma: the British Columbia Cancer Agency experience. Gynecol Oncol. 2005;98:54-8.
11. Rao GG, Rogers P, Drake RD, Nguyen P, Coleman RL. Phase I clinical trial of weekly paclitaxel, weekly carboplatin and concurrent radiotherapy for primary cervical cancer. Gynecol Oncol. 2005;96:168-72.
12. Lee MY, Wu HG, Kim K, Ha SW, Kim KS, Kim IA, et al. Concurrent radiotherapy with Paclitaxel/Carboplatin chemotherapy as a definitive treatment for squamous cell carcinoma of uterine cervix. Gynecol Oncol. 2007;104:95-9.

Cite this article as: Sujindra E, Chaturvedula L. Radiation versus paclitaxel chemo radiation in the treatment of locally advanced carcinoma of cervix. Int J Reprod Contracept Obstet Gynecol 2016;5:3572-5.