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Original Research Paper

Oncology

OUTCOME AND TOXICITY OF CONCURRENT CHEMOTHERAPY WITH CARBOPLATIN ALONG WITH RADIATION IN LOCALLY ADVANCED CARCINOMA OF THE CERVIX

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KEYWORDS :

INTRODUCTION-

Cervical cancer is the third most common cancer in women worldwide with global estimates of 529,800 new cases and 275,100 deaths in 2011[1]. Developing countries have higher incidence of cervical cancer cases and deaths occur because of lack of effective screening procedures, socio- economic challenge, pattern of healthcare delivery and social factors[2]. Cervical cancer is the second most common cancer in India in women accounting for 22.86% of all cancer cases in women and 12% of all cancer cases in both men and women[3]. Rural women are at higher risk of developing cervical cancer as compared to their urban counterparts[4]. Cervical cancer is the third largest cause of cancer mortality in India accounting for nearly 10% of all cancer related deaths in the country[5].

Concurrent chemoradiotherapy (CCRT) is the mainstay treatment for locally advanced carcinoma of the cervix. Various chemotherapeutic agents are used along with radiation.

Several studies have shown the superiority of platinum based therapy, combined with radiation. Based on these premises the concomitant administration of radiotherapy plus weekly cisplatin may be considered as a reasonable standard of care. However despite the benefits obtained with the addition of platinum based chemotherapy the cure rates of locally advanced squamous cell carcinoma have reached a plateau in recent years[6,7].

Radiation with weekly cisplatin yields promising results nephrotoxicity becomes limiting factor especially in patients with parametrial involvement in whom renal function is already compromised . That's-why we need to study and observe outcome and toxicity with carboplatin, an analogue of cisplatin, with similar mechanism of action and less nephrotoxicity.

Carboplatin: Its mechanism of action is mediated by the formation of platinum DNA adducts. Since 1999, carboplatin, an analogue of cisplatin, with a similar mechanism of action, has been used with radiation therapy in much institution for the treatment of locally advanced cervical carcinoma. Mechanisms that underlie the interaction between the drugs and radiation therapy may include inhibition of the tumors sublethal damage repair systems and an increase in the radio-sensitivity[8].

MATERIAL METHODS

Inclusion Criteria

Biopsy confirmed , locally advanced unresectable , Stage IIB – IIIC AJCC 8th , Cervix cancer , KPS > 60 % , age > 20 years < 69 years ,

Exclusion criteria

Patient not willing to give informed consent , age more than 79 years , Biopsy inconclusive , metastatic tumours

Study Design

Observational , randomised , prospective carried out at Govt. Mahatma Gandhi Memorial Medical College , Indore , Madhya pradesh , India in the year 2018-2019.

Total 35 biopsy proven cases of cancer cervix received carboplatin (AUC 2 weekly) as concurrent chemotherapy patients were treated upto 46 Gy in 20 fractions using external beam radiotherapy , 5 fractions per week , 2.3 Gy per fraction followed by HDR brachytherapy 7.5 Gy per fraction weekly for three weeks.

Statistics all statistical calculations were done using **SPSS 20 ,Toxicity assessment** Toxicity criteria were by RTOG/ EORTC.

RESPONSE EVALUATION

Complete response (CR) was defined as the complete absence of disease 6 weeks. Partial response (PR) was defined as a reduction of disease by at least 50% in the sum of all measurable products of the longest perpendicular

diameters of measurable tumor masses for at least 6 weeks, with no growth of other lesions or appearance of new lesions. stable diseases (SD)was defined as reduction in lesion by less than 50%, or increase by less than 25%. Progressive disease (PD) was defined as an increase by at least 25% of tumor lesions or appearance of new lesions.

Observation and results

Out of 35 patients 18 patients in between 51-60 yrs of age,15 patients 61-69 yrs of age, 2 patients were 41-50 yrs of age. 7 cases were stage IIB , 12 cases belongs to stage IIIA, 10 cases were stage IIIB and rest 6 cases belongs to stage IIIC.

Patient Characteristics (Table 1)

Patient Characteristics	Number
Total Patients	35
Age 20 – 30 Years	Nil
Age 31 – 40 Years	Nil
Age 41-50 Years	2
Age 51 – 60 Years	18
Age 61 – 69 Years	15
Stage	
IIB	7
IIIA	12
IIIB	10
IIIC	6

RESPONSE

In the present study disease assessment after concurrent chemoradiotherapy Complete response seen in 31 patients and partial response seen in 3 patients and 1 patient reports stable disease. None patient presented with progressive disease.

Table2 Response

Response	(n= 35)
CR	31
PR	2
SD	1
PD	0

Toxicity

Hematological toxicity grade 3 observed in 26 patients and grade 4 toxicity in 2 patients. Grade 3 skin reaction observed in 27 patients and grade 4 skin reaction seen in 4 patients. Renal toxicity observed grade 1 in 23 patients only. Nausea and vomiting notice in 18 and 14 patients ,grade 2 and grade 3 respectively

Table 3 Toxicity

Toxicity	**cases**
Hematological Toxicity	
Grade 3	**26**
Grade 4	**2**
Skin reaction	
Grade 3	**27**
Grade 4	**4**
Renal toxicity	
Grade 1	**23**
Nausea & Vomiting	
Grade 2	**18**
Grade 3	**14**

DISCUSSION

Definitive concurrent chemoradiotherapy is the standard treatment of the advance stage carcinoma of cervix (7). Cisplatin and 5 FU were the drugs commonly used in combination with radiotherapy (9)(10)(11) . Despite good response their use is restricted by their toxicities . situation is further worsened by the presence of hydronephrosis in patients suffering from Ca cervix III B so we studied effects and toxicities of carboplatin as concurrent chemotherapy in locally advanced cancer cervix.

In our study we used weekly carboplatin at a dose of 100 mg/m2 as a radiation sensitizer in patients at AUC2 as had been recommended and were also used in other studies (8).

In our study most patients received 5 cycles of weekly carboplatin . Complete response was seen in 31 (88 %) patients and partial response was seen in 3 (8.5 %) patients and 1 patient reported stable disease. None patient presented with progressive disease. All these results were comparable in terms of efficacy to the studies evaluating the response rates using cisplatin as concurrent chemotherapy which is standard of care (7) (9) (10).

In our study grade 3 and grade 4 hematologic toxicity were observed in 74 % and 5 % cases respectively which was a matter of concern but was managed aggressively with blood and blood products. Radiation to pelvic bone marrow could be a contributing factor to this.

Grade 3 Skin toxicity was seen in 77 % percent cases and 11 percent cases had grade 4 skin reaction. Poor hygiene could be a contributing factor in this , as all the patients belonged to low socioeconomic status and illiterate background Incidence of renal toxicities were low as only grade 1 (65 %) renal toxicity was observed this was very low as compared to standard regimen containing concurrent cisplatin chemotherapy. Carboplatin is known to have very low nephrotoxicity.
Incidence of nausea vomiting were similar to standard regimens.

CONCLUSION

Carboplatin was administered to the patients of cancer cervix along with radiation. Myelosuppression was the major toxicity observed but was manageable , outcomes were similar to standard protocol. This study concludes that carboplatin can also be used as radiosensitizer in locally advanced cancer cervix

REFERENCES

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011;61:1–22.
2. Rose PG, Bundy BN, Watkins EB, Thigpen JT, Deppe G, Maiman MA, Clarke-Pearson DL, Insalaco S. Concurrent cisplatin-based chemoradiation improves progression free and overall survival in advanced cervical cancer: results of a randomized Gynecologic Oncology Group study. N Engl J Med. 1999;340(1144):53
3. http://screening.iarc.fr/doc/WHO_India_CCSP_guidelines_2005.pdf
4. Karthigeyan, K.; Cervical cancer in India and HPV vaccination.;2012; Indian J Med Paediatr Oncol.; 33(1): 7–12
5. World Health Organisation. The Global Burden of Disease: 2004 Update Geneva, WHO, 2009b.
6. Rotman M, Pajak TF, Choi K, Clery M, Marcial V, Grigsby PW, Cooper J, John M. Prophylactic extended-field irradiation of para-aortic lymph nodes in stages IIB and bulky IB and IIA cervical carcinomas: ten-year treatment results of RTOG 79-20. Jama. 1995 Aug 2;274(5):387-93.
7. Rose PG, Ali S, Watkins E, Thigpen JT, Deppe G, Clarke-Pearson DL, Insalaco S. Long-term follow-up of a randomized trial comparing concurrent single agent cisplatin, cisplatin-based combination chemotherapy, or hydroxyurea during pelvic irradiation for locally advanced cervical cancer: a Gynecologic Oncology Group Study. Journal of clinical oncology. 2007 Jul 1;25(19):2804-10.
8. Higgins RV, Naumann WR, Hall JB, Haake M. Concurrent carboplatin with pelvic radiation therapy in the primary treatment of cervix cancer. Gynecologic oncology. 2003 Jun 30;89(3):499-503
9. Whitney CW, Sause W, Bundy BN, Malfetano JH, Hannigan EV, Fowler Jr WC, et al. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stages IIB–IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group study. J Clin Oncol 1999;17(5):1339–48.
10. Eifel PJ, Winter K, Morris M. Pelvic irradiation with concurrent chemotherapy versus pelvic and para-aortic irradiation for high-risk cervical cancer: An update of Radiation Therapy Oncology Group trial (RTOG) 90–01. J Clin Oncol 2004;22(5): 872–80.
11. Peters III WA, Liu PY, Barrett II RJ, Gordon Jr W, Stock RJ, Berek JS, et al. Cisplatin, 5- fluorouracil plus radiation therapy are superior to radiation therapy as adjunctive therapy in high-risk, early-stage carcinoma of the cervix after radical