TREATMENT OF ADVANCE CARCINOMA CERVIX BY CHEMORADIOTHERAPY

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SUMMARY

Carcinoma cervix is the most common female malignancy in India. The most common problem we are facing is that majority of the patients present with stage Ib & IIIb disease. Since intracavitory application is the essential part of curative radiotherapy it is possible in only 55% of such advanced cases. In order to improve the local regression after external RT, chemoradiotherapy was started. Twenty four hours 5FU infusion for five days was given along with external RT. The dose of 5FU was 1 gm/m²/day along with 45 Gy / 4.5 to 5 wks of external radiation. Out of total 30 patients 80% (n = 24) have shown good clinical regression and intracavitory application could be possible. The toxicity of regimen was not severe except severe throm ophlebitis at local sites which developed in 4 patients.

INTRODUCTION

The Selectron LDR two patients system was installed in our hospital in 1986 with 40 mci of caesium. Since then 485 patients of carcinoma cervix have been treated till March 1992. The most important problem which we were facing, was that 70 to 80% of patients came with advanced lesions, usually stage IIIb or late stage IIb thus causing the problem of high local failure, since dose of external RT (usually 50 Gy / 25 fr) was only sufficient in 55% of the cases in regressing the local disease, adequately enough to allow intracavitory application. In rest of the patients (45%) treatment had to be completed by external RT, which resulted in a very low complete response rate. In order to improve the local regression by external RT, recently concurrent chemoradiation was started. Since majority of our patients come from low socioeconomic strata, a relatively cheaper drug 5 FU was selected which has shown good effect in Ca cervix as a single agent as well as in combination. Only preliminary results in terms of frequency of

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intracavitory application possible after chemoradiation, complete response rate at the end of treatment and acute toxicity have been discussed.

MATERIAL AND METHOD

Till date 30 patients have been treated and included in this study. Out of thirty, 22 (73%) were of stage IIIb and 8 (27%) of late stage IIb. Among the IIIb patients, 16 (73%) had bilateral parametrium involvement upto lateral pelvic wall while 6 patients (27%) (Table I) had one parametrial disease short of lateral pelvic wall. All stage IIb patients had disease in both parametriums. All patients had squamous cell carcinoma predominantly grade II and III. All stage IIIb patients had mild hydronephrosis as diagnosed by ultrasound.

Treatment started with external RT and 5 FU infusion. 5 FU was given in a dose of 1gm/m^2 body surface area / day, dissolved in 1 litre of normal saline. Twenty four hours continuous infusion was given for 5 days from day 1 of radiotherapy. Same schedule of 5 FU infusion was repeated from day 17 to day 21. The dose of external RT was 45 Gy / 4.5 to 5 weeks 2nd schedule of 5 FU infusion was withdrawn after 6 cases since patient compliance was very poor (Table II). Patients were examined 2 to 3 weeks after external RT and intracavitory application was done if local regression was found good. The selectron dose was 30 Gy at point A.

Table I

Break up of the Patients

Stage	Parametrium upto LBW*	No. of patients (%)
IIIb	Bilateral	16 (73%)
	Unilateral	6 (27%)
Total		22 (100%)
IIb		8 (100%)
Grant Total		30 (IIb + IIIb)

* Lateral pelvic wall

RESULTS

On analysing all the thirty patients we have found that in 80% (n=24) of the patients local regression was good after 2 to 3 weeks of external RT and intracavitory application could be done in them. In 20% (n=6) of the cases intracavitory application could not be done because of poor local regression and further external RT was given in these cases to bring total dose to 70 Gy / 35 Fr in 7 weeks by shrinking field technique. All of these patients were stage IIIb, who had bilateral parametrium involvement. To determine the overall response rate all patients were examined 6 to 8 weeks after completion of treatment. Out of 24 patients who had intracavitory application, 18 patients (75%) showed no evidence of disease, while 6 patients (25%) had thickened parametrium. But it was difficult to decide whether active disease was present in parametrium. Presently these patients are put on close follow up. Out of 6 patients who were given external RT only, 50% showed no evidence of disease while

Table II

Protocol for concurrent chemoradiotherapy

Days 1 2 3 4 5.....17 18 19 20 21.....34 35

Ext RT. ----------

5 FU [1gm/m^2] [1gm/m^2*]

* Withdrawn after 6 cases

Table III

Results

No. of patients	Ext. RT.	I/C	Total dose at point 'A'	* NED. 6 to 8 week after treatment
24 (80%)	45 Gy	30	75 Gy	18 (75%)
6 (20%)	70 Gy	—	70 Gy	3 (50%)

* No evidence of disease

other 50% had residual disease in cervix as well as parametrium (Table III). Regarding toxicity of this regimen, all patients had mild to moderate diarrhoea, nausea and vomiting which were controlled by conservative treatment. The only significant toxicity of 5 FU infusion was, thrombophlebitis at the site of infusion which occurred in All the patients. It was of mild degree except in four patients who developed severe thrombophlebitis. It was, however controlled by antibiotics, anti-inflammatory drugs and local dressing with sumag.

DISCUSSION

Carcinoma cervix is the most common malignancy among females in India. Diagnosis at very advanced stage is most frequent problem, for the physicians. In Cancer Hospital, Gwalior, 80% of the females present with stage IIB & IIIb disease which give poor locoregional control and overall survival rate (Perez et al. 1988). Considerable research effort is currently being put into improving pelvic control and survival rates in patients with advanced carcinoma of the cervix. These efforts mainly have been focussed in three major different directions, interstitial implants (Prempree 1983), neoadjuvant (sequential) chemotherapy (Thomas et al. 1990). Since with sequential chemotherapy total time of the treatment is prolonged markedly which may allow the tumour to repopulate, as has been shown in head and neck cancers (Hall, 1988) we focussed our attention to use concurrent chemotherapy.

The chemotherapeutic agent 5 FU was choosen because of the following reasons : (1) clinical data by Cummings et al (1984) have shown local control rate of 90% in patients with squamous cell carcinoma of the anal canal and Keane et al (1985) have shown 70% tumour regression in the patient with carcinoma of oesophagous. (2) 5 FU have shown good effect in Ca cervix as a single agent as well as in combination (Perez and Brady 1988). (3) Invitro data by Byfield et al (1982) also suggested that the addition of infusional 5 FU to radiation therapy would enhance the radiation effect. (4) Since, majority of our patients come from lower socio-economic class, a relatively cheaper drug is affordable by them.

Initially two cycles of 5 FU were administered with a gap of 2-3 weeks. But patients usually refused to undergo second infusion, thus after 6 cases, the second term of 5 FU infusion was withdrawn. The preliminary results have shown good response after chemotherapy and frequency of intracavitory applications increased markedly as compared to radiation alone (80% Vs 55%).

CONCLUSION

Majority of carcinoma cervix patients in our country present in very advanced stage and treatment results are disappointing. Transperineal interstitial implantation could improve the results but facilities are available only at a few centres in our country. Chemotherapy either before or concomittent with radiation are being evaluated at many centres. We also started this pilot study to evaluate the results of concomittent chemoradiation and drug 5 FU was selected mainly because of its lower price. Initial results are encouraging. Though at this stage, no definite conclusion can be drawn as total number of patients is less but we may hope good results in future since the present study is still going on. Whether this regimen has any impact on overall survival or disease free survival is yet to be seen.

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