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RESEARCH

Palliative chemotherapy in recurrent carcinoma cervix: experience from a regional cancer centre in southern India

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Aims: To evaluate the clinical outcome and complications with two different palliative chemotherapy regimens in recurrent cervical carcinoma.
Methods and materials: Forty (40) women with recurrent cervical squamous cell carcinoma were treated with palliative chemotherapy using paclitaxel plus cisplatin or single-agent docetaxel. Clinical outcome and toxicities were analysed. The parameters in two arms were compared using Student's t-test and statistical analysis was done using R software.
Results: At a median follow up of 1.35 years the clinical outcome was complete response/partial response in 50% and 60% and progressive disease in 20% and 10% of the patients with either paclitaxel/cisplatin or docetaxel, respectively, which was not statistically significant. Stable disease (SD) was 30% in both arms. Toxicity included nausea, seen in all the patients in both arms, and diarrhoea, seen in 90% and 70% of the patients in the two arms, respectively. Grade II to III neutropenia was seen in 10% of patients with paclitaxel/cisplatin and none with docetaxel. Hypersensitivity was encountered in 40% and 30% in the two arms, respectively.
Conclusion: There was no significant difference in clinical outcome and morbidity in patients with either paclitaxel/cisplatin or single-agent docetaxel. Further prospective clinical trials with larger study groups and longer follow-up are required to substantiate these claims.

Keywords: docetaxel, paclitaxel/cisplatin, palliative chemotherapy, recurrent cervical cancer

Introduction

Cervical cancer is one of the common cancers seen in developing countries worldwide. It is also the most common cancer in women presenting at Kidwai Memorial Institute of Oncology, Bangalore, India, where this study was conducted. Notwithstanding the fact that it is curable if detectable at an early stage a considerable number of cases do recur in spite of adequate treatment. Palliative chemotherapy is offered to patients who develop local regional recurrence and the outcomes of this are variable.

There is a paucity of data with regard to the optimal palliative chemotherapy regimen in such cases.

Most of the studies reported in the literature are either case series, have a small sample size or are controversial.[5–22]

Against this background, we embarked on a retrospective study to identify the optimal regimen with regard to clinical outcome and toxicity between two chemotherapy schedules commonly used at our institute, i.e. paclitaxel with cisplatin or single-agent docetaxel.

Methods and materials

This was a retrospective study conducted at Kidwai Memorial Institute of Oncology (KMIO), Bangalore. The study population comprised 40 patients with recurrent squamous cell carcinoma of the cervix, who were treated with palliative chemotherapy. The two common regimens of chemotherapy used in first-line salvage setting at our institute were paclitaxel plus platinum (cisplatin) or single agent docetaxel. All the patients received six cycles of either of the above regimens. The decision for a chemotherapy regimen was based on issues like affordability, insurance coverage and tolerability.

Baseline parameters such as age, performance score (KPS), 'T' size, nodal status, HPV status and histopathological grading of tumours (Table 1) were comparable between the two groups.

Clinical features

All the patients in the present study had a history of white discharge per vagina. Other symptoms like bleeding per vagina and low back pain were occasionally noted.

All the patients in the present study had a good performance score. General physical examination was essentially normal in all patients.

Chemotherapy

Informed consent was taken from all patients. Baseline CT scan of abdomen and pelvis, CBC, LFT, RFT, HIV/HBsAg, and histpathological report were collected.

Twenty patients each received paclitaxel+cisplatin and docetaxel respectively. Response was evaluated using clinical examination findings and CT scan findings after completion of six cycles of chemotherapy using RECIST criteria.

A toxicity profile was assessed during and after chemotherapy. After completion of chemotherapy, patients were reviewed every month during the first three months of follow-up, once in

Table 1: Baseline parameters

Serial no.	Variable	Arm A	Arm B	*t*-value	*p*-value
1.	Age (years)	45.5 ± 13.2	42.2 ± 6.68	0.062	0.543
2.	Tumour size in cm (range)	4.25 ± 2.38 (1.5–10)	3.35 ± 0.74 (2.5–5)	1.14	0.268
3.	Nodal status				
	N0	10	12	–	0.9
	N1	10	8		
4.	KPS	87 ± 5	90 ± 6	–	0.8
5.	HPV				
	Negative	6	8	–	0.9
	Positive	14	12		
6.	SCC grade				
	III	14	12		
	II	4	6	–	1.0
	I	2	2		

Mean ± standard deviation was calculated for each parameter and compared using Student's t-test.
None of the baseline parameters in arm A and arm B is significantly different.
A *p*-value < 0.05 was taken as significant.

Table 2: Response to chemotherapy

Serial no.	Response	Arm A (%)	Arm B (%)	*p*-value
1.	CR	2 (10%)	0 (0%)	0.78
2.	PR	8 (40%)	12 (60%)	
3.	SD	6 (30%)	6 (30%)	
4.	PD	4 (20%)	2 (10%)	

Table 3: Toxicity profile

Serial no.	Toxicity	Arm A	Arm B	*p*-value
1.	Nausea	20 (100%)	20 (100%)	1.0
2.	Diarrhoea	5 (25%)	2 (10%)	0.57
3.	Neutropenia	2 (10%)	0 (0%)	1.0
4.	Hypersensitivity	8 (40%)	6 (30%)	1.0

two months during the next six months and once in three months thereafter.

Response and toxicity were documented at each visit. Results were tabulated and analysed using Student's t-test using R software (https://www.r-project.org/).

Paclitaxel+cisplatin (arm A)

Paclitaxel 175 mg/m^2 was administered in normal saline using a glass bottle and codon set over three hours, after premedication with diphenhydramine, a 5HT3 inhibitor, corticosteroids and an H2 receptor blocker.

Cisplatin 100 mg/m^2 was administered in normal saline over three hours with adequate hydration and electrolyte supplementation, following paclitaxel.

Oral steroids, an H2 receptor blocker and a 5HT3 blocker were advised for three days following chemotherapy. The above combination was repeated every 21 days. CBC, LFT, RFT and electrolytes were done prior to each cycle.

Docetaxel (arm B)

Docetaxel 120 mg/m^2 was administered in normal saline using a glass bottle and codon set over two hours, after premedication with diphenhydramine, a 5HT3 inhibitor, corticosteroids and an H2 receptor blocker.

Oral steroids, an H2 receptor blocker and a 5HT3 blocker were advised for three days following chemotherapy. The above combination was repeated every 21 days. CBC, LFT, RFT and electrolytes were done prior to each cycle.

Results

At a median follow-up duration of 1.4 years in arm A and 1.3 years in arm B response to chemotherapy was analysed and was found to be complete response (CR) or partial response (PR) in 50% and 60% of patients, progressive disease (PD) in 20% and 10% of patients in arm A and arm B, respectively, which was not significantly different; 30% of patients in each arm had Stable disease (SD). Two patients in arm A and none in arm B had CR (Table 2).

Toxicity profile

All patients were reviewed during chemotherapy and toxicity was documented at each visit. Nausea was seen in 100% of patients in both arms of the study. Two cases of neutropenia were seen in arm A. Diarrhoea was seen in 25% and 10% respectively. Hypersensitivity was seen in 40% and 30% of patients in arm A and arm B, respectively (Table 3).

Discussion

Carcinoma of the uterine cervix is currently the commonest malignancy affecting women in India. Worldwide, chemotherapy has been used in recurrent cervical carcinoma with variable results.[5–22] At present, cisplatin in combination with paclitaxel is the standard-of-care chemotherapy in the palliative management of cervical cancer.

The combination of paclitaxel with cisplatin was evaluated in a phase II study by the Gynecologic Oncology Group (GOG) and was found to be highly active in recurrent squamous cell carcinoma of the cervix with an overall response rate of 46.3%. Paclitaxel was given at a dose of 135 to 170 mg/m^2 as a 24-hour infusion along with cisplatin 75 mg/m^2 over three hours. Myelosuppression was the dose limiting toxicity.[1]

The combination of paclitaxel with cisplatin was found to be superior to cisplatin alone with respect to response rate and progression-free survival in 280 patients in a phase III trial by GOG. The dose of cisplatin was 50 mg/m^2 and paclitaxel 135 mg/m^2 administered every 21 days for six cycles.[2]

Single-agent docetaxel at 100 mg/m^2 once in 21 days was found to have minimal activity in refractory squamous cell cancer of the cervix in a GOG phase II study with 8.7% partial response, 34.8% stable disease and 39% progressive disease. Myelosuppression, infection, gastrointestinal toxicity and constitutional effects were commonly seen.[3]

A small phase II study evaluated weekly docetaxel at 35 mg/m^2, which showed only limited activity in recurrent squamous cell cancer of the cervix. With a median of two cycles, there were no objective responses to chemotherapy.[3]

Against this background, we retrospectively studied the role of a paclitaxel/cisplatin combination versus single-agent docetaxel chemotherapy in recurrent squamous cell carcinoma of the cervix.

We analysed 20 cases in each arm. The two arms were well matched with regard to age, performance, HPV status, nodal status and histological grade. At a median follow-up duration of 1.3 years, the overall response rate was 50% with paclitaxel/cisplatin and 60% with docetaxel. Progressive disease was seen in 20% and 10% of patients in arm A and arm B, respectively; 30% of patients in each arm had stable disease.

The excellent results seen in our study compared with the published literature could be attributed to the fact that all the patients completed six cycles of the planned chemotherapy and the higher dose of chemotherapy: paclitaxel (175 mg/m^2), cisplatin (100 mg/m^2) and docetaxel (120 mg/m^2).

Neutropenia, diarrhoea, nausea and hypersensitivity were the common toxicities associated with chemotherapy in both arms of the study.

Conclusion

We conclude that, in our series of 40 patients with recurrent cervical cancer treated with palliative chemotherapy, there was no difference in clinical outcome and complication rates with either paclitaxel/cisplatin or single-agent docetaxel.

Prospective studies with a larger sample size and longer follow-up are warranted in the future.

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