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RESEARCH ARTICLE

CONCURRENT CHEMORADIATION WITH WEEKLY CISPLATIN AND PACLITAXEL IN LOCALLY ADVANCED CARCINOMA CERVIX

Preethi A, Ragavendra A, Selvalakshmi S., Durga Prasad R., Senthilkumaran M. and Madhumathi S.
Department Of Radiation Oncology, Madras Medical College Hospital, Chennai, India.

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Abstract

Introduction: Carcinoma cervix is the most common gynaecological malignancy in women. Concurrent chemoradiotherapy is an effective treatment for locoregionally advanced squamous cell carcinoma of the cervix, with established benefits in both organ preservation and survival.

Aims:1. To assess the immediate locoregional response rates of locally advanced squamous cell carcinoma of the cervix treated with concurrent chemoradiotherapy using weekly low dose cisplatin and low dose paclitaxel followed by HDR intracavitary brachytherapy. 2. To assess the acute toxicity.

Materials and methods: This is a single arm prospective study in which 30 patients with cervical carcinoma of stages IB2-IIIB, presenting to our hospital, were given concurrent chemoradiation: EBRT 50Gy/25# with weekly Cisplatin 30mg/m^2 and Paclitaxel 30mg/m^2 followed by intracavitary brachytherapy 8Gy/2# and response was assessed, both clinical and radiological, at the end of 6 weeks after completion of therapy, using RECIST criteria. Toxicity was assessed using RTOG morbidity scoring.

Results: Clinically, there was complete locoregional response in 27 patients (90%), partial response in 3 patients (10%). Acute toxicities were observed but they were manageable. Diarrhea presented as grade I, II and III in 5 (16.7%), 3 (10%) and 2 (6.7%) patients respectively. Grade Ihaematological toxicity was seen in 7 patients (23.3%) and grade II in 3 patients (10%) during the 5th week of chemo-radiation. Grade I and II skin reactions were seen in 7 patients (23.3%) with grade III reactions in one patient. Grade I bladder toxicity is seen is 2 patients (6.7%).

Conclusion: This study shows including a taxane as a radiosensitiser, in the standard concurrent chemoradiation with weekly cisplatin schedule, yields better loco-regional response with acceptable toxicity, especially in locally advanced stages and those with pelvic nodal involvement.

Introduction:-

Carcinoma Cervix is one of the most common malignancies in the world, standing third among the women worldwide and first among women in developing countries. However, effective screening techniques developed

Corresponding Author:- Ragavendra A, drragavendra84@gmail.com
Address:- Govt. Coimbatore Medical College Hospital, Coimbatore, Tamil Nadu, India.

during the recent times, for the detection of pre-invasive lesions, have led to the decrease in incidence of invasive cervical carcinoma. But it still continues to be a major public health problem in the developing countries.

Carcinoma of the cervix is the commonest malignancy among women in India constituting about 20-50% of all malignancies [1]. Thus India bears a major burden as far as cervical cancer is concerned, not only in terms of disease incidence and progression but also mortality and is one of the important causes of cancer deaths in the world.

Chemotherapy has been widely used for the purpose of palliation in stage IVB cancers. Earlier radiotherapy alone was used with curative intent for stages IB2 and higher stages. Nowadays, concurrent chemoradiation has been approved as the standard of treatment for treatable stages of cervical carcinomas. The earlier technique of radiation alone has resulted in reduced locoregional control rates and survival when compared to concurrent chemoradiation especially in higher stages. This is because of larger size of tumor, poor tumor geometry and higher rates of central hypoxia. This is responsible for the higher proportion of residual disease which can lead to further progression and locoregional extension and distant metastasis and eventually leading to death. Hence there is a great need for better local control to improve survival rates. There are several methods to improve locoregional control rates and increasing the gap between survival curves of tumor and organs at risk. Many radio-sensitisers, oxygen enhancing agents, cytotoxic drugs and immunogenic agents have been used in several trials. Of all these, concurrent chemoradiation with conventional fractionation has been proved to increase locoregional control rates and better survival with acceptable toxicities. There is a synergistic effect between chemotherapy and radiotherapy leading to enhanced cell death and tumor regression.

Several drugs such as Cisplatin, 5-FU, Hydroxyurea and Mitomycin have been used in the treatment of locally advanced cervical cancers and have shown significant action. Some more drugs are under trial like Paclitaxel, Gemcitabine and Carboplatin. However the standard of care for locally advanced cervical cancers remains to be Cisplatinum based chemoradiation. This has reduced the mortality by a statistically significant 30%. This has been proven by several landmark trials like GOG, RTOG and SWOG where different combinations of chemotherapeutic drugs have been experimented. According to these studies, in Feb 1999, NCI (National Cancer Institute) has confirmed that concurrent Cisplatin based chemo-radiotherapy has greater therapeutic efficacy when compared to standard radiotherapy alone in locally advanced cervical cancers.

Cisplatin acts as a radiosensitiser as well as combats the micrometastasis due to systemic spread thus acting on both locoregional and systemic control. Cisplatin is a cell cycle non-specific drug. It radio-sensitises the hypoxic tumor cells and inhibits repair of potentially lethal damage. Paclitaxel is the most important microtubule stabilizing drug. It inhibits depolymerisation of tubulin in the spindle apparatus, thereby inducing apoptosis in dividing cells. There is mitotic arrest at G2-M transition and thus increasing sensitivity to radiation leading to cell death.

Since the early 70s, the Gynaecological Oncology Group (GOG) has been conducting several trials using many agents. Initially, hydroxyurea was used as a radiosensitiser. Maximum benefit was found with cisplatin in terms of tumor regression in both early stages and recurrent or metastatic tumors. Thus the standard treatment of cisplatin-based concurrent chemoradiation was implemented from 1979 showing an overall survival of 49% for all stages [5]. Complete remission of 89% was seen in stage III. Potish et al and Twiggs et al studied the effect of weekly cisplatin for better response [6,7]. Phase II trials of concurrent chemoradiation using cisplatin were conducted [8-9]. The above studies favoured cisplatin based regimens as they showed better disease-free survival and overall survival.

Souhami et al evaluated 50 patients with carcinoma cervix stage IIA-IVA in a phase II trial with concurrent chemoradiation with weekly Cisplatin 30mg/m^2 [10]. Complete response was seen in 88%. The 4 yr- survival rate was 65%. Studies like GOG -85[11], GOG -120[12], GOG -123[13], RTOG -90 -01[14], SWOG -87 -97[15] showed favourable results supporting chemoradiation by improved rates of complete response and disease-free survival with reduced mortality rates when compared to conventional radiation alone.

Studies with concurrent paclitaxel alone[16] compared weekly cisplatin with weekly paclitaxel and found no significant difference in local control and toxicity. Paclitaxel is an effective agent by itself to produce maximum benefits along with radiation in carcinoma cervix as radio-sensitizer. By adding paclitaxel to cisplatin, optimum benefits are expected along with manageable toxicity.

JACCRO GY-01 trial[17] using weekly cisplatin and paclitaxel showed Favourable local control with acceptable toxicity. PRAGYAT THAKUR (phase III trial)[18] compared weekly cisplatin and paclitaxel with cisplatin alone and showed better rates of complete response in trial arm with better Disease Free Survival. PIGNATA et al[19] found maximum tolerable dose of cisplatin and paclitaxel as 30mg/m^2 and 50mg/m^2 and achieved a tumor response rate of >90%. DISILVESTRO et al[20]: found maximum tolerable dose of cisplatin and paclitaxel as 40mg/m^2 and 40mg/m^2 and achieved a tumor response rate of 89% with acceptable toxicity. MIGLIETTA et al[21] used cisplatin and paclitaxel and achieved complete response rate of 100%.

Hence a study has been designed with Primary Objective: To assess the immediate locoregional response rates of locally advanced squamous cell carcinomas of the cervix treated with the study protocol and to observe the radio-sensitivity effect of paclitaxel, when added to cisplatin during concurrent chemoradiotherapy for carcinoma cervix; Secondary Objective: To assess acute toxicity to the treatment.

Materials and methods:-

A single arm prospective study was designed with thirty consecutive patients having inclusion criteria of: Biopsy proven squamous cell carcinoma of the uterine cervix, Age 20- 65 years, Stage IB2, IIA2, IIB, IIIA, IIIB (FIGO 2009), Signed informed consent prior to protocol initiation, treatment naive, Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0-2, Diabetes and hypertension under control, Hb ≥10gm%, total count ≥4000, platelet count ≥1,00,000, good renal function and liver function. All patiens underwent LFT, viral markers, Cystoscopy and Proctoscopy, if indicated, Cardiology evaluation, USG abdomen, CT scan or MRI pelvis, Chest X ray, blood grouping and typing, Anaesthetic evaluation and fitness, Weekly Complete blood count, Renal Function test (RFT) before each course of chemotherapy.

TREATMENT PROTOCOL: External beam radiotherapy 50Gy/25# over 5 weeks with Weekly Concurrent Chemotherapy CDDP 30mg/m^2 and Paclitaxel 30mg/m^2, followed by HDR intracavitary brachytherapy 16Gy/2# given after 1 week of EBRT at weekly interval.

EBRT TARGET VOLUME: Whole pelvis – uterus, cervix, vagina, parametria along with the pelvic and common iliac group of lymph nodes.

SIMULATION AND EXECUTION: X-ray simulation was taken with patient in the prone position with comfortably full bladder (to avoid irradiation of the small bowels during EBRT). If the field separation is <20cm, patient was treated by AP/PA fields only and if >20cm, four-field technique was used.

ICA PROTOCOL: After external beam radiation, patient was assessed for intra-cavitary brachytherapy application. If found fit for the application, they were considered for HDR intra-cavitary brachytherapy.

CHEMOTHERAPY PROTOCOL: The patients were pre-medicated with Dexamethasone 12hrs and 6hrs before administration of chemotherapy. Adequate hydration was given with 1 litre of RL 24 hours before chemotherapy. Half an hour before chemotherapy, 500 ml of RL, ondansetron 4mg, Ranitidine 50mg, Mannitol 100ml were given followed by infusions of 30 mg/m^2 Paclitaxel in 500 ml NS over 2 hours and 30 mg/m^{2}Cisplatin in 500 ml NS over 2 hours. EBRT was delivered 1 hour after the chemotherapy.

OVERALL TREATMENT TIME is 7 weeks. Response was assessed six weeks after completion of concurrent chemoradiation and brachytherapy, with CT scan by using RECIST criteria. Both clinical and radiological response assessment was done. Toxicities assessment was done using RTOG toxicity grading.

Results:-

Most of the patients belong to 41-50 years group. Mean age at presentation was 48.4 years. Pre and post-menopausal were equally distributed. Most of the patients were multiparous. More than 80% of the patients had ECOG PS of 0-1. About 37% of patients were anemic before start of treatment; treated with blood transfusions. About 37% required transfusion during therapy. Most patients were in stage II B and III B (94%). Two patients had extension of disease into lower one-third of vagina (III A). Around 60% of patients had bilateral parametrial involvement. 57% had pelvic LN involvement. Many patients had poorly differentiated histology.

63.3% of the patients completed the proposed 5 cycles of chemotherapy; others received only 4 cycles due to gastrointestinal toxicity or haematological toxicity.All the thirty patients had completed the treatment and were available for assessment after 6 weeks. Complete or partial response was seen in all the patients with none having static or progressive disease. There were no treatment related deaths. 27 (90%) patients showed complete response. This included 13 patients with stage IIB and 11 patients with stage IIIB (92.8% and 84.6% respectively).

There was a significant beneficial outcome in patients with ECOG 1, accounting to 83.3% of the patients who showed complete response. The rate of complete response increased with increasing levels of haemoglobin. There was 100% complete response in the group with haemoglobin levels more than 11g%. Three patients with low haemoglobin levels at presentation contributed to the group with partial response. Complete response was observed in both well differentiated and poorly differentiated groups.

There was complete disappearance of pelvic nodes in the 17 patients who had lymph nodal involvement.Patients with bilateral parametrial disease were shown to have inferior response compared to unilateral disease. There was 100% complete response in the unilateral parametrial involvement group when compared to 83.3% in the bilateral group.

There was only one case which presented with grade III skin reaction. 40% and 13.3% had presented with grade I and II reactions respectively. 63.3% and 16.7% presented with grade I and II vaginal mucositis respectively. 60% of the patients had grade I upper GI toxicity which included predominantly nausea and vomiting. This can be attributed to the emetic effect of Cisplatin. Grade I rectal toxicity was observed in 50% of the patients while 10% had grade II toxicity in the form of diarrhoea and proctitis. Only one patient presented with grade I bladder toxicity in the form of increased frequency of micturition and dysuria. 66.7% of the patients developed grade I small bowel toxicity in the form of abdominal pain. 23.3% presented with grade I toxicity and 10% presented with grade IIhaematological toxicity. There were no cases of renal impairment.

Discussion:-

Invasive cervical carcinoma is the second most common cause of mortality among cancer patients in India. The limitations of single modality regimens have paved the way for several newer modalities of treatment strategies to obtain maximal results. To achieve this goal, concurrent chemoradiation is an ideal method to conform to the concept of ‘maximal therapy with minimal time’ so that the entire treatment is completed within the stipulated ‘window of curability’.

Cisplatin is an important drug which has a strong foundation, both as a single agent and as part of combination therapies in concurrent chemoradiation schedules. The synergistic effect of cisplatin and radiotherapy has been established and well accepted. The various cisplatin based chemoradiation regimens have shown response rates from 74% to 100% with complete response in 63-87%. Cisplatin is now the most standard and acceptable chemotherapy drug used in the treatment of carcinoma cervix. Analysis of patient and disease characteristics was done and a detailed assessment provided better understanding of the factors leading to more rationale treatment strategies along with better optimization of various combinations of radiotherapy with additional modalities of management thereby leading to highest local pelvic control with acceptable toxicity, thus tailoring to the therapeutic needs of patients. To enhance the radio-sensitive effect and cytotoxicity of chemotherapy and radiotherapy, paclitaxel was added along with cisplatin.

Detailed analysis of the results obtained during this study has shown the importance of several patient and disease characteristics which have a major role in affecting therapeutic response and thus tumor control. The method of statistical analysis used in this study is the Chi-square test.

This present study, using cisplatin and paclitaxel in concurrent chemoradiation in locally advanced carcinoma cervix, was compared with previous conventional studies using cisplatin alone, during the years September 2003 to July 2006, in our department. Comparison between these two studies was done as they had only one variable. The addition of paclitaxel was the only difference between the present and previous studies. The response was assessed 6 weeks, after the completion of treatment.

1. 100% complete response in both studies - associated factors: a.ECOG – 1,b.Parametrium involved only on one side.
2. Favourable response in both studies – associated factors:a.Tumor stage IIB, b.Hemoglobin>11g%.

3. Poor response in both studies – associated factors:a.Performance status – ECOG 2 and more, b.Hb status - <10g% ,c.Stage – IIIB, d.Bilateralparametrial involvement

The present study which included cisplatin and paclitaxel in weekly schedules was therefore delivered mainly to improve response in such individuals. Due to tumor bulk, low haemoglobin status, thus reducing oxygen supply to tumor, thereby making it less radiosensitive, and poor performance status of the patients, the standard regime was not able to achieve the expected response. The present study is therefore done to assess the response in such individuals, looking for beneficial outcomes.

But the above results are not statistically significant due to the inclusion of a small sample size. Comparison with the immediate complete response rates of various studies including international, with radiation and cisplatin given concurrently in locally advanced cervical carcinoma has revealed that the immediate response rates of our study is comparable with the other studies.

There was more occurrence of bone marrow suppression in the present study because of the combined effect of radiation to pelvic hematopoietic tissues and a chemotherapy regimen containing two drugs. The toxicity patterns of the studies with cisplatin and paclitaxel with radiation, studies with concurrent cisplatin-based chemo-radiation, studies conducted in our institution were analysed and tabulated.

Table 1:- Distribution Of Patient Demographics.

S. No.	Demographics	Frequency	Proportion
1.	**Age**		
	31-40	7	23
	41-50	12	40
	51-60	9	30
	>60	2	7
2.	**Menopausal status**		
	Pre-menopausal	16	53
	Post-menopausal	14	47
3.	**Parity**		
	1	2	7
	2	15	50
	3	9	30
	4	3	10
	5	1	3
4.	**ECOG performance status**		
	0-1	25	83
	2	5	17
5.	**Hb level**		
	<10 gm%	11	37
	10-11 gm%	10	33
	>11 gm%	9	30
6.	**FIGO STAGE**		
	I B2	2	7
	II B	14	47
	III A	1	3
	III B	3	43
7.	**Vaginal Extension**		
	Upper 2/3	23	77
	Lower 1/3	2	7
8.	**Parametrial Extension**		
	Unilateral	10	33
	Bilateral	18	60

9.	**Pelvic Lymph nodes**		
	Enlarged	17	57
	Not enlarged	13	43
10.	**Differentiation**		
	Well differentiated	3	10
	Moderately differentiated	11	37
	Poorly differentiated	16	53

Table 2:- Demographics Vs Response Assessment.

S. No.	Demographics	Complete response Frequency (Proportion)	Partial response Frequency (Proportion)
1.	**ECOG PS**		
	1	25 (83)	
	2	2 (7)	3 (10)
2.	**Hb level**		
	<10 gm%	8 (27)	3 (10)
	10-11 gm%	10 (33)	
	>11 gm%	9 (30)	
3.	**Differentiation**		
	Well differentiated	2 (7)	1 (3)
	Moderately differentiated	10 (33)	1 (3)
	Poorly differentiated	15 (50)	1 (3)
4.	**Parametrial Extension**		
	Unilateral	10 (33)	0
	Bilateral	15 (50)	3 (10)

Table 3:- Stage Group Wise Response Assessment.

		CR		PR	
Stage	**No. of patients**	**No.**	**%**	**No.**	**%**
I B2	2	2	100	0	-
II B	14	13	92.8	1	7.2
III A	1	1	100	0	-
III B	13	11	84.6	2	15.4
Total	30	27	90	3	10

Table 4:- Comparison Of Previous Vs Present Study.

Factor	Previous Study		Present Study	
	No. of CR	**CR %**	**No. of CR**	**CR %**
ECOG-1	6	100	25	100
Unilateral parametrial involvement	11	100	10	100
IIB	11/13	88	13/14	92.8
Hb>11g%	7/9	77	9/9	100
Age <60 yrs	11/13	84	25/28	89
Hb<11 g%	17/20	85	18/21	86
B/L parametrial involvement	13/15	85	15/18	84
Tumor stage IIIB	9/11	82	11/13	85

Table 5:- Toxicities Encountered In Present Study:

RTOG Toxicity	Grade 1		Grade 2		Grade 3	
	N	%	N	%	N	%
Skin toxicity	12	40.0	4	13.3	1	3.3
Vaginal mucositis	19	63.3	5	16.7	-	-
Small bowel toxicity	18	60.0	2	6.7	-	-
Rectal toxicity	15	50.0	3	10.0	-	-
Bladder toxicity	1	3.3	-	-	-	-
Hemato toxicity	7	23.3	3	10.0	-	-
Renal toxicity	-	-	-	-	-	-

Table 6:- Comparison With International Studies:

Name of study	No. of patients	Chemo Schedule	CR %
Runowicz et al 31	32	Cisplatin 20mg/m2, D1-5, every 21 days	91%
Fields et al 30	55	Cisplatin 20mg/m2, D1-5, every 21 days	87%
Calkins et al 13	30	Cisplatin 50mg/m2 D1-17 5FU D2, 3, 4, 5 & 18, 19, 20, 21	-
JACCRO GY-01 trial 39	68	Cisplatin 30mg/m2 and Paclitaxel 50mg/m2 weekly	76.5%
Pragyat Thakur et al- Indira Gandhi Med College, Shimla and PGI Chandigarh 40	81	Cisplatin 30mg/m2 and Paclitaxel 50mg/m2 weekly	84%
Miglietta et al43	27	Cisplatin 75mg/m2 and Paclitaxel 175mg/m2 every 21 days	100%
Previous study	26	Cisplatin weekly 40mg/m2	88%
Present study	30	Weekly Cisplatin 30mg/m2 & Paclitaxel 30mg/m2	90%

Table 7:- Comparison With Previous Studies In Our Institution: (Past 5 Years).

Study	Dose Of Radiation (Gy)			Chemotherapy Schedule	Cr
	Whole pelvis	PM	PointA		
Hyper fractionated RT	50.4	65	82	-	75%
Weekly CDDP-conventional RT	50	60	76	Weekly Cisplatin- D1 of every week	88%
Concurrent CDDP with conventional RT	50	60	76	Cisplatin 20mg/m2 D1-5, D21-25	90%
Hyper fractionated RT with CDDP & 5FU	57.6	65	83	Cisplatin D1,17 5FU D2,3,4,5 & 18,19,20,21	84%
Hyper fractionated RT with CDDP	57.6	65	83	Weekly Cisplatin D1 of every week	92%
Present study	50	60	76	Cisplatin and Paclitaxel, D1 of every week	90%

Table 8:- Toxicities Encountered.

Systemic toxicity	Previous study	Present study

Hematological	6 (20%)	17 (56.6%)
Renal	-	-

Table 9:-

Acute effects	RTOG Grade	Previous Study	Present Study
Skin	1	13 (50%)	12 (40%)
	2	13 (50%)	4 (13.3%)
	3	-	1 (3.3%)
Vaginal Mucositis	1	26 (100%)	19 (63.3%)
	2	-	5 (16.7%)
Small Bowel	1	-	18 (60%)
	2	26 (100%)	2 (6.7%)
Rectum	1	13 (50%)	15 (50%)
	2	13 (50%)	3 (10%)
Bladder	1	18 (70%)	1 (3.3%)

Table 10:- Toxicity Patterns Of Other Studies With Concurrent Cisplatin-Based Chemo-Radiation – Comparison:

Study	Treatment	Organ	Toxicity (Max %)
RTOG 90-01 36	CDDP+RT	Rectum	Gr-4 (8%)
GOG -123 35	CDDP+RT	Hematological	Gr-3 (18%) Gr-4 (5%)
GOG -120 34	CDDP+RT	Hematological	Gr-3 (21%)

Table 11:- Toxicity Patterns Of Studies With Cisplatin And Paclitaxel With Radiation – Comparison:

Study	Treatment	Organ	Toxicity (Max %)
DISILVESTRO et al 42	Conventional EBRT+ICA+WeeklyCisplatin and Paclitaxel	Small intestine	Gr-3: 10.5%
		Hematological	Gr-3: 36.8%
PIGNATA et al 41	Conventional EBRT+ICA+WeeklyCisplatin 30mg/m2 and Paclitaxel 55mg/m2	Vaginal mucosa	Gr-2: 5.5%
		Small intestine	Gr-2: 5.5%
		Rectum	Gr-3: 16.7%
		Bladder	Gr-1: 11.1%
PRAGYAT THAKUR, Indira Gandhi Medical College, Shimla, PGI Chandigarh 40	Conventional EBRT+ICA+ Weekly Cisplatin and Paclitaxel	Skin	Gr-3: 2%
		Small intestine	Gr-3: 20%
		Hematological	Gr-3: 35%
JACCRO GY-01 TRIAL 39	Conventional EBRT+ICA+ Weekly Cisplatin and Paclitaxel	Cumulative Late toxicity: Grade 1: 13.2% Grade 2: 5.9% Grade 3: 2.9% Grade 4: 2.9%	

Table 12:- Toxicity Patterns Of Studies Conducted In Our Institution – Comparison:

Study	Treatment	Organ	Toxicity (Max %)
Hyper-fractionated RT	Hyper-fractionated EBRT + ICA	Skin	Gr-2: 10%
		Bladder	Gr-2: 10%
		Small intestine	Gr-2: 10%
Concurrent Chemo-radiation	Conventional EBRT+ CisplatinD1-5,D21-25	Skin	Gr-2: 50%
		Vaginal Mucosa	Gr-1: 100%
		Small intestine	Gr-2: 100%

		Rectum	Gr-2: 50%
		Bladder	Gr-1: 70%
Hyper-fractionated RT with Chemo	Hyper-fractionated EBRT+ ICA+ Cisplatin D1&17 5FU D2,3,4,5& D22,23,24,25	Skin	Gr-3: 11%
		Vaginal Mucosa	Gr-2: 26%
		Small intestine	Gr-4: 10%
		Rectum	Gr-4: 4%
		Bladder	Gr-2: 18%
Concurrent chemo-radiation with weekly CDDP (previous study)	Conventional EBRT+WeeklyCisplatin, D1,6,11,16,21	Skin	Gr-2: 50%
		Vaginal Mucosa	Gr-1: 50%
		Small intestine	Gr-2: 100%
		Rectum	Gr-2: 50%
		Bladder	Gr-2: 4%
Hyper-fractionated RT with weekly Cisplatin	Hyper-fractionated EBRT+ ICA+ Cisplatin weekly, D1,6,11,16,21	Skin	Gr-2: 33%
		Vaginal Mucosa	Gr-2: 4%
		Small intestine	Gr-2: 100%
		Rectum	Gr-3: 2%
		Bladder	Gr-2: 4%
Conventional RT with weekly cisplatin and paclitaxel	Conventional EBRT+ ICA+ weekly Cisplatin and Paclitaxel	Skin	Gr-3: 3.3%
		Vaginal Mucosa	Gr-2: 16.7%
		Small intestine	Gr-2: 6.7%
		Rectum	Gr-2: 10%
		Bladder	Gr-1: 3.3%

Figure 1:- X-Ray Simulation – AP / Lateral.

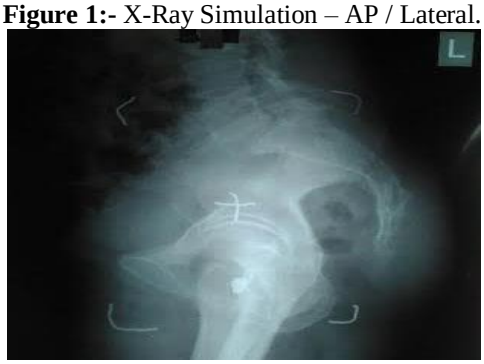


Figure 2:- Brachytherapy - Simulation And Planning.

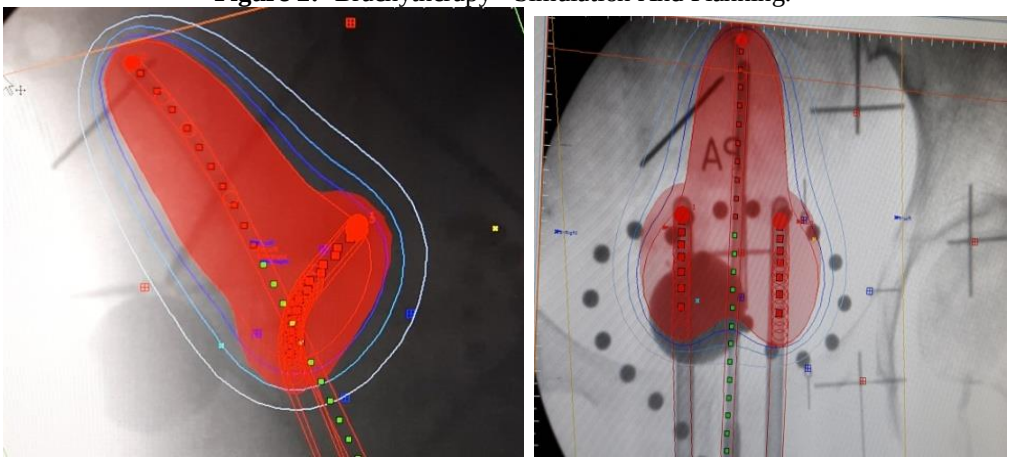
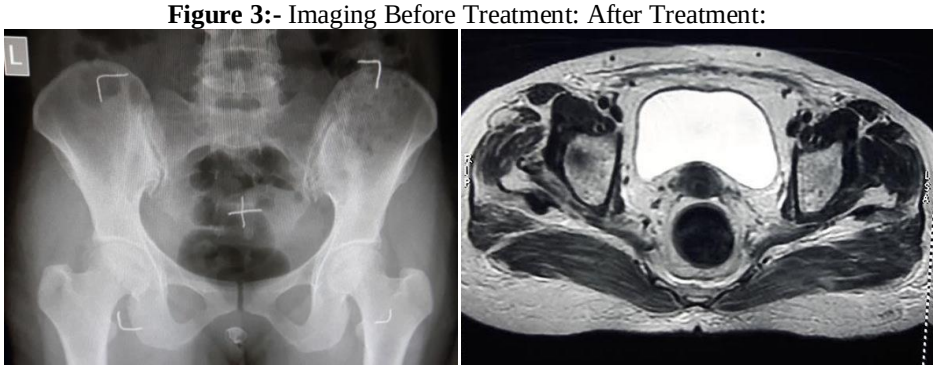


Figure 3:- Imaging Before Treatment: After Treatment:



Conclusion:-

The stage of the tumor and the volume of disease directly influence the treatment outcome in cervical carcinoma patients. Larger the volume, more hypoxic is the tumor. The large incidence of local failure observed in patients treated with radiation alone is attributed to the presence of hypoxic tumor cells which are radio-resistant as oxygen is important for the toxic action of radiation. By adding cisplatin to radiation, a large benefit has been observed. Paclitaxel has the property of radio-sensitisation by redistribution and accumulation of cells in the radio-sensitive phase of the cell cycle thus showing an enhanced effect in hypoxic cells. Concurrent chemotherapy using cisplatin and paclitaxel with conventional radiation has been used in this study for this purpose of improving response in bulky disease and those with regional nodal involvement. The patients who were benefitted by this study included: Stage III B, those with pelvic nodal involvement, low Hemoglobin status.

The aim of this study, which was to improve local control with concurrent chemo-radiation, was thus fulfilled with manageable toxicity. This schedule is therefore a feasible option in an institution set up like ours and must be considered for further randomized controlled trials.

Conflicts of interest:
Nil.

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