



Oncology

CLINICAL OUTCOMES OF COMPUTED TOMOGRAPHY BASED INTRACAVITARY BRACHYTHERAPY TREATMENT IN CERVICAL CANCER PATIENTS ATTENDING TERTIARY CARE HOSPITAL .

Dr. Swapan Kumar Mallick* Associate Professor, Department of Radiotherapy, Malda Medical College and Hospital, Malda, West Bengal. *Corresponding Author

Dr. Jayanta Biswas Assistant Professor, Department of General Surgery, NRS Medical College and Hospital, Kolkata, West Bengal.

ABSTRACT Cervical cancer is one of the most common cancers in women . The aim of our study is to evaluate toxicity, compliance, and response by Computed Tomography based Intracavitary Brachytherapy treatment in patients of cervical carcinoma . This study was conducted in the Department of Radiotherapy, Government Medical College from December 2018 to May 2020, meeting specified Inclusion and Exclusion Criteria. The prognostic outcome of each patient were assessed on the following-parameters: Acute and late Side effects, Loco-regional control for complete or partial response and recurrence. On analysing the pattern of response assessment all patients have complete response(100%) after CT based Brachytherapy. ICRT significantly improve loco regional response but increases incidence of haematological and mucosal toxicity, which being manageable.

KEYWORDS : Cervical Cancer, Cisplatin, Computed Tomography, Intracavitary Brachytherapy.

INTRODUCTION:

Cervical cancer is the third most common cancer in women worldwide with an estimated annual death rate > 275000^[1,2]. Most factors associated with an increased risk of cervical cancer are early age of first intercourse, multiple sexual partners, a male partner with a history of multiple sexual partners, early age of first childbirth, low socio-economic status, a large number of pregnancies, a history of sexually transmitted disease, including gonorrhoea, chlamydia, herpes simplex virus II, and/or human immunodeficiency virus (HIV) and HPV transmission^[3,4]. Most cases in developing countries are diagnosed in the locally advanced stage^[5]. The early stages of cervical cancer may be completely asymptomatic^[6,7]. Symptoms of advanced disease may include loss of appetite, weight-loss, fatigue, pelvic pain, sciatic pain, swollen leg, Foul- smelling vaginal discharge, heavy bleeding from vagina, leaking of urine or faeces from the vagina^[8].

Cervical carcinoma in early stages is quite radiosensitive, however, in locally advanced stages, the long-term outlook has consistently remained grim on account of central or peripheral failures. Concurrent chemo radiation with ,radio-sensitizer like Inj. Cisplatin given every week followed by computed tomography based Intracavitary Brachytherapy(ICRT) has become the standard of treatment in locally advanced cervical carcinoma. According to recent published literature approximately half of locally advanced disease fails in treated pelvic area^[9,10]. Standard treatment regimen for such cases has remained external beam radiation with concurrent chemotherapy followed by brachytherapy wherever possible^[11]. Definitive radiation therapy consists of a combination of external beam radiotherapy and brachytherapy; the addition of brachytherapy represents an integral part of definitive radiation therapy for cervical cancer shown to improve overall survival^[12,16].

MATERIALS AND METHODS :

Patients with locally advanced cervical cancer attending the Radiotherapy Out Patient Department (OPD), Government Medical College, Kolkata, from December 2018 to May 2020, meeting specified Inclusion and Exclusion Criteria, willing to participate in the study. Pre-treatment diagnostic evaluation consisted of a gynecological examination and a panel of laboratory and radiological tests: hematology and biochemistry blood test, chest radiography, computed tomographic/magnetic resonance imaging scan of the abdomen and pelvis, and intravenous urography. Patient were treated with EBRT, 50Gy in 25 fractions over 5 weeks, with concurrent chemotherapy (Injection cisplatin 50mg weekly on the day of EBRT) followed by computed tomography based HDR brachytherapy(7 Gy/3 fraction). Response was assessed using the Response Assessment Criteria in solid tumours. Resist (RECIST) version 1.1.

During treatment patients will be reviewed weekly. After treatment completion, patients will be reviewed monthly for six months. And after that, they will be reviewed every 3 months till the end of study. A complete physical and pelvic examination was conducted at each

follow up visit. If there was any suspicion of pelvic recurrence, CECT/MRI scan and biopsy was performed.

RESULTS:

This single institution study was conducted from December 2018 to May 2020. Total 30 patients were assessed for eligibility. Ultimately, 23 patients were included in the study. Acute toxicities and locoregional control were assessed using the common terminology criteria for adverse events (CTCAE) version 4.0. Patient tolerated the treatment well with few toxicities, like nausea, vomiting ,diarrhoea, neutropenia, thrombocytopenia, anemia,vaginal mucositis, cystitis, proctitis during the ICRT treatment. Response assessment prior to Brachytherapy was 73.9% patients CR with residual disease remaining 26.1% patients PR.

Table 1- Age Distribution:

DISTRIBUTION OF AGE OF PATIENTS	
AGE GROUP	NO. OF PATIENTS (%)
31-40 yrs	1 (4%)
41- 50 yrs	7 (31%)
51-60 yrs	12 (52%)
61-70 yrs	3 (13%)

Majority of the patients were of age group of 51 to 60 years(52%). Median age was 55 years.

Menopausal Status

Chart 1. Menopausal Status

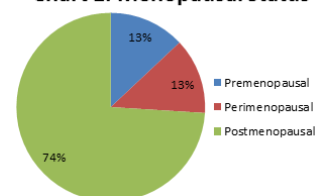


Fig 1: Menopausal Status

Majority of the patients were post menopausal.

Stage Distribution:

Chart 2. Stage Distribution

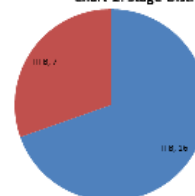


Fig 2: Stage Distribution

Majority of the patients had FIGO stage IIB (69.6%)

Acute skin Toxicity

Chart 3. Acute Skin Toxicity

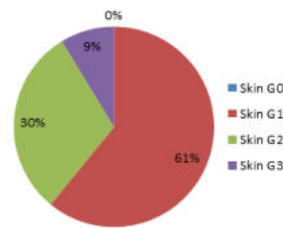


Fig3: Acute skin Toxicity

Acute skin Toxicity is a common side effect of radiation therapy that experience by 70% to 100% of patients. Erythema to dry or wet desquamation i.e G1 skin toxicity were maximum number. Reaction occur within 1 to 4 weeks of treatment. Ulceration may occur in more severe cases.

Genitourinary Toxicity

Chart 4. Genitourinary Toxicity

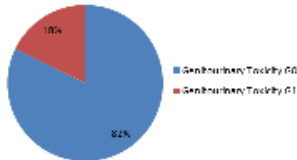


Fig 4: Genitourinary Toxicity

Genitourinary toxicities were dysurea and vaginal mucosities. G1 Genitourinary toxicity is 82% cases.

Gastrointestinal Toxicity

Chart 5. Gastrointestinal Toxicity

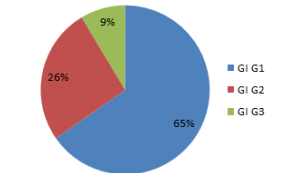


Fig 5: Gastrointestinal Toxicity

Most frequent Gastrointestinal toxicity were nausea, vomiting anorexia and diarrhoea and proctitis.

Haematological Toxicity:

Chart 6. Haematological Toxicity

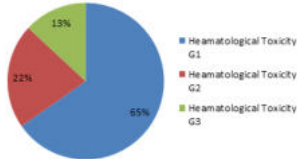


Fig 6: Haematological Toxicity

Most frequent haematological toxicity was anaemia.

Table 2- Response To Post EBRT Treatment

RESPONSE	NO OF PATIENTS(%)
CR	17 (73.9%)
PR	06 (26.1%)

Response assessment prior to BT was 73.9% Complete Response(CR) with residual disease remaining 26.1% patients Partial Response(PR). At the end of brachytherapy response assessment was done clinically and radiologically where patients were showing complete response(CR) with few of them experiencing some complication. The study aims to establish a benchmark for cervical cancer management in terms of tumor control, complications, dose specification, and a prospective assessment of quality-of-life.

DISCUSSION:

In our country, cervical cancer is the second most cancer in female and most of the patient come in an advanced stage in our OPD. The current

standard treatment of locally advanced cervical cancer includes External Beam Radiotherapy with weekly Injection cisplatin followed by intracavitary Brachytherapy [13,14]. Computed tomography (CT) based three-dimensional (3D) planning and more recently more sophisticated image-based planning (Intensity Modulated Radiotherapy) has been widely accepted and implemented for external beam radiotherapy. Intracavitary Brachytherapy (ICBT) is the integral component of treatment of locally advanced cervical carcinoma. HDR Ir192 and Co60 source has significant clinical different between the two isotopes in dose prescribing, treatment planning, and resultant isodose distributions[15]. All patients received EBRT of 50Gy in 25 fractions over 5 weeks with concurrent Cisplatin of 40mg/m2 followed by High dose rate computed tomography based intracavitary brachytherapy. The external beam portion of treatment encompasses treatment to the pelvic lymph nodes, parametria, and primary tumour to a dose adequate to control microscopic disease. The addition of brachytherapy serve to boost the gross tumour, and improves disease control and survival [16,17,18,19,20]. To compare 2D versus 3D planning was the French STIC study by Brunaudet et al [21]. In this cohort patients were treated with EBRT plus chemotherapy followed by brachytherapy. At 24 months local relapse free survival was 74% and 79%, while grade 3-4 toxicity rates were 23% vs 3% in the 2D versus 3D groups respectively and overall survival 65% versus 74%. Charra Brunaud et al [22] also found out that 3 D based ybrachytherapy has improved local control with half the toxicity observed with 2D dosimetry. Banerjee et al [23] concluded that progression from 2D to 3D based imaging and treatment planning for cervical cancer brachytherapy has improved local control, reduced toxicity, and improved overall survival for women.

This study along with continued improvements in imaging, contouring, dosimetry, quality assurance, physics, and brachytherapy delivery promise to perpetuate the advancement of image-based brachytherapy to optimize outcomes for locally-advanced cervical cancer patients.

CONCLUSION:

Computed Tomography based Brachytherapy tissue delineation seems adequate for evaluation of Organ at Risk(OAR) and target tissues, they are defined CT based countouring, 3D imaged-based brachytherapy which allows volumetric optimization improving tumor coverage and critical organ sparing which potentially increases local control, reduces toxicities, and helps predict outcomes.

REFERENCES:

- Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin. 2011;61:69-90.
- Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005;55:74-108.
- DeVita, Hellman, and Rosenberg's Cancer Principles & Practice of Oncology, 9th Ed: p. 1315.
- Bruni L, Barrionuevo-Rosas L, Albero G, Aldea M, Serrano B, Valencia S, Brotons M, Mena M, Cosano R, Muñoz J, Bosch FX, de Sanjosé S, Castellsagué X. ICO Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in India. Summary Report 2014-12-18.
- Kumar, Vinay; Abbas, Abul K.; Fausto, Nelson; & Mitchell, Richard N. (2007). Robbins Basic Pathology (8th ed.) ed. Saunders Elsevier. p. 718-721. ISBN 978-1-4160-2973-1.
- Canavan TP, Doshi NR (2000). "Cervical cancer". Am Fam Physician 61 (5): 1369-76. PMID 10735343. <http://www.aafp.org/afp/20000301/1369.html>. Retrieved 2007-12-01.
- Nanda, Rita (2006-06-09). "Cervical cancer". MedlinePlus Medical Encyclopedia. National Institutes of Health. <http://www.nlm.nih.gov/medlineplus/ency/article/000893.htm>. Retrieved 2007-12-02.
- Vasishtha S, Varghese A, Ragheb A (2007) Patterns of failure in cervical carcinoma and outcome of salvage therapy: a retrospective study. Gul J Oncolog 1: 43-49.
- Perez CA, Breaux S, Madoc-Jones H, Bedwinek JM, Camel HM, et al. (1983) Radiation therapy alone in the treatment of carcinoma of uterine cervix. I. Analysis of tumor recurrence. Cancer 51: 1393-1402.
- Perez CA (1998) Uterine cervix. In: Perez CA, Brady LW (eds) Principles and practice of radiation oncology. (3rd edn). Lippincott-Raven Publishers, Philadelphia.
- Keys HM, Bundy BN, Stehman FB, Mudderspach LI, Chafe WE, et al. (1999) Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. N Engl J Med 340: 1154-1161.
- Montana GS, Hanlon AL, Brickner TJ, Owen JB, Hanks GE, Ling CC, Komaki R, Marcial VA, Thomas GM, Lanciano R. Carcinoma of the cervix: patterns of care studies: review of 1978, 1983, and 1988-1989 surveys. Int J Radiat Oncol Biol Phys. 1995;32:1481-1486.
- Lanciano RM, Martz K, Coia LR, Hanks GE. Tumour and treatment factors improving outcome in stage IIIB cervix. Int J Radiation Oncol Bio-Phys 1991;20:95-100.
- Peteret DG, Pearcey R. Literature analysis of high dose rate brachytherapy fraction schedules in the treatment of cervical cancer; is there an optimal fractionation schedule? Int J Radiation Oncol Bio-Phys 1999;43:359-66
- Palmer A, Mzenda B, Hayman O, Hosseini-Ashrafi M, Queen Alexandra Hospital, Portsmouth Hospitals, NHS Trust, The Physics, Economics and Clinical Use of Co-60 for High Dose Rate Brachytherapy. Phys. Med. Biol. 54: 7417-7434
- Lanciano RM, Won M, Coia LR, Hanks GE. Pretreatment and treatment factors associated with improved outcome in squamous cell carcinoma of uterine cervix: A final report of the 1973 and 1978 patterns of care studies. Int J Radiation Oncol Bio-Phys 1991;20(4):667-676.
- Hanks GE, Herring DF, Kramer S. Patterns of care outcome studies. Results of the national practice in cancer of the cervix. Cancer. 1983;51(5):959-967.

18. Coial, Won M, Lanciano R, Marcial VA, Martz K, Hanks G. The patterns of care outcome study for cancer of the uterine cervix. Results of the second national practice survey. *Cancer*. 1990;66(12):2451-2456.
19. Montana GS, Martz KL, Hanks GE. Patterns and sites of failure in cervix cancer treated in the USA in 1978. *Int J Radiation Oncol Bio-Phys* 1991;20(1):87-93.
20. Logsdon MD, Eifel PJ, Figo IIB. Squamous cell carcinoma of the cervix; An analysis of prognostic factors emphasizing the balance between external beam and intracavitary radiation therapy. *Int J Radiation Oncol Bio-Phys* 1999;43(4):763-775.
21. Brunaudet C, Levitchi M, Delannes M. Dosimetric. Clinical results of a French prospective study of 3D brachytherapy for cervix carcinoma. *Radiother Oncol*. 2011;99(S57).
22. Charra-Brnaud C, Harter V, Delannes M, Haie-Meder C, Quetin P, Kerr C, Castelain B, Thomas L, Peiffer D. Impact of 3D image-based PDR brachytherapy on outcome of patients treated for cervix carcinoma in France: results of the Frnch STIC prospective study. *Radiother Oncol*. 2012;103:305-313.
23. Banerjee; Brachytherapy in the treatment of cervical cancer: a review *Int J Womens Health*. 2014;6: 555-564.