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ORIGINAL ARTICLE

ASSESSMENT OF ACUTE GASTRO-INTESTINAL AND GENITO-URINARY TOXICITIES IN THE CERVICAL CANCER PATIENTS USING COBALT-60 BASED HIGH DOSE RATE INTRA CAVITARY BRACHYTHERAPY

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Key Message:

The acute gastrointestinal and genitourinary toxicities of high-dose-rate intracavitary brachytherapy using Co-60 is low compared to Ir–192, thus it is more suitable for low economic country.

ABSTRACT

Context: Recently introduced Cobalt-60 HDR source has longer half life of 5.2 years compared with 73.8 days of Ir-192, more economical and attractive for low resource settings.
Aim: The purpose of this study to know acute gastrointestinal and genitourinary toxicities associated with Co-60 source in HDR ICRT of cervical cancer patients and its comparison with similar toxicities in Ir-192 based HDR ICRT.
Settings and Design: Prospective study
Methods and Material: The study was completed on 65 patients of carcinoma cervix. External beam radiotherapy (EBRT) of dose 45-50 Gy in 25 fractions @ 180-200cGy per fraction delivered over 5 days per week using teletherapy Cobalt 60 machine. ICRT was started after one week of completion of EBRT. Fletcher suite applicators were used for brachytherapy in all patients. Total 3 sessions of ICRT, 7Gy each, were delivered 72 hours apart. The acute gastro-intestinal and genito-urinary toxicities were assessed using Common Terminology Criteria for Adverse Events version 4.03 (CTCAE). The only highest grade of GU and GI toxicity was used for final analysis and patients were kept in follow up for 3 months in this study.
Statistical analysis used: Comparison with previous studies
Results: Only 2 patients (3%) had grade 3 acute diarrhea. In other studies, the reported rates of acute toxicities ≥ grade 3 ranged from 0%–8% for gastrointestinal and 0%–3% for genitourinary toxicities.
Conclusions: The acute gastrointestinal and genitourinary toxicities of high-dose-rate intracavitary brachytherapy using Co-60 radionuclide source is low and comparable with Iridium-192. Additionally, Cobalt 60 has economic advantage over Ir-192. Thus, it is more suitable for low economic resource settings.

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INTRODUCTION

Carcinoma cervix is the second most common malignancy among females of India (Ferlay *et al*., 2015). According to Globocan 2012 database, the incidence of this cancer in India was 123,000 (Bray *et al*., 2013). It is one of the malignancies that have been effectively treated with radiotherapy (Landoni *et al*., 1997). In early stages of carcinoma cervix, surgery has same results as radiotherapy. For advanced stages, the external beam radiotherapy followed by high dose rate (HDR) intracavitary brachytherapy (ICRT) constitutes the main treatment (Fletcher and Shukovsky, 1975). Iridium 192 (Ir-192) radionuclide sources is widely used for HDR ICRT. This is because of easier to manufacture Ir-192 in smaller size for brachytherapy applications and its high specific activity and rapid fall of dose. Cobalt-60 (Co-60) HDR source was available but unpopular because of bigger source size compare to Ir-192 (Chao *et al*., 2002). It is now possible to produce miniaturized size of Cobalt-60 radionuclide for HDR applications. This has been also shown to have identical geometric and dosimetric properties with Ir-192 (Ballester *et al*., 2005). The advantages of Co-60 over Ir-192 are its longer half life of 5.2 years compared with 73.8 days for Ir-192. This shows that instead of changing the Ir-192 source every 3-4 months, Co-60 source can be changed every 6-8 years which is

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a more economical and attractive for low resource settings. Few radiation experts are concerned with the higher energy of Co-60 (1.25MeV) compared with Ir-192 (0.6MeV). They mainly concerns for possible increase in toxicity to patients due to this higher energy. Therefore, this study was carried out to assess the acute gastro-intestinal and genito-urinary toxicities associated with Co-60 as HDR source and these were compared with the patients of carcinoma cervix treated with Ir-192 HDR ICRT.

MATERIALS AND METHODS

This study was conducted prospectively on the patients of carcinoma cervix with FIGO stage IB_2 to IIIB. ICRT applications were done using Fletcher suit applicators and Co-60 based HDR remote after loaded brachytherapy unit. As per departmental guidelines informed consent of every patient was taken before procedure.

Inclusion Criteria

1. Cases to be done in between May, 2016 to September, 2016.
2. FIGO stage IB_2 to IIIB.
3. Pathologically proven.
4. No major co morbidity.
5. Adequate vaginal space.

Exclusion Criteria

1. Post-op.
2. Re-irradiation.
3. Inadequate vaginal space.
4. Patient who not giving consent.

Source of Data

Total 67 patients of carcinoma cervix were enrolled in this study in between May 2016 to September 2016. 2 patients were lost follow up for further analysis during the study period. Hence, these patients were de-registered for final statistical analysis.

Method

External beam radiotherapy (EBRT) of dose 45-50 Gy in 25 fractions @ 180-200cGy per fraction delivered over 5 days per week using teletherapy Cobalt 60 machine. ICRT was started after one week of completion of EBRT. Fletcher suite applicators were used for brachytherapy in all patients. Total 3 sessions of ICRT, 7Gy each, were delivered 72 hours apart. The procedures were done under general anesthesia after getting pre-anesthetic clearance. Vaginal examination was done in each patient to know appropriate size of ovoids. The angle and length of the central tandem required was assessed by using uterine sound. Cleaning and draping of pelvic area was done using povidone iodine solution. A Foley's catheter was inserted into the urinary bladder and the balloon inflated with 7 cc (according to ICRU 38[13]) of diluted urograffin dye. After serial dilatation of the cervical os, the most suitable central tandem was inserted into the uterus such that keel gets fixed at the level of external os. The ovoids was placed in right and left vaginal fornix equidistant from the central tandem. The vagina was packed with gauze to further displace the bladder anteriorly and the rectum posteriorly to minimize the dose to these organs and to immobilize the applicators. An additional rectal marker was placed in rectum to identify the ICRU 38 rectal points. AP and lateral orthogonal marker X-rays with the help of reconstruction box was taken with C-arm X-ray machine. The orthogonal pictures were reconstructed and treatment planning was done with treatment planning system. Multiple points consistent with ICRU 38 were located and used for treatment planning as like Point A (Tod and Meredith, 1953), Bladder reference point, rectal reference point. The bladder point dose was kept to <90% of point A or a total of <75 Gy (±5%). Rectal dose was kept up to <80% of point A or total <70 Gy (±5%). Dwell positions were optimized to minimize the doses to rectum and bladder points. The acute gastro-intestinal (GI) and acute genito-urinary (GU) toxicities were assessed using Common Terminology Criteria for Adverse Events version 4.03 (CTCAE) (CTCAE, 2010). The only highest grade of particular GU and GI toxicity was used for final analysis of this study. In acute GI toxicities, proctitis, diarrhoea, nausea and vomiting were included. In acute GU toxicities, cystitis, urinary frequency and urinary urgency were included. All patients were kept in follow up for total 3 months in this study.

The Assessment of GI and GU toxicities was done as per schedule

- First assessment – at the time of last HDR ICRT application
- Second assessment- one month later to last HDR ICRT application
- Third assessment-two month later to last HDR ICRT application
- Fourth assessment- three month later to last HDR ICRT application

The patients with grade 3 or higher toxicities were hospitalized as per department's protocol and managed accordingly.

RESULTS

Table 1. Patient characteristics

Sr. No.	Attributes	Group character
1.	Median age(years)	50
2.	FIGO stage(no. of patients)	
	I	2
	II	25
	III	38
3.	Median duration of observation(days)	90
4.	ICRT	
	Dose per fraction(Gy)	7
	Median length of uterine cavity(cm)	5
	Median ovoid size	Medium

Total 7 parameters were analyzed of acute complication in HDR brachytherapy

1. **Acute Proctitis:** Maximum no. of patients i.e 32 had Gr I and 5 patients had Gr II toxicity.
2. **Diarrhea:** Maximum no. of patients i.e 32 had Gr I, 6 had Gr II and 2 patients (3%) had Gr III toxicity.
3. **Nausea:** Gr I toxicity was observed in 7 patients (10.7%).
4. **Vomiting:** 8 patients had Gr I and one patient had Gr II toxicity.
5. **Acute Cystitis:** 24 patients had Gr I and one patient had Gr II toxicity.

Table 2. Comparison of acute GI and GU toxicities with Atara Ntekim Co-60 based HDR brachytherapy 2008 study

Study	Toxicity						
	Proctitis	Diarrhea	Nausea	Vomiting	Cystitis	Urinary frequency	Urinary urgency
Atara Ntekim *et al*.	57	62	11	10	40	40	40
Our study	56.92	61.53	10.76	13.84	38.46	40	35.38

Table 3. Comparison of ≥III GI and GU acute toxicity in previous studies of chemo-radiation using Ir-192 as HDR source

Study	HDR Gy/fr	EBRT	EQD2	GI toxicity %	GU toxicity %
Chung *et al* 2005	25/5	45/25	75.50	2	0
Chen *et al* 2006	24/4	45/25	72.25	4.3	0
Shakespeare *et al* 2006	31.8/6	45/25	86.65	0	0
Atara Ntekim *et al* 2008 (with Co-60)	19.5/6	45/22	70.25	3	0
Our study	21/3	50/25	79.75	3.07	0

Table 4. Comparison of some early (≤ grade II) GI and GU acute toxicities in the previous studies

Study	Toxicity (%)					
	Proctitis	Diarrhea	Nausea	Vomiting	Cystitis	GU
Chung *et al* 2005	-	77	44	-	-	22
Chen *et al* 2006	-	-	-	-	-	5.7
Shakespeare *et al* 2006	4.8	-	-	-	23.8	-
Atara Ntekim *et al* 2008 (with Co-60)	57	59	11	10	40	40
Our study	56.92	58.46	10.76	13.84	38.46	40

6. **Urinary frequency:** Gr I toxicity was observed in 26 patients (40%).
7. **Urinary urgency:** Grade I toxicity was observed in 23 patients (35.3%).

The above studies done (Table 3) on Ir-192 based ICRT have grade-III acute GI toxicities and no acute GU toxicities similar to our study. Abbreviations: [HDR – High dose rate, EBRT – external beam radiation therapy, GI – Gastrointestinal, GU – Genitourinary]. Above data (Table 4) shows the comparison of acute toxicities ≤ grade-II. There were similar toxicities profiles as our study.

DISCUSSION

Carcinoma cervix is the second most common malignancy among females of India (Ferlay *et al*., 2015). Because of lacking proper screening facilities, majority of the patients usually presents in advanced stages (Singh and Chauhan, 2015). Hence, a combination of external beam radiotherapy and brachytherapy gives high cure rate especially with concurrent use of cisplatin based chemotherapy in these stages. HDR ICRT by Iridium-192 is widely used and discussed in the literature. Reports on Cobalt 60 HDR ICRT are very scanty because earlier sources sizes were larger and comparatively higher energy. It is now possible to produce miniaturized size of Co-60 radionuclide source. The advantages of CO-60 over Ir-192 are its longer half life of 5.2 years compared with 73.8 days for Ir-192 source (Chao *et al*., 2002). The available HDR Brachytherapy systems with Co-60 sources include the Ralston remote after loader manufactured by Shimadzu Corporation of Japan and the BEBIG Multisource/Gyne Source remote after loader manufactured by BEBIG GmbH of Germany. This study was aimed to know about the acute toxicities of Co-60 based HDR ICRT. Our results have shown that HDR ICRT done with Co-60 radionuclide source was well tolerated.

There was no grade 3 or 4 acute genitourinary toxicity among all the patients. Only 2 patients (3%) had grade 3 acute diarrhea that necessitated treatment suspension for one-two week. In other studies, the reported rates of acute toxicities ≥ grade 3 ranged from 0%–8% for gastrointestinal and 0%–3% for genitourinary toxicities (Ntekim *et al*., 2010; Chen *et al*., 2006; Shakespeare *et al*., 2006; Chung *et al*., 2005). The early (≤grade 2) gastrointestinal and genitourinary toxicities experienced by patients in this study might be higher compare to other studies as because most authors ignored these mild symptoms hence mostly higher toxicities were reported and if reported, consistent scoring criteria was not used. We found that the acute genito-urinary toxicities in Co-60 based HDR ICRT were tolerable and manageable and acute toxicities profiles are also similar with Ir-192 based applications. However the risk of late treatment related toxicity is yet to be evaluated.

Conclusion

The acute gastrointestinal and genitourinary toxicities of high-dose-rate intracavitary brachytherapy using Co-60 radionuclide source is low and comparable with Iridium-192. Additionally, Cobalt 60 has economic advantage over Ir-192. Thus, it is more suitable for low economic resource settings.

Conflict Of Interest

NIL

REFERENCES

Ballester, F., Granero, D., Perez-Calatyud, J., Casal, E., Agramunt, S. and Cases, R. 2005. Monte Carlo dosimetric study of the BEBIG Co-60 HDR source. *Phys Med Biol,* 50:309-16.

Bray, F., Ren, J.S., Masuyer, E., Ferlay, J., *et al*. 2013. Estimates of global cancer prevalence for 27 sites in the adult population. *Int J Cancer,* 132:1133-45.

Chao, K.S., Perez, C.A. and Brady, L.W. 2002. Physics and Dosimetry of High Dose Rate Brachytherapy in radiation oncology management decisions. Lippincott Williams & Wilkins Philadelphia 2002;2:89-94.

Chen, S.W., Liang, J.N., Hung, Y.C. *et al*. 2006. A control cohort comparison with radiation alone on treatment outcome and complications of concurrent weekly cisplatin plus external beam radiotherapy and high-dose rate brachytherapy for advanced cervical cancer. *Int Journal Radiation Oncology,* 66:1370–77.

Chung, Y.L., Jian, J., Cheng, S. *et al*. 2005. A phase 1/11 study of extended-field radiotherapy and High- Dose Rate brachytherapy with concurrent and adjuvant cisplatin-based chemotherapy for locally advanced cervical cancer. *Gynecologic Oncology,* 97:126–35.

CTCAE, V. 2010. 4.03: June 14, U.S. Dept of health and human service.

Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., *et al*. 2015. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer,* 136:E359-86.

Fletcher, G.H. and Shukovsky, L.J. 1975. The interplay of radiocurability & tolerance in the irradiation of human cancers. *J Radiol Electrol Med Nucl,* 56:383-400.

International Commission of Radiation Units and Measurements. Dose and Volume Specification for Reporting Intracavitary Therapy in Gynaecology. Bethesda, MD: ICRU; 1985. (Report No: 38).

Landoni, F., Maneo, A, Colombo, A. *et al*. 1997. Randomized study of radical v/s radiotherapy for IB-IIA cervical cancer. Lancet, 350:535-40.

Mandal, A., Asthana, A.K. and Aggarwal, L.M. 2007. Clinical significance of cumulative biological effective dose and overall treatment time in the treatment of carcinoma cervix. *J of Med Phys,* 32:68–72.

Ntekim, A., Adenipekun, A., Akinlade, B. and Campbell, O. 2010. A Prospective Study of High Dose Rate Brachytherapy in the treatment of cervical cancer, preliminary experience with Co-60 Radionuclide source. *Clin Med Insights Oncol,* 4:89-94.

Raksha, A., Yousefi Kashi, A.S., Hoseini, S.M. *et al*. 2015. Evaluation of Survival and Treatment Toxicity with High Dose Rate Brachytherapy with Cobalt-60 in carcinoma cervix. *Iran J Cancer Prev,* 8:3573.

Shakespeare, T.P., Lim, K.H.C., Lee, K.M., Back, M.F., Mukhrerjee, R. and Lu, J.D. 2006. Phase II Study of the American brachytherapy Society guidelines for the use of HDR Bracytherapy in the treatment of cervical carcinoma. *Int J Gynecol Cancer,* 16:277-82.

Singh, J.K. and Chauhan, R. 2015. Management of Locally Advanced Cancer Cervix an Indian Perspective. *Rev Recent Clin Trials,* 10:298-301.

Tod, M. and Meredith, W.J. 1953. Treatment of cancer of the cervix uteri-a revised "Manchester method". *Br J Radiol,* 26: 252.

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