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The Dosimetric Comparison of Doses Distribution of Co^{60} Based High Dose Rate Intracavitary Brachytherapy Delivered Under General Anaesthesia v/s Conscious Sedation in Cervical Cancer Patients

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Abstract: ***This study compare prospectively the dosimetric distribution of doses delivered to point A, bladder and rectal reference point using CO^{60}based ICRT under general anaesthesia v/s conscious sedation in cervical cancer patients. This study was conducted prospectively on 80 applications of ICRT in carcinoma cervix patients with stage IB_2 to IIIB. 40 applications in group AG(anaesthesia group) and 40 applications in group CS(conscious sedation group) those planned from October, 2015 to November, 2015. ICRT was done using Fletcher suit applicators (central tendem and two vaginal ovoids) and the machine named Eckert and Zeigler HDR remote after loading. In each application dose of 6 Gy was prescribed to point 'A' and doses at bladder and rectal reference points ($bladder_{ref}$ and $rectal_{ref}$) were noted and compared in both groups. Student 't' test was used to compare significance difference. Demography and clinical characteristics were comparable in both groups. The mean dose to $bladder_{ref}$ in group AG ranges from 17.7-69.2% (1.07-4.14 Gy) and in Group CS from 15.54-74.24% (0.93-4.45Gy).P value is 0.130(insignificant). The mean dose to $rectal_{ref}$ in group AG ranges from 32.5-77.73% (1.95-4.78 Gy) and in Group CS it ranges from 21.07-79.16% (1.26-4.75 Gy). P value is 0.126 (insignificant). So avoiding general anaesthesia doesn't result in inferior dosimetry in HDR brachytherapy in carcinoma cervix.***

Keywords: oncology

1. Introduction

Cervical cancer is one of the leading causes of death in reproductive age group of women. According to GLOBACAN 2012 database[1], the incidence of cervical cancer in India was 123, 000 among 1.2 billion people. Multiple randomized trials done in past proved that in early stages of carcinoma cervix surgery has equivalent treatment outcome as radiotherapy.[2] For advanced stages, i. e., from bulky stage IB2 and IIA to Stage IVA, external beam radiotherapy (EBRT), followed by intracavitary radiotherapy (ICRT) or intracavitary brachytherapy (ICBT) constitutes the main treatment[3]. Concurrent weekly inj. cisplatin 35-40mg/$m^2$is given with EBRT from stage IB2 onwards[4].

ICRT is an important treatment in the management of cervical carcinoma.[5] It is a mean to deliver the required dose of brachytherapy to cervix and parametrium with relative sparing of the adjoining normal structure.[6]

According to ABS guidelines, [16]brachytherapy should be done under general anaesthesia (GA). It provides good analgesia and muscle relaxation, although it has shown to be associated with higher complications (hypotension, bradycardia etc).[10]For general anaesthesia pre-anaesthetic clearance is required. Institute with heavy burden of patients and less manpower, it is very time consuming. Sometimes it is very difficult to manage complications too.

On the other side, brachytherapy in conscious sedation is simple and convenient to practice, not requiring preanasthetic clearance but may cause pain, discomfort and poor muscle relaxation, which may lead to compromising dosimetry.
Our centre is having heavy load of cervical cancer patients. Due to increased load, we have started ICRT with conscious sedation to treat more patients as in higher burden settings.

So the aim of this study is to know the effect of general anaesthesia vs. conscious sedation in dosimetric distribution in cervical cancer patients treated with HDR brachytherapy source being CO^{60}.

2. Aims and Objectives

To compare prospectively the dosimetric distribution of doses delivered to point A, bladder and rectal reference point using CO^{60}based ICRT under general anaesthesia v/s conscious sedation in cervical cancer patients.

3. Review of Literature

Daya N. Sharma et al[9] (2012) has done a study that compared the dosimetry of high-dose-rate intracavitary brachytherapy (HDR-ICBT) performed with and without general anesthesia /spinal anesthesia (GA/SA) in patients with cervical carcinoma. They retrospectively retrieved the records of 138 HDR-ICBT applicator insertions performed in 46 patients: 69 performed with GA/SA (anaesthesia group known as AG) in 23 patients and 69 performed without GA/SA (non anaesthesia group known as NAG) in 23 patients. The intracavitary brachytherapy (ICBT) application was done with central tandem and two vaginal ovoids. For each ICBT plan, a high-dose-rate (HDR) dose of 7 Gy was prescribed to point A. From each plan, the doses to Point B right (B_R), Point B left (B_L),

bladder and rectal reference points ($Bladder_{ref}$ and $Rectal_{ref}$) were recorded and compared in the two groups. Student's t-test was applied to find out the significance of difference. The two groups were comparable in term of demography and clinical characteristics. Mean Point B_L doses in AG and NAG were 1.89 Gy (27% of Point A dose) and 1.82 Gy (26% of Point A dose), respectively. Mean Point B_R doses in AG and NAG were 1.91 Gy (27% of Point A dose) and 1.85 Gy (26% of Point A), respectively (p-value 0.7). The mean dose to $Bladder_{ref}$ in AG and NAG was 5.03 Gy and 4.90 Gy, respectively (p-value 0.6). The mean dose to $Rectal_{ref}$ was significantly higher in AG than NAG (5.09 Gy vs.4.49 Gy, p-value 0.01). Although based on conventional 2D dosimetry planning, this study has demonstrated that avoiding GA/SA does not result in inferior HDR-ICBT dosimetry.

Bhanabhai H et al[12] (2013) done a study of pain assessment during conscious sedation for cervical cancer HDR brachytherapy. From January 2009 to October 2010, 20 patients (median age: 45 years) underwent 57 procedures. The median duration of the procedure was 1.4 hrs and no significant cardiovascular events were noted. The total dose of intravenous midazolam used ranged 0.5mg-8.5mg (median: 2.5mg). The total dose of intravenous morphine equivalent used ranged 2.5mg-60mg (median: 8mg). The maximum pain score during procedure was 0-10(median 4.7). The mean and median pain scores during the procedure were 1.4 and 1.1 respectively. The period of recovery from conscious sedation was relatively brief (median discharge time: 1 hr). So we are able to demonstrate that patients undergoing HDR brachytherapy for cervical cancer can achieve good pain control with conscious sedation.

Anker CJ et al[15](2013) has done a study on effect of brachytherapy technique and patient characteristics on cervical cancer implant dosimetry. From 1998 to 2008, 31 patients with cervical cancer with full dosimetric data were identified who received definitive external beam radiation and HDR brachytherapy with tandem and ovoid applicators. Patients underwent a median of 5 brachytherapy procedures (range, 3 to 5), with a total of 179 procedures for 31 patients. For all brachytherapy treatments, the average ratios between the doses for the rectal, bladder, vaginal surface and pelvic sidewall reference points to those at point A were 0.49, 0.59, 1.15 and 0.17, respectively. In general decreased OAR dose Co-60 versus Ir-192 in HDR brachytherapy: Scientific and as associated with a lower stage, younger age, increased ovoid size, and increased tandem length and earlier implant number. Increased tandem curvature significantly increased bladder dose and decreased rectal dose. Intravenous anaesthesia usage was not correlated with improved dosimetry.

4. Materials and Methods

This study was conducted prospectively on 80 applications of ICRT in carcinoma cervix patients with stage IB_2 to IIIB. At our centre EBRT with or without concurrent chemotherapy followed by ICRT is the mainline treatment.

EBRT dose 45-50 Gy in 25 fractions @ 180-200cGy per fraction treated 5 days per week over 5-6 weeks was given using teletherapy Cobalt 60 machine through antero-posterior and postero-anterior (AP/PA) portal to pelvis using SAD technique with concurrent chemotherapy if indicated.

ICRT was started after 1 week of EBRT completion. The four sessions @ 6 Gy /session was given with a gap of at least 72 hrs between each session.

ICRT was done using Fletcher suit applicators and the machine named Eckert and Zeigler HDR remote after loading brachytherapy unit with CO^{60} radionuclide source. As per departmental guidelines informed consent of every patient was taken in written before brachytherapy.

Inclusion criteria:

1. Applications done from October, 2015 to November, 2015.
2. Stage IB_2 to IIIB.
3. Pathologically proven.
4. No sign of co morbidity.
5. Adequate vaginal space.

Exclusion criteria:

1. Post-op.
2. Re-irriadition.
3. Inadequate vaginal space.
4. Pt. who didn't give consent.

Grouping was done at systemically odd and even basis in which all odd number patients was in group AG(anaesthesia group) and even number was in CS(conscious sedation group) those planned from October, 2015 to November, 2015.

Group AG: ICRT done under general anaesthesia.

In group AG, every patient underwent pre-anaesthetic clearance (PAC). Patient was admitted one day before the procedure for preparation like overnight empty stomach and enema.

Group CS: ICRT done in conscious sedation in 40.

In group CS Inj. Midazolam 0.5-8mg(median 2.5mg)[12] in the form of slow i.v. infusion was used with antiemetic support and rescue for pain was inj. Tramadol 2mg/kg. Since the procedure was done under mild sedation, so there was no need for PAC or patient staying empty stomach. Post procedure rescue for pain in either group was inj. Tramadol 2mg/kg.

The rest of procedure was same in both the groups. Patient was made to lie in lithotomy position. PS/PV examination was done to know the vaginal space and direction of uterus, to assess the angle and length of the central tandem required. Cleaning and drapping of pelvic area was done using Povidone ioidine solution. A Foley's catheter was inserted into the urinary bladder and the balloon was

inflated with 7 cc (according to ICRU 38)[19] of diluted Urograffin dye to identify the bladder reference points. Fletcher suite applicator was used for brachytherapy in all the patients. After serial dilation of the cervical os, the most suitable central tandem was inserted through the cervical os into the uterus such that keel fixed at the level of external os. The code of central tandems available according to length and angle varies from LAR 02-01 to LAR 06-01. The ovoids were 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 rectum points.

Orthogonal X-rays with the help of recobox (reconstruction box) done with C-arm X ray machine.

The orthogonal view was reconstructed and treatment planning was done with BEBIG HDR plus 2.5 treatment planning system.

Dose prescription was specified to point "A". Multiple points consistent with ICRU 38 were located and used for treatment planning and dose optimization to point A, bladder and rectum.

Calculation of data was compiled in master chart and statics was calculated with software SPSS (statistical package for the social sciences) 23.0version[22].

5. Observation

Patient characteristics:

Table A: Showing patient characteristics

Sr. No.	Attributes	Group AG	Group CS
1.	Median age (years)	40	45
2.	FIGO stage (no. Of patients) I II III	 2 7 1	 3 6 1
3.	Median EBRT dose (Gy)	50	50
4.	Median duration of treatment (days)	58	60
5.	ICRT Average applicator insertion time in OT (minutes) Dose per fraction (Gy) Median length of uterine cavity (cm) Median ovoid size	40 6 5 Medium	30 6 5 Medium

The two groups are well matched to various demographic and clinical characteristics of patients.

Total 6 Parameters were analyzed { Dose to point A_1, Dose to point A_2, Bladder max dose($B_{max.}$), Bladder mean dose(B_{mean}), Rectal max dose(R_{max}) Rectal mean dose(R_{mean})}

Dose to point A1-

Table 1: Showing target A1 dose distribution in group AG&CS.

Target A1 dose	Group AG	Group CS
4.5-5	0	2
5-5.5	8	9
5.5-6	22	14
6-6.5	9	13
6.5-7	1	2

Target A1 (point A to the right on x axis) dose ranges from 5.04-6.36 Gy with the average dose of 5.69Gy in Group AG. The target A1 dose in group CS ranges from 4.91-6.92 Gy with the average dose being 5.92Gy.

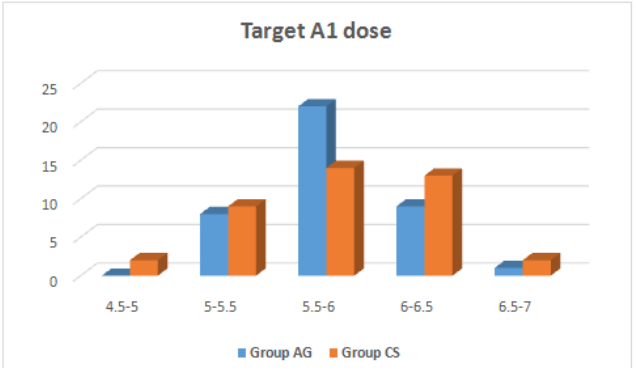

Figure 1: Showing target A1 dose distribution in group AG&CS

Dose to point A2-

Table 2: showing target A2 dose distribution in group AG&CS

Target A2 dose	Group AG	Group CS
4.5-5	1	0
5-5.5	7	10
5.5-6	20	18
6-6.5	10	8
6.5-7	2	4

The target A2 (point A to the left on x-axis) dose in Group AG ranges from 5.06-6.44 Gy with the average dose being

5.75Gy. In group CS the target A2 dose ranges from 4.77-6.76 Gy with the average dose of 5.97 Gy.

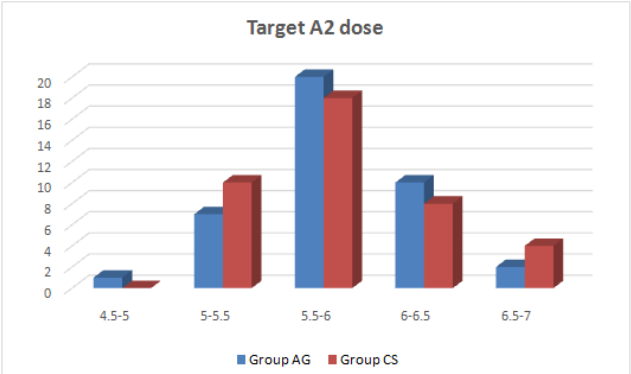

Figure 2: Showing target A2 dose distribution in group AG&CS

Bladder max dose

Table 3: Showing bladder max dose%. distribution in group to AG and CS.

Bladder max dose %	Group AG	Group CS
21-40	8	10
41-60	11	13
61-80	11	11
81-100	8	5
101-120	2	1

The max bladder dose in group AG ranges from 27.5-114.7 % (1.65-6.88Gy) and in group CS it ranges from 21.2-111% (1.27-6.66 Gy).

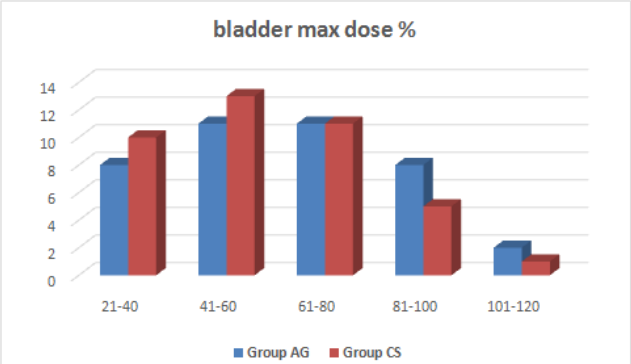

Figure 3: Showing bladder max dose %. distribution in group AG&CS

Bladder mean dose

Table 4: Showing bladder mean dose%. distribution in group AG&CS.

Bladder mean dose %	Group AG	Group CS
0-20	3	3
21-40	21	20
41-60	14	16
61-80	2	1

The mean bladder dose in group AG ranges from 17.7-69.2% (1.07-4.14 Gy) and in Group CS from 15.54-74.24% (0.93-4.45Gy).

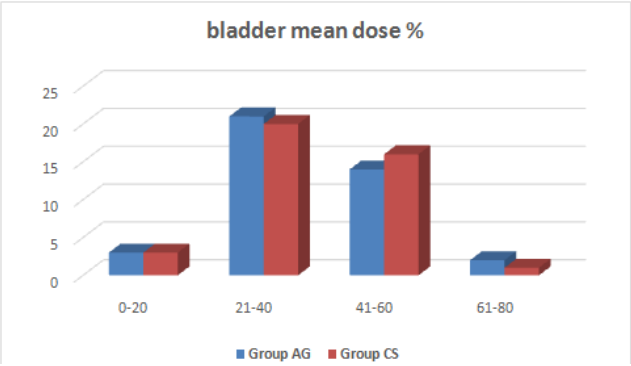

Figure 4: Showing bladder mean dose% distribution in group AG&CS

Rectum max dose-

Table 5: Showing Rectum Max dose% distribution in group AG&CS

Rectum max dose %	Group AG	Group CS
21-40	3	6
41-60	14	14
61-80	14	14
81-100	9	6

The max. rectum dose in group AG ranges from 26.2-90.4% (1.99-5.42 Gy) and in group CS it ranges from 25.5-90% (1.53-5.45Gy).

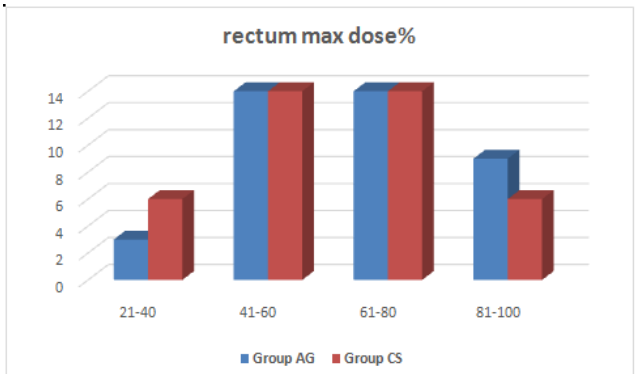

Figure 5: Showing Rectum Max dose% distribution in group AG&CS

Rectum mean dose-

Table 6: Showing Rectum mean dose% distribution in group AG&CS.

Rectum mean dose %	Group AG	Group CS
21-40	4	10
41-60	27	17
61-80	9	13

The mean rectum dose (TABLE 6, FIG. 6) in group AG ranges from 32.5-77.73% (1.95-4.78 Gy) and in Group CS it ranges from 21.07-79.16% (1.26-4.75 Gy).

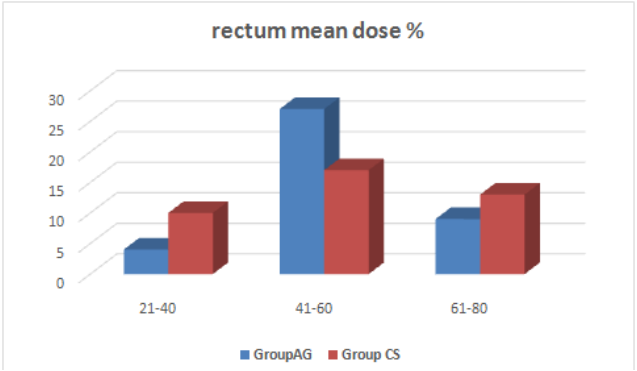

Figure 6: Showing Rectum mean dose% distribution in group AG&CS

6. Results

TABLE 'A' showing two groups AG and CS are well matched to various demographic and clinical characteristics of patients.
Target A1 (point A to the right on x axis) dose ranges from 5.04-6.36 Gy with the average dose of 5.69Gy in Group AG. The target A1 dose in group CS ranges from 4.91-6.92 Gy with the average dose being 5.92Gy(TABLE 1, FIG.1). P value is 0.327 (insignificant).

The target A2 (point A to the left on x-axis) dose in Group AG ranges from 5.06-6.44 Gy with the average dose being 5.75Gy. In group CS the target A2 dose ranges from 4.77-6.76 Gy with the average dose of 5.97 Gy(TABLE 2, FIG.2). P value is 0.640 (insignificant).

The max bladder dose (TABLE 3, FIG. 3) in group AG ranges from 27.5-114.7 % (1.65-6.88Gy) and in group CS it ranges from 21.2-111% (1.27-6.66 Gy). P value is 0.044(significant).

The mean bladder dose (TABLE 4, FIG. 4) in group AG ranges from 17.7-69.2% (1.07-4.14 Gy) and in Group CS from 15.54-74.24% (0.93-4.45Gy).P value is 0.130(insignificant).

The max. rectum dose (TABLE. 5, FIG. 5) in group AG ranges from 26.2-90.4% (1.99-5.42 Gy) and in group CS it ranges from 25.5-90% (1.53-5.45Gy).P value is 0.054(insignificant).

The mean rectum dose (TABLE 6, FIG. 6) in group AG ranges from 32.5-77.73% (1.95-4.78 Gy) and in Group CS it ranges from 21.07-79.16% (1.26-4.75 Gy). P value is 0.126(insignificant).

7. Discussion

In Daya n Sharma et al study total 138 procedures were done, 69 in anaesthesia group(AG) and 69 in non anaesthesia group(NAG). For each ICRT 7 Gy was prescribed to point A. The mean dose to Bladder reference points in AG and NAG was 5.03gy and 4.90gy, respectively (p value 0.6). The mean dose to Rectal reference points in AG and NAG was 5.09gy and 4.90gy, respectively (p value 0.01). No significant difference in dose distribution in AG and NAG group.

In our study total 80 procedures were done, 40 in anaesthesia group(AG) and 40 in non anaesthesia that is conscious sedation group(CS). For each ICRT 6 Gy delivered to point A.

Target A1 (point A to the right on x axis) dose ranges from 5.04-6.36 Gy with the average dose of 5.69Gy in Group AG. The target A1 dose in group CS ranges from 4.91-6.92 Gy with the average dose being 5.92Gy. P value is 0.327 (insignificant).

The target A2 (point A to the left on x-axis) dose in Group AG ranges from 5.06-6.44 Gy with the average dose being 5.75Gy. In group CS the target A2 dose ranges from 4.77-6.76 Gy with the average dose of 5.97 Gy. P value is 0.640 (insignificant).

The max bladder dose in group AG ranges from 27.5-114.7 % (1.65-6.88Gy) and in group CS it ranges from 21.2-111% (1.27-6.66 Gy). P value is 0.044(significant).

The mean bladder dose in group AG ranges from 17.7-69.2% (1.07-4.14 Gy) and in Group CS from 15.54-74.24% (0.93-4.45Gy).P value is 0.130(insignificant).

The max. rectum dose in group AG ranges from 26.2-90.4% (1.99-5.42 Gy) and in group CS it ranges from 25.5-90% (1.53-5.45Gy).P value is 0.054(insignificant).

The mean rectum dose in group AG ranges from 32.5-77.73% (1.95-4.78 Gy) and in Group CS it ranges from 21.07-79.16% (1.26-4.75 Gy). P value is 0.126(insignificant).

So there was no significant difference in dose distribution of doses delivered to point A, bladder and rectal reference point with 60 Gy reference volumes in AG and CS group.

8. Conclusion

Intracavitary brachytherapy in carcinoma cervix can be done under conscious sedation without compromising dosimetric distribution.

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