RESEARCH COMMUNICATION

High Dose Rate Cobalt-60 Afterloading Intracavitary Therapy of Uterine Cervical Carcinomas in Srinagarind Hospital - Analysis of Complications

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Abstract

Objectives: To evaluate complications in uterine cervical cancer patients treated with teletherapy combined with high dose rate(HDR) cobalt-60 brachytherapy. Materials and Methods: A retrospective study of uterine cervical cancer patients, stages IB-IVB (International Federation of Gynecologists and Obstetricians recommendations), treated by radiotherapy alone between April 1986 and December 1988 was conducted. The patients received teletherapy 50Gy / 25 fractions, five fractions per week to the whole pelvis together with HDR Cobalt -60 afterloading brachytherapy of 850 cGy/ fraction weekly to point A for 2 fractions. Results: The study subjects were 141 patients with uterine cervical cancer. The mean age was 49 years with a range of 30-78. The mean tumor size was 4.1 cms in diameter (range 1-8 cms). Mean follow-up time was 2.9 years (range 1 month - 6.9years). The treatments resulted in a 96.5% complete response rates but morbidity rates of grade 1 and grade 2 radiation proctitis of 27.0%, and 10.6 %.The grade 1 and grade 2 radiation cystitis were 1.4%, and 1.4 %. At the level of grade 3 radiation complications, 0.71% of radiation proctitis and 0.71% small bowel obstruction were observed. The mean onset time to develop radiation proctitis after complete treatment was 15 months with a range of 6-61 months, for radiation cystitis was 30 months (range 9 - 47 months) and for small bowel obstruction was 53 months in the one case it occurred. Conclusion: Combined teletherapy along with high dose rate Cobalt -60 brachytherapy of 850 cGy/ fraction, weekly to point A for 2 fractions for uterine cancer demonstrated a slightly higher incidence of grade 2 radiation proctitis. Therefore, treatment using HDR-60 brachytherapy less than 850 cGy per fractionation for decreasing the grade 2 and grade 3 radiation morbidity is recommended.

Keywords: Uterine cervical carcinoma - teletherapy - high dose rate Cobalt - 60 brachytherapy - complications

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Introduction

Carcinoma of the uterine cervix has been recognized to be the major problem in developing countries particularly in Thai women (Vatanasapt et al., 1993; 1995; Sriplung et al., 2003). Most of the patients were found to be in advanced stages burdened with large tumor volumes at their first visit (Tungsubutra et al., 1985; 1985; Tangvoraphongchai et al., 1989; Pesee et al., 1995). The large tumor volumes in addition to the advanced staging of cases resulted in the radioresistant tumors.These were contributing factors limit the effectiveness of radiation therapy. In addition, the time gap between teletherapy and brachytherapy in most patients was reported to be more than 2 weeks and was due to limitation of hospital facilities (Tungsubutra et al., 1985; 1985; Tangvoraphongchai et al., 1989; Pesee et al., 1995). These problems were the factors influencing the selection of high dose rate Cobalt - 60 brachytherapy fractionation. Definitive radiotherapy alone is the standard treatment in uterine cervical cancer (Symonds 2003). There is no consensus on the best technique of brachytherapy (Visser et al., 2001; Symonds, 2003). Concomitant chemotherapy and radiotherapy improves overall and progression-free survival , reduces local and distant recurrence in selected patients(Green et al., 2001). Acute toxicity, particularly leucopenia and gastrointestinal effects, however, were increased in combined therapy of all trials(Symonds, 2003).

The reviews of the optimal fractionation schedule for treating uterine cervical cancer using HDR brachytherapy is still unknown(Petereit et al., 1999). The once weekly HDR brachytherapy combined with properly adjusted external beam pelvic irradiation is a safe and effective treatment (Le Pechoux et al., 1995).The report of combined teletherapy 50Gy/ 25 fractions together with three fractions of 10 Gy brachytherapy to point A demonstrates less than 6 % of severe complications (Mosalaei et al., 2006). In addition, increased morbidity rates with higher doses more than 7 Gy at point A per fraction have been reported (Ortan et al., 1991).

Therefore the retrospective study was conducted to determine whether the complication rates of uterine

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cervical carcinoma treatment using combined teletherapy 50Gy/25 fractions together with high dose rate Cobalt - 60 brachytherapy of 850 cGy/ fraction to point A weekly for 2 fractions, now designated as current combined treatment (CCT) between April 1986 and December 1988.

Materials and Methods

This study was performed at Radiotherapy Division, Department of Radiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand 40002. Inclusion criteria were: (1) uterine cervical cancer FIGO stages IB-IVB treated with radiotherapy alone between April 1986 and December 1988 (2) using HDR Cobalt -60 afterloading brachytherapy of 850 cGy/ fraction to point A for 2 fractions, once weekly fractionation. (3) complete treatment. Exclusion criteria were : (1) uterine cervical carcinoma treated by other fractionation schedules.(2) incomplete treatment.

The staging of the diseases has been classified by the tumor clinic committee of gynecologists and radiation oncologists according to International Federation of Gynecologists and Obstetricians (FIGO) recommendations(International Federation of Gynecologists and Obstetricians, 1995). This project has been approved by the Human Ethics Committee of Khon Kaen University (HE470104).

Grading of complications was defined according to Perez, et al (1984) :- Grade1:Minor symptoms, seft-limited or responding to simple outpatient management. Grade2: Major symptoms, repeated occurrences which often required hospitalization for diagnosis and for nonsurgical management. Grade3:Complications which require major surgery for correction or life threatening.

The complications and the onset time to develop radiation complications after complete treatment were analyzed as percentages.

All patients were treated with Cobalt-60 teletherapy units.The prescribed dose of teletherapy was 5000 cGy / 25 fractions, five fractions per week to the whole pelvis through AP and PA 15x15 cm2 or 16x16 cm 2 port.The ports were extended to 15x 18 cm 2 for the patients with stage IIIA. In addition, the parametrial boosts of 200 cGy for 3-5 days after the completion of brachytherapy were used to treat stage IIIB patients with massive tumors at the parametrium. Brachytherapy was performed by using high dose rate Cobalt -60 brachytherapy (RALSTRON 20-B) about 2-4 weeks after completion of teletherapy with doses of 850 cGy/ fraction to point A for 2 fractions, once weekly. The point A doses were approximately 75.50 Gy for early stages, and approximately 81.50 - 85.50 Gy for advanced stages.

Results

Patient characteristics are summarized in Table 1, the outcome of treatments in Table 2 and the details of complications in Tables 2-4.

Table 1. Patient Characteristics

Characteristics	Total 141 cases
Age groups(range)	Age in years(%)
30-39 years	24/141 (17%)
40-49 years	44/141 (31.2%)
50-59 years	48/141 (34%)
60-69 years	19/141 (13.5%)
70-79 years	6/141 (4.3%)
Mean age in years(range)	49.98 (30-78 y)
Stage of Diseases	Number of cases(%)
Stage IB	4/141 (2.8%)
Stage IIA	6/141 (4.3%)
Stage IIB	36/141 (25.5%)
Stage IIIA	2/141 (1.4%)
Stage IIIB	89/141 (63.1%)
Stage IVA	2/141 (1.4%)
Stage IVB	2/141 (1.4%)
Median tumor size (range) in cms.	4.1(1-8) cms
Gross appearance	Number of cases(%)
Exophytic	99/141 (70.2%)
Ulcerative	21/141 (14.9%)
Infiltrative	14/141 (9.9%)
Others	7/141 (5.0%)
Follow up time	
Mean (range) years	2.94 years (1 mo.-6.92 years)
Pathology	Cases and percentages
Squamous cell carcinomas	131/141 (92.9%)
Adenocarcinomas	9/141 (6.4%)
Adenosquamous cell carcinoma	1/141 (0.7%)

Table 2. The Outcome of Treatment

Outcome	Cases (%)
Complete response	136/141 (96.5%)
Residual diseases at cervix	4/141 (2.8%)
Residual diseases (cervix+parametrium)	1/141 (0.7%)

Table 3. Type and Grade of Radiation Complication

Complication	Cases (%)
Radiation proctitis Grade 1	38/141 (26.95%)
Radiation cystitis Grade 1	2/141 (1.4%)
Radiation proctitis Grade 2	15/141 (10.64%)
Radiation cystitis Grade 2	2/141 (1.4%)
Radiation proctitis Grade 3	1/141 (0.71%)
Small bowel obstruction	1/141 (0.71%)

Table 4. Onset Time to Develop Complications

Onset (months)	Radiation proctitis	Radiation cystitis	Small bowel obstruction	Total cases (%)
0-6	4	0	0	4 (2.8%)
6-12	20	1	0	21 (14.89%)
13-18	14	0	0	14 (9.93%)
19-24	9	0	0	9 (6.38%)
25-30	3	1	0	4 (2.8%)
31-36	1	0	0	1 (0.7%)
37-42	1	1	0	2 (1.4%)
43-48	0	1	0	1 (0.7%)
49-54	1	0	1	2 (1.4%)
61	1	0	0	1 (0.7%)
Total (%)	54 (38.3%)	4 (2.8%)	1 (0.7%)	59 (41.8%)

Discussion

The optimal dose of HDR brachytherapy is suggested to be 29 Gy ±2 Gy at point A, with 4 to 5 fractions of 600 to 700 cGy delivered over 4 to 5 weeks for uterine cervical cancer stage I and II has been reported(Arai et al., 1992). This HDR fractionation has been reported to have the radiation morbidities of grade 3 and 4 as 4.1% of rectosigmoid colon, 1.2% of bladder, and 1.1% of small intestine(Arai et al., 1992). The effective fractionation of using teletherapy 45 Gy to the whole pelvis with four HDR fractions of 6 Gy to point A for stage II and III uterine cervical cancer has been reported to be safe(Ferrigno et al., 2005). The 5-year actuarial incidence of rectal, bladder, and small bowel late complications is 16%, 11%and 14% according to Ferrigno et al (2005). Perez CA, et al reported the grade 2 and grade 3 radiation complications of 10% and 8% and approximately 25% of the patients who experienced these radiation complications demonstrated more than one sequele (Arai et al., 1992). The severe grade 3 complication rates of 5.9 % in cervical cancer treated with three fractions of 10 Gy to point A have been reported (Mosalaei et al., 2006). The reviews of radiation complications demonstrated 2.7% - 10.7% of grade 3 radiation complications(Perez et al., 1984; Boonvisuth et al., 1989).

The current study had 96.5% of a high complete response rates (Table 2) but morbidity rates of grade 1 and grade 2 radiation proctitis of 26.95%, and 10.64 %.The grade 1 and grade 2 radiation cystitis were 1.4%, and 1.4 %. At the level of grade 3 radiation complications, 0.71% of radiation proctitis and 0.71% of small bowel obstruction were observed. In addition, severe anemia initiated by suffering of grade 2 rectal bleedings led to hospitalizations and blood transfusions for the patients.

The mean onset time to develop radiation proctitis after complete treatment was 15 months with a range of 6-61 months. The mean onset time to develop radiation cystitis after complete treatment was30 months over a range of 9 - 47months. The onset time to develop small bowel obstruction was 53 months (Table 4).

Combined teletherapy along with high dose rate Cobalt -60 brachytherapy of 850 cGy/ fraction, weekly to point A for 2 fractions for the uterine cancer demonstrated a slightly higher incidence of grade 2 radiation proctitis. The treatments resulted in a 96.5% complete response rates but morbidity rates of grade 1 and grade 2 radiation proctitis of 26.95%, and 10.64 %.The grade 1 and grade 2 radiation cystitis were 1.4%, and 1.4 %. At the level of grade 3 radiation complications, 0.71% of radiation proctitis and 0.71% of small bowel obstruction were observed. Therefore, the treatment of using HDR-60 brachytherapy less than 850 cGy per fractionation for decreasing the grade 2 and grade 3 radiation morbidity was recommended.

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