นิพนธ์ต้นฉบับ • **Original Article**

ความจำเป็นในการตรวจระดับฮีโมโกลบินทุกสัปดาห์ในผู้ป่วยมะเร็งปากมดลูกที่ได้รับรังสีรักษา

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The Necessity of Weekly Hemoglobin Level Monitoring in Cervical Cancer Patients Receiving Radiotherapy

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หลักการและเหตุผล: ภาวะโลหิตจางในผู้ป่วยมะเร็งปากมดลูกที่ได้รับรังสีรักษามีผลลดทั้งความสามารถในการควบคุมโรคเฉพาะที่และอัตราการรอดตายของผู้ป่วย มีคำแนะนำให้ตรวจระดับฮีโมโกลบิน (hemoglobin: Hb) ก่อนการให้รังสีรักษาและตรวจระดับ Hb ทุกสัปดาห์ในระหว่างการให้รังสีรักษา คณะผู้วิจัยมีความประสงค์ที่จะทราบว่าการตรวจระดับ Hb ในผู้ป่วยมะเร็งปากมดลูกที่ได้รับรังสีรักษาโดยไม่ได้รับยาเคมีบำบัดร่วมด้วยมีความจำเป็นต้องทำทุกสัปดาห์หรือไม่

วัตถุประสงค์: เพื่อประเมินคุณค่าของการตรวจระดับ Hb ทุกสัปดาห์ในผู้ป่วยมะเร็งปากมดลูกที่ได้รับรังสีรักษา

รูปแบบการศึกษา: การศึกษาเชิงพรรณนา

สถานที่ศึกษา: โรงพยาบาลมหาวิทยาลัยเชียงใหม่

วัสดุและวิธีการ: จากเวชระเบียนผู้ป่วยมะเร็งปากมดลูกในหน่วยมะเร็งวิทยานรีเวชที่ได้รังสีรักษาในช่วงพฤษภาคม พ.ศ. 2543 ถึงพฤษภาคม พ.ศ. 2545 ได้รวบรวมลักษณะทางคลินิก ผลการตรวจนับเม็ดเลือด (complete blood count: CBC) ทุกสัปดาห์ เพื่อประเมินระดับ Hb เวลาและจำนวนครั้งในการให้เลือดทดแทน

ผลการศึกษา: มีผู้ป่วยในการศึกษาครั้งนี้ทั้งหมด 113 ราย พบว่า 54 ราย (ร้อยละ 47.8) มีระดับ Hb ก่อนให้รังสีรักษา

Background: Several studies have demonstrated that anemia is one of the poor prognostic factors for cervical cancer patients treated with radiotherapy. We questioned the necessity of weekly hemoglobin level monitoring in these patients. This study was conducted to evaluate the value of weekly hemoglobin level measurement in cervical cancer patients receiving radiotherapy.

Objective: To evaluate the value of weekly hemoglobin (Hb) level measurement in cervical cancer patients receiving radiotherapy.

Design: Descriptive study.

Setting: Chiang Mai University Hospital.

Materials and Methods: The medical records of cervical cancer patients admitted in gynecologic oncology ward between May 2000 and May 2002 were reviewed to evaluate the clinical characteristics and weekly Hb level. Measurement outcomes include grade 2-4 hematologic toxicity, Hb nadir, week of Hb nadir and the number of blood transfusion.

Results: There were 113 cervical cancer patients receiving radiotherapy in the study period. Fifty-four patients (47.8%) had Hb level at presentation < 10 g/dL.

น้อยกว่า 10 g/dL ในผู้ป่วยกลุ่มนี้มีภาวะโลหิตจางระดับ 2-4 ในช่วงสัปดาห์ที่ 1-4 อยู่ 21-30 คนต่อสัปดาห์ หรือเฉลี่ย 23.5 คน (ร้อยละ 43.5) ต่อสัปดาห์ และ 5-22 คน หรือเฉลี่ย 15.3 คน (ร้อยละ 28.3) ต่อสัปดาห์ในสัปดาห์ที่ 5-8 มีผู้ป่วย 59 ราย ที่มีระดับ Hb ก่อนให้รังสีรักษามากกว่าหรือเท่ากับ 10 g/dL ในกลุ่มนี้พบว่ามีภาวะโลหิตจางระดับ 2-4 อยู่ 7-9 คนหรือเฉลี่ย 7.5 คน (ร้อยละ 12.7) ต่อสัปดาห์ในช่วง 4 สัปดาห์แรก และ 3-8 คนหรือเฉลี่ย 5.8 คนต่อสัปดาห์ในช่วงสัปดาห์ที่ 5-8 ผู้ป่วยที่มีระดับ Hb ก่อนให้รังสีรักษามากกว่าหรือเท่ากับ 11 g/dL พบว่ามีภาวะโลหิตจางระดับ 2-4 เพียงร้อยละ 0.8 ในสัปดาห์ที่ 1-4 และร้อยละ 4.9 ในสัปดาห์ที่ 5-8 มีผู้ป่วยที่ได้รับเลือดทดแทนจำนวน 47 คน (ร้อยละ 41.6) ในจำนวนนี้มีผู้ป่วย 42 คน (ร้อยละ 89.4) มีระดับ Hb ก่อนให้รังสีรักษาน้อยกว่า 10 g/dL ส่วนผู้ป่วยที่เหลืออีก 5 คน (ร้อยละ 10.6) มีระดับ Hb ก่อนให้รังสีรักษามากกว่าหรือเท่ากับ 10 g/dL ($p < 0.001$) มีเพียง 1 คนในกลุ่มที่มีระดับ Hb ก่อนให้รังสีรักษามากกว่าหรือเท่ากับ 11 g/dL ที่ได้รับเลือดทดแทน และไม่มีผู้ป่วยรายใดเลยที่มีระดับ Hb ก่อนให้รังสีรักษามากกว่าหรือเท่ากับ 12 g/dL ที่ต้องได้รับเลือดทดแทน

สรุป: ผู้ป่วยมะเร็งปากมดลูกที่มีระดับ Hb ก่อนให้รังสีรักษาน้อยกว่า 10 g/dL ควรได้รับการตรวจระดับ Hb ทุกสัปดาห์ในระหว่างการให้รังสีรักษา สำหรับผู้ป่วยที่มีระดับ Hb ก่อนให้รังสีรักษามากกว่าหรือเท่ากับ 11 g/dL อาจตรวจระดับ Hb ในระยะเวลาที่ห่างขึ้นได้

คำสำคัญ: มะเร็งปากมดลูก, รังสีรักษา, ระดับฮีโมโกลบิน

Among these patients, grade 2-4 anemia was found in 21-30 patients per week with a mean of 23.5 (43.5%) in week 1-4. Between week 5-8, grade 2-4 anemia was found in 5-22 patients per week with a mean of 15.3 (28.3%). Among 59 patients with Hb level at presentation ≥ 10 g/dL, grade 2-4 anemia was found in 7-9 patients per week with a mean of 7.5 (12.7%) in the first 4 week. After week 4, grade 2-4 anemia was found in 3-8 patients per week with a mean of 5.8 (9.8%). Patients with Hb level at presentation ≥ 11 g/dL, grade 2-4 anemia was found in only 0.8% and 4.9% in week 1-4 and week 5-8, respectively. Fourty-seven patients (41.6%) received a blood transfusion. Among these patients, 42 patients (89.4%) had a Hb level at presentation < 10 g/dL, the remaining 5 patients (10.6%) had a Hb level at presentation ≥ 10 g/dL($P < 0.001$). Only one patient with Hb level at presentation ≥ 11 g/dL received a blood transfusion. No blood transfusion was administered in patients with Hb at presentation ≥ 12 g/dL.

Conclusions: For cervical cancer patients with Hb level at presentation < 10 g/dL, weekly Hb level should be checked during radiotherapy. Among those with Hb level at presentation ≥ 11 g/dL, Hb level may be checked less frequently.

Key words: Hemoglobin level, cervical cancer, radiotherapy

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Introduction

Several studies have demonstrated that anemia is one of the poor prognostic factors for cervical cancer patients treated with radiotherapy.[1-8] It is believed that anemia is a tumor-associated indicator of severely aggressive cervical carcinoma. Although the exact mechanism of anemia is not fully understood, recent studies suggest that changes in iron metabolism, suppression of erythroid progenitor cells by tumor released cytokines, impaired erythropoietin response on erythroid progenitor cells, or even hemorrhage are the causes of pretreatment tumor-associated anemia.[9-10] The association between anemia and poor patient outcome is in part due to increased tumor hypoxic fraction with subsequent relative radioresistance resulting from impaired tumor oxygenation.[11-13] However, the hemoglobin level during or after radiotherapy, rather than the hemoglobin level at the time of presentation, reportedly is strongly predictive for the risk of local failure and impaired disease free and overall survival in patients with carcinoma of the cervix.[1-2]

Hemoglobin correction is associated with a lowering of tumor radioresistance and improved survival.[1-2, 14-16] It is recommended that all patients with carcinoma of the cervix who will be treated with radiotherapy have their hemoglobin level measured at presentation and at least weekly during radiotherapy.[2] However, radiotherapy usually causes anemia after fourth week of pelvic radiation.

Although, concurrent chemoradiation is the standard treatment for patients with advanced cervical cancer,[17-21] some patients who are of old age, poor performance, or impaired kidney function receive only radiotherapy. We questioned the necessity of weekly hemoglobin level monitoring in these patients. Accordingly, this study was conducted to evaluate the value of weekly hemoglobin level measurement in cervical cancer patients receiving radiotherapy.

Methods and materials

The medical records of cervical cancer patients admitted in gynecologic oncology ward at Chiang Mai University Hospital between May 2000 and May 2002 were retrospectively reviewed. The criteria for admission of cervical cancer patients in gynecologic oncology ward are age > 60 years, poor performance status, anemia and hemorrhage.

The retrospective survey included patients with the following criteria: histologically proven cervical carcinoma, International Federation of Gynecology and Obstetrics (FIGO) stage IB to IVA, radical radiotherapy without concurrent chemotherapy. The World Health Organization criteria were used for histologic classification. Patients who received total doses of radiation to point A < 35 grays (Gy), previous radical or standard hysterectomy, neoadjuvant or concurrent chemotherapy were excluded from the study.

All patients received radical radiotherapy to the pelvis. Radical pelvic radiotherapy was given with the aim of cure. The pelvis was treated by external beam radiotherapy with a linear accelerator of 4-6 MV within a standard, four-field box. The treatment field was set to extend 3 cm beyond the known extent of disease and to encompass iliac and lower common iliac lymph nodes. Fractions of 2 Gy were delivered 5 days a week over a period of 5-6 weeks for a total dose of 50-56 Gy and external irradiation was withheld if the white blood cell count (WBC) < 3000 /mm^3 or absolute neutrophil count (ANC) < 1500 / mm^3. External beam radiotherapy was followed by intracavitary, high-dose rate brachytherapy in 2-4 insertions after completion of external beam radiotherapy. The dose to point A (a reference location 2 cm superior to the external cervical os and 2 cm lateral to the cervical canal) was 30 Gy, for a cumulative dose of 75 Gy and the cumulative dose to point B (3 cm lateral to point A) was 55 Gy.

A complete blood count was determined by venous puncture before commencing radiotherapy and every 7 days thereafter. It has been departmental policy to transfuse patients with hemoglobin level < 10 g/dL before and during radiotherapy in an attempt to raise hemoglobin level ≥ 10 g/dL and to maintain this value over the entire course of radiotherapy. Patients who were anemic at diagnosis usually received one or two units of packed red blood cell transfusion at the time of treatment planning 2-3 days before radiotherapy was initiated.

Data collected from the patient records that were used to characterize the time course of anemia, hematologic toxicity and blood transfusion practice included presenting hemoglobin level, hemoglobin levels, WBC, platelet count taken during the course of radiotherapy, and the number and timing of blood transfusions received by the patient. Presenting hemoglobin level was defined as the earliest hemoglobin level recorded in relation to disease prior to commencement of radiotherapy. The average weekly nadir hemoglobin level was calculated by averaging the weekly nadir hemoglobin levels for each patient and was used as an estimate of patient hemoglobin during radiotherapy.

In addition, the following patient-, treatment-, and tumor-related data also were collected: patient age, FIGO staging, histologic type, tumor size, total radiation dose, fraction size, and treatment energy, total treatment time, number of intracavitary insertions, dose to point A and dose rate of intracavitary radiation.

The main measurement outcomes were grade 2-4 hematologic toxicity, hemoglobin nadir, week of hemoglobin nadir and the number of blood transfusion during radiotherapy. Grade 2-4 hematologic toxicities in our study mean Hb level of < 10.0 g/dL, WBC of < 3000 / mm^3, ANC < 1500 /mm^3 or platelet count of < 75000 /mm^3. We aimed to keep Hb level of ≥ 10.0 g/dL in all patients throughout treatment.

Statistical calculations were performed using SPSS software version 10.0 for Windows. Clinical characteristics among group, hemoglobin level at presentation < 10 g/dL and ≥ 10 g/dL, were described using mean and frequency for continuous and categorical variables. Chi-square test and Fisher's exact test were used to compare characteristics among groups. Comparison of mean hemoglobin values was done with a t-test for binary variable and the ANOVA test for variables with more than 2 degrees of freedom.

Results

During the study period, there were 113 patients enrolled in this study. The average patient age was 59.3 years (range, 25-83 years). We divided patients in 2 groups; one had hemoglobin level at presentation < 10 g/dL and the other one had hemoglobin level at presentation ≥ 10 g/dL. Patients' characteristics including FIGO staging, histologic type, tumor gross appearance, tumor size, hemorrhagic complication among group, hemoglobin level at presentation < 10 g/dL and ≥ 10 g/dL were shown in Table 1. Patients with hemoglobin level at presentation < 10 g/dL had younger age (56.6 years vs 61.7 years, p = 0.025), more advanced stage (stage III-IV 60.7% vs 39.3%, p = 0.003), larger tumor size (tumor size > 4 cm 68.2% vs 31.8%, p < 0.001) and higher incidence of hemorrhage (81% vs 19%, p < 0.001) than patients with hemoglobin level at presentation > 10 g/dL. The details of the reason for admission of cervical cancer patients in gynecologic oncology ward were shown in Table 2.

Table 1. Clinical characteristics among hemoglobin level at presentation groups

Characteristics	Hb < 10 g/dL (N = 54) (%)	Hb ≥ 10 g/dL (N = 59) (%)	p-value
Age (years)			0.025
Mean + SD	56.6 ± 13.4	61.7 ± 10.1	
Range	25-82	37-83	
FIGO staging			0.003
I	3 (5.6)	5 (8.5)	
II	14 (25.9)	30 (50.8)	
III	32 (59.3)	20 (33.9)	
IV	5 (9.3)	4 (6.8)	
Histologic type			0.555
SCC	48 (88.9)	53 (89.8)	
Others	6 (11.1)	6 (10.2)	
Gross appearance			0.937
Exophytic	25 (46.3)	23 (39.0)	
Endophytic	19 (35.2)	30 (50.8)	
Ulcerative	10 (18.5)	6 (10.2)	
Tumor size			< 0.001
< 4 cm	24 (44.4)	45 (76.3)	
> 4 cm	30 (55.6)	14 (23.7)	
Hemorrhage	47 (87.0)	11 (18.6)	< 0.001

Table 2. The reason for admission of cervical cancer patients in gynecologic oncology ward

Reasons	Frequency (%) (N = 113)
Old age	64 (56.6%)
Hemorrhage	59 (52.2%)
Chronic renal failure	5 (4.4%)
Fever	3 (2.7%)
Pyometra	2 (1.7%)
Vesico-vaginal fistula	1 (0.9%)
Medical disease*	6 (5.3%)

* Medical disease; hypertension, diabetes mellitus, cerebrovascular accident, deep vein thrombosis, chronic obstructive pulmonary disease

Table 3. Association of hemoglobin levels with clinical characteristics

Characteristic	No. of Patients (N = 113)	Hb at presentation (Mean + SD)	p-value	Nadir Hb (Mean + SD)	p-value
Stage			0.027		0.499
I	8	10.7 ± 2.2		9.8 ± 1.3	
II	44	10.6 ± 1.7		9.4 ± 1.5	
III	52	9.5 ± 1.9		8.8 ± 1.1	
IV	9	9.2 ± 2.1		8.9 ± 1.8	
Histologic type			0.306		0.193
SCC	101	10.1 ± 1.9		9.2 ± 1.4	
Others	12	9.8 ± 1.9		8.9 ± 1.6	
Tumor size (cm)			< 0.001		0.001
≤ 4	69	10.6 ± 1.8		9.5 ± 1.3	
> 4	44	9.2 ± 1.8		8.6 ± 1.3	

Table 4. Grade 2-4 anemia during radiotherapy among hemoglobin level at presentation groups

Hb at presentation (g/dL)	Mean patient number of grade 2-4 anemia/ 4 weeks	
	Week 1-4 mean (%)	Week 5-8 mean (%)
Hb < 10 (N = 54)	23.5 (43.5)	15.3 (28.3)
Hb ≥ 10 (N = 59)	7.5 (12.7)	5.8 (9.8)
Hb ≥ 11 (N = 37)	0.3 (0.8)	1.8 (4.9)
Hb ≥ 12 (N = 12)	0 (0)	1.0 (4.8)

Table 5. Hemoglobin nadir and blood transfusion during radiotherapy

Details	Hb at presentation < 10 g/dL (N = 54) (%)	Hb at presentation ≥ 10 g/dL (N = 59) (%)	p-value
Nadir Hb (g/dL)			
Mean	8.1 ± 0.9	10.1 ± 1.1	<0.001
Range	5.3-10.0	7.2-12.2	
Nadir week (mode)	3	5	
Blood transfusion			
No. of patients	42 (77.8)	5 (8.5)	<0.001

Fifty-four patients (47.8%) had a hemoglobin level at presentation < 10 g/dL, 59 patients (52.2%) had a hemoglobin level at presentation ≥ 10 g/dL. Thirty-seven patients (32.7%) and 21 patients (18.5%) had a hemoglobin level at presentation ≥ 11 g/dL and ≥ 12 g/dL, respectively. For all patients, the mean hemoglobin level at presentation was 10.1 g/dL (range, 5.2-14.3 g/dL).

The association of hemoglobin levels with clinical and histopathologic features was shown in Table 3. The mean hemoglobin level at presentation was correlated significantly with FIGO stage (p = 0.027) and tumor size (p < 0.001). Patients with tumor size ≤ 4 cm had mean nadir hemoglobin of 9.5 ± 1.33 g/dL compare with 8.6 ± 1.35 g/dL in patients with tumor size > 4 cm (p = 0.001). No other significant association of nadir hemoglobin with FIGO stage or histologic type was found.

105 from 113 patients (92.9%) had their hemoglobin levels measured during 6 to 8 weeks of radiotherapy (range, 4-8 weekly measures). Patients with hemoglobin level at presentation < 10 g/dL, grade 2-4

anemia was found in 21-30 patients per week with a mean of 23.5 (43.5%) in week 1-4. Between week 5-8, grade 2-4 anemia was found in 5-22 patients per week with a mean of 15.3 (28.3%). Among 59 patients with hemoglobin level at presentation ≥ 10 g/dL, grade 2-4 anemia was found in 7-9 patients per week with a mean of 7.5 (12.7%) in the first 4 week. After week 4, grade 2-4 anemia was found in 3-8 patients per week with a mean of 5.8 (9.8%). Patients with hemoglobin level at presentation ≥ 11 g/dL, grade 2-4 anemia was found in only 0.8% and 4.9% in week 1-4 and week 5-8, respectively (Table 4). Neutropenia grade 2-4 was found in 0-3 patients per week with a mean of 2.4 (2.1%). Thrombocytopenia grade 2-4 was found in 0-1 patients per week with a mean of 0.3 (0.3%).

The mean nadir hemoglobin level was 9.1 g/dL (range, 5.3-12.2 g/dL). The median week of nadir hemoglobin was 4. Nadir hemoglobin and week of nadir hemoglobin among hemoglobin level at presentation groups were shown in Table 5. Nadir hemoglobin was found in week 3, 5, 6 in patients with hemoglobin level at presentation < 10 g/dL, ≥ 10 g/dL, and ≥ 11 g/dL, respectively.

Fourty-seven patients (41.6%) received a blood transfusion. Among these patients, 42 patients (89.4%) had a hemoglobin level at presentation < 10 g/dL, the remaining 5 patients (10.6%) had a hemoglobin level at presentation ≥ 10 g/dL ($p < 0.001$) (Table 5). Only one patient with hemoglobin level at presentation ≥ 11 g/dL received a blood transfusion. No blood transfusion was given in patients with hemoglobin level at presentation ≥ 12 g/dL. Thirty-six patients (76.6%) received a blood transfusion prior to commencement of radiotherapy, and 11 patients (23.4%) received a blood transfusion during radiotherapy. Twelve patients (25.5%) received a single blood transfusion, and 35 patients (74.5%) received more than one blood transfusion. The median number of blood transfusions was 2 (range, 1-7 transfusions). Fourty-two patients (77.8%) of patient with hemoglobin level at presentation < 10 g/dL received a blood transfusion. Twelve patients (22.2%), who had not received a blood transfusion, had a hemoglobin level at presentation in the range of 8.7-9.9 g/dL. The reasons for not administering blood transfusion to these patients were lack of packed red blood cell or whole blood and some patients had hemoglobin level ≥ 10 g/dL in the later period despite not receiving blood transfusion.

Ninety-one percent of patients who were transfused (43/47 patients) received a blood transfusion before or during the first 3 weeks of radiotherapy. Among these patient, 42 patients had hemoglobin level at presentation < 10 g/dL, 1 patient had hemoglobin level at presentation 10.2 g/dL. Four patients (8.5%) received a blood transfusion in week 5-7, all of these patients had hemoglobin level at presentation ≥ 10 g/dL.

Discussion

It has been reported that anemia is associated with both impaired local control and decreased overall survival in large series of patients with cervical carcinoma.[1-2,3,7] In patients who have had definitive radiotherapy without chemotherapy for carcinoma of the cervix, the hemoglobin value during or even after radiotherapy was highly predictive for survival. This was not the case for the hemoglobin at presentation.[1,2] In a Canadian multicenter survey,[2] the 5-year survival rates were 74% for patients with an average weekly nadir hemoglobin (AWNH) ≥ 12 g/dL, 52% for patients with AWNH levels 11.0-11.9 g/dL, and only 45% for patients with an AWNH < 11 g/dL. Similar findings were reported in another study of 386 patients who were treated with radiotherapy for locally advanced cervical carcinoma. Multivariate analysis demonstrated that a hemoglobin level of < 10 g/dL before radiation therapy was not relevant prognostically. In contrast, patients with at least one value below an hemoglobin value of 10 g/dL during therapy had an 80% increased risk of local regional failure compared with patients with all of their hemoglobin values ≥ 10 g/dL.[1]

In our institute, weekly CBC check-up in cervical cancer patients treated by radiotherapy has been performed for many years. Patients with hemoglobin level of < 10 g/dL before and during radiotherapy had to receive a blood transfusion to raise hemoglobin level up to ≥ 10 g/dL and to maintain this value over the entire course of radiotherapy.

In previous studies, the mean hemoglobin level at presentation was correlated significantly with FIGO stage of disease, tumor size and lymph node status.[2,22] However, Obermair and associates[14] reported no significant association of hemoglobin at presentation or nadir hemoglobin with FIGO stage, tumor size, parametrial involvement, histologic grading, or histologic type. In our

study, the mean hemoglobin level at presentation was associated significantly with FIGO stage ($p = 0.027$) and tumor size ($p < 0.001$) but not associated significantly with histologic type. The mean nadir hemoglobin also associated significantly with tumor size ($p = 0.001$), but not associated significantly with FIGO stage and histologic type.

Grade 2-4 anemia was found more frequently in patients with hemoglobin level at presentation of < 10 g/dL than patients with hemoglobin level at presentation of ≥ 10 g/dL (43.5% vs 12.7% in week1-4, 28.3% vs 9.8% in week 5-8). The prevalence of anemia that decreased during week 5-8, when compare with that of week 1-4, reflected our policy in keeping Hb > 10 g/dL. Patients with hemoglobin level at presentation ≥ 11 g/dL, grade 2-4 anemia was found in only 0.8% in week 1-4 and 4.9% in week 5-8.

Patients with hemoglobin level at presentation < 10 g/dL, nadir hemoglobin was found mostly in week 3, compare with week 5 in patients with hemoglobin level at presentation ≥ 10 g/dL, and was found late to week 6 if hemoglobin level at presentation was ≥ 11 g/dL.

Grogan and associates[2] reported on 630 patients who received radical radiotherapy. One hundred fifty-two patients (25%) received a blood transfusion, 58% received a single blood transfusion, 42% received more than one blood transfusion. Seventy-four percent of patients who were transfused received a blood transfusion before and during the first 3 weeks of radiotherapy. In our study, 41.6 % of patients received a blood transfusion. Eighty-nine percent of patients who were transfused had hemoglobin level at presentation < 10 g/dL. Only one patient with hemoglobin level at presentation ≥ 11 g/dL received a blood transfusion and no one with hemoglobin level at presentation ≥ 12 g/dL received a blood transfusion. Because of the criteria for admission of patients in our gynecologic oncology ward are old age, poor performance, anemia and hemorrhage, so most of the patients in our study were more likely to receive a blood transfusion prior to commencement of radiotherapy.

We recommend that patients with hemoglobin level at presentation of < 10 g/dL should continue weekly hemoglobin level monitoring. For patients with hemoglobin level at presentation of ≥ 11 g/dL, hemoglobin level measurement may be performed late to a few weeks after commencement of radiotherapy and the frequency of hemoglobin level monitoring should be individualized.

In conclusion, for cervical cancer patients with hemoglobin level at presentation of < 10 g/dL, weekly hemoglobin level should be checked during radiotherapy. Among those with hemoglobin level at presentation ≥ 11 g/dL, hemoglobin level may be checked less frequently.

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References

1. Girinski T, Pejovic-Lenfant MH, Bourhis J, Campana F, Cosset JM, Petit C, et al. Prognostic value of hemoglobin concentrations and blood transfusions in advanced carcinoma of the cervix treated by radiation therapy: results of a retrospective study of 386 patients. Int J Radiat Oncol Biol Phys1989; 16: 37-42.
2. Grogan M, Thomas GM, Melamed I, Wong FLW, Pearcey RG, Joseph PK, et al. The importance of hemoglobin levels during radiotherapy for carcinoma of the cervix. Cancer 1999; 86: 1528-36.
3. Hong JH, Chen MS, Lin FJ, Tang SG. Prognostic assessment of tumor regression after external irradiation for cervical cancer. Int J Radiat Oncol Biol Phys 1992; 22: 913-17.
4. Lowrey GC, Mendenhall WM, Million RR. Stage IB or IIA-B carcinoma of the intact uterine cervix treated with irradiation: a multivariate analysis. Int J Radiat Oncol Biol Phys 1992; 24: 205-10.
5. Fyles AW, Pintilie M, Kirkbride P, Levin W, Manchul LA, Rawlings GA. Prognostic factors in patients with cervix cancer treated by radiation therapy: results of multiple regression analysis. Radiother Oncol 1995; 35: 107-17.
6. Pedersen D, Sogaard H, Overgaard J, Bentzen SM. Prognostic value of pretreatment factors in patients with locally advanced carcinoma of the uterine cervix treated by radiotherapy alone. Acta Oncol 1995; 34: 787-95.

7. Werner-Wasik M, Schmid C, Bornstein L, Ball HG, Smith DM, Madoc-Jones H. Prognostic factors for local and distant recurrence in stage I and II cervical carcinoma. Int J Radiat Oncol Biol Phys 1995; 5: 1309-17.
8. Kagei K, Shirato H, Nishioka T. High-dose-rate intracavitary irradiation using linear source arrangement for stage II and III squamous cell carcinoma of the uterine cervix. Radiother Oncol 1998; 47: 207-13.
9. Mercadante S, Gebbia V, Marazzo A, Filosto S. Anaemia in cancer: pathophysiology and treatment. Cancer Treat Rev 2000; 26: 303-11.
10. Spivak JL. Cancer-related anemia: its causes and characteristics. Semin Oncol 1994; 21: 3-8.
11. Bush RS. The significance of anemia in clinical radiation therapy. Int J Radiat Oncol Biol Phys 1986; 12: 2047-50.
12. Rubin P, Casarett GW. In: Clinical radiation pathology. Philadelphia: Saunders, 1968: 103.
13. Hirst DG. Anemia: a problem or an opportunity in radiotherapy?. Int J Radiat Oncol Biol Phys 1986; 12: 2009-17.
14. Obermair A, Cheuk R, Horwood K, Janda M, Bachtiary B, Schwanzelberger B, et al. Impact of hemoglobin levels before and during concurrent chemoradiotherapy on the response of treatment in patients with cervical carcinoma: preliminary results. Cancer 2001; 92: 903-8.
15. Lavey RS, McBride WH. Influence on hematocrit on tumor oxygenation and sensitivity to radiation. Eur J Cancer 1993; 29: 216.
16. Thews O, Koenig R, Kelleher DK, Kutzner J, Vaupel P. Enhanced radiosensitivity in experimental tumours following erythropoietin treatment of chemotherapy-induced anaemia. Br J Cancer 1998; 78: 752-6.
17. Peters WA, Liu PY, Barrett RJ II, Stock RJ, Monk BJ, Berek JS, et al. Concurrent chemotherapy and pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. J Clin Oncol 2000; 18: 1606-13.
18. Keys HM, Bundy BN, Stehman FB, Muderspach LI, Chafe WE, Suggs CL III, et al. Cisplatin, radiation, and adjunct hysterectomy compared with radiation and adjuvant hysterectomy for bulky Stage IB cervical carcinoma. N Engl J Med 1999; 340: 1154-61.
19. Morris M, Eifel PJ, Lu J, Grigsby PW, Levenback C, Stevens RE, et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. N Engl J Med 1999; 340: 1137-43.
20. Whitney CW, Sause W, Bundy BN, Malfetano JH, Hannigan EV, Fowler WC Jr., et al. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in Stage IIB-IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group study. J Clin Oncol 1999; 17: 1339-48.
21. Rose PG, Bundy BN, Watkins EB, Thigpen JT, Deppe G, Maiman MA, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. N Engl J Med 1999; 340: 1144-53.
22. Kapp KS, Poschauko J, Geyer E, Berghold A, Oechs AC, Petru E, et al. Evaluation of the effect of routine packed red blood cell transfusion in anemic cervix cancer patients treated with radical radiotherapy. Int J Radiat Oncol Biol Phys 2002; 54: 58-66.