

# Protective efficacy of vitamin B<sub>12</sub> combined with far-infrared radiation on radiation-induced skin damage in the treatment of pelvic tumours

Qin Ge MD, Cen-ming Yu MD, Jing Cai MD, Chun-xia Chu MD, Guo-dong Xie MD, Ji-Zhong Zhao MD

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**OBJECTIVE:** To determine the protective efficacy of vitamin B<sub>12</sub> combined with far-infrared radiation on radiation-induced skin damage in the treatment of acute and chronic pelvic tumours.

**METHODS:** One hundred patients requiring radiation therapy were randomly assigned to one of two groups: 50 patients were assigned to the control group and received usual care; the 50 patients assigned to the experimental group were, in addition to usual care, given vitamin B<sub>12</sub> (0.25 mg/mL) injections to radiation-sensitive perineal skin and subsequently treated with far-infrared radiation beginning the first day of radiotherapy. Far-infrared radiation treatment was performed at a light distance of 40 cm at a temperature of 28°C to 32°C for 25 min twice per day.

**RESULTS:** The incidence of acute skin reactions in the two groups was statistically different ( $P < 0.05$ ). The incidences of grades I, II, III and IV radiation-induced skin damage in the experimental group were 60.0%, 30.0%, 10.0% and 0%, respectively; in contrast, the incidences in the control group were 26.0%, 54.0%, 18.0% and 2.0%, respectively. Grades II to IV skin reactions in the experimental group were remarkably less severe than those of the control group. When a radiation treatment dose of  $< 40$  Gy was used, the incidences of acute radiation-induced dermatitis in the control and experimental groups were 66% and 34%, respectively ( $P < 0.05$ ).

**CONCLUSION:** Vitamin B<sub>12</sub> combined with far-infrared radiation had a markedly protective effect on acute radiation-induced skin damage in the treatment of pelvic cancers. Moreover, the treatment improved patient quality of life and was clinically valuable.

**Key Words:** *Far-infrared; Radiation dermatitis; Pelvic tumours; Radiation therapy; Vitamin B<sub>12</sub>*

Radiation therapy is an important tool in the treatment of pelvic malignancies such as advanced colorectal, anal, cervical and prostate cancers, and other metastatic diseases involving the pelvic region. Radiation-induced dermatitis is one of the most common complications of radiation therapy. It can severely affect patient quality of life and, due to the unique physiological nature and anatomical location of perineal skin, which is thin, wrinkled, difficult to expose and poorly ventilated, the efficacy of clinical treatments is generally poor. Given the poor local blood supply and lymphatic drainage in the pelvic region, patients spontaneously develop skin injury postirradiation. To prevent or mitigate radiation-induced skin reactions, skin protectants are needed. In the present study, we aimed to determine whether vitamin B<sub>12</sub> combined with far-infrared radiation could prevent or lessen the severity of radiation-induced dermatitis during the course of radiation therapy.

## METHODS

### Clinical data

The present study enrolled 100 patients with pelvic tumours who were seen at the authors' institution between July 2013 and February 2014. Thirty-six cases of colorectal cancer, four cases of anal cancer, 45 cases of cervical cancer and 15 cases of prostate cancer were pathologically diagnosed. The study sample consisted of 77 men and 23 women, with a median age of 56 years (range 38 to 70 years). Inclusion criteria included a Karnofsky Performance Status score  $\geq 70$ , with no serious heart, lung, liver or kidney dysfunction, and no contraindications to radiotherapy. Patients were randomly assigned into two groups: the control group, which received standard treatment; and the experimental group, which received vitamin B<sub>12</sub> injection and far-infrared radiation to the perineal skin in addition to standard treatment.

### Treatment

All patients were initially treated with radiation. To determine the precise location and extent of the tumour, patients were positioned prone on a table with their head stabilized, and underwent 16-slice spiral computed tomography (CT) scan using a slice thickness of 5 mm. Data were transferred to the Pinnacle3 8.0 program design system; an experienced radiologist and two physicians calculated gross tumour volume (GTV) based on the CT images of tumour and lymph node metastasis. The GTV was used to determine clinical target volume (CTV), which included lymphatic drainage area. Planning target volume was then calculated based on GTV and CTV; approximately 0.5 cm to 1.0 cm was added to the margins to account for setup errors, visceral activity and other factors, and to avoid organs at risk, including the bladder, the lower small intestine and the femoral head. Patients were treated using three-dimensional conformal radiation or intensity modulated radiation therapy, using 6 MV x-rays and a noncoplanar five-field arrangement. The doses corresponding to 95% of planning target volume were 50 Gy to 76 Gy per 25 to 38 fractions (1.8 Gy/fraction to 2 Gy/fraction; five fractions per week).

A total of 50 patients in the control group received conventional care. Detailed explanations regarding the efficacy of radiation and its importance were provided to patients before radiotherapy. Patients were advised to wear soft, loose-fitting, absorbent clothing to avoid friction; use a warm, soft cloth to wash, and avoid scrubbing the skin with hot water and bath soap; and avoid the use of iodized oil, alcohol and other disinfectants, and irritating ointments. Antibacterial agents were applied to the skin after it had been cleaned.

The patients in the experimental group were treated with vitamin B<sub>12</sub> injections (0.25 mg/mL) and subsequently underwent far-infrared

Department of Radiation Oncology, Nantong Tumor Hospital, Nantong, People's Republic of China

Correspondence: Dr Chun-xia Chu, Jiangsu Nantong, Nantong Tumor Hospital, Nantong 226361, People's Republic of China.

Telephone 13813606819, e-mail ccx519466@sina.com



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**TABLE 1**  
Clinical characteristics of patients in the experimental and control groups

Characteristic	Group		P	$\chi^2$
	Experimental	Control		
Sex				
Male	39	38	0.055	0.814
Female	11	12		
Age, years				
≤60	34	33	0.044	0.834
>60	16	17		
Tumour Node Metastasis staging				
II	38	39	0.055	0.814
III	12	11		
Lymph node metastasis				
No	29	31	0.018	0.894
Yes	21	19		
Degree of differentiation				
High	24	23	0.039	0.843
Low	26	27		

Data presented as n unless otherwise indicated

**TABLE 2**  
Incidence of acute skin injury postradiation

Group	Grade of skin damage*				
	0	I	II	III	IV
Experimental group (n=50)	0 (0)	30 (60.0)	15 (30.0)	5 (10.0)	0 (0)
Control group (n=50)	0 (0)	13 (26.0)	27 (54.0)	9 (18.0)	1 (2.0)

Data presented as n (%). \*0 – no skin change; grade I – follicular dark erythema or hair loss, dry desquamation and decreased sweating; grade II – tenderness or new-onset erythema, flaky moist desquamation, moderate edema; grade III – outside skin folds fusion, moist desquamation, pitting edema; and grade IV – ulcers, bleeding and necrosis.  $\chi^2=9.57$ ,  $P<0.05$

light therapy (TCM Medical Instrument Co, Ltd, Chongqing God horse brand, China) to easily damaged skin in the radiation field. Far-infrared radiation treatment was performed at a light distance of 40 cm at a temperature of 28°C to 32°C for 25 min twice per day.

### Efficacy

The skin in the radiation field was evaluated daily throughout the entire course of radiotherapy in both groups.

### Evaluation criteria

Using the CTC 3.0 standard (1), radiation-induced skin damage was classified according the following grades: 0 – no skin change; grade I – follicular, dark erythema or hair loss, dry desquamation and decreased sweating; grade II – tenderness or new-onset erythema, flaky moist desquamation, moderate edema; grade III – outside skin fold fusion, moist desquamation, pitting edema; and grade IV – ulcers, bleeding and necrosis.

### Statistical analysis

Data were analyzed using SPSS version 16.0 (IBM Corporation, USA).  $\chi^2$  test analysis was used to compare differences between the groups; a two-sided  $P<0.05$  was considered to be statistically significant in all analyses.

## RESULTS

### Clinical data

The clinical characteristics of the two groups showed no significant differences ( $P>0.05$ ) (Table 1).

**TABLE 3**  
Comparison of wound healing times

Group	Healing time, days	Healed wounds, %
Experimental (n=50)	8.1±2.5	77.3±2.88
Control (n=50)	11.9±4.4	57.3±2.31
P	<0.05	<0.05

Data presented as mean ± SD unless otherwise indicated

### Incidence of acute radiation-induced skin damage

The incidence of acute radiation-induced skin damage was 100% in both groups. However, its severity in the experimental group was significantly lower than that of the control group. In particular, the incidence of grade II acute skin damage was significantly less severe compared with the control group ( $P<0.05$ ), as shown in Table 2. In the control group, one patient exhibited grade IV skin damage, which interrupted radiation therapy; however, he showed significant improvement 15 days after antibacterial cleaning, drugs and other treatment.

### Wound healing

The mean healing time in the control group was significantly longer than that in the experimental group (Table 3).

### Radiation dose

The number of patients who developed skin damage in the control group and the experimental group was 66% (33 of 50) and 34% (17 of 50), respectively, when the radiation dose was <40 Gy ( $\chi^2=11.18$ ;  $P=0.001$ ).

## DISCUSSION

Acute radiation-induced skin damage, also known as acute radiation dermatitis, is a common complication of radiotherapy. The incidence and severity of acute radiation dermatitis is related to radiation wavelength, the irradiated volume and interpatient differences, among many other factors. Its pathogenesis is believed to result from dysregulation of DNA synthesis and differentiation, leading to a series of skin reactions and, ultimately, damage. As reported, several drugs, including antibiotics and hormones, have been used for the treatment of acute radiation-induced skin damage. Unfortunately, the results have been disappointing. The incidence of acute skin damage following exposure to radiation has been reported to be as high as 90% (2). In recent years, many attempts have been made to alleviate the severity of damage. Suping et al (3) treated 24 patients who experienced skin damage following irradiation using a topical agent (MEBO, Sekanjalo Healthcare, South Africa), while Zhimei (4) treated 38 patients with special dressings. Li et al (5) and Wu et al (6) used JUC, and antimicrobial spray and dressing, and peptide to prevent acute radiation dermatitis in 29 and 120 cases, respectively. Therefore, effective methods of ameliorating radiation-induced skin damage have practical significance for clinical care.

Vitamin B<sub>12</sub> is produced by the liver and is involved in several biochemical metabolic reactions. It promotes the repair of damaged skin mucous membranes and vascular endothelial cells, reduces spasm and occlusion of blood vessels, improves local blood flow and prevents the deterioration of wound infection. In addition, it reduces the excitability of pain fibres C and AG, leading to an analgesic effect (7,8). Vitamin B<sub>12</sub> injections to the skin in the radiation field benefit the wound by reducing irritation and pain, preventing rupture and enhancing new epithelial resistance to radiation, thereby promoting healing of the skin (9). Chen et al (10) used a vitamin B<sub>12</sub> solution treat radiation-induced moist dermatitis. The cure rate at 10 days was 100%, which was significantly different from the control group (48%).

Light at the far-infrared end of the visible spectrum has wavelengths of 0.76 µm to 1000 µm. Its use in the medical field began abroad in the 1920s, and did not appear in China until the 1950s. Far-infrared radiation is useful for the dilation of blood vessels and restoring blood flow, and for repair and adjustment of other biological systems that cause imbalances in the body. It plays an important role in

promoting tissue repair and wound healing through anti-inflammatory effects. Far-infrared radiation has been shown to promote cellular DNA synthesis, enhance cellular metabolism and maintain cell membrane function in animal experiments (11). Far-infrared radiation has been used widely in burn care for many years except radiation-induced skin damage (12-16). Although radiation-induced skin damage is unique, its physiological characteristics are similar to burn injury.

Currently, effective measures to prevent or delay the occurrence of radiation dermatitis and reduce the extent of injury are lacking. The prevention of wound infection depends on the development of new technologies and methods of care. Both vitamin B<sub>12</sub> and far-infrared have biological effects of repair in damaged skin and mucous membrane cells, but using them in combination has an additive effect, thus providing enhanced protection from the effects of radiation. The results of the present study showed that grade II, III or IV radiation-induced skin damage was significantly more serious, with a longer average healing time, in the control group compared with the experimental group, suggesting that the combination of vitamin B<sub>12</sub> injections supplemented with far-infrared radiation mitigates the severity of skin injury postradiation. It has been shown that erythema develops when skin is irradiated with as little as 5 Gy, and epithelial exfoliation and ulceration (wet reaction) occur with doses of approximately 20 Gy to 40 Gy, often resulting in serious prolonged healing of ulcers (17). To date, there have been no effective measures or drugs to treat skin damage

induced by radiation. When mild skin reactions occur, patients are encouraged to adhere to radiotherapy. When severe reactions occur, patients are given anti-inflammatory treatment, debridement, dressings and other symptomatic treatment, with skin wound healing time of up to two to four weeks, which can seriously affect quality of life. Moreover, because of interruption to radiation therapy, tumour control time is reduced, further decreasing the survival rate of patients (18). We showed that higher doses of radiation increased the frequency and severity of acute radiation-induced skin damage. When the radiation dose was >40 Gy, more patients in the experimental group developed skin damage. In contrast, at doses <40 Gy, radiation-induced skin damage was more prevalent in the control group. The difference was statistically significant, indicating that the combination of vitamin B<sub>12</sub> injections and far-infrared radiation therapy prolonged the length of acute radiation-induced skin injury.

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