

EXPERIMENTAL STUDY

Role and mechanism of radiological protection cream in treating radiation dermatitis in rats

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Abstract

OBJECTIVE: To explore the role and mechanism of a radiation protection cream (Rp) in the treatment of radiation dermatitis, and to accumulate necessary technical information for a new drug report on Rp.

METHODS: High-performance liquid chromatography was used to establish the method of measuring the main effective ingredients of sovereign and

adjuvant herbs of Rp drugs, and to formulate the draft quality standards of Rp. A total of 48 Sprague-Dawley male rats were randomly divided into the Model, Trolamine cream (Tc), Rp and Blank groups according to a random number table method. The skin of each rat's buttocks was irradiated using an electron linear accelerator to establish an acute radiation dermatitis model. The histological changes were observed under light microscopy and electron microscopy during wound healing and the effect of Rp on rat fibroblast Ku70/80 gene expression was detected at the transcriptional level.

RESULTS: Pathological examination revealed that Rp protected the cellular and subcellular structures of skin after irradiation, promoting the proliferation and restoration of collagen fibers. Ku70/80 mRNA expression levels in the Rp and Tc groups were higher than that in the model group ($P < 0.05$). Moreover, The majority of grade radiation dermatitis relative to the Model, Rp and Tc groups for reducing grade III and IV dermatitis efficiency were 85.7% and 69.2% ($P < 0.05$), respectively. The efficacy of Rp group in treating radiation dermatitis was better than the Trolamine cream group by 16.5% ($P < 0.05$).

CONCLUSION: Compared with Tc, Rp had certain advantages in the efficacy and performance to price ratio. Thus, Rp is considered an effective alternative formulation for the prevention and treatment of radiation dermatitis.

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Key words: Radiological health; Skin cream; Radiation dermatitis; Pharmacology

INTRODUCTION

Radiation dermatitis is the most common complication of radiation oncology treatment. Radiation-induced skin reactions of erythema occur in approximately 87% of patients receiving radiotherapy, in which the incidence of moist desquamation is 10%-15%.¹ Moist desquamation also occurs at the end of radiotherapy in about 10% of breast cancer patients.² The prevention and treatment of radiation dermatitis has been a concern of radiotherapy professionals. Effective protection is a key tool in the treatment of radiation dermatitis. Trolamine cream is a commonly imported drug with good clinical efficacy, but is quite expensive. In clinical applications, Trolamine cream (Tc) does not exhibit significant therapeutic effects in patients with grade II lesions or skin blister-ulceration, skin touch pain, edema, and epithelial flaky moist exfoliation that constantly expand.

The main causes of radiation skin damage are X-, β -, and γ -rays. X- and γ -rays can penetrate through the skin to the subcutaneous tissue. They can even damage bones and sometimes generate long-term ulcers. β -rays (E-Line) cause local damage and external irradiation commonly leads to skin damage.³ The criteria of the radiation therapy oncology group (RTOG) are still being used to evaluate toxicity.⁴ These criteria are still considered the standard bases for evaluation of radiation-induced skin reactions. However, further research is needed to inform clinical practice. Simonen *et al*⁵ spectrophotometrically measured damage due to low doses of radiation because it is difficult to detect small changes with the naked eye. Nuutinen *et al*⁶ evaluated the degree of radiation injury by measuring the capacitance rate. Extensive necrosis and damage of the dermal layer connective tissue and collagen fibers can be observed under a light microscope.⁷ Under an electron microscope, mitochondria and various organelles show vacuolar degeneration, nuclei apoptosis, nuclear condensation and changes in collagen fibers. Radiation causes acute radiation-induced ulcer formation, and decreases the expression levels of several growth factors and their receptors, leading to the formation of granulation tissue, which affects the entire process of wound healing.^{8,9} Radiation mainly kills tumor cells by causing DNA double-strand breaks. Studies found that Ku70/80 mRNA is involved in the regulation of DNA replication and that Ku deletion results in lower DNA replication in mammals.¹⁰ A previous study observed that irradiation significantly increased Ku70/Ku80 mRNA and protein expression levels in normal fibroblasts, in which Ku70/80 proteins are soluble protein fragments.¹¹ Ku can suppress the generation of apoptosis.¹² DNA fragments promote Ku and DNA connection and damage repair, thereby inhibiting apoptosis. In recent years, Ku has attracted attention in tumor prognosis and diagnosis.¹³⁻¹⁵ Previous studies demonstrated that the transcript level of Ku70/80 increased with the

DNA damage activity.¹⁶⁻²² In the present study, we investigated the effect of Rp on Ku70/80 gene expression at the RNA level using real-time polymerase chain reaction (PCR) method and found that Rp can up-regulate Ku70/80 gene expression and promote the repair of cell DNA damage caused by radiation.

To date, numerous topical medicines are clinically used for the treatment of radiation dermatitis. These medicines include unilateral or compound Traditional Chinese Medicine (TCM), corticosteroids, vitamins, minerals, antibiotics and disinfectants. Radiation is a fiery toxin, causing muscle desquamation, hot itch, ulcers, blood heat-induced erythema, blood stasis-induced pigmentation, and burning-induced blood stagnation and meridian obstruction. Danggui (*Radix Angelicae Sinensis*), Baixianpi (*Cortex Dictamni Radicis*) and Zicao (*Radix lithospermi*) are used as sovereign herbs; Kushen (*Radix Sophorae Flavescentis*), Baizhi (*Radix Angelicae Formosanae*) and Gancao (*Radix Glycyrrhizae*) are used as adjuvant herbs; and Xuejie (*Sanguis Draconis*) blood and Bingpian (*Borneolum Syntheticum*) are used as assistant herbs. They are combined with a broad-spectrum antibiotic chloramphenicol powder from Western Medicine. Baixianpi (*Cortex Dictamni Radicis*) has a wide range of antibacterial and antifungal functions and can eliminate dampness. Zicao (*Radix lithospermi*) can cool blood and detoxify the blood, in which the lethal scattered blood heat has a unique effect on ionization burns. Danggui (*Radix Angelicae Sinensis*), Gancao (*Radix Glycyrrhizae*) and Baizhi (*Radix Angelicae Formosanae*) can nourish the blood, cause myogenic sores and detoxify fluid. Bingpian (*Borneolum Syntheticum*) can reduce fever, decrease swelling and prevent corrosion. It is also myogenic, eliminating itching and burning discomfort sensations. The broad-spectrum antibiotic chloramphenicol powder can enhance the antibacterial effect of prescription herbs. An effective and cost-effective method for preventing and treating dermatitis based on radiation dermatitis-grading criteria, individual differences in circumstances and a patient's economic status should be developed. In the present study, we used traditional herbal medicines that have been tested and their efficacies have been confirmed through clinical applications and animal experiments.

MATERIALS AND METHODS

Drug prescriptions

Danggui (*Radix Angelicae Sinensis*) 30 g, Baixianpi (*Cortex Dictamni Radicis*) 30 g, Gancao (*Radix Glycyrrhizae*) 15 g, Kushen (*Radix Sophorae Flavescentis*) 15 g, Baizhi (*Radix Angelicae Formosanae*) 15 g, Zicao (*Radix lithospermi*) 3 g, Xuejie (*Sanguis Draconis*) 3 g, and Bingpian (*Borneolum Syntheticum*) 3 g were used. Chloramphenicol powder (5 g) was added to strengthen the antibacterial effect of the herbs.

Drug preparation process

Radiological protection cream (Rp) group: sesame oil

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