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RESEARCH REPORT

Role of triamcinolone in radiation enteritis management

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Abstract

AIM: To investigate the role of triamcinolone in the management of acute and chronic enteritis caused by pelvic radiotherapy.

METHODS: Twenty-eight patients with rectum adenocarcinoma or endometrium adenocarcinoma were studied. We compared the results of 14 patients treated with injected triamcinolone acetonide (TA) with those of 14 patients who were not treated with TA. For the TA group, 40 mg of TA was injected intramuscularly on the 1st, 11th and 21st d of radiotherapy; the control group received no injections. All of the study participants had a median age of 65 years, had undergone postoperative radiotherapy and were evaluated weekly using Radiation Therapy Oncology Group and the European Organization for Research and Treatment of Cancer Acute Morbidity Score Criteria, and complete blood counts for every 10 d.

RESULTS: Triamcinolone was found to effectively prevent and treat radiation-induced acute gastrointestinal (enteritis) and genitourinary (cystitis) side effects (P = 0.022 and P = 0.023). For the lower GI side effect follow up, 11 patients in the control group had Grade 2 toxicity and 3 patients had Grade 1 toxicity. In the TA group, 5 patients had Grade 2 toxicity and 9 patients had Grade 1 toxicity. For the genitourinary system side effect follow up, 4 patients had Grade 2 toxicity and 6 patients had Grade 1 toxicity. Additionally, 2 patients had Grade 2 toxicity and 2 patients had Grade 1 toxicity. The neutrophil counts did not differ between the TA group and the control group. There was no meaningful difference between age groups and primary cancers. At the 12th mo of follow up, there were no differences between groups for chronic side effects.

CONCLUSION: Triamcinolone is a moderately potent steroid, that is inexpensive and has a good safety profile. It would be beneficial for reducing medical expenses related to treatment of radiation induced enteritis.

Key words: Radiotherapy; Enteritis; Cystitis; Triamcinolone

Core tip: Radiation enteritis, proctitis and cystitis are acute side effects of radiotherapy of the pelvic region that change patients' performance status and can interrupt the radiotherapy program. An important effort should be made to treat the side effects and to provide patient follow-up. Many drugs are available to treat the side effects, and although supportive digestive supplements may be used, the medical expenses associated with tratment are increasing, and the patients are suffering. In this study, we evaluated the role of triamcinolone acetonide, which is moderately effective, low-priced and easy to use, in the management of acute gastrointestinal and genitourinary system side effects.

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INTRODUCTION

Radiotherapy of the pelvic region is commonly used for a significant percentage of patients with rectosigmoid and genitourinary system tumors to target the lymphatic region and the primary tumor bed. Radiation enteritis, proctitis and cystitis are acute side effects that change patients' performance status and may interrupt the radiotherapy program. Intestinal mucosa with a high mitotic rate, is affected by radiotherapy, and tenesmus, diarrhea and hematochezia may be seen. To treat these side effects, antispasmotics, antidiarrhetics, analgesics, antiinflammatory drugs and intravenous serum replacement are often used in certain cases. Chemotherapy, older age, pelvic inflammatory disease, peritoneal adhesion after operation, diabetes mellitus, hypertension and collagen vascular diseases are also risk factors for radiation induced side effects. The total radiation dose, dose of fractions and scheme of radiotherapy affect the situation directly. Many studies have examined reducing the rate of radiation enteritis by treatment positioning or by providing palliative medical treatments. Doctors make as an important efforts to treat the side effects and provide patient follow-up; however, the associated medical expenses are increasing, and patients are suffering as a result. Although the use of steroids for radiation-induced proctitis is reported in the literature, in this study, we evaluated the role of triamcinolone asetonide (TA), which is moderately effective and easy to use, for the management of acute gastrointestinal system (GIS) and genitourinary system (GUS) side effects of pelvic radiotherapy.

MATERIALS AND METHODS

Patients

Patients with diabetes mellitus, pelvic inflammatory disease, hypertension, collagen vascular disease, and fungal-viral infections were excluded. From December 2008 to December 2010, 28 patients had pelvic conformal radiotherapy with conventional fraction sizes of 4 fields for a total of 50.0 to 50.4 Gy that was planned postoperatively. The upper limit of the treatment field was the L5-S1 intervertebral space, and the lower limit of V40 of the intestines within the treatment volume was 90%. Six of the patients had endometrial cancer, and 22 had rectal cancer. The median age of all the patients was 65. Chemotherapy was applied for the rectal cancer patients concomitantly as 5-fluorouracil (425 mg/m^2 twice every 3 wk) and folinic acid (25 mg/m^2). The patients were divided into two equal groups. The patients' characteristics are summarized in Table 1.

For the TA group patients, 40 mg of TA was injected intramuscularly on the 1st, 11th and 21st d of radiotherapy; the patients in the control group received no injections. For both groups, medical support was also planned if needed. Evaluations were performed weekly during radiotherapy using the Radiation Therapy Oncology Group and the European Organization for Research and Treatment of Cancer (RTOG/EORTC) Acute Radiation Morbidity Scoring Criteria, and complete blood counts were performed every 10 d (http://www.rtog.org/ResearchAssociates/AdverseEventReporting/AcuteRadiationMorbidityScoringCriteria.aspx).

Statistical analysis

Statistical assessment was conducted using SPSS V13 program. Normality was tested using Shapiro-Wilk W test ($P < 0.05$) and Pearson's χ^2 test was used to test for meaning ($P < 0.05$).

RESULTS

For the lower GI side effect follow-up, 11 patients in the control group had Grade 2 toxicity and 3 patients had Grade 1 toxicity. In the TA group, 5 patients had Grade 2 toxicity and 9 patients had Grade 1 toxicity. For the GUS side effect follow-up, 4 patients in the control group had Grade 2 toxicity and 6 patients had Grade 1 toxicity. In the TA group, 2 patients had Grade 2 toxicity and 2 patients had Grade 1 toxicity. For GIS and GUS, Grade 2 toxicities occured on the 21st (median) day and Grade 1 toxicities occured on the 14th (median) day. The neutrophil numbers decreased with Grade 1 toxicity in 3 patients from each group on the 21st day. The patient score frequencies are summarized in Table 2.

The statistical analysis showed that TA was effective for preventing and treating acute radiation-induced GIS side effects from pelvic radiotherapy when Grade 1 and Grade 2 toxicities were compared ($P = 0.022$). TA was also effective for preventing and treating acute radiation-induced GUS side effects from pelvic radiotherapy when Grade 0 and Grade 1-2 toxicities were compared ($P = 0.023$). The neutrophil counts did not differ between the groups. There was no meaningful difference between age groups and primary cancers. At the 12 mo follow up, there were no differences between groups in terms of chronic side effects.

DISCUSSION

Small bowels are highly sensitive, dose-limiting organs for pelvic or abdominal radiotherapy[1]. The fraction size, fractionation schema, dose and volume of the treatment site are important factors in radiation-induced enteropathy. Additionally, patient-dependent factors, such as genetic factors, are minimally defined, as the methods for this treatment are not highly sensitive[2]. During radiation, matrix metalloproteinase2 (MMP2) and tumor necrosis factor (TNF) are secreted by the cells at the site[3,4]. After their induction by radiation, transient mucosal atrophy and plasma cells and polymorphonuclear leucocytes are accommodated. Inflammatory reactions and endothelium loss, microabcesses, mucosal ulcers, water-electrolyte loss and bacterial infiltration are seen as a cascade[5-7]. Typically, 8 to 12 mo after radiotherapy, obliterative endarteritis occures as a vascular occlusion, followed by tissue growth factor (TGF)-induced tissue ischemia, necrosis and fibrosis[8,9]. Additionally, angiogenesis and chronic

Table 1 Patient properties

	Rectum Ca	Endometrium Ca	Total
Patient number	22	6	28
Median age	66	64	65
Female	12	6	
Male	10		
TA group	11 (6 male)	3	14
Control group	11 (4 male)	3	14

TA: Triamcinolone acetonide.

Table 2 Score frequencies for acute radiation morbidity

		GIS	GUS	Neutrophils
TA	Grade 0	0	10	11
	Grade 1	9	2	3
	Grade 2	5	2	0
Control	Grade 0	0	4	11
	Grade 1	3	6	3
	Grade 2	11	4	0

GIS: Gastrointestinal system; GUS: Genitourinary system; TA: Triamcinolone acetonide.

inflammation are seen after vascular endothelial growth factor (VEGF) secretion[10].

There are many studies using patient positioning and medical palliation to decrease the rate of radiation-induced enteritis. There are varying results for the prone positions during radiotherapy. A 16% decrease in the small bowel median dose has been reported with the use of belly board, but its applicability for patients has been criticized[11,12]. No wide-range study has evaluated the treatment effects of aminosalicylates. For the treatment of radiation-induced enteropathy, there are preliminary results for amifostine, but additional data are needed[13]. According to a double-blind Phase Ⅲ study of pelvic radiotherapy in 120 patients, glutamine is not effective for the treatment of acute radiation enteritis[14].

In contrast, glucocorticoids are used for a vast number of inflammatory diseases. Long term use cause side effects. These drugs inhibit MMP2 secretion and prevent leucocytes infiltrations and TNF-induced inflammatory and angiogenic steps. Steroids are effective agents for preventing leucocyte infiltration, mucosal inflammation and edema[15,16]. Based on these molecular aspects, steroids would be appropriate agents to prevent or attenuate the tissue reaction to radiation.

In a study of 24 patients receiving radiation therapy, the steroid treatment methylprednisolone was reported to improve parenteral nutrition and clinical effects in 8 wk[17]. The rectal use of beclamethasone was also reported to be effective for preventing radiation-induced mucosal changes and rectal bleeding in a randomized study of 120 patients[18].

Periocular injections of TA have been reported to be effective for treating symptomatic macular edema and retinopathy after radiotherapy. The same group designed a prospective randomized study of 163 patients and reported that TA is effective for preventing macular edema[19,20].

In our study, the acute GIS and GUS side effects of pelvic radiotherapy patients were evaluated. These patients often require relevant medication and follow up. It is likely that the acute side effects of radiation arise from patient-dependent factors in the first weeks of conventional fractions rather than the total radiotherapy dose itself. A steroid drug would be preferable because it might prevent the tissue reactions to radiation at some molecular steps.

The long-term use of oral or intravenous steroids may have many side effects; consequently, doctors usually avoid such use. Nevertheless, TA has a good safety profile and is a member of a moderately effective steroid group. In our study, TA was used every 10 d intramuscularly, which is an easy pattern of administration. As a result, TA was found to be effective for preventing and treating radiation-induced acute GIS and GUS side effects.

Compared with other drugs and support products, TA would be beneficial for reducing the medical expenses associated with treating radiation-induced enteritis. To precisely assess the role of TA in preventing and treating radiation-induced side effects, a double-blind randomized study and laboratory confirmation are needed. We think that, our study contributes additional data about preventing and treating radiation-induced side effects and the safety of steroid use in radiation oncology.

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The study analysis was done after Gazi University Noninvasive Clinical Studies Committee permission.

COMMENTS

Background

Many drugs are available to treat the side effects of radiation-induced enteritis. Supportive digestive supplements are used; however, the associated medical expenses are increasing, and patients are suffering as a result. In this study, the authors evaluated the role of triamcinolone acetonide, which is moderately effective, low-cost and easy to use, to manage acute gastrointestinal and genitourinary system side effects.

Research frontiers

Steroids are effective agents to prevent leucocyte infiltration, mucosal inflammation and edema. Based on these molecular aspects, steroids should be appropriate agents to prevent or attenuate the tissue reaction to radiation. In a study of 24 patients undergoing radiation therapy, the steroid treatment methylprednisolone was reported to improve parenteral nutrition and clinical effects in 8 wk. The rectal use of beclamethasone is also reported to be effective for preventing radiation-induced mucosal changes and rectal bleeding in a randomized study of 120 patients.

Innovations and breakthroughs

Periocular injection of triamcinolone acetonide (TA) has been reported to be effective for treating symptomatic macular edema and retinopathy after radiotherapy. The same researchers designed a prospective randomized study of 163 patients and reported that TA is effective for preventing macular edema.

Applications

The authors evaluated the effects of injected TA in 14 patients compared the results with those of 14 untreated patients. For the TA group, 40 mg of TA was injected intramuscularly on the 1st, 11th and 21st d of radiotherapy; the control

group received no injections.

Terminology

RTOG/EORTC Acute Morbidity Score Criteria: "Toxicity criteria of the Radiation Therapy Oncology Group and the European Organization for Research and Treatment of Cancer".

Peer review

Triamcinolone was found to be effective for preventing and treating radiation-induced acute gastrointestinal system (enteritis) and genitourinary system (cystitis) side effects. Triamcinolone is a moderately potent steroid with a low price and a good safety profile. It would be beneficial for reducing medical expenses associated with the treatment of radiation-induced enteritis.

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