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Hyperbaric Oxygen Therapy for Radiation-Induced Cystitis and Proctitis

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Summary

Hyperbaric oxygen therapy (HBOT) is a low-risk, noninvasive treatment that can improve pelvic radiation toxicity. In a retrospective analysis of the efficacy of HBOT for treating hemorrhagic cystitis and proctitis secondary to pelvic- and prostate-only radiotherapy, we found that HBOT is appropriate for radiation-induced hemorrhagic cystitis once less time-consuming therapies have failed to resolve the bleeding and that it is efficacious in the short and long term, with minimal side effects.

Purpose: To provide a retrospective analysis of the efficacy of hyperbaric oxygen therapy (HBOT) for treating hemorrhagic cystitis (HC) and proctitis secondary to pelvic- and prostate-only radiotherapy.

Methods and Materials: Nineteen patients were treated with HBOT for radiation-induced HC and proctitis. The median age at treatment was 66 years (range, 15–84 years). The range of external-beam radiation delivered was 50.0–75.6 Gy. Bleeding must have been refractory to other therapies. Patients received 100% oxygen at 2.0 atmospheres absolute pressure for 90–120 min per treatment in a monoplace chamber. Symptoms were retrospectively scored according to the Late Effects of Normal Tissues—Subjective, Objective, Management, Analytic (LENT-SOMA) scale to evaluate short-term efficacy. Recurrence of hematuria/hematochezia was used to assess long-term efficacy.

Results: Four of the 19 patients were lost to follow-up. Fifteen patients were evaluated and received a mean of 29.8 dives: 11 developed HC and 4 proctitis. All patients experienced a reduction in their LENT-SOMA score. After completion of HBOT, the mean LENT-SOMA score was reduced from 0.78 to 0.20 in patients with HC and from 0.66 to 0.26 in patients with proctitis. Median follow-up was 39 months (range, 7–70 months). No cases of hematuria were refractory to HBOT. Complete resolution of hematuria was seen in 81% ($n = 9$) and partial response in 18% ($n = 2$). Recurrence of hematuria occurred in 36% ($n = 4$) after a median of 10 months. Complete resolution of hematochezia was seen in 50% ($n = 2$), partial response in 25% ($n = 1$), and refractory bleeding in 25% ($n = 1$).

Conclusions: Hyperbaric oxygen therapy is appropriate for radiation-induced HC once less time-consuming therapies have failed to resolve the bleeding. In these conditions, HBOT is efficacious in the short and long term, with minimal side effects. © 2012 Elsevier Inc.

Keywords: Hyperbaric oxygen therapy, Radiation-induced cystitis, Radiation-induced proctitis, Late radiation tissue injury, Radiation toxicity

Introduction

External-beam radiotherapy (EBRT) is a noninvasive treatment targeting malignant cells and surrounding tissue. Technological advances have resulted in greater treatment efficacy while significantly reducing the level of toxicities. Nevertheless, late radiation tissue injuries (LRTI), which include radiation-induced cystitis and proctitis, are side effects of treatment to the pelvis

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that remain a concern. In LRTI, tissues undergo a progressive deterioration marked by a reduction of small blood vessels and fibrosis, supplanting the normal tissue until localized hypoxia compromises normal function (1). These events may be exacerbated by infection or surgical involvement in the affected area. Moreover, the most damaging effects of radiotherapy are due to obliterative endarteritis. If present, hemorrhagic cystitis (HC) typically presents between 6 months and 10 years after radiotherapy, with its prevalence reaching 6.5% in patients with cervical cancer who received pelvic radiation (2). Patients typically present with hematuria, anemia, urinary frequency, dysuria, and incontinence or retention secondary to clots obstructing the urethra. Review of the literature has suggested methods of treatment including simple bladder irrigation, cystoscopic fulguration, intravesical treatment with alum or formalin, hydrodistention, hyperbaric oxygenation, internal iliac embolization, and, as a final resort, cystectomy with urinary diversion. However, these treatments have failed to demonstrate optimal efficacy (3).

Likewise, radiation-induced proctitis occurs as a late toxicity of radiotherapy mostly in patients with prostate and cervical cancer, because of the proximity of these structures to the rectum. The symptoms of proctitis include pain, diarrhea, bowel incontinence, and rectal bleeding. It has been reported that 2%–11% of patients with irradiated prostate and cervical cancer develop this constellation of symptoms; however, some authors argue that the actual incidence is unknown (4, 5). Five percent of all radiation-induced proctitis cases reach severe grades of 3–5 on the Radiation Therapy Oncology Group scale (6). Past treatments have included oral medications, rectal suppositories of steroids and formalin, and endoscopic coagulation procedures, although the efficacy is inconsistent and no standard of care exists (7).

A few researchers have reported on both radiation cystitis and proctitis in the same study. They concluded that patients with both conditions benefit similarly from hyperbaric oxygen therapy (HBOT) (8–10). We report the short- and long-term responses to HBOT of patients with radiation-induced HC and proctitis to compare its safety and efficacy when applying it to these two conditions.

Methods and Materials

Patients were treated with HBOT between October 2004 and December 2009 at our institution. The charts of patients who had pelvic or prostate radiotherapy and subsequently developed rectal or bladder LRTI as evident from hematochezia and/or hematuria were reviewed retrospectively. The condition must have been present for several months and refractory to other therapies.

Patients were screened for unacceptable patient-specific risks to HBOT, namely, susceptibility to rupture of the tympanic membrane, optic neuritis, or pneumothorax. Patients had to be evaluated and cleared before treatment by an otolaryngologist and an ophthalmologist and had to have an up-to-date chest radiograph.

A total of 19 patients were treated with HBOT: 15 patients for radiation-induced HC and 4 for radiation-induced proctitis. The mean age at treatment was 66 years (range, 15–84 years). Four patients were not evaluable after HBOT. Three of them died shortly after treatment because of complications of their cancer. No patients died secondary to their bleeding. One patient who could not be evaluated was lost to follow-up. Patient diagnoses, previously attempted therapy for LRTI, and radiotherapy regimen/dosing are illustrated in Table 1.

Radiation treatments

The range of EBRT doses was 50.0–75.6 Gy to the prostate or pelvic region. Fifteen patients were initially treated for prostate adenocarcinoma; 3 were treated for squamous cell carcinoma of the cervix and vulva; and 1 was treated for alveolar rhabdomyosarcoma of the rectum. The majority of the whole-pelvis fields were constructed using computed tomography–based three-dimensional conformal radiotherapy; a total of 45 Gy was delivered to the pelvic field; respective doses were delivered to the prostate or cervix. Radiation boosts to the cervix were delivered via brachytherapy. The majority of the patients who had radiation to the prostate bed received only intensity-modulated radiotherapy (IMRT); however, not all treatment records were available. In fact, 2 patients with prostate cancer and 1 patient with cervical cancer did not have recorded radiotherapy doses because they were treated at a different institution, and the treating institution did not keep records of the patients dating back more than 10 years.

Hyperbaric oxygen therapy

Hyperbaric oxygen therapy was administered in a monoplace compression chamber pressurized over 10 min to a treatment pressure of 2.0 ATA. The overall treatment duration ranged from 90 to 105 min, with treatments scheduled daily, 5 days per week for 30–40 dives. Sessions varied in time and duration to ensure patient comfort. Each patient was initially scheduled for 90 min. If they complained of discomfort or ear pain, the pressure would be increased more slowly within the chamber, which would increase the duration of the session by 10 minutes. This process would minimize the likelihood that tympanic membrane tubes would be required for pressure equilibrium. All patients were scheduled for 30 dives. If the patient did not achieve a complete response after 30 dives, an additional 10 dives were added in the hope of obtaining a complete response.

Quality of life assessment

Patients with refractory radiation cystitis and proctitis were retrospectively evaluated according to the Late Effects of Normal Tissues—Subjective, Objective, Management, Analytic (LENT-SOMA) scales (11) on the basis of their documented signs and symptoms—and were scored accordingly. This scale is an anatomic-specific morbidity scoring system. It provides an order of severity of radiation-induced complications (Tables 2 and 3). Short-term efficacy of HBOT was assessed using this scale (from end of treatment up to 4 weeks after HBOT); long-term efficacy was determined by recurrence and severity of hematuria or hematochezia. Long-term outcome included only patients with at least 6 months of follow-up from end of HBOT.