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Clinical Investigation

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.

Table 1 Patient demographics and responses to HBOT

Patient no.	Age at HBOT (y)	Primary diagnosis	Total RT dose (Gy)	Toxicity	Previous therapy attempted but symptoms refractory	Dives (*n*)	Severity of pre-HBOT bleeding	Pre-HBOT LENT-SOMA score	Post-HBOT LENT-SOMA score	Time to bleeding recurrence after HBOT (mo)	Severity of post-HBOT bleeding*
1	83	Prostate AC	67.0	HC	CBI	30	I	0.79	0.35	–	–
2	84	Cervical SCC	External RT + HDR	HC	CBI, CCE	30	P	0.93	0.00	3†	I
3	76	Prostate AC	72.0 total, 45.0 to pelvis	HC	CBI	25	P	0.93	0.00	–	–
4	67	Prostate AC	66.0	HC	CBI	30	I	1.14	0.14	–	–
5	55	Vulvar SCC	50.0	HC	CBI	18	P	1.14	0.29	17	I
6	75	Prostate AC		HC	CBI, CCE	23	P	0.93	0.71	2‡	P
7	63	Prostate AC	75.6 total, 45.0 to pelvis	HC	LC, alum	32	R	0.71	0.21	PR to HBOT	O
8	70	Prostate AC	75.6	HC	CCE	40	I	0.43	0.25	PR to HBOT	O
9	15	Rectal alveolar RMS	59.4	HC		30	I	0.43	0.00	–	–
10	73	Prostate AC		HC	BI, Fulg	30	I	0.71	0.07	–	–
11	76	Prostate AC	72.0 total, 45.0 to pelvis	HC	CBI, CCE	10	P	0.43	0.14	28	I
12	67	Prostate AC	66.0	Proctitis	SE	30	O	0.36	0.27	–	–
13	55	Prostate AC	^{125}I seeds, 145 Gy	Proctitis	SE	40	P	0.86	0.14	–	–
14	77	Prostate AC	75.6	Proctitis	SE, PC, FE	40	P	0.93	0.50	Bleeding refractory to HBOT	P
15	70	Prostate AC	75.6 total, 45.0 to pelvis	Proctitis	FE, APC	40	P	0.50	0.00	PR to HBOT	O

Abbreviations: AC = adenocarcinoma; APC = argon plasma coagulation; BI = bladder irrigation; CBI = continuous bladder irrigation; CCE = cystoscopic clot evacuation; FE = formalin enema; Fulg = fulguration; HBOT = hyperbaric oxygen therapy; HC = hemorrhagic cystitis; HDR = high dose rate; LENT-SOMA = Late Effects of Normal Tissues—Subjective, Objective, Management, Analytic; LC = laser cautery; PC = photocoagulation; PR = partial response; RT = radiotherapy; RMS = rhabdomyosarcoma; SCC = squamous cell carcinoma; SE = steroid enema.

* Severity of bleeding: O = occasional; I = intermittent; P = persistent.

† Patient developed bladder cancer diagnosed after HBOT.

‡ Patient had existing myelodysplastic syndrome.

Table 2 Late effects of normal tissues—subjective, objective, management, analytic scale for proctitis (rectum)*

Parameter	Grade 1	Grade 2	Grade 3	Grade 4	Scoring	Instructions
Subjective						
Tenesmus	Occasional urgency	Intermittent urgency	Persistent urgency	Refractory	——	Score the 14 SOM parameters with 1−4
Mucosal loss	Occasional	Intermittent	Persistent	Refractory	——	
Sphincter control	Occasional	Intermittent	Persistent	Refractory	——	
Stool frequency	2−4/d	4−8/d	>8/d	Uncontrolled diarrhea	——	
Pain	Occasional and minimal	Intermittent and tolerable	Persistent and intense	Refractory and excruciating	——	
Objective						
Bleeding	Occult	Occasionally >2/wk	Persistent/daily	Gross hemorrhage	——	(Score = 0 if there are no toxicities)
Ulceration	Superficial ≤ 1 cm^2	Superficial >1 cm^2	Deep ulcer	Perforation, fistulae	——	
Stricture	>2/3 normal diameter with dilation	1/3−2/3 normal diameter with dilation	<1/3 normal diameter	Complete obstruction	——	
Management						
Tenesmus and stool frequency	Occasional, ≤ 2 antidiarrheals/wk	Regular, >2 antidiarrheals/wk	Multiple, >2 antidiarrheals/d	Surgical intervention/ permanent colostomy	——	Total the scores and divide by 11†
Pain	Occasional nonnarcotic	Regular nonnarcotic	Regular narcotic	Surgical intervention	——	
Bleeding	Stool softener, iron therapy	Occasional transfusion	Frequent transfusions	Surgical intervention/ permanent colostomy	——	
Ulceration	Diet modification, stool softener	Occasional steroids	Steroids per enema, hyperbaric oxygen	Surgical intervention/ permanent colostomy	——	
Stricture	Diet modification	Occasional dilatation	Regular dilatation	Surgical intervention/ permanent colostomy	——	
Sphincter control	Occasional use of incontinence pads	Intermittent use of incontinence pads	Persistent use of incontinence pads	Surgical intervention/ permanent colostomy	——	
Analytic						LENT score: ——
Barium enema		Assessment of lumen and peristalsis			Y/N Date:	
Proctoscopy		Assessment of lumen and mucosal surface			Y/N Date:	
CT		Assessment of wall thickness, sinus and fistula formation			Y/N Date:	
MRI		Assessment of wall thickness, sinus and fistula formation			Y/N Date:	
Anal manometry		Assessment rectal compliance			Y/N Date:	
Ultrasound		Assessment of wall thickness, sinus and fistula formation			Y/N Date:	

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† In contrast to the divisor of 11 shown here from the original source (11), we divided our proctitis scores by 14, as was done in the largest randomized controlled trial to date of radiation-induced proctitis (5).

Table 3 Late effects of normal tissues—subjective, objective, management, analytic scale for cystitis (bladder/urethra)*

Parameter	Grade 1	Grade 2	Grade 3	Grade 4	Scoring	Instructions
Subjective						
Dysuria	Occasional and minimal	Intermittent and tolerable	Persistent and intense	Refractory and excruciating	——	Score the 14 SOM parameters with 1−4
Frequency	3−4-h intervals	2−3-h intervals	1−2-h intervals	Hourly	——	
Hematuria	Occasional	Intermittent	Persistent with clot	Refractory	——	
Incontinence	<Weekly episodes	<Daily episodes	≤2 pads/undergarments/d	Refractory	——	
Decreased stream	Occasionally weak	Intermittent	Persistent but incomplete obstruction	Complete obstruction	——	
Objective						
Hematuria	Microscopic, normal hemoglobin	Intermittent macroscopic, <10% decrease in hemoglobin	Persistent macroscopic, 10−20% decrease in hemoglobin	Refractory, >20% decrease in hemoglobin	——	(Score = 0 if there are no toxicities)
Endoscopy	Patchy atrophy or telangiectasia without bleeding	Confluent atrophy or telangiectasia with gross bleeding	Ulcerations into muscle	Perforation, fistula	——	
Maximum volume	>300−400 cm^3	>200−300 cm^3	>100−200 cm^3	≤100 cm^3	——	
Residual volume	25 cm^3	>25−100 cm^3	>100 cm^3	−		
Management						
Dysuria	Occasional nonnarcotic	Regular nonnarcotic	Regular narcotic	Surgical intervention	——	Total the scores and divide by 14
Frequency	Alkalization	Occasional antispasmodic	Regular narcotic	Cystectomy	——	
Hematuria/ telangiectasia	Iron therapy	Occasional transfusion or single cauterization	Frequent transfusion or coagulation	Surgical intervention	——	
Incontinence	Occasional use of incontinence pads	Intermittent use of incontinence pads	Regular use of pad or self-catheterization	Permanent catheter	——	
Decreased stream	−	<Once-daily self-catheterization	Dilatation, >once-daily self-catheterization	Permanent catheter, surgical intervention	——	
Analytic						LENT score: ——
Cystography	Assessment of mucosal surface				Y/N Date:	
Volumetric analysis	Assessment of bladder capacity in milliliters				Y/N Date:	
Contrast radiography	Assessment for ulcers, capacity and contractility				Y/N Date:	
Ultrasound	Assessment of wall thickness, sinus and fistula formation				Y/N Date:	
Electromyography	Assessment of sphincter activity using intralumenal pressure transducer, contraction pressure and volume curves				Y/N Date:	

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Results

Of those with sufficient follow-up, the indication for HBOT was radiation-induced HC in 11 patients and radiation-induced proctitis in 4 patients. The proportion of patients who developed LRTI secondary to IMRT was similar to that of those who developed it secondary to three-dimensional conformal radiotherapy. A mean of 29.8 HBOT sessions, referred to as dives, were performed (range, 10–40). Fifteen patients treated with HBOT were assessed for short-term efficacy of HBOT. Long-term efficacy (at least 6 months of follow-up from end of HBOT) could be assessed in 11 of the 15 patients. For the long-term patients, the median length of follow-up was 39 months (range, 7–70 months).

Hemorrhagic cystitis

The median time from completion of radiotherapy to presentation of hematuria was 30 months (range, 5–324 months). All 11 HC patients showed improvement in their LENT-SOMA score after HBOT. The mean pretreatment LENT-SOMA score for HC patients was 0.78, which was reduced to 0.20 shortly after HBOT was completed. A diagram is provided in Fig. 1 as a visual aid to the following description of patient outcomes.

Nine of 11 HC patients (81%) had complete resolution of their hematuria during treatment or shortly after the completion of treatment. Four of the 9 patients with HC who initially had a complete resolution experienced recurrence of hematuria. The severity of recurrence in 3 of these patients was less than the severity of the first episode before HBOT. For example, the hematuria was characterized as "persistent" before HBOT and "intermittent" on recurrence. The median time from completion of HBOT to recurrence of hematuria was 10 months (range, 2–28 months). One of the patients who had recurrence of hematuria also developed prostate cancer recurrence. This patient's recurrent hematuria was self-limiting after 2 months. Another patient who had recurrence of hematuria underwent another course of HBOT with 30 additional dives and again had complete resolution. This patient's radiotherapy initially included combined-modality external-beam and brachytherapy for cervical cancer. Subsequently, this patient was diagnosed with bladder cancer. At the time of this submission, this patient experienced recurrence of hematuria for a second time and was treated with transurethral resection of the bladder and cystoscopic clot evacuation. Another patient with recurrence had several comorbidities, including myelodysplastic syndrome that transformed into acute leukemia. This patient was treated with frequent transfusions and underwent further HBOT at another facility and was lost to subsequent follow-up.

Two of the 11 patients with HC experienced partial response to HBOT. One of these patients improved from "refractory" (4 points on the cystitis scale) to "occasional" bleeding (1 point on the scale); the other improved from "intermittent" (2 points on the scale) to occasional bleeding.

One patient with proctitis developed HC 23 months after completion of HBOT for rectal bleeding. He refused additional HBOT to treat the HC and instead relied on cystoscopy with cauterization. This patient experienced recurrence of hematuria 42 months later and was treated with continuous bladder irrigation; however, the bleeding was refractory. At the most recent follow-up, this patient received a formalin injection that resolved the bleeding for the time being.

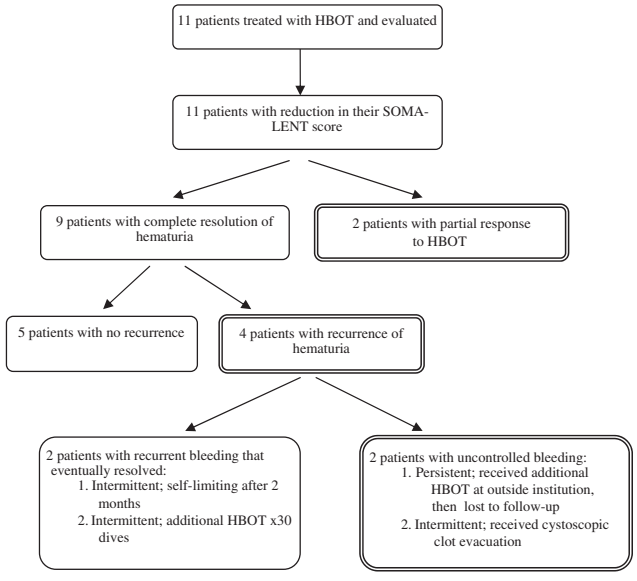

Fig. 1. Outcomes of patients with hemorrhagic cystitis. HBOT = hyperbaric oxygen therapy; SOMA = Subjective, Objective, Management, Analytic; LENT = Late Effects of Normal Tissues.

Proctitis

The median time from completion of radiotherapy to presentation of hematochezia was 10.5 months (range, 3–37 months). All 4 patients with proctitis showed an improvement in their LENT-SOMA score after HBOT. Their mean pretreatment LENT-SOMA score was 0.66, which was reduced to 0.26 shortly after HBOT was completed. A diagram is provided in Fig. 2 as a visual aid to the following description of patient outcomes. Two of the 4 proctitis patients had complete resolution of their hematochezia. Neither patient experienced recurrence. One patient had partial resolution of hematochezia after HBOT; this patient's bleeding improved from "intermittent" (3 points on the proctitis scale) to "occasional" (2 points on the scale) after HBOT. This patient's bleeding was self-limiting after several months. One patient had persistent bleeding refractory to 40 dives of HBOT. This patient's hematochezia resolved 11 months after HBOT with the aid of steroid and formalin enemas.

Adverse effects of HBOT

The most common side effect of HBOT was otalgia, which was resolved with the placement of tympanostomy tubes. This side

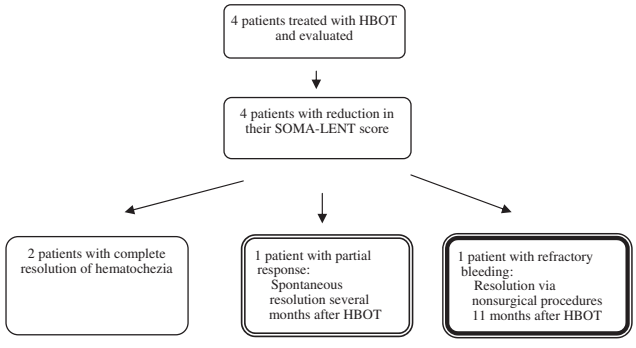

Fig. 2. Outcomes of patients with proctitis. HBOT = hyperbaric oxygen therapy; SOMA = Subjective, Objective, Management, Analytic; LENT = Late Effects of Normal Tissues.

effect occurred in 33% of the patients ($n = 5$) and was considered a minor side effect. No major adverse effects were observed secondary to HBOT.

Discussion

The use of IMRT in the treatment of pelvic malignancies allows better conformal dosing and decreased radiation to adjacent organs. Relatively newer methods of radiation delivery (*i.e.*, image-guided radiotherapy) should further decrease radiation complications. Through daily localization of the prostate with image-guided radiotherapy, the margins around the prostate could be tightened, thereby allowing delivery of a smaller dose to the bladder and rectum. Although less frequently encountered because of improved technology, radiation-induced bleeding remains an area of concern in a small percentage of patients.

At normal atmospheric pressure, oxygen saturation reaches its full potential by binding to all available hemoglobin sites. The mechanism behind HBOT maximizes the amount of oxygen being delivered to tissue by using high pressure to enable more oxygen to dissolve in the plasma.

A small number of case reports of successful reversal of radiation-induced hematuria by use of HBOT were first reported in the mid-1980s (12). The rationale for using HBOT was based on reports from the early and mid-1970s of healing mandibular osteoradionecrosis with HBOT, along with surgical debridement and antibiotics (13). More recently, an updated Cochrane review in 2009 examined eight randomized controlled trials comparing the effect of HBOT with that of no HBOT on LRTI prevention or healing. The reviewers suggested that, for people with LRTI affecting tissues of the head, neck, anus, and rectum, HBOT is associated with improved outcomes (14). However, they did not find useful randomized studies to support the efficacy of HBOT for other tissues, including the bladder.

One of the first prospective studies to assess HBOT for HC ($n = 40$) reported a complete response in 75% of patients, with only 3 patients experiencing recurrent hematuria after a mean follow-up of 29 months (15). A recent retrospective study of 60 patients with HC showed complete resolution or marked improvement in 80% of cases treated with an average of 33 sessions (16). The study with the longest median follow-up of 5.1 years reported similar short-term results but poor long-term outcomes. Only 27% of these patients ($n = 3$) achieved long-term complete resolution when treated with a median 40 sessions (17). This outcome exemplifies the importance of reporting on the long-term efficacy in studies that evaluate HBOT for cystitis.

Our experience showed good short-term efficacy, in which 81% of patients with HC had complete resolution of hematuria. Those who did not experience complete resolution of hematuria showed marked improvement after completion of HBOT and gradually achieved spontaneous resolution of bleeding. The outcome of 2 of 4 of the patients who experienced recurrence of hematuria may have been confounded by comorbidities. For example, 1 patient developed bladder cancer, and the other had acute leukemic transformation of pre-existing myelodysplastic syndrome. In both cases, hematuria was an expected finding secondary to their disease. All 4 patients who experienced recurrence had pre-HBOT bleeding characterized as "persistent," whereas, 5 of 7 of those who did not experience recurrence had "intermittent" pre-HBOT bleeding. Therefore, more severe bleeding at presentation may increase the likelihood of experiencing recurrence after treatment.

Further support for this therapy is exemplified in the patient who initially had proctitis and later developed HC but refused an addition round of HBOT for his new LRTI. This patient was treated with several methods to resolve bleeding that did not include HBOT and subsequently developed recurrence of hematuria. In comparison with the patients with HC whose hematuria recurred after they completed HBOT, this patient experienced recurrent bleeding that was as severe as his initial episode and that was refractory to several treatments until resolution was finally achieved for the time being. In comparison, those with recurrence who were treated with HBOT experienced bleeding that was less severe than their initial episode and responded well to additional treatment. This finding can help enhance the perspective of outcome with respect to HBOT.

The role for HBOT in radiation-induced proctitis has not been reported in the literature to the extent that it has been reported for HC. Nonetheless, observational studies have shown complete resolution of symptoms in a large proportion of patients treated with HBOT whose symptoms were refractory to other treatment (6, 18). A relatively large double-blind crossover trial with long-term follow-up evaluating HBOT for radiation proctitis recently showed a statistically significant clinical response rate of 89% in the HBOT arm compared with 63% in the control group (5).

A limitation of our study was the small sample of patients with radiation-induced proctitis, which makes it difficult to deduce specific trends. Nevertheless, our results showed improvement in patients receiving HBOT for proctitis. All of their LENT-SOMA scores decreased, and half of them had complete resolution of hematochezia after treatment. The patient who experienced partial response eventually achieved spontaneous remission. Only 1 of the proctitis patients still has problems with rectal bleeding. Thus, patients treated for radiation-induced proctitis greatly benefited from HBOT. A unique feature of our study is the inclusion of both conditions, which has been reported in few other studies.

Complications of HBOT have been described as barotraumatic lesions caused by compression or expansion of enclosed gas volumes, which can be localized to the nasal sinuses, teeth, lung, inner ear, and most commonly the middle ear. Five of our patients (33%) experienced middle ear equalization changes manifesting as otalgia, a proportion similar to those reported previously (19). Each of these patients responded well to tympanostomy tube placement and completed their remaining dives. Peripheral circulatory disorders with refractory ulcers or nonhealing wounds have been identified as independent risk factors for pressure equalization problems after therapy (20). However, the impact is of low significance for the current subset of patients because it is a comorbid feature of those undergoing HBOT for indications other than radiation-induced HC or proctitis.

Conclusions

Although the widespread use of IMRT has enabled radiation oncologists to achieve sharp contrasts of doses applied to structures close to each other, serious radiation-induced injuries still persist in a small percentage of patients. Hyperbaric oxygen therapy is effective in resolving or improving the symptoms of radiation-induced HC irrespective of the patient's overall prognosis. Our results are in agreement with those of other studies examining the effectiveness of HBOT in treating HC and proctitis.

In particular, it is a legitimate approach for patients with HC who have failed with other treatments. Although we obtained favorable results, our small sample size of patients with proctitis makes it difficult to state conclusions regarding the efficacy of HBOT for this condition. The literature lacks abundant randomized clinical trials to evaluate the long-term efficacy for both conditions. However, our results, along with those from many other small studies, have shown sufficient evidence to support this approach. As a result, HBOT can be added to the interventions at a clinician's disposal to treat such patients.

The merit of directly examining responses in both conditions may help revise the rationale for discrepancies in insurance coverage between radiation-induced hemorrhagic cystits and proctitis in patients with different plans. Currently, no major insurance plan covers both conditions. As we have shown, HBOT is a reliable option for both toxicities, especially those whose symptoms are refractory to other treatments. Hopefully, as a result of mounting evidence similar to that determined by our study, coverage will be extended to both conditions. This change may lead to heightened patient confidence that serious adverse effects of radiation can be treated safely, rendering the patients more likely to proceed with radiotherapy to treat their malignancies.

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