Hyperbaric Oxygen Treatment, Alpha-Tocopherol and Ascorbic Acid Are Effective For Reducing Late Radiation-Induced Side Effects of Pelvic Radiotherapy

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Objectives
Pelvic radiotherapy (RT) is a key aspect in the management of genitourinary (GU) and gynecologic (GYN) malignancies. Pelvic irradiation may result in urinary and intestinal toxicities. Late radiation-induced normal tissue toxicity can be difficult to manage and significantly impact quality of life. To better appreciate radiation-induced late effects and their potential management, we undertook an analysis of a prospective treatment protocol designed to investigate the efficacy of hyperbaric oxygen therapy (HBOT), oral alpha-tocopherol (AT) and ascorbic acid (AA) in patients with pelvic radiation disease.

Methods
An REB approved retrospective review of a prospective adult radiation late effects (LE) treatment protocol was conducted. Twenty patients referred to a multidisciplinary late effects clinic at a tertiary care cancer center were screened to identify those with GU and GYN malignancies who had received pelvic RT. Patient, tumor and treatment factors were abstracted and analyzed. The median time to LE onset, LE symptoms, maximal initial Common Terminology Criteria for Adverse Events Version 4.0 (CTCAE) grade, LE treatment and duration and maximal post CTCAE grade were analyzed.

Translation of Late Effects into a Scale

Grade 1+
Asymptomatic, signs are minimal and neither interfere with functional endpoints nor impede mobility. Most often, management is restrained, interventions and medication are not required.

Grade 2+
Symptomatic, moderate findings clinically or in the laboratory, that may alter functional endpoints without impact on QOL or ADL. Medications and non-surgical interventions can be used and be useful.

Grade 3+
Effects are indicative of severity of symptoms and signs, which persist over time. Disruption of mobility, working, and numerous functional endpoints. More serious interventions, such as hospitalization or surgery, are often indicated.

Grade 4+
Effects are potentially life threatening, catastrophic, disabling and result in loss of limb, bowel, or organ function.

Grade 5+
Fatal

Results
The primary symptoms were bleeding (18) and diarrhea (2), and the secondary symptoms were rectal pain (10), bladder symptoms (7) and diarrhea (3). The median maximal CTCAE grade at initial consult was 3 (3-4). 16 received HBOT. A median of 40 (36-41) treatments per patient were performed. No major adverse events attributable to HBOT were reported. Ten received oral AT and AA as antioxidant therapy. The median duration was 16 months (3-27). No side effects were reported with their use. The median duration of follow-up from LE symptom onset was 58 months (1-141). At the time of last assessment, median maximal CTCAE grade was 1 (1-3) with a median change of 2. A paired sample t-test revealed a significant difference in CTCAE grades (p = 0.0001). Following HBOT and AT and AA, persistent reductions in CTCAE grades were observed for all patients. Rectal and urinary bleeding resolved or improved in 16 patients.

Conclusion
HBOT, alpha-tocopherol and ascorbic acid appear non-invasive and effective interventions for radiation proctitis and cystitis. For the patient population failed by conventional interventions, further trials of HBOT and AT and AA are warranted.