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FINAL TECHNICAL REPORT
F49620-92-J-0183

"The Role of Hyperbaric Oxygen as a
Prophylaxis for Radiation Enteritis"

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Abstract

C3H mice were used to study the effects of post radiation treatments of hyperbaric oxygen (HBO) on preventing onset of radiation enteritis. Fifty mice were irradiated in the abdominal pelvic regions with identical radiation doses of 3000 CGY in 10 fractions over two weeks. The mice were randomly divided into a control and a study group of 25 each. The control group received no other treatment while being maintained with standard nutritional support. The study group received 30 HBO treatments (90 min of 100% oxygen at 2.4 ATA for 5 days/week for 6 weeks) starting 7 weeks after radiation therapy. All mice were sacrificed at 7 months and examined for signs of radiation damage. A numerical scoring system was used to quantitatively evaluate radiation damage to tissue. A score of +30 was determined for the radiation control group consisting of 21 surviving animals while a score of only +3 was noted for the HBO treated study group consisting of 25 surviving animals. Stretch meter examination showed that 7 of 21 control animals possessed stenotic lesions while only 4 of 25 HBO-treated animals were affected. Histological examination for submucosal fibrosis is presently in progress with no apparent differences noted thus far. This study indicates that post-radiation HBO treatments can significantly reduce small bowel radiation damage in mice.

BACKGROUND

Radiation enteritis is a rare but very serious complication of abdominal radiation. Under certain circumstances, its incidence is as high as 19%. Other than surgical resection of the affected part, there is no effective treatment. In its most serious expression, it is a life threatening disorder. The inherent tolerance of the small bowel limits the dose of abdominal radiation which can be safely delivered. An effective prophylactic measure could prevent enteritis and possibly even permit a more aggressive radiation dosage scheme with a resultant increase in tumor control.

Several clinical studies and a few laboratory studies have shown efficacy for HBO (Hyperbaric Oxygen Therapy) when used therapeutically for radiation necrosis. There have also been a few reports demonstrating the utility of HBO as a prophylaxis for mandibular radiation necrosis when given prior to tooth extractions from the mandibles of irradiated patients.

MATERIAL AND METHODS

The study was a controlled animal trial using the C3H mouse as the animal model. Fifty mice were irradiated with identical radiation dose fractionation schemes of 3000 CGy whole abdominal pelvic radiation in 10 fractions over two weeks. Seven weeks after the irradiation, animals were randomly assigned to a control and a study group. The control group received no additional intervention other than standard nutritional support and maintenance in the animal colony.

The study group received a course of 30 HBO treatments beginning 7 weeks after completion of the radiation. HBO treatments were given daily 5 days per week over 6 weeks and consisted of 90 minutes of 100% oxygen at 2.4 ATA. A small animal HBO chamber was utilized (Bethlehem Manufacturing on loan from the Hyperbaric Medicine Division of Armstrong Laboratory).

Radiation was delivered using a 250 kVp beam through a single anterior portal at a dose rate of 65 cGY per minute. Three additional animals received no radiation and no HBO. Seven months after completion of radiation, all animals were euthanized and examined for objective signs of radiation damage. Three segments of ileum just proximal to the ileocecal valve from each animal were taken for further study.

RESULTS

A scoring system was developed to quantitate gross evidence of radiation damage to the small bowel. Animals were assessed a score of +1 for each of the following findings: white ischemic bowel, grossly narrowed segments, grossly dilated segments, rigid segments, and adhesions.

Twenty-one of 25 animals were available in the radiation only arm. A score of +30 was determined for this group with at least one positive finding in 14 of 21 animals. All 25 animals were available in the combined HBO/radiation group. A score of +3 was determined for this group with abnormal findings in only 3 of 25 animals.

An electronic stretch meter device was also used to determine lumen size and distensibility of the bowel. Stretch meter determination showed pronounced stenosis in 13 specimens from 7 of 21 radiation only group animals. The same determination showed pronounced stenosis in 6 specimens from 4 of 25 HBO/radiation group animals. Stretch meter determinations showed an increase in rigidity to 150% or more of average control values in 12 segments from 9 animals in the radiation only group and in no segments from animals in the combined radiation/HBO group.

Histologic examination of the small bowel segments is under way. So far, no significant difference in the amount of measurable submucosal fibrosis has been seen. Further determinations to be

done include the number and quality of mucosal villi as well as the degree of visible vascular stenosis.

CONCLUSION

The study with the determinations to date shows a significant reduction in objective signs of small bowel radiation damage.