Physiological Monitoring of Patients Undergoing Radiation Therapy under High-Pressure Oxygen

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From the University of Washington School of Medicine, Seattle Physiological Monitoring of Patients Undergoing Radiation Therapy under High-Pressure Oxygen

There have been numerous clinical trials of radiation treatment of patients exposed to pure oxygen at elevated pressures since Churchill-Davidson's initial work. With rare exception, such hyperbaric radiation therapy has been administered in few, irregularly spaced exposures per patient. Inasmuch as the results and sequelae of conventional radiation therapy are based on administration in approximately equal daily increments for overall periods of several weeks, this disparity of application compromises useful comparison of hyperbaric and conventional radiation therapy, as related to augmentation of radiation responsiveness of tumor and radiation-produced sequelae.

It seems necessary to determine whether conscious, unmedicated patients with cancer can be subjected to flowing pure oxygen under increased pressure each day for 30–40 minutes for an overall period of 4–6 weeks, while undergoing radiation therapy. For reasons outside the scope of this discussion, our trial is being conducted with an intrachamber pressure of 30 p.s.i.

Although several patients have been treated elsewhere in this manner without gross unacceptable side effects, it would seem necessary to study the patients' physiological tolerance of the method in order to determine whether it has a broad range of applicability. Any "physiological price" of application would need to be subtracted from gains achieved in control of tumor.

There are reports of: (1) refusal of patients to enter the compression chamber; (2) lung damage; (3) central nervous system effects – i.e. convulsions, physiological changes in the brain, disturbed mentation and other neurological changes; (4) retinal damage; (5) otalgia and ear infections; (6) hematological changes; (7) endocrine changes; (8) cardiovascular changes; (9) alterations of the bacterial flora which might affect the airway and intestinal tract; (10) microscopic liver changes.

These reported physiological damages in man and animals are not directly applicable to the conditions of daily 40-minute exposures of humans to pure flowing oxygen under 30 p.s.i., but they create a demand for careful physiological assessment of these patients.

The patients selected for our study harbor lesions which have a reputation of infrequent control by conventional treatment methods, but which have sufficient biological predictability to allow observations on local control of tumor. The neoplasms include: cancer of the uterine cervix, stage III because of parametrial extension; carcinoma of the hypopharynx, especially those lesions arising in or involving the piriform fossa; cancer of the pharyngeal tongue; cancer of the thoracic esophagus; cancer of the urinary bladder with deep invasion of the muscular wall; inoperable cervical lymph node metastases from primary well-differentiated

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squamous-cell or adenocarcinomas; and selected tumors such as melanoma and fibrosarcoma, notoriously poorly responsive to radiation.

Because of our interest in evaluating pulmonary and cerebral function, lung and intracranial neoplasms have been excluded.

Pulmonary function: There is a voluminous literature on pulmonary pathology produced in animals breathing oxygen under increased pressure. Changes such as focal atelectasis; pulmonary edema; alteration of lung volume, diffusion capacity and blood gases have been produced using high pressures for long periods.

Eight patients have had serial pulmonary function studies by C. Lenfant, M.D. The pre-treatment exam includes chest X-ray, N₂ washout, N₂ washin and arterial blood gas measurements (O₂, CO₂, N₂). Then N₂ washout, N₂ washin and arterial-alveolar differences in P_{O₂}, PCO₂ and PN₂ are repeated each week during treatment. Within two weeks after completion of treatment, the exhaustive pre-treatment battery is rerun. Periodic follow-up exams are scheduled and are in progress.

There has been no alteration of pulmonary function on any patients except one, a 58-year-old male receiving mediastinal irradiation for squamous-cell carcinoma of the esophagus. He received a calculated dose of 5200 rads in 79 days to opposing mediastinal fields 7 X 16 cm. By three weeks after treatment, he noted inspiratory difficulty and cough. There was a marked roentgenographic change within the irradiated field (slide). Pulmonary function was decreased about 50% in all parameters. Four weeks later there has been modest symptomatic improvement of his breathing and objective evidence of progression of the extensive esophageal tumor.

Ears: Otalgia, serous otitis, tympanic membrane perforation and infection of the skin of the external canal have been reported in patients subjected to oxygen at 30 p.s.i.

On the basis of weekly examination on 8 patients, there has been no observation of infection or serous otitis. The tympanic membranes have remained intact with pre-treatment light reflex. On the basis of gross auditory acuity tests (watch tick, tuning fork at 256 v.p.m.), there has been no alteration except in one patient who experienced sudden unilateral deafness after blowing his nose prior to treatment. This did not improve during the 8 weeks of treatment, nor has it since treatment.

More sophisticated testing is scheduled. This will include auditory acuity tests to various pitches and measurement of slight variations in the surface of the tympanic membrane incident to changes in eustachian tube pressure.

Eyes: Retinal detachment, hypotony, conjunctivitis and iritis have been produced in dogs subjected to oxygen at elevated pressures for long periods.

Six patients have been examined before and after the treatment course by Dr. David McIntyre. Examination has included visual acuity and refraction, slit-lamp exam, retinal observation and ocular tension determination. There have been no changes.

CNS: A dramatic effect of great concern associated with administration of oxygen under elevated pressure has been generalized focal seizures, noted in both animals and humans. These convulsions reported during compression and decompression have led to the use of general anesthesia in several clinical trials. Hiccoughing, tinnitus and dizziness also have been attributed to oxygen toxicity.

There has been no such event in about 300 compression cycles in our study.

Electroencephalographic monitoring during pressurization, scheduled early in our study, will not start for another month because of technical problems related to

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adaptation of French equipment to an English chamber by an Italian electro-encephalographer.

All of our patients have a neurological exam to include cranial nerve function, cerebellar function, motor function, cutaneous sensation and deep tendon reflexes prior to treatment and at weekly intervals during treatment. No changes have been noted to date.

Cardiovascular system: Multiple changes such as right heart change in the ECG, elevation of the mean arterial tension, decrease of heart rate and cardiac output have been reported in animals subjected to high-pressure oxygen.

In multiple observations on our patients, there has been no significant change in cardiac rate or rhythm or in peripheral arterial blood pressure. Electrocardiographic monitoring, scheduled to start soon, has been delayed for technical reasons, as previously stated.

Hematopoietic tissue: Significant rises in hematocrit have been reported in dogs subjected to 30 p.s.i. for several hours. There has been no such change in our patients.

Liver and kidney function: Although microscopic liver changes have been reported, it is unlikely that liver or kidney functions will be altered. Creatinine clearance, PSP, BSP and transaminase screening tests have been completed in two patients without pertinent finding.

Summary

A detailed program has been initiated for the physiological assessment of cancer patients subjected to daily pressurization at 30 p.s.i. of free-flowing oxygen in conjunction with radiation therapy. A modest amount of accumulated data has failed to show significant alteration of pulmonary function, central nervous system, cardiovascular system, hematopoietic tissue, eyes or ears.

From the Tumor Institute of the Swedish Hospital, Seattle

The Management of the Cancer Patient by Radiation Therapy with Hyperbaric Oxygen

Comments on the Prevention and Treatment of Complications

By O. WILDERMUTH

At the present time

we conclude from our experience to date that the complications of hyperbaric radiotherapy seen in the area of treatment – in the normal tissues as well as the tumor – are entirely dependent upon the radiation dose

except in a small group of instances when normally non-vascularized tissue is present in the radiation field. Manipulations of radiation dosage have been considered necessary for various reasons

to be reviewed. The avascular tissues that may appear in the field of radiation are cartilage the lens of the eye

the cornea

etc. Since their normal existence is maintained by diffusion from the surface where contact with the body vascularity is maintained

it is obvious that a new response to radiation beyond

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