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Effects of radiotherapy after hyperbaric oxygenation on malignant gliomas

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Summary The purpose of this non-randomized trial was to evaluate the efficacy of radiotherapy combined with hyperbaric oxygen (HBO) in patients with malignant glioma. Between 1987 and 1997, 29 patients in whom computerized tomography (CT) or magnetic resonance imaging (MRI) scans showed post-operative residual tumours were locally irradiated with nitrosourea-based chemotherapy. Treatments were consecutively combined with HBO at two institutions since 1991 and 1993. Fifteen patients were irradiated daily after HBO, and the periods of time from decompression to irradiation were within 15 and 30 min in 11 and four patients respectively. Fourteen other patients were treated without HBO. Tumour responses were assessed by CT or MRI scans and survival times were compared between the treated groups. In the HBO group, 11 of 15 patients (73%) showed ≥ 50% tumour regression. All responders were irradiated within 15 min after decompression. In the non-HBO group, four of 14 patients (29%) showed tumour regression. The median survivals in patients with and without HBO were 24 and 12 months, respectively, and were significantly different ($P < 0.05$). No serious side-effects were observed in the HBO patients. In conclusion, irradiation after HBO seems to be a useful form of treatment for malignant gliomas, but irradiation should be administered immediately after decompression.

Keywords: malignant glioma; hyperbaric oxygenation; radiation therapy; clinical trials

Malignant gliomas, comprising the majority of primary brain tumours in adults, have a very poor prognosis. Traditional therapies, such as surgery, radiotherapy and some chemotherapeutic agents, have been used in various combinations in the search for a curative regimen. Radiotherapy has a major role in the adjuvant therapies for malignant gliomas. Despite notable technical advances in both the surgical and radiotherapeutic treatment approaches to malignant gliomas during the last decade, patient survival has not improved. The presence of hypoxic tumour cells is thought to be a major reason for tumour resistance to radiotherapy (Gray et al, 1953; Hall, 1994).

Molecular oxygen has long been recognized as one of the most powerful modifiers of cellular radiation sensitivity. For example, oxygen has been reported to increase, by a factor of approximately 3, the biological effect of ionizing radiation on mammalian cells in which radiation is performed under well-oxygenated conditions as compared to anoxic conditions (Gray et al, 1953). Thus hyperbaric oxygen (HBO) exposure, which improves the oxygen supply to hypoxic tumour cells, was used in combination with radiotherapy to treat malignant gliomas (Chang, 1977; Dowling et al, 1992). The previous combination method in which irradiation was administered during HBO exposure was hazardous to patients and a complex technique, and as a result HBO has not been routinely adopted with radiotherapy to treat malignant gliomas (Chang, 1977; Jain, 1990; Dische, 1991).

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Exposure to HBO produces tissue oxygenation, and the increased PO_2 persists in normal tissues for certain periods after decompression (Wells et al, 1977). We hypothesized that if PO_2 in malignant gliomas remains elevated after HBO exposure, the resulting improvement in irradiation after decompression may lead to enhanced tumour control. In our previous pilot study, we reported that all patients who received HBO experienced regression of their residual tumours (Kohshi et al, 1996). Consequently, we evaluated the effectiveness and safety of this new approach to treat malignant gliomas.

MATERIALS AND METHODS

Patient selection

At our University Hospital of Occupational and Environmental Health between 1987 and 1997, and at Amakusa Medical Center between 1990 and 1997, 72 cases with newly diagnosed malignant gliomas were locally irradiated after tumour debulking or biopsy. Patients have been consecutively treated by radiotherapy combined with HBO at the above two institutions since 1991 and 1993 respectively. Eligibility criteria included:

1. all patients were above the age of 16 years
2. anaplastic astrocytoma or glioblastoma multiforme was pathologically verified according to the World Health Organization classification (Kleihues et al, 1993)
3. measurable disease was exhibited on pre-treatment contrast-enhanced computerized tomography (CT) or magnetic resonance imaging (MRI) scan
4. Karnofsky Performance Scale (KPS) score was 60 or greater at the time of assignment (Karnofsky et al, 1948)