Oxygenation Measurements in Head and Neck Cancers during Hyperbaric Oxygenation

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Background: Tumor hypoxia has proven prognostic impact in head and neck cancers and is associated with poor response to radiotherapy. Hyperbaric oxygenation (HBO) offers an approach to overcome hypoxia. We have performed pO2 measurements in selected patients with head and neck cancers under HBO to determine in how far changes in the oxygenation occur and whether a possible improvement of oxygenation parameters is maintained after HBO.

Patients and Methods: Seven patients (five male, two female, age 51–63 years) with squamous cell cancers of the head and neck were investigated (six primaries, one local recurrence). The median pO2 prior to HBO was determined with the Eppendorf histograph. Sites of measurement were enlarged cervical lymph nodes (n = 5), the primary tumor (n = 1) and local recurrence (n = 1). Patients then underwent HBO (100% O2 at 240 kPa for 30 minutes) and the continuous changes in the oxygenation during HBO were determined with a Licox probe. Patients had HBO for 30 minutes (n = 6) to 40 minutes (n = 1). HBO was continued because the pO2 had not reached a steady state after 30 minutes. After decompression, patients ventilated pure oxygen under normobaric conditions and the course of the pO2 was further measured over about 15 minutes.

Results: Prior to HBO, the median tumor pO2 in the Eppendorf histography was 8.6 ± 5.4 mm Hg (range 3–19 mm Hg) and the pO2 measured with the Licox probe was 17.3 ± 25.5 mm Hg (range 0–73 mm Hg). The pO2 increased significantly during HBO to 550 ± 333 mm Hg (range 85–984 mm Hg, p = 0.018). All patients showed a marked increase irrespective of the oxygenation prior to HBO. The maximum pO2 in the tumor was reached after 10–33 minutes (mean 17 minutes). After leaving the hyperbaric chamber, the pO2 was 282 ± 196 mm Hg. All patients maintained an elevated pO2 for further 5–25 minutes (138 ± 128 mm Hg, range 42–334 mm Hg, p = 0.028 vs the pO2 prior to HBO).

Conclusions: Hyperbaric oxygenation resulted in a significant increase in the tumor oxygenation in all seven investigated patients. A significant increase at the point of measurement could be maintained for several minutes after decompression and after leaving the hyperbaric chamber.

Key Words: Head and neck cancer · Hypoxia · Hyperbaric oxygenation

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erstoffatmung über 5–25 Minuten signifikant erhöht (138 ± 128 mm Hg, Spanne 42–334 mm Hg, p = 0.028 gegenüber dem pO2 vor HBO).

**Schlussfolgerungen:** Hyperbare Oxygenierung führte bei diesen Patienten zu einer signifikanten Verbesserung der Oxygenierung, die über Minuten nach der Dekompressionsphase anhielt. Für eine klinische Studie könnte deshalb ein strahlensensibilisierender Effekt auch dann erreicht werden, wenn die Bestrahlung nicht simultan, sondern unverzüglich nach einer HBO erfolgt.

**Schlüsselwörter:** Kopf-Hals-Tumoren · Hypoxie · Hyperbare Oxygenierung

**Introduction**

The presence of hypoxic cells in solid cancers and their possible impact on the response of tumors to radiotherapy has been demonstrated in numerous studies over the past decades. Several recent clinical investigations with advanced techniques for measuring hypoxia have supported a prognostic impact of hypoxia in various cancer sites, especially in head and neck cancers [2, 6, 10, 19, 22]. Hypoxic cancer showed a poor response to radiotherapy. Modulation of tumor hypoxia has therefore again gained clinical interest [26].

Hyperbaric oxygenation (HBO) offers one approach to overcome hypoxia. Several randomized studies investigating HBO as radiosensitizer were performed 30–40 years ago [1, 4, 5, 7, 8, 11, 13–15, 21, 23–25, 27]. This approach was left because of technical problems and because pharmacological targeting of hypoxic cells by hypoxic cell sensitizers was considered more effective at that time. A recent meta-analysis of the historical studies, however, suggests an improvement in local control in head and neck cancers by the use of additional HBO [20].

It is currently not possible to combine modern radiation therapy techniques (e.g. individual patient fixation, 3D-conformal therapy) simultaneously with hyperbaric oxygenation. Recent experimental studies in animals, however, suggest that the oxygenation parameters in tumors may not only improve during HBO, but also maintain improved for minutes after HBO [16]. This would suggest that a possible clinical benefit by HBO might be expected if the radiation is administered immediately after HBO. A clinical study in glioblastomas supports this hypothesis [17].

For to investigate the changes of tumor tissue oxygenation during HBO, we have performed pO2 measurements in a small number of selected patients with head and neck cancers under HBO. The objective was to determine in how far changes in the oxygenation occur and whether a possible improvement of oxygenation parameters is maintained after HBO. The study was designed as a “proof of principle” investigation.

**Patients and Method**

Seven patients (five male, two female, age 51–63 years) with squamous cell cancers of the head and neck were investigated (six primaries, one local recurrence). All patients underwent oxygenation measurements with the Eppendorf histograph. The method and results have been recently described [2, 3, 9]. Sites of measurement were enlarged cervical lymph nodes (n = 5), the primary tumor (n = 1) and the local recurrence (n = 1).

Immediately prior to the start of radiotherapy, patients underwent one HBO session in a hyperbaric chamber (100% O2 at 2.5 atm) for one time. The scheduled time for the HBO session was 30 minutes. In one patient, the duration of HBO was extended to 40 minutes because the tumor showed steady increase in the oxygenation after 30 minutes. Prior to HBO, a permanent oxygen probe (Licox probe) was inserted into the tumor (same site as used for pO2 histography) under CT guidance. The Licox probe allows continuous measurement of the oxygen partial pressure in a small volume. After decompression, patients ventilated pure oxygen under normobaric conditions and the course of the pO2 was further measured over about 15 minutes.

**Results**

The raw data and a summary of the results are given in Table 1. The median tumor pO2 in the Eppendorf histography was 8.6 ± 5.4 mm Hg (range 3–19 mm Hg). Five patients had a median pO2 ≤ 10 mm Hg. The frequency of hypoxic readings with a pO2 < 5 mm Hg ranged from 5 to 51% (mean: 33 ± 18%).

The pO2 measured with the Licox probe was 17.3 ± 25.5 mm Hg (range 0–73 mm Hg) prior to the start of HBO. The pO2 increased significantly during HBO to 500 ± 333 mm Hg (range 85–984 mm Hg, p = 0.018, Wilcoxon test). All patients showed a marked increase irrespective of the oxygenation prior to HBO (Figure 1). The increase was 85–984 mm Hg (mean 533 ± 333 mm Hg). The maximum pO2 in the tumor was reached after 10–33 minutes (mean 17 minutes).

After the end of the decompression period when leaving the hyperbaric chamber, the pO2 was 282 ± 196 mm Hg. All patients maintained an elevated pO2 over further 5–25 minutes during ventilation of 100% oxygen under normobaric conditions (138 ± 128 mm Hg, range 42–334 mm Hg, p = 0.028 vs the pO2 prior to HBO, Wilcoxon test).

A simultaneous transcutaneous measurement of the pO2 in normal tissue was also performed. The maximum cutaneous pO2 during HBO ranged from 765 to 1610 mm Hg and did not correlate with the tumor pO2.