HYPERBARIC OXYGEN THERAPY OF BURNS

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Treatment results considering integument and upper respiratory tract burns are unsatisfactory. The introduction of novel management methods in case of burn wounds, infections of the injured area, and immunity disturbances, lead towards a significant reduction in mortality. In spite of the above-mentioned conservative therapy of burn disease often leads towards patient death.

The search for new therapeutic methods, technically justified is connected with the introduction of hyperbaric oxygen in the treatment of burns. Oxygen is the basic energetic material without which life ceases to exist. Disturbances in the supply of vascular oxygen are characteristic in case of extensive burns. The idea of introducing significant amounts of oxygen by means of another method is tempting. Oxygen directly transported through tissues by means of increased pressure, without the participation of hemoglobin is favorable, considering tissue anoxia. Edward Teller, the father of the hydrogen bomb underlined the role of hyperbaric oxygen in the transportation of free molecular oxygen to the cells, which enables its metabolic use without energy exchange, even in case of circulatory insufficiency (1).

History

Mention of hyperbaric oxygen therapy was already found in the 5-th century B.C. In 1662, the British clergyman-Henshaw constructed the first oxygen chamber called the domicilium. Compressed air (21% of oxygen) was used in the treatment of infections, scurvy, arthritis, and rickets (2).

With the discovery of oxygen hyperbaric chambers were used in the treatment of leprosy. In the 20-th century, hyperbaric oxygen chambers were created, being applied in the treatment of patients with heart diseases. Military medicine created foundations for the treatment of decompression disease.

Boerema was the father of contemporary oxygen therapy introducing hyperbaric oxygen in the fifties of the 20-th century, as adjunctive treatment in case of congenital heart diseases (3). Brummelkamp in 1959 observed the inhibition of anaerobic infections following hyperbaric oxygen therapy (4). Smith, Sharp and co-authors in 1962 applied hyperbaric oxygen therapy in case of severe carbon dioxide intoxication (5, 6).

The use of the above-mentioned method in case of burn therapy can be connected with the observations of Wad and co-authors, who, during treatment of carbon dioxide intoxication observed much faster healing of II° burns, considering coal miners (7). Gruber in 1970, based on numerous experimental investigations on rats demonstrated tissue anoxia in the area of the deep burns, which inclined towards the use of hyperbaric oxygen therapy (8).

The first hyperbaric chambers were used in the treatment of decompression disease in divers. Nowadays, the above-mentioned disease entity is the main indication for such manage-
The technological development enabled to construct safe chambers and search for the therapeutic indications of numerous diseases, and complications of hyperbaric oxygen therapy. Many hyperbaric therapy centers were created, especially in the USA. Considering the northern states of the United States there were 83 active hyperbaric therapy centers during the period between 1971 and 1978. Nowadays, there are more than 260 such centers, mostly treating patients with decompression disease and air embolisms, due to injuries sustained during diving, as well as carbon dioxide intoxication, osteitis and osteoradionecrosis (9). In Poland, during the seventies of the past century numerous experimental investigations were undertaken (prof. Tadeusz Orłowski) evaluating the influence of hyperbaric oxygen therapy on the healing of skin grafts (10), burn wounds (11), and coagulation system in case of burns (12). Other studies concerned indications towards hyperbaric oxygen therapy and treatment of gas gangrene wounds (13-16).

The authors from Gdańsk also investigated the application of hyperbaric oxygen therapy in the management of burn wounds (17).

Russian hyperbaric chambers used in Poland during those days were of poor technological quality. Explosions and fires were often observed, although luckily not in Poland, mostly connected with personnel neglect and mistakes.

The clinical application of these chambers in the management of burn wounds during the seventies of the past century, in Poland, did not exist. This was connected with the imperfection of the equipment.

Mechanism of action

The concentration of oxygen at sea level amounts to 0.3 ml in 100 ml of blood. Normal tissue perfusion is observed after the extraction of 5-6 ml of oxygen from 100 ml of blood. Respiration by means of 100% oxygen under normal pressure increases the amount of diluted blood oxygen by five-fold (1.5 ml in 100 ml), while in case of 3 atmospheres of pressure-6 ml per 100 ml (18, 19, 20).

Hyperbaric oxygen is dissolved in the human plasma with its level remaining quite high. Tissue and skin pO2 measurements demonstrated that the oxygen content is 10-fold greater, as compared to respiration in case of normal pressure. Hyperoxia, that is increased oxygenation, leads towards generalized contraction of arterioli without the deterioration of oxygen distribution (21, 22).

The primary influence of hyperbaric oxygen therapy on the human organism is as follows:

– hyperoxygenation,
– decreased number of gas alveoli in blood (23).

Increased tissue oxygenation (hyperoxygenation) exerts influence on the increased volume of tissue oxygen and extracellular tissue saturation. Thus, its application in case of oxygen transportation disturbances to the cells, due to decreased number or lack of oxygen carriers, anemia, cachexia, reduced microcirculatory vascularization, such as in case of crush wounds, increased pressure fascial space syndromes, endangered tissue flaps, and tissue edema, which reduce oxygenation (24, 25).

The decompression disease and air embolisms are connected with the release of alveoli to the blood. According to Boyle’s law the volume of gas in a closed space is reversely proportional to the pressure exerted by the gas. Higher pressure than atmospheric reduces gas alveoli preventing from the formation of new alveoli. The above-mentioned is used in the treatment of decompression disease and air embolisms.

During hyperbaric oxygen therapy the following are observed:

– angiogenesis, which is of significant value in case of ischemia of chronic wounds and post-radiation necrosis, facilitating natural tissue alimentation (26, 27);

– vascular contraction, which reduces stromal fluid transudation and edema development. A favorable effect would be desired in case of crush syndromes, burns, and directly after the injury (28);

– aerobic bacteria growth inhibition (4). Oxygen in case of increased pressure is bactericidal for some anaerobic bacteria (Clostridium perfringens) (29) and bacteriostatic for some Escherichia and Pseudomonas species (30, 31).

– increased proliferation of fibroblasts (32, 33).

– increased activity of free radical leucocytes (34). Local ischemia favors inflammation and reduces the antibacterial defense system through the secretion of free oxygen radicals by neutrophils (PPM). Hyperbaric oxygen therapy reconstructs the ability to secrete killer radicals (34, 35);

– blockage of toxins, which is characteristic of Clostridium alpha-toxins (36, 37);
synergistic activity of oxygen with selected antibiotics, being indispensable for transmembrane transport. The above-mentioned concerns fluoroquinolones, amphotericin B and aminoglycosides (38);

the favorable effect in case of the reperfusion syndrome. An important role is attributed to the activity of neutrophils on the walls of ischemic vascular microcirculation in the reperfusion syndrome, being characteristic of “clamping shock”, and increased tissue destruction in case of the crush syndrome, increased pressure fascial space syndrome, and newly created skin flaps. The above-mentioned syndrome also appears in case of deep burn wounds when the initially ischemic tissue is suddenly subjected to fluid saturation by means of fluid resuscitation. Reperfusion trauma is mainly caused by the release of free oxygen radicals from PPM adhering to the wall of the vascular microcirculation (39, 40). A significant role is attributed to the prevalence of the intercellular adhesive molecule ICAM1 over cellular nitrogen oxide (NO), which stimulates PPM towards endothelial adherence (41, 42). According to Buras and co-authors the favorable effect of hyperbaric oxygen therapy in case of the reperfusion syndrome would consist in the attenuation of ICAM1 formation by means of increased cellular NO production (43);

reduced tissue edema. Tissue edema in case of burn wounds leads towards fluid displacement in the human organism and increased tissue pressure, impairing microcirculation and thus, oxygen exchange. The extent of tissue damage following thermal injuries is a dynamic phenomenon characterized by primary tissue necrosis and vascular disturbances. The stasis zone, apart from xerosis is also subjected to necrosis, and in the hyperemic zone the distribution of oxygen is disturbed. This mechanism would most likely be responsible for the therapeutic effect of oxygen in case of increased pressure. Vascular contraction in the necrotic zone decreases the risk of generalized edema and reduces the fluid demand. Oxygen supply would be possible by means of its tissue distribution. Experimental investigations on mice demonstrated a significant reduction of generalized burn edema after hyperbaric oxygen therapy. However, one should underline the important fact that oxygen therapy was initiated directly after the injury (44);

inhibition of tissue damage. Nylander and co-authors demonstrated that numerous hyperbaric chamber sessions increased the ATP level and decreased the lactate level. The reduction of phosphorylase activity, which is a sensitive indicator of muscular cell damage, was observed following hyperbaric oxygen therapy (45). Experimental animal study results often confirmed the above-mentioned observations, although many did not show the favorable effect of hyperbaric oxygen therapy on the healing of burn wounds. Ikeda and co-authors noted a reduction of post-radiation edema (46). Ketchum and co-authors in 1967 observed a reduction in the healing time of burn wounds and number of infections (47), which was also confirmed by Härtwig and co-authors in 1974 (48). Bleser and co-authors observed a reduction of burn shock symptoms and four-fold increased survival in burned animals (surface of 30%), as compared to animals not subjected to hyperbaric oxygen therapy (49, 50);

inhibition of early burn wound conversion. The role of hyperbaric oxygen therapy in the inhibition of early burn necrosis conversion was underlined by Germonpre and co-authors. Considering the area of necrosis, oxygen supplementation by means of tissue saturation would be independent of vascular damage, being partially connected with fluid resuscitation leading towards symptoms of “clamping shock” and ensuing local complications increasing necrosis. However, there is lack of an unequivocal answer as to the main cause of conversion during shock. Free oxygen radicals, inflammatory cytokines, and stromal hemodynamic conditions play the major role. Experimental studies performed on rats subjected to burns of 5% of their body surface demonstrated an inhibition of wound necrosis following hyperbaric oxygen therapy and piracetam administration (51). A similar effect was observed by Kaiser and co-authors who demonstrated subcutaneous tissue edema reduction after scalding (52). On the other hand, Perrins observed no positive influence of hyperbaria on burn wounds (53).
Clinical studies

An encouraging and beneficial influence of hyperbaric oxygen therapy on destruction processes in case of burn wounds presented in experimental studies lead towards the initiation of clinical trials confirming the efficacy and need of burn wound management by means of hyperbaric chambers.

Many investigations were undertaken, considering the influence of hyperbaric oxygen therapy on numerous concomitant diseases. Treatment results in case of animal and human burn wounds are often contradictory. Controlled investigations in humans are limited. The postulated favorable effect of hyperbaric oxygen therapy in case of burn wounds consists in the reduction of edema following vascular contraction, as a result of hyperoxia, collagen formation, and improved phagocyte bactericidal activity.

During the past two decades one can observe significant progress in the management of burn wounds including improved respiratory care, local and general antibiotic therapy optimization, early wound excision and parenteral nutrition. The question whether hyperbaric oxygen therapy in addition to conventional treatment, considering burn centers, is beneficial, remains the key issue.

In 1974, Hart in his clinical trials demonstrated that hyperbaric oxygen therapy decreases the fluid demand in case of shock, accelerates the healing process, and reduces mortality, in comparison to the non-treated group of patients (61).

According to data presented by Merol and co-authors in 1978, 37 patients with burn wounds showed faster healing of burn wounds, as compared to non-treated wounds (62).

Lee et al. investigated patients, aged between 15 and 45 years with the burned surface ranging between 35-70%, demonstrating that the mortality index in case of patients subjected to hyperbaric oxygen therapy amounted to 6.8%, in comparison to the non-treated group, where mortality amounted to 14.8% (63).

The study undertaken by Niegoda and co-authors from the Department of Hyperbaric Medicine, Travis Air Force Base, United States, is a copy of the study presented by Hammarlund and co-authors from Helsinborg, Sweden. The randomized study concerned 12 volunteers subjected to hyperbaric oxygen the-
therapy, due to ultraviolet radiation burns. Hyperbaric oxygen therapy reduced the wound area, its congestion and the amount of exudate. Epidermization lesions were not observed. Thus, the authors consider hyperbaric oxygen therapy to be beneficial in the management of superficial skin wounds (64). The Swedish authors came to the same conclusions (65).

Niu and co-authors demonstrated a statistically significant decrease of mortality in case of 266 severely burned patients, who were additionally subjected to hyperbaric oxygen therapy, as compared to the 609 patients without the above-mentioned therapy. The duration of therapy was similar in both groups (66).

According to Cianci and co-authors hyperbaric oxygen therapy was responsible for the statistically significant decrease in the duration of the hospitalization, without an increase in treatment costs, considering patients with burn wounds between 18%-39% of their body surface (67).

The same author analysed the therapeutic costs in case of patients with burn wounds comprising 19%-50% of their body surface. Hyperbaric oxygen therapy significantly shortened the hospitalization and the number of therapeutic procedures, which enabled to save 31 600 $ in every patient (68).

Grossman and co-authors described the treatment of 800 burn patients demonstrating that hyperbaric oxygen therapy is the only adjuvant method in case of standard resuscitation and does not replace proper management. However, they observed decreased morbidity and mortality index, and shorter hospitalization, as compared to previously treated burn patients (69).

Waissbren and co-authors demonstrated significant harmfulness of hyperbaric oxygen therapy. They observed no favorable effect of the above-mentioned method on the duration of therapy, average number of patient deaths, and hospitalizations. However, the authors observed increased frequency of renal damage and positive bacteriological blood cultures under the form of sepsis (70).

According to Leach and co-authors there are no convincing data as to the application of hyperbaric oxygen therapy in case of burn wounds. Randomized, controlled studies demonstrated that the average hospitalization period, use of skin grafts and mortality, were similar to patients that were not subjected to hyperbaric oxygen therapy. Additionally, adverse effects which are usually moderate can be life-threatening after hyperbaric oxygen therapy. Moreover, the cellular, biochemical and physiological mechanisms of hyperbaric oxygen therapy are not fully accepted (23).

Brannen and co-authors performed a randomized evaluation of 125 burn patients admitted to the hospital within 24 hours of trauma, comparing their age, extent of the burn wound and presence or absence of an inhalatory injury. Patients were subjected to hyperbaric oxygen therapy by means of 2 atmospheres for a period of 90 minutes, twice daily, minimum of 10 sessions or maximum of one session per % of the surface of their burn wound. The control group was treated similarly, hyperbaric oxygen therapy excluded. No statistically significant differences between both groups were observed, considering mortality, number of operations, and duration of the hospitalization. In case of this large clinical trial the beneficial effect of hyperbaric oxygen therapy, considering burn wounds was not proved (71).

There is chaos considering literature data on hyperbaric oxygen therapy. On one hand, numerous experimental investigations undertaken on animals demonstrated the influence of the above-mentioned method on tissue oxygenation, level of free oxygen radicals, tissue edema, muscular level of high-energy compounds, stasis zone in the burned tissue, healing of deep burn wounds, fluid demand in case of burn shock, inflammation and mortality. Thus, one can observe the favorable effect of the above-mentioned therapeutic method. On the other hand, clinical study results significantly differ considering the influence of hyperbaric oxygen therapy on mortality, duration and costs of treatment, as well as the actual value of the method in case of burn wounds.

Hyperbaric chambers, both for a single patient and those seating many are expensive and are not produced in Poland. Many centers in our country are interested in hyperbaric oxygen therapy, which seems to be simple and easy. However, does the actual therapeutic value of the method justify the need to equip the few burn centers in Poland with such hyperbaric chambers?

Based on World Health Organization data, one can find a report of the Regional Committee in Sydney, Australia, dated September 22-26, 1997 (48 sessions), which demonstrated that
hyperbaric oxygen therapy is an example of a medical technology developing rapidly, quite promising, although data concerning its efficacy and cost-effectiveness are unconvincing (72).

In Great Britain, before creating a hyperbaric oxygen therapy center in the West Midlands scientific literature concerning the above-mentioned method was followed through. Since 1968, only 13 randomized studies were found, which showed no convincing data. Apart from the established indications towards hyperbaric oxygen therapy, which comprise decompression disease, and air and gas embolisms there is no convincing evidence of the efficacy of the method in case of burn wounds (73).

The European Consensus Conference recommends hyperbaric oxygen therapy only as an optional method in the treatment of burns (lowest in the 3-scale HBO indications), suggesting its application only in case of extensive burns, exceeding 20% of the body surface (74).

During the last European conference dedicated to hyperbaric oxygen therapy (2004), the method was considered as optional in the management of deep burn wounds, exceeding 20% of the body surface. Thus, the above-mentioned method is not a lifesaver. The method is considered as supportive therapy without scientific justification. In case of less severe burns hyperbaric oxygen therapy is not recommended (75).

The above-mentioned is often in contradiction to the belief of many applying the method. However, scientific and literature data are scarce and poorly elaborated, considering the methodology. Thus, limited indications towards the application of the method. Cochrane’s last analysis concerning treatment of burn wounds confirmed the above-mentioned. When analyzing literature data randomized studies were considered as most valuable, comparing patients subjected to hyperbaric oxygen therapy and those not treated by means of the method. Four such studies were found, although only two satisfactorily fulfilled the assumed conditions and did not confirm the efficacy of hyperbaric oxygen therapy. The above-mentioned is insufficient to implement hyperbaric oxygen therapy in the management of burn wounds. Only a few studies are methodologically correct (76).

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