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REVIEW / DERLEME

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Hyperbaric Oxygen Therapy in Crush Injuries and Compartment Syndrome

Crush Yaralanmalar ve Kompartman Sendromunda Hiperbarik Oksijen Tedavisi

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Abstract

Hyperbaric oxygen (HBO) therapy is a medical treatment method based on breathing 100% oxygen from a mask, hood placed over the head, endotracheal tube, or space at pressures higher than (1 atmosphere absolute =760 mmHg) in completely closed single or multi-person hyperbaric chambers. The most common emergencies in which HBO therapy is used are carbon monoxide poisoning and decompression sickness. However, acute traumatic ischemias such as crush injury and compartment syndrome that cause tissue hypoxia are among the indications for effective HBO therapy. This review aims to share general information about HBO therapy and its use in crush injury and compartment syndromes. Thus, the role of HBO therapy in reducing morbidity and mortality when used together with necessary surgical and medical treatments has been emphasized.

Keywords: Hyperbaric oxygen therapy, crush injury, compartment syndrome, fasciotomy, amputation

Öz

Hiperbarik oksijen (HBO) tedavisi, tamamen kapalı tek ya da çok kişilik basınç odalarında, (1 atmosphere absolute =760 mmHg) daha yüksek basınçlarda, maske, başlık, endotrakeal tüp ya da ortamdan %100 oksijen solutulması esasına dayalı medikal bir tedavi yöntemidir. HBO tedavisinin en sık kullanıldığı durumlar karbonmonoksit zehirlenmesi ve dekompresyon hastalığıdır. Bununla birlikre crush yaralanma ve kompartman sendromu gibi doku hipoksisine neden olan akut travmatik iskemiler de HBO tedavisinin etkin olarak kullanıldığı durumlar arasındadır. Bu derlemede HBO tedavisi hakkında genel bilgilerin ve crush yaralanması ve kompartman sendromlarında kullanımına ait bilgilerin paylaşılması amaçlanmıştır. Bu sayede HBO tedavisinin gerekli cerrahi ve medikal tedavilerle birlikte kullanıldığında morbidite ve mortaliteyi azaltmadaki rolü vurgulanmıştır.

Anahtar Kelimeler: Hiperbarik oksijen tedavisi, crush yaralanma, kompartman sendromu, fasiyotomi, ampütasyon

Introduction

Hyperbaric oxygen (HBO) therapy is a treatment method based on intermittent breathing of 100% oxygen from a mask, hood placed over the head, endotracheal tube, or environment at pressures higher than 1 [atmosphere absolute (ATA) =760 mmHg] in completely closed single or multi-person hyperbaric chambers (Figures 1, 2). The pressure should be at least 1.4 ATA or more for clinical effect[1]. Indications determined by the Ministry of Health in Turkey are decompression sickness and arterial gas embolism, carbon monoxide and cyanide poisoning, necrotizing soft tissue infections, necrotizing fasciitis, clostridial myonecrosis (gas gangrene), crush injury, compartment syndrome and other acute traumatic ischemias, diabetic and non-diabetic chronic ulcers, thermal burns, radiation injuries, chronic

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refractory osteomyelitis, sudden and painless vision loss, sudden deafness, avascular necrosis, and some brain abscesses[1,2]. Each treatment is administered for 90-120 minutes, at pressures between 2 and 3 ATA and in one or more sessions per day depending on the condition of the disease[3].

The use of HBO in modern medicine began in 1937 with the treatment of decompression in patients by Benkhe and Shaw. Scientific societies named the European Undersea Biomedical Society were established in 1965 and the Undersea Medical Society in 1967. In Turkey, studies on underwater medicine started in the same years.

The Marine and Undersea Medicine Department was established by Professor Maide İmşit at İstanbul University, İstanbul Faculty of Medicine in 1981, and it was transformed into a department in 1989. The name of the specialty and department was changed to "Undersea Medicine and Hyperbaric Medicine". Currently, HBO therapy services are provided in 54 secondary and tertiary hospital centers in public and private sector in Turkey.

Mechanism of HBO Therapy

The HBO treatment session consists of three phases. The first stage is called diving (compression), in which the ambient pressure is increased until the treatment pressure. The second stage is the treatment stage in which the patient breathes 100% oxygen. The last stage is the stage where the pressure is reduced to 1 ATA and is called ascent or decompression.

HBO therapy exerts its effect through the direct (mechanical) effect of high pressure and increased partial pressure of oxygen.

Mechanical Effect of HBO

According to Boyle's gas law, at a constant temperature, the pressures and volumes of gasses are inversely proportional. With increasing pressure, the volumes of gasses in the circulation and tissues decrease. In addition, the surface tension of the bubbles is inversely proportional to their size. The mechanical effect of pressure is best observed for treating arterial or iatrogenic gas embolisms and decompression sickness. In these diseases that require urgent treatment, tissue perfusion can be restored as the bubbles shrink and deflate under high pressure[4].

Figure 1. Monoplace pressure chamber (Hipertech, Turkey)

Figure 2. Multiplace pressure chamber at the İzmir City Hospital, Clinic of Underwater and Hyperbaric Medicine, Baroks, Turkey

Effects of Dissolved Oxygen

Antihypoxic Effect

The second effect of HBO treatment is an increase in partial oxygen pressure. According to Henry's gas law, there is a direct proportionality between the partial pressures of gasses and their solubility at a constant temperature. Even if the amount of oxygen in the breathing air is increased under normal conditions, it is not possible to increase the oxygen carried to the tissues by hemoglobin. However, because of the increase in the partial pressure of inhaled oxygen under hyperbaric conditions, the amount of oxygen dissolved in the plasma also increases (Figure 3)[4,5]. By breathing 100% oxygen at 3 ATA, the dissolved oxygen in 100 mL of blood increased to 6.8 mL (1.5) (Table 1). Thus, without the need for oxyhemoglobin, sufficient oxygen is provided to meet the needs of the tissues. This effect of HBO is particularly evident in cases of carbon monoxide intoxication and cyanide poisoning.

Antiedema Effect

The antiedema effect of HBO occurs due to both the reduction of vasoconstriction and total perfusion and the prevention of fluid transfer to the extravascular compartments by fixing the increased permeability due to hypoxia[6].

Antitoxic Effect

HBO has an antitoxic effect by inhibiting the production of toxins or their effect on metabolism. It shows its effect on CO poisoning through CO metabolism. Owing to the high partial pressure of oxygen obtained with HBO, the refunction of the mitochondrial respiratory chain is ensured by the dissociation of CO from hemoproteins and the prevention of tissue hypoxia[4,5]. The best example of this is the inhibition of alpha toxin production by *Clostridium perfringens*, which is the most common cause of gas gangrene.

Antibacterial Effect

HBO treatment achieves its antibacterial effect in three different ways. It acts directly on bacteria, increases the effect of antibiotics such as aminoglycoside, fluoroquinolone, vancomycin, and teicoplanin, and improves the immune system response by increasing the antibacterial functions of polymorphonuclear leukocytes and macrophages. HBO treatment has a bactericidal effect on anaerobic bacteria and a bacterşostatic effect on aerobic bacteria[7,8].

Effect on Wound Healing

Wound healing occurs in the stages of inflammation, proliferation, and remodeling/maturation. The main problems associated with delayed healing wounds are

Table 1. Effect of pressure on arterial O_2[5]

Total pressure		Ideal dissolved oxygen content (vol%)	
ATA	**mmHg**	**Breathing air**	**Berahting 100% O_2**
1	760	0.32	2.09
1.5	1140	0.61	3.26
2	1520	0.81	4.44
2.5	1900	1.06	5.62
3	2280	1.31	6.80
4	3040	1.80	O_2 not administered at pressure >3 ATA
5	3800	2.30	
6	4560	2.80	

ATA: Atmosphere absolute

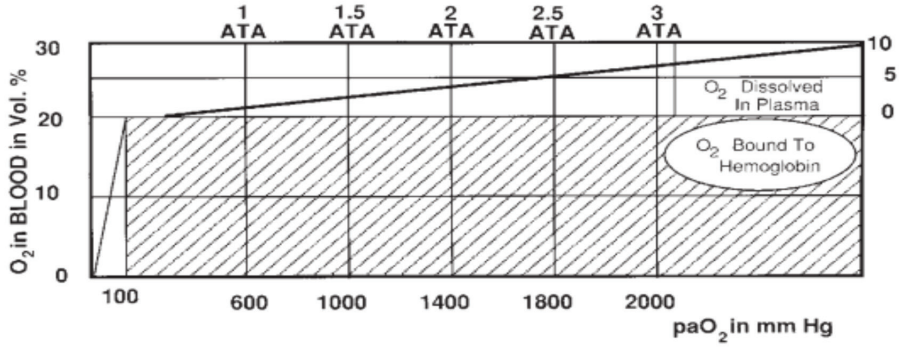

Figure 3. Oxygen uptake curve under HBO in humans[5]

HBO: Hyperbaric oxygen

tissue hypoxia and infections. HBO therapy increases the oxidative and non-oxidative functions of neutrophils during the inflammatory phase of wound healing[8]. During the proliferation stage, it provides the necessary vascularization for fibroblasts and endothelial cells to form the tissue matrix and perform neovascularization. With HBO therapy, the synthesis, release, and stabilization of collagen are performed. Because of the increase in tissue hydroxyproline, ATP, and phosphocreatinine levels with HBO, the fibroblast-collagen matrix support required for neovascularization is provided. In addition, by increasing the bactericidal activities of leukocytes, optimum conditions for wound healing are obtained. In the maturation and restructuring phase, the formation of cross-links between collagen fibers and the strengthening of connective tissue are also achieved by HBO therapy[9].

Indications for HBO Therapy

Indications for HBO therapy are determined by the European Committee for Hyperbaric Medicine and the Undersea and Hyperbaric Medical Society, and consensus reports and indications are published with evidence levels (Tables 2, 3)[1,10]. Indications for HBO therapy determined by the "Regulation on Private Health Institutions Applying HBO Therapy" published by the Ministry of Health in Turkey in 2001 are given in Table 4[2].

Table 2. Recommendations on the indications accepted for HBOT (there was no Level A evidence)[10]

Condition	Level of evidence		Agreement level
Type 1	**B**	**C**	
CO poisoning	X		Strong agreement
Open fractures with crush injury	X		Strong agreement
Prevention of osteoradionecrosis after dental extraction	X		Strong agreement
Osteoradionecrosis (mandible)	X		Strong agreement
Soft tissue radionecrosis (cystitis, proctitis)	X		Strong agreement
Decomprssion illness		X	Strong agreement
Gas embolism		X	Strong agreement
Anaerobic or mixed bacterial infections		X	Strong agreement
Sudden deafness	X		Strong agreement

Side Effects and Risks of HBO Therapy

The side effects of HBO therapy include high-pressure side effects and high-pressure oxygen inhalation toxic effects. The most common side effect that we encounter in our daily practice is middle ear barotrauma due to high pressure. Ear equalization maneuvers are taught to the patient before the

Table 2. Continued

Condition	Level of evidence		Agreement level
Type 2			
Diabetic foot lesions	X		Strong agreement
Femoral head necrosis	X		Strong agreement
Compromised skin grefts and musculo-cutaneous flaps		X	Strong agreement
Central retinal artery occlusion		X	Strong agreement
Crush injury without fracture		X	Agreement
Osteoradionecrosis (bones other than mandible)		X	Agreement
Radio-induced lesions of soft tissues (other than cystitis and proctisis)		X	Agreement
Surgery and implant in irradiated tissue (preventive treatment)		X	Agreement
Ischemic ulcers		X	Agreement
Refractory chronic osteomyelitis		X	Agreement
Burns, 2nd degree more than 20% BSA		X	Agreement
Pneumatosis cystoides intestinalis		X	Agreement
Neuroblastoma, stage IV		X	Agreement
Type 3			
Brain injury (acute and chronic TBI, chronic stroke, post anoxic encephalopathy) in highly selected patients		X	Agreement
Radio-induced lesions of larynx		X	Agreement
Radio-induced lesions of CNS		X	Agreement
Post-vascular producer reperfusion sydrome		X	Agreement
Limb replantation		X	Agreement
Selected non-gealing wounds secondary to systemic processes		X	Agreement
Sicckle cell disease		X	Agreement
Interstitial cystitis		X	Agreement

CNS: Central nervous system, HBOT: Hyperbaric oxygen therapy, BSA: Body surface area, TBI: Traumatic brain injury

Table 3. Uses of HBO approved by Undersea and Hyperbaric Medical Society, USA[5]
Air or gas embolism
Carbon monoxide poisoning and carbon monoxide poisoning complicated by ciyanide poisoning
Clostridial myonecrosis (gas gangrene)
Compromised skin grafts and flaps
Crush injury, compartment syndrome and other acute traumatic ischmias
Decompression sickness
Enhanement of healing in selected problem wounds
Exceptional anemia resülting from blood loss
Intracranial abcess
Necrotizing soft tissue infections (of subcutaneous tissue, muscle or fascia)
Radiation tissue damage (osteoradionecrosis)
Refractory osteomyelitis
Sensory neural hearing loss
Skin grafts and flaps
Thermal burns
HBO: Hyperbaric oxygen

Table 4. Indications for hyperbaric oxygen therapy in Turkey[2]
Decompression sickness
Air or gas embolism
Carbon monoxide, cyanide poisoning, acute smoke inhalation
Gas gangrene
Necrotizing infections of soft tissue (subcutaneous, muscle, fascia)
Crush injuries, compartment syndrome and other acute traumatic ischemia
Enhancement of healing in selected problem wounds (diabetic and non-diabetic)
Chronic refractory osteomyelitis
Excessive blood loss
Radiation necrosis
Skin grafts and flaps (compromised)
Thermal burns
Brain abscess
Anoxic encephalopathy
Sudden sensory neural hearing loss
Retinal artery occlusion
Acute osteomyelitis of the skull bones, sternum and vertebrae

treatment, and the patient's ear equalization is ensured by the guidance of the assistant personnel accompanying the treatment. However, the presence of edema and congestion in the respiratory tract may prevent equalization. In such cases, treatment may be interrupted until the patient recovers. In uncooperative children and unconscious patients, prophylactic tympanocentesis may be required to avoid barotrauma.

Lung barotrauma occurs either because of the expansion of the trapped air in the decompression phase due to lesions such as cysts, caverns, bullae, and blebs in the lung or because of the patient's breathlessness during the exit phase of the treatment. Pulmonary barotraumas can be observed as alveolar rupture, pneumothorax, pneumomediastinum, subcutaneous emphysema, and gas embolism[3,11,12]. To prevent these side effects, the patient should be evaluated with respiratory system examination and chest X-ray before treatment. In suspected cases, further investigations may be required.

Inhalation of 100% oxygen at pressures of 2 ATA or higher may produce toxic effects on the central nervous system (CNS). This effect manifests itself in the form of tonic-clonic contractions in the patient. To avoid this side effect, air breaks are administered in HBO therapies. In various studies, it has been reported that the frequency of CNS oxygen toxicity is 1-6/10000 HBO therapy sessions[12,13]. Prodrome symptoms can be observed in less than half of the cases. These include muscle twitching, fixed gaze in the eyes, auditory hallucinations, tunnel vision, restlessness, and anxiety[12]. As soon as the signs of toxicity are observed, the patient's oxygen mask is removed, the cabin pressure is kept constant, and the patient is allowed to breathe from the ambient air. Thus, the symptoms regress. Oxygen toxicity does not cause sequelae. The subsequent treatment of the patient can be continued as planned. However, as a precaution, longer air breaks can be given for these patients[11-13]. Pulmonary oxygen toxicity does not occur with routine HBO therapy. It is usually seen in long-term treatment scedules such as decompression sickness or arterial gas embolism. Symptoms begin with substernal pain on deep inspiration. With continued exposure, pleuritic chest pain, cough, and dyspnea occur. Symptoms disappear with the cessation of oxygen exposure[11,13].

Myopia occurs at a rate of 25-100% in long-term treatments with HBO and reverts within a few weeks after treatment is stopped[13]. Cataract is a very rare side effect. Claustrophobia is mostly seen in single rooms. Although anxiety is rare in

multi-person pressure chambers, very few require sedation. The presence of auxiliary personnel in the pressure room is a factor preventing claustrophobia.

Contraindications to HBO Therapy

The absolute contraindication for HBO is untreated pneumothorax. Relative contraindications include conditions such as borderline heart failure, pregnancy, uncontrolled asthma, obstructive pulmonary diseases, epilepsy, asymptomatic lung lesions on X-ray, lesions such as bulla-bleps that may cause air trapping, and a history of chest or ear surgery[3,11,12]. Pacemakers produced recently can generally be used safely under pressures below 3 ATA. However, the reliability of the batteries of pacemakers under pressure should be checked from the user manuals.

Crush Injuries

Crush injuries are serious injuries that result from the exposure of any part of the body to high-energy trauma or pressure, such as dents, traffic accidents, or gunshot wounds. In these injuries, at least two of the bone, soft tissue, nerve, and vascular structures are affected, and the viability of the affected tissue is threatened. In cases where treatment is delayed, irreversible damage may occur. In severe crush injuries, osteomyelitis, non-union of the fractures, unsuccessful flaps, and amputations are seen in approximately 50%[14]. In injured tissues, there is a gray zone between the minimally affected area and the areas of irreversible damage. The aim of this treatment is to maintain the vitality of the tissues in the partially viable gray zone and to prevent further tissue damage. For this, immediate tissue perfusion is required. Decreased blood flow and thrombosis in microvessel impair tissue perfusion and cause tissue hypoxia. Because of hypoxia at the cellular level, cells lose their water content and bacterial defense systems become irreversible due to insufficient energy production. In addition, leakage of intracellular fluid into the intercellular space and extravasation from blood and lymphatic vessels lead to edema formation[15]. Consequently, edema, ischemia, hypoxia, and deterioration in microcirculation around the injured area create a vicious circle with secondary ischemia.

Treatment of Crush Injuries

In crush injuries, diagnosis should be made without delay and treatment should be started quickly to minimize the permanent damage that may occur not only in the damaged tissue but also in the surrounding tissues. This is because the complication rate is high and requires surgery at rates exceeding 50%, even under most conditions[14,15]. Therefore, the treatment of crush injuries requires a multidisciplinary approach. The primary goal of treatment is to restore circulation. The vitality of the extremity depends on the time elapsed between injury and treatment. Tissue hypoxia in crush injuries is caused by ischemia. By preventing hypovolemia and blood loss, the patient's hemodynamics should be fixed, and antibiotherapy should be arranged. Another primary treatment is the debridement of necrotic tissue in open wounds. However, care must be taken to protect living tissues at this time.

HBO Therapy

HBO therapy in crush injuries is an adjunctive treatment method that should be used in the early period to reduce edema formation and provide hyperoxygenation in hypoxic tissues[15].

HBO therapy is recommended by international HBO societies along with open fractures or isolated crush injuries[1,10]. Because tissue infection and necrosis may be associated with severe open fractures, HBO therapy should be initiated in the early period. In the presence of host or injury-related risk factors, HBO therapy should be considered even if the injury is less severe[10]. Similarly, HBO therapy is recommended in cases where there are open wounds where tissue viability is at risk due to infection, even if there is no fracture. HBO therapy is generally recommended as 90 min at 2.4 ATA, three sessions a day in the first 24 h, and then two sessions a day[14,15].

Compartment Syndrome

Compartment syndrome is a situation in which increased pressure within the myofascial compartment threatens the circulation and function of tissues in that area. Crush injuries of the extremities, especially long-term tourniquet applications, tight plaster and bandages, burns, ischemia-reperfusion injury, or toxic coma are the conditions that occur as a result of long-term compression of the extremity. The most important criterion in the diagnosis of compartment syndrome is the presence of trauma. Classical diagnostic criteria, defined as 6P, are pain (disproportionate to trauma), extremity pallor, pressure, paralysis, paresthesia, pulselessness, and progression of symptoms. The diagnosis is confirmed by increasing complaints and rising intracompartmental pressure in hourly repetitive examinations[15]. Pain that does not respond

to analgesics and increases with passive stretching is typical in this patient. Intracompartmental pressure is not a direct indicator of tissue damage, and there are different tolerance levels among patients. Note that the greater the initial soft tissue damage, the higher the intracompartmental pressure. In patients who are unconscious or uncooperative, intracompartmental pressure measurements should be routinely performed[14]. When the interstitial fluid pressure in the compartment exceeds the capillary perfusion pressure, the flow within the capillary bed is blocked and the compartment contents become ischemic. Thus, ischemia, necrosis, and loss of function occur in the tissue. In these cases, surgical decompression of the compartment, ie fasciotomy, is required in the presence of neuropathy. Thus, tissue perfusion is restored. However, tissue necrosis is not always reversible[14,15].

HBO Therapy for Compartment Syndrome

It shows its effect in HBO compartment syndrome by restoring perfusion with the hyperoxygenation it provides in the tissue. Thus, oxygen delivery to the tissue is ensured and the vitality of hypoxic tissues is preserved. The other effect is to reduce intracompartmental pressure by reducing tissue edema with vasoconstriction due to hyperoxia[16]. In experimental models, it has been shown that HBO therapy reduces the intracompartmental volume[17]. HBO therapy cannot be used instead of fasciotomy, which is the main treatment for compartment syndrome. However, in cases where surgery will be delayed, the patient can be treated with HBO to control the compartment pressure. Hyperoxia also stimulates collagen synthesis and fibroblast proliferation and induces neovascularization. Thus, it is possible to control infection in fasciotomy wounds and limit muscle necrosis (Figure 4)[16,17].

In the literature, it has been reported that amputations can be reduced with the use of HBO in two randomized controlled studies on the use of HBO therapy in acute traumatic ischemia[18,19]. The use of vacuum-assisted closure systems together with HBO therapy in the follow-up of fasciotomy wounds provides a synergistic effect and earlier closure of wounds[20]. In another study, a decrease in amputation rates was noted with HBO therapy in crush injuries with open fractures[21]. In the first multicenter, randomized controlled clinical study in which HBO therapy was used in acute musculoskeletal trauma, it was shown that HBO therapy was effective in reducing tissue necrosis and infections[22].

Figure 4. Fourteen-year-old girl who was trapped under the rubble for 3 hours

a, b: Before treatment, c, d: After 25 sessions of HBO therapy and surgical closure

HBO: Hyperbaric oxygen

According to official records, 17,127 people lost their lives in the 7.8 magnitude Marmara Earthquake that occurred in 1999. HBO therapy was widely used for the first time in this earthquake, and its results have been published by various researchers. Sever et al.[23] reported that 28 of 639 patients underwent HBO therapy and were followed up because of crush syndrome and acute renal failure. While mortality was 15.2% in patients who did not receive HBO therapy, no death was recorded in the HBO receiving group (p=0.002)[23]. In another study by Kazancioglu et al.[24], they reported that 8 of 37 cases, followed up for crush syndrome and acute renal

failure, underwent HBO therapy. They revealed that, although no difference was observed in the hemodialysis duration of eight patients who were treated with HBO therapy, no major amputation was required in the HBO group, whereas major amputation was performed on three of the group that did not receive HBO therapy[24]. In the 52 case series of Yildiz et al.[25], it was reported that the most important factor protecting earthquake survivors from amputation was the time to start HBO therapy. In the experimental compartment syndrome study of Aydin et al.[17], HBO therapy was not as effective as fasciotomy alone or fasciotomy + HBO therapy in reducing intracompartmental pressure; however, the group with the least tissue necrosis and infection was the isolated HBO receiving group. This situation has been associated with infection and tissue damage caused by fasciotomy[17]. In the special issue of Turkish association of Orthopedics and Traumatology, titled Earthquake Injuries, published in May 2022, although the subject was evaluated in all its aspects, the subject of HBO therapy was not discussed[26].

Conclusion

Crush injuries and compartment syndromes are injuries that occur massively during earthquakes. Anatolia, one of the most complex regions in the world in terms of earthquake activity, is located in the middle of the Arabian, African, and Eurasian plates. Tens of thousands of our citizens have lost their lives in major earthquakes in our country, which has faced devastating earthquakes for centuries. In the 1999 Marmara Earthquake, many patients who were treated at the İstanbul Medical Faculty and GATA Haydarpaşa Hospitals were also given HBO therapy. In the published studies, it has been revealed that the success rates of patients who receive HBO therapy are significantly higher than those of others. In the same way, HBO therapy was started as soon as possible in the Kahramanmaraş-centered earthquake that occurred on February 6, 2023 and was effective in 11 provinces in regional hospitals with HBO facilities.

However, patients in other hospitals did not have such a chance. When the results of these patients, who are still under treatment in various centers, are published, it will be possible to compare the patient groups who did not receive HBO therapy.

Today, because of developments in orthopedics, plastic surgery, and vascular surgery, protection of the extremities in crush injuries and compartment syndrome can be achieved at a higher rate than in the past. However, amputations may still be inevitable because of infection, tissue necrosis, and repetitive surgeries.

HBO therapy provides tissue perfusion by regressing edema and hypoxia in both compartment syndrome and crush injuries and since it reduces the patient's need for repetitive surgery with additional infection control in fasciotomy ulcers. Therefore, we strongly recommend this adjunctive therapy. In this way, it is possible to both reduce amputation rates and obtain a more functional extremity. In order for more patients to benefit from this treatment in the early period, it is necessary to know more about the subject and to be kept in mind by specialists in pediatrics, plastic surgery, and cardiovascular surgery, especially in the field of orthopedics. Because we can encounter hundreds, sometimes thousands, of patients at the same time in major disaster situations such as earthquakes, it is important that patient triage for HBO therapy is carried out with pre-made action plans in such cases.

Ethics

Authorship Contributions

Surgical and Medical Practices: F.A., A.K., Concept: F.A., A.K., Design: F.A., A.K., Data Collection or Processing: F.A., A.K., Analysis or Interpretation: F.A., A.K., Literature Search: F.A., A.K., Writing: F.A., A.K.

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