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Review Article

Hyperbaric Oxygen Therapy as an Accelerator in Regenerative Medicine

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Abstract

Regenerative medicine is the study of using the regenerative capability of the body to heal or replace degraded tissues or organs. An example of a regenerative medicine is Hypobaric Oxygen Therapy (HBOT). HBOT is a treatment that has been recognized by a variety of professionals that has a vast number of healing properties that include increased oxygen delivery to tissues which accelerates wound healing and reduces inflammation; mobilizes stem cells which repair damaged tissues; inhibits oxidative stress which is damaging to cells and tissues; and reduces apoptosis which is the programmed cell death occurring as a response to an injury. These healing properties can be used to accelerate the treatment of injuries including chronic wounds, various neurological disorders, and various sports injuries. This paper will aim to use HBOT as a basis to investigate the capabilities of regenerative medicines and how it has the potential to replace traditional medicine.

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Introduction

Regenerative medicine is the study of harnessing the regenerative capabilities of the human body [1]. Regenerative medicine has the potential to heal or replace tissues and organs that degraded by age, disease, or trauma, that can be an innovative solution towards the growing aging population [2,3]. Currently, the population of people aged 60 years and over is 1.4 billion and expected to reach up to 2.1 billion in 2050 [4]. Current studies in regenerative medicines focus on stem cells and its proliferation [5]. The potential of stem cell therapies can delay and possibly reverse aging effects due to the characteristics of the cells [6]. It is believed the reduction in stem cell activity declines the regenerative potential of the cells [7].

A current therapy considered a regenerative medicine is Hyperbaric Oxygen Therapy (HBOT). HBOT is a therapeutic approach which exposes the user towards pressurized

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oxygen via an elevated atmospheric pressure in a hyperbaric chamber (Figure 1) [8,9].

There have been a number of studies that have discussed the use of hyperbaric chamber in regenerative medicine [10,11]. HBOT is considered as a regenerative medicine, as it helps treat various injuries and diseases by using the regenerative properties of the body [12]. The approach is a non-invasive alternative which helps athletes rehabilitate and recover from injuries and general fatigue [13]. The rehabilitative and recovery nature of this medicine can help with the increased rate of sports injuries within children and adolescents along with professional athletes [14,15].

Michael Phelps, Novak Djokovic, Tiger Woods are among the list of pros who are said to use HBOT. HBOT is also beneficial for the public due to the potential of skeletal muscle repair, neurological treatment, and various other treatments [16-18].

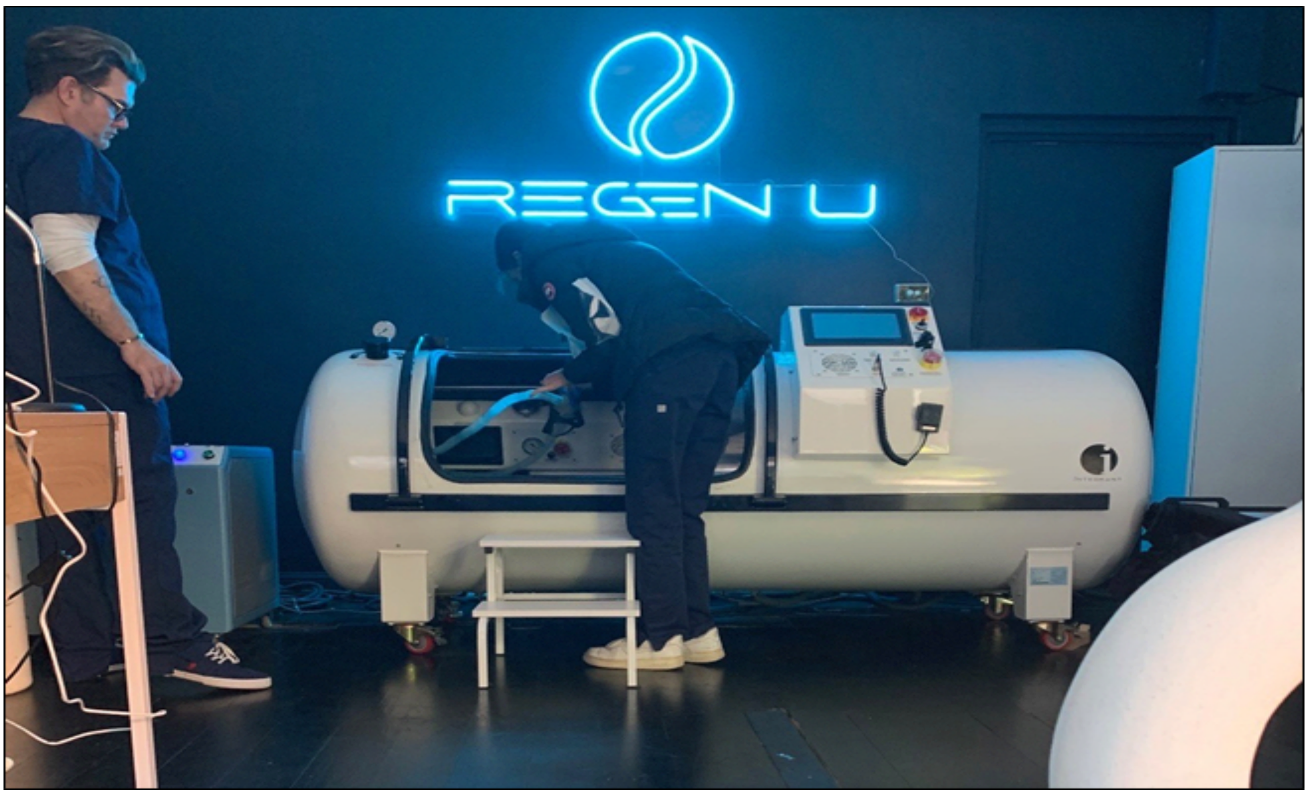

Figure 1: A series 1 integrant hard-shell tank (2-2.4 atmospheres) closed 100% respiratory loop system at a Regen U clinic.

Healing properties of HBOT

Oxygen is fundamental in helping individuals recover from injuries and fatigue. It has also been used in the beauty industry with celebrities such as the Kardashians, Madonna, and Justin Bieber amongst users. HBOT vastly increases the oxygen pressure in arterial blood to ~ 266.6 kPa, increasing the blood to tissue oxygen gradient aiding on the healing of inflammatory and microcirculatory disorders [19]. In the event of an injury, blood vessels are damaged and interrupts blood flow. This can result in tissue hypoxia,

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deterring oxygen flow less than the metabolic demand of the tissue damaging the cells leading to cellular death and apoptosis [20,21]. According to the FDA, there are specific diseases/disorders which HBOT can be used as a medical device for, along with possible complications in using HBOT. The FDA approves HBOT applications provided in (Table 1). This list is not exhaustive for the conditions that benefit from HBOT [22,23].

Disorders/Diseases cleared by FDA for use of HBOT	Possible complications according to FDA
Air and gas bubbles in blood vessels	Ear and sinus pain
Anaemia(severe anaemia when blood transfusions cannot be used)	Middle ear injuries, including tympanic membrane rupture
Burns(severe and large burns treated at a specialized burn centre)	Temporary vision changes
Carbon monoxide poisoning	Lung collapse (rare)
Crush injury	
Decompression sickness(diving risk)	
Gas gangrene	
Hearing loss(complete hearing loss that occurs suddenly and without any know cause)	
Infection of skin and bone(severe)	
Radiation injury	
Skin graft flap at risk of tissue death	
Vision loss (when sudden and painless in open eye due to blockage of blood flow)	
Wounds(non-healing, diabetic foot ulcers)	

Table 1: FDA approved disorders/diseases to be healed by HBOT and the possible complications according to the FDA [22].

Sports injuries

With the rise of participation in competitive sports at a younger age, the incidence of injuries within sports have increased drastically [24,25]. This is exasperated by the incidence and burden rates of sports injuries with people aged 15+years in Victorian hospitals accumulating $375 million in sports and lower limb injuries [26]. These lower body injuries consist of various ligament ruptures, muscular strains and contusions, ankle sprains and various fractures. increasing interest has been given to the incidence of concussion, which has an estimated 1.6 to 3.8 million incidences annually [27].

Because of the concussions effect upon the individuals motor function further injuries can occur [28,29]. The use of HBOT can be beneficial towards athletes as the enhancement of oxygen can reduce oedema, mitigate infection, have anti-inflammatory effects, and mitigate ischemia-reperfusion injury [30].

This can help reduce the effects of concussive injuries. HBOT can be shown to vastly accelerate the rate of return to full activities

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in conjunction with physiotherapy, as can be shown by the graph within (Figure 4) [31]. Muscular strains are the most common type of injuries, and stem from overuse and fatigue [32,33]. Current solutions consist of these injuries are not agreed upon, including treatments like rest, ice, compression, bandaging, physiotherapy, and medications [34].

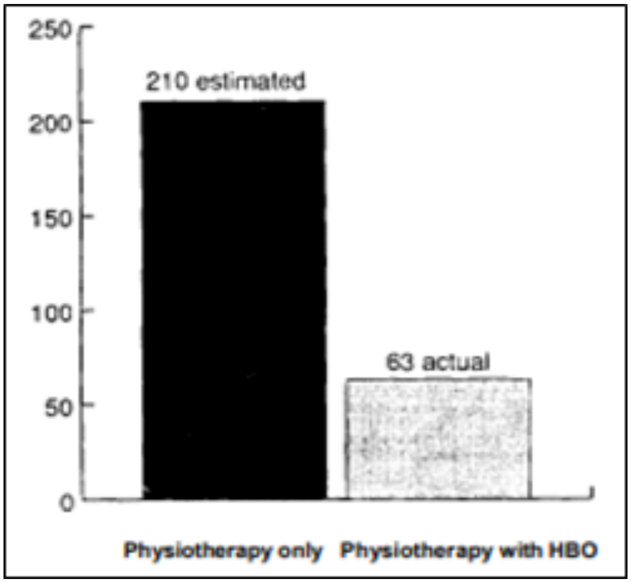

Figure 2: Difference in outcome between expected and actual duration of injuries with physiotherapy in conjunction with HBOT in 20 simple injuries [32].

Chen, et al., reported that HBOT reduced the muscular enzyme levels along with improving pain intensity and interference and in other studies alleviating the lactate elevation post-exercise [35,36].

The elevated oxygen levels allow the enhancement of performance in athletes while using HBOT during exercise.

This increases VO2max, power, and VO2AT linked to increased mitochondrial respiration and mass [37].

Stem cells and wound healing

Several studies propose the mobilization of stem cells via HBOT by engrafting injured tissues giving the therapeutic effects of HBOT [38].

The mobilization of stem cells is an imperative feature of wound healing as it advances through three stages: the inflammatory phase, the proliferation phase, and the remodeling phase [39]. HBOT is then shown to increase the proliferation within the intestinal stem cells of mice without adverse effects to oxidative metabolism [11,40]. HBOT was successfully completed on a patient within a tertiary care hospital of the armed forces as seen in the sequential photographs of the diabetic patient within (Figure 2) [41]. Furthermore, hypoxia is shown to be the leading factor of compromised skin grafts, hence the hyperoxia, angiogenesis, leukocyte function enhancement and antimicrobial actions of HBOT improves the survival rate of compromised skin grafts [42,43].

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Figure 3: Progress of necrotised soft tissue in a 53-year-old male diabetic treated via HBOT [42].

Stroke, Traumatic Brain Injury (TBI), Spinal Cord Injuries (SCI) and neurological disorders

According to further studies, diseases such as TBI, SCI, stroke and other neurological diseases account for a substantial burden to the global health systems and economies. In 2016 27.08 million new cases of SCI and 0.93 new cases of SCI [44]. When looking at the Years Lived with Disability (YLD's), TBI caused 8.1 million YLD's and SCI caused 9.5 million YLD's [44]. Strokes contribute to one of the highest causes of burden to the neurologic and cerebrovascular disease at 58.1% of total Disability-adjusted life years (DALY) as seen in (Figure 3) [45]. When observing the potential interventions which can reduce stroke and ischemic heart disease by 10%, a projected $25 billion annually can be saved [45]. Several clinical trials provide evidence of cerebral plasticity, leading to brain function and quality of life improvements for post-stroke patients [46]. HBOT inhibits oxidative stress, which is considered as an integral factor to cerebral ischemic and hemorrhagic injuries [47]. In SCI, increased apoptosis can be caused by further inflammation within the spinal cord along with oxidative stress. HBOT helps neutralize these issues which can ease or diminish the neurological deficits [48]. Clinical studies were made with animals that were induced with TBI. These studies showed decreased apoptosis, decreased apoptosis-related proteins, reduced transmembrane mitochondrial potential, and reduced inflammatory responses when treated by HBOT [49].

Cons

There are negatives when considering HBOT. Due to the chamber being highly pressurized and oxygen rich, it increases the flammability of the materials [50,51]. This can be minimized by using tanks that have closed respiratory circuits and breathing 100% oxygen through a mask. Many of the general

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population are claustrophobic, hence being an inconvenience [52]. Another possible hazard in high oxygen breathing is oxygen toxicity, which can cause fast twitching, nausea, visual changes, and tachycardia [53]. This monomized by using appropriate protocols with air brakes. Complications including middle ear barotrauma, development of nuclear cataract and myopia, barosinusitis, and other concerns related to effects of pressure can be triggered by HBOT [54-57]. The one absolute contraindication to hyperbaric is active pneumothorax [58].

Conclusion

Hyperbaric Oxygen Therapy is beneficial and overall encourages healing with minimal downside. Trained staff must be used to operate this form of medicine like any other . With the activation of stem cell proliferation, HBOT has many medical and lifestyle applications.

A major example is in (Figure 2) where the healing of the wound being influenced due to stem cell proliferation rather than a physical skin graft. HBOT potentiates the body's ability to heal itself and is a potent adjuvant to other treatments.

It is becoming a cornerstone in regenerative technologies to both activate and speed recovery cycles.

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