Meta-Analysis

A Comparative Analysis of HBOT and L-HBOT: An Innovative Possibility to Enhance HBOT?

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ABSTRACT

Oxygen is a vital component of wound healing. When trauma occurs, causing a wound, it is difficult to get oxygen to the wound site because of the damage that is present. Hyperbaric oxygen chamber therapy (HBOT) is employed to combat hypoxia in wounds by having the patient inhale high concentrations of oxygen at elevated atmospheric pressures, accelerating the rate at which oxygen dissolves into the bloodstream at a faster rate. HBOT has been used to treat a variety of conditions like diabetic foot ulcers, Crohn's disease, and chronic wounds. Yet, the limited body of literature and the risk of complications have limited the application of HBOT. Medical professionals have proven the significance of oxygen on wound healing from stimulating most of the vital functions to initiating the production of certain genes, oxygen is the keystone for successful complete wound healing. On the other hand, the risk of oxygen toxicity is one of the main contraindications of HBOT. Contrary to common knowledge, recent studies have shown that HBOT administered at a lower atmospheric pressure with a lower oxygen concentration can decrease this risk significantly. Low-pressure hyperbaric oxygen therapy (L-HBOT) may still be as effective as traditional high-pressure hyperbaric oxygen therapy (H-HBOT) without the unpredictable complications that medical professionals are unsure of. In all, this review aims to analyze recent studies to provide a clear comparison between these two variations of HBOT.

Keywords: Hyperbaric oxygen chamber therapy (HBOT); low-pressure; wound healing; medical device; chronic wounds; diabetic foot ulcers (DFU)

INTRODUCTION

Oxygen is essential to life as it allows the body to grow and heal. When the body lacks oxy gen, it cannot survive much less heal (1). The purpose of hyperbaric oxygen chamber therapy (HBOT) is to utilize the natural healing capabilities of oxygen and to promote efficient wound healing. HBOT is a widely accepted treatment option for hypoxic conditions and has proven to be effective (2). It has been shown to increase the efficacy of wound healing, especially in treating certain conditions that require an increase in oxygen, or neovascularization (3, 4). HBOT operates by having the patient inhale high concentrations of oxygen at a pressure higher than sea level (1.0 atmosphere absolute ATA), allowing the body to absorb more oxygen (Figure 1). The oxygen that HBOT administers increases

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neovascularization, and the production of reactive oxygen species (ROS), endothelial cells, and fibroblasts, and catalyzes the production of certain genes that have crucial roles in wound healing (3, 5). The increased number of ROS plays a pivotal role in fighting infections at the wound site. However, excessive production of ROS can overwhelm the immune system leading to cellular damage and increased apoptosis (6). Both fibroblasts and endothelial progenitor cells are essential for angiogenesis and wound healing. Despite these benefits, HBOT is not without its challenges. The risk for oxygen toxicity raises concerns as different tissue wounds as the level of oxygen needed for different tissue types often varies.[6] Secondly, the cost and level of difficulty in producing a standardized treatment plan give us reasons to consider looking into other variations of HBOT that can mitigate some of these disadvantages (4).

Low-pressure hyperbaric oxygen chamber therapy (L-HBOT) presents a promising alternative to conventional HBOT. This variation of the traditional high-pressure hyperbaric oxygen chamber therapy (H-HBOT) utilizes lower atmospheric pressure when administering oxygen that is not as concentrated, allowing for the patient to receive similar therapeutic effects while simultaneously decreasing the risk for oxygen toxicity as the oxygen is a much weaker concentration (5). These therapeutic properties are why HBOT is so effective against chronic wounds. Chronic wounds are characterized as wounds that stay in the inflammatory phase of wound healing because of the hypoxic state the wound is in.[2] The decreased rate of angiogenesis found in wounds due to hypoxia and inflammation causes wounds to not progress into the subsequent stages of wound healing (5). One of the most common types of chronic wounds is diabetic foot ulcers (DFU). According to the World Health Organization, there is a mortality rate of 45% in patients diagnosed with DFU when it comes time for their 5-year checkup. The cause for this extreme rate is not purely based on DFU itself but a combination of conditions that are in accordance with DFU. Approximately 1 in 20 people with diabetes develop foot ulcers and 15% of patients with DFU need amputation (5). Another study conducted to examine the results of L-HBOT on diabetic foot ulcers showed healing results only 16 hours after treatment. This increase in healing time is proven to be caused by the increase in oxygen (7). The overwhelming prevalence of chronic wounds that require drastic surgical interventions should advocate for more studies to look for much less invasive treatment options and HBOT has shown to be a promising possibility (3).

L-HBOT has been proven to be a much safer option, but in this literature review, the aim is to compare the results of traditional HBOT to L-HBOT to gain further insight into the efficacy of L-HBOT. By the end of this literature review, the question to be addressed is: How does the efficacy of traditional high-pressure hyperbaric oxygen therapy compare to low-pressure hyperbaric oxygen therapy in treating chronic wounds without negative complications?

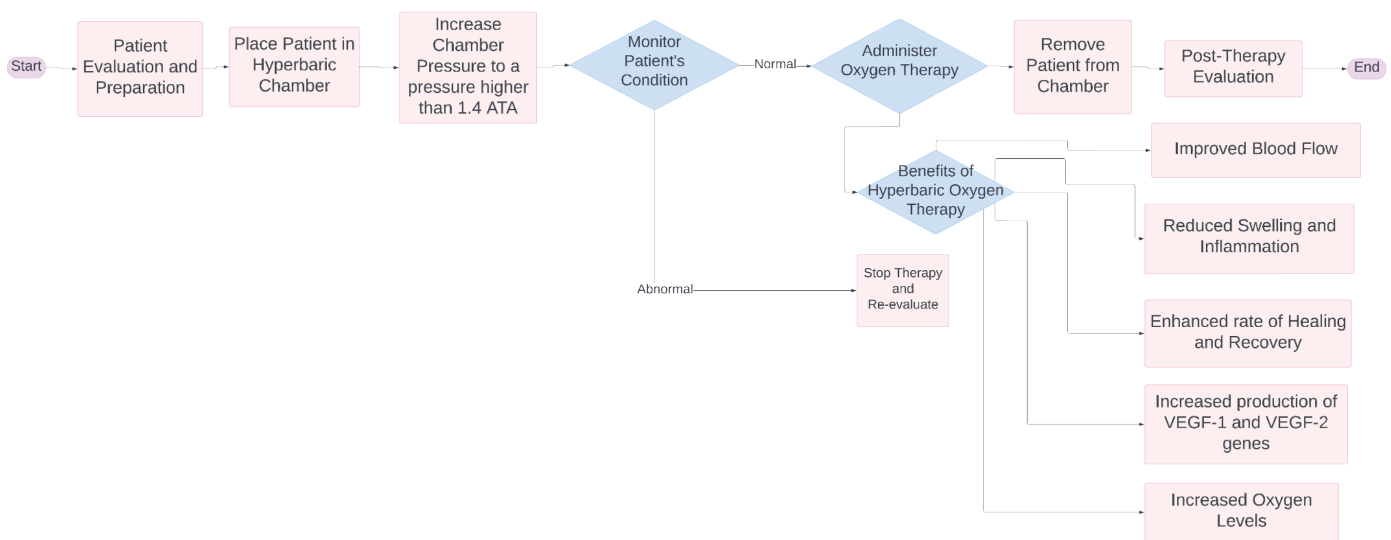

Figure 1. Flow Chart Explaining Hyperbaric Oxygen Therapy Treatment Protocol.

METHODS

In this literature review, I screened for studies in the current literature that looked at HBOT indicated for promoting wound healing that is found on Pubmed and Google Scholar utilizing the keywords, “Hyperbaric oxygen chamber therapy.” In this review, studies where HBOT was administered at 2.0 ATA or less, were considered low-pressure hyperbaric oxygen chamber therapy because traditional HBOT is recommended at 2.0 - 3.0 ATA (5). In addition to the general search of studies relating to HBOT, the term “wound healing” was added to the search for studies tapered specifically towards the effects of HBOT on wound healing.

We evaluated studies that assessed HBOT efficacy on wound healing strictly within the human patient population. The studies were not all randomized controlled trials so there are possibilities for bias in the results. In addition, some of the analyzed studies had limitations due to various factors, including restricted resources such as funding and time, small sample sizes, and limited access to specialized HBOT facilities. These considerations should be taken into account.

The studies included chronic wounds, burns, crush injuries, acute superficial wounds, DFU, and other wound-related injuries. All superficial wound injuries were included in our review if they were treated with a high concentration of oxygen at an atmospheric pressure higher than 1.4 ATA.

Although the focus of this review was on HBOT treatment with 2.0 ATA or less, treatments that used 2.0 - 3.0 ATA were also included to compare the benefits of both traditional HBOT and L-HBOT so that I could comprehensively answer the presented research question.

RESULTS

After consideration, 13 separate studies on HBOT were included in this literature review for analysis. The primary outcome for all of these studies showed that HBOT was an effective treatment option regardless of the protocol. Both traditional HBOT administered at $\geq$ 2.1 ATA and L-HBOT administered at 1.4-2.0 ATA had increased therapeutic effects on wound healing.

Chronic Wounds: Diabetic Foot Ulcers (DFU)

Huang et al conducted research on the effects HBOT had on diabetic foot ulcers (DFU), a common and serious complication for diabetic patients. Patients with diabetes often feel anxious because of the increased possibility of developing DFU (3). Diabetes affects 347 million people worldwide, and 1 in 20 of these diabetic patients develop DFU (5). These patients start to see skin tissue on their feet disintegrate, which leads to ulcers that eventually become chronic wounds because of the patient’s diabetes (3). The ulcers develop into chronic wounds since diabetes hinders blood flow. The poor blood circulation causes the wound to become hypoxic, a common cause of chronic wounds. If this condition continues to worsen, often times the only treatment option is amputating the whole leg. Of all DFU patients, 15% end up needing amputations because of their chronic wounds. This should encourage us to look into less drastic interventions when dealing with DFU.

HBOT combats this condition by bringing high concentrations of oxygen to the wound allowing for the wound to heal. Additionally, Huang et al state that HBOT increases multiple functions in the body that promote wound healing. It was reported that there was an increase in the production of reactive oxygen species (ROS), fibroblasts, and endothelial progenitor cells. The increased ROS production rate has both therapeutic and detrimental effects. Lastly, HBOT was seen to increase the production of hypoxia-inducible factors (HIFs) and vascular endothelial growth factor (VEGF). Under normal circumstances, HIF-1 is inhibited by prolyl hydroxylase domain (PHD) enzymes, however, when wounds become hypoxic the PHD enzymes are inhibited to allow for the HIF-1 gene to be released. The HIF-1 and HIF-2 bond together to form a protein complex, which in turn binds to DNA in the nucleus of the cells, increasing angiogenesis. This is the body’s response to mild hypoxic conditions, however, the body will start to fail, the more hypoxic the wound becomes. The body is unable to respond to severe hypoxia so HBOT steps in to increase oxygenation at the wound site, circumventing the body’s natural limitations (6).

L-HBOT’s effectiveness in treating diabetic foot ulcers (DFU) has been demonstrated by Huang et al, reporting substantial improvements in healing rates when treated with 2.0 ATA compared to the group without HBOT. Within 30 days of treatment, HBOT notably reduced wound size. Many patients experienced complete healing, leaving behind smooth skin without scarring. Secondly, L-HBOT has been proven to significantly decrease the rate of amputations caused by DFU. Finally, the complications observed were mild or reversible, such as temporary barotrauma during treatment. L-HBOT has demonstrated efficacy comparable to traditional HBOT, with a reduced risk of oxygen toxicity due to the lower pressure at which oxygen is delivered, which allows the body more time to adapt. These factors underscore a promising future for L-HBOT in the treatment of wound healing (3).

Superficial Wounds: Burns, Post Surgical Wounds, and Crush injuries

Similarly, after reading multiple studies on superficial wounds, the consensus that has emerged is that L-HBOT significantly increases the rate of healing along with decreasing the risk of needing drastic surgical interventions (6, 8, 9).

Burns

In a study conducted by Hart et al, it was reported that burn injuries treated with HBOT healed approximately twice as fast as those treated using normal procedures without HBOT. The researchers employed a sham group to compare the results of the group treated with L-HBOT at 2.0 ATA. The sham group reported a median healing time of 43.8 days compared to the group that used L-HBOT, which had a mean healing time of 19.7 days. This is a significant decrease in healing time. However, three patients in the HBOT group had sinus barotrauma. While the study, did not explicitly state the cause of the barotrauma but it should be noted that their HBOT sessions lasted 90 minutes and they did not disclose the oxygen concentration they used. Nonetheless, the study concluded a drastic increase in the rate of wound healing with only a small amount of reversible complications, further supporting the efficacy of L-HBOT.

Crush Injuries

Similar to the results seen in burn injuries, crush injuries had approximately doubled the success rate when treated with HBOT at 2.5 ATA. The rate of complete wound healing was 56% in the control group compared to 96% seen in the group treated with HBOT (9). In all the primary outcome was the doubled rate of complete wound healing when using HBOT (8).

Post Surgery Wounds

Historically, HBOT was utilized as a cosmetic tool to help post-cosmetic surgery patients recover more rapidly. Conditions such as postoperative ecchymosis are healed at a significantly faster rate when treated with L-HBOT. In a study conducted by Strong and Jacono, patients treated with 2.0 ATA L-HBOT had a 35% decrease in ecchymosis, 10 days after surgery. It should be noted that treatment sessions only lasted 60 minutes, and no complications were reported (2).

Assisting Flaps and Skin Grafts

Surgical interventions are often necessary when injuries are so severe that our body is unable to heal naturally. After surgical intervention, the damaged state of the wound site poses a challenge for reconstructive techniques due to the increased fibrosis, poor vascularity, and poor granulation tissue formation which leads to low success rates (10). Multiple studies have reported that HBOT significantly increases the success rate of flaps and skin grafts. For instance, a study conducted by Perrins DJ reported that when split-skin grafts were treated along with L-HBOT at 2.0 ATA, there was a continuous trend that indicated a higher rate of complete survival of the skin graft. In that trial, 95% of the graft being healthy indicated complete healing. Furthermore, that study did not indicate any HBOT-related complications which is consistently the case when using L-HBOT (8, 11). L-HBOT promotes neovascularization, which combats the challenge of poor vascularity at the wound site. The increased blood flow along with the increased amounts of oxygen in the blood stream when using L-HBOT, brings adequate amounts of oxygen to the wound site. Additionally, L-HBOT accelerates healing by enhancing critical wound-healing processes. Overall, L-HBOT contributes to the success of skin grafts and flaps through increased blood flow, elevated oxygen levels, and accelerated formation of granulation tissue (10).

DISCUSSION

This study aimed to explore both the therapeutic properties and limitations of HBOT to provide a more comprehensive understanding of its clinical application (8). Multiple studies affirm that HBOT accelerates wound healing, elevates oxygen levels, and increases neovascularization. However, the complications associated with HBOT have spurred interest in alternative methods to achieve similar therapeutic effects without the adverse side effects.

Throughout this study, I have analyzed current literature and clinical trials on L-HBOT, and the findings indicate a promising future for this treatment. L-HBOT offers the same therapeutic benefits as traditional HBOT but at lower pressure, significantly reducing the severity and frequency of complications. While HBOT is already recognized as a safe treatment, L-HBOT further minimizes complications, making them less severe, shorter in duration, and largely reversible.

After reviewing studies where HBOT was used to treat superficial wounds, chronic wounds, and assist with skin grafts and flaps, it is clear that HBOT is highly effective for treating superficial wounds and those particularly difficult to heal due to oxygen or blood supply deficiencies. Since L-HBOT effectively increases both oxygen levels and neovascularization, it is a great adjunctive treatment option for these types of wounds, including burns, crush injuries, and skin ulcers (2, 5, 8).

In the study conducted by Hart et al. on burns, patients receiving L-HBOT experienced a significant increase in the healing rate, attributed to the increase in neovascularization and granulation tissue formation.[12] The increased blood flow to the wound site delivers essential nutrients and oxygen, promoting tissue formation, which is also enhanced by L-HBOT. However, the complications reported in this study were likely due to the treatment sessions being 90 minutes, with no breaks. Studies that included shorter session lengths or 5-minute breaks between portions of the sessions have shown fewer complications (13, 14). This highlights the importance of taking breaks during sessions because prolonged exposure to high concentrations of oxygen is the direct cause of oxygen toxicity or other HBOT-related complications. The body can become overwhelmed by high amounts of oxygen, leading to avoidable complications. Nonetheless, future studies with randomized trials and larger patient pools are needed to support this, but there is a promising solution to the contraindications of L-HBOT (13).

Conversely, this literature review also indicates that administering HBOT at higher pressures often produces desired effects more quickly and with fewer treatment sessions, likely due to Henry's law (15). This law states that the amount of gas dissolved in a liquid is proportional to the gas's partial pressure on the liquid's surface (10). Therefore, higher pressure results in more oxygen dissolving into the bloodstream, raising oxygen levels. While this can accelerate treatment and wound healing, it also increases the risk of oxygen toxicity and other HBOT-related complications. Overall, higher-pressure HBOT can yield faster therapeutic effects, but L-HBOT offers a safer alternative with similar benefits to traditional HBOT.

One of the key challenges encountered during this literature review was the scarcity of literature focused on L-HBOT. Traditional HBOT has been studied extensively but L-HBOT is remains a newer area of study, with dosing protocols of L-HBOT still under examination. Furthermore, the studies that did include L-HBOT had small patient pools, were non-randomized controlled trials, or lacked resources like time and money. This could introduce sampling bias and limit the generalizability of the findings in the studies. As a result, future studies are needed to address these gaps and further explore the potential advantages of L-HBOT over the traditional protocols.

CONCLUSION

L-HBOT and traditional HBOT are both viable and safe treatment options in wound healing. Although this is true, L-HBOT offers several advantages, particularly because L-HBOT is more versatile and has fewer complications compared to traditional HBOT, while still being equally effective. L-HBOT promotes the essential functions needed for wound healing while minimizing the potential adverse side effects, making it a compelling alternative to traditional HBOT. Despite these advantages, a significant limitation lies in the need for more extensive literature and clinical trials supporting L-HBOT. As a novel approach, L-HBOT has the potential to influence the development of future medical devices and clinical care, offering healthcare professionals more flexible and safer options for patient care. Continued research is essential to uncover the full picture of its benefits and limitations, ensuring that L-HBOT can contribute meaningfully to advancements in wound management and treatment.

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DECLARATION OF CONFLICT OF INTERESTS

The author declares that there are no conflicts of interest regarding the publication of this article.

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