Does hyperbaric oxygenation therapy benefit in the treatment of non-healing wounds in diabetic patients?

C Novaleski

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Abstract

As the incidence of diabetes mellitus type II is steadily increasing in our society, diabetic non-healing lower extremity wounds are complicating patient care. Hospitalization and amputation rates relating to diabetic lower extremity wounds are increasing causing concern relating to quality of life and healthcare expense. Treatment of these wounds can be difficult and alternative therapy such as hyperbaric oxygenation (HBO) is being used in clinical practice. A review of four studies challenging the HBO benefit in treating diabetic lower extremity non-healing wounds demonstrates a significant increase short term healing rates and reduction in amputation rates. However, results demonstrate no significant increase in long term healing rates. Multiple studies have been linked to the Undersea and Hyperbaric Medical Society, creating possible bias. More non-bias research should be performed to clearly demonstrate HBO benefits for diabetic non-healing wounds and to guide practitioners in treating diabetics with non-healing wounds.

INTRODUCTION

With the rise in diabetes mellitus type II (DM-II) in our country, peripheral neuropathy and subsequent diabetic foot wounds are becoming increasingly common among the adult population. Treatment is limited in these patients and often results in amputation due to secondary osteomyelitis. As much as 50% of all amputations in the US are due to diabetes (1). Among these diabetes-related amputations 9% are of the foot, 31% are of the lower leg and 30% are above the knee amputations (1). This not only decreases the quality of life for the patient, but also puts a financial strain on the US healthcare system (1).

Hyperbaric oxygenation (HBO) is a controversial therapy that is FDA approved to aid in the treatment of non-healing wounds in diabetic patients. This treatment involves multiple intervals of 100% oxygen inhaled at pressures greater than sea level (1). HBO often requires months of therapy and can be quite expensive. Practitioners prescribing HBO frequently face conflicts with insurance coverage.

Decreasing the incidence of amputations and further reducing overall health care costs may justify the use of this treatment. The controversy stems from the lack of studies using high-level evidence to support HBO therapy in non-healing wounds. Since the FDA approval of HBO there have only been a few studies performed to challenge this topic (12,13,14,15). It is important to review these early studies that assisted in the approval of HBO as well as the newer supportive data and opposing data when approaching this topic. Thus, the purpose of this paper is to review the data on HBO therapy and determine its benefit in treating non-healing wounds in diabetic patients.

BACKGROUND

Diabetes mellitus (DM) is defined as hyperglycemia due to a defect in insulin secretion, improper functioning of insulin, or both. DM is classified into two categories. DM type I (DM-I) is also known as juvenile onset diabetes. This disease is an abrupt autoimmune response in which the body destroys the insulin producing beta cells in the pancreas. This destruction leads to diminished or absent endogenous insulin production. DM-II accounts for 90% of all cases of diabetes (2). It is traditionally known as adult onset diabetes, but this term is no longer being used to describe this disorder due to the increased incidence of DM-II in adolescence. DM-II is a chronic disease process in which there is gradual impairment of the insulin producing beta cells, decreased insulin secretion and a decrease in tissue sensitivity to insulin (2).

DM-II is in insidious disease process. Approximately 1 in 16

people in the US have DM and are unaware of it (2). High fat and high carbohydrate meals lead to increased glucose levels in the blood, which the insulin must clear from the bloodstream. Simultaneously this lifestyle of excessive caloric intake with decreased activity leads to increased body fat and obesity. Thus adipose tissue and other body tissue become resistant to insulin. The beta cells are able to compensate for this resistance but eventually become exhausted, leading to defects in insulin production and secretion.

Poor glucose control leads to various complications. Microvascular complications include retinopathy, nephropathy and neuropathy. Macrovascular complications consist of cardiovascular disease, dyslipidemia, coronary artery disease and hypertension (HTN), including increased risk for stroke and myocardial infarction. Diabetic peripheral neuropathy is one of the most frequently occurring complications which affects in the lower extremities and in more severe states, affects in the upper extremities, decreasing sensation and sometimes causing chronic pain to these areas (2). Nerve fiber loss is caused by both metabolic and ischemic components. Chronic hyperglycemia allows glucose to combine with amino acids and leads to the formation of irreversible advanced glycosylation end products (AGE) (3). Increased AGE concentrations cause vascular injury associated with microvascular complications of diabetes (3). Cell metabolism is decreased due to increased collections of sorbitol (3). Oxidative stress is observed at high rates in uncontrolled hyperglycemia and causes peripheral nerve damage (3). Thickened endoneural blood vessel walls with increased vascular occlusions leads to ischemia (3). In addition, diabetics are not able to restore peripheral nerves adequately due to loss of neutrophic peptides typically involved in nerve repair (3).

In addition, diabetics are at higher risk for infection (4). Hyperglycemia can impair the immune response which reduces the ability to fight infection. Vascular insufficiency leads to ischemia of the surrounding tissues, resulting in impaired wound healing. A decreased sensation in the lower extremities due to peripheral neuropathy diminishes a diabetic's ability to feel trauma or pain in the affected areas.

Risk factors for diabetic peripheral neuropathy include factors associated with developing diabetes and poor glucose control. DM-I is linked to heredity. Obesity, sedentary lifestyles, aging and gestational DM are associated with the development of DM-II. Genetic components also seem to have a role in DM-II. As obesity becomes an epidemic in our society, DM-II is becoming more common in adolescence and young adulthood (2). Regulating glucose is the most important factor in preventing diabetic neuropathy or retarding its progression. However, this is a progressive disease and glucose control will not reverse the damage.

DM-II is reaching epidemic rates in the US, while DM-I accounts for only 10% of all cases of diabetes (2). “Nearly 800,000 new cases of DM are diagnosed per year in the US and approximately 15% will develop lower extremity ulcers at some point in their lives” (5). About 2 million people in the US experience impaired wound healing (5). More than 160,000 hospitalizations per year involve lower extremity non-healing wounds (5). This condition also accounts for $1 billion of US healthcare costs annually (5).

Typically, lower extremity infections begin with a minor trauma and ulcer formation. Diabetic ulcers are more susceptible to infection due to ischemia, neuropathy and impaired healing. Ulcers are further defined by the Wagner scale which ranges from grade 0 to 5 (6). This scale is used to classify wounds; the higher the grade, the more severely the wound is infected. The Wagner scale is useful in determining standards for diagnostic procedures and treatment.

Grade 0 is defined as a high risk extremity without ulceration (6). Prevention of trauma and infection is the goal for grade 0 extremities. This can be accomplished through routine examination of the extremities and well controlled blood glucose levels. Also, therapeutic shoes which provide greater depth may be worn to help prevent trauma.

Grade 1 ulcers are superficial, involving the full skin thickness but not underlying tissues. Grade 2 ulcers are deep, penetrating down to ligaments and muscle without bone involvement or abscess formation (6). Symptoms of infection associated with grade 1 and 2 ulcers may include systemic illness such as fever, chills and tachycardia. A clinical diagnosis of infection can be made if two of the following criteria are present at the affected area: erythema, warmth, tenderness or swelling (7). Pus or sinus tract formation at the wound site may aid in diagnosis. An increased white blood cell (WBC) count, increased erythrocyte sedimentation rate (ESR) and positive may be present (7). Wound cultures may be performed to determine the causative bacteria and may help guide antibiotic therapy. Imaging is used to confirm or rule out osteomyelitis and

determine presence or absence of an abscess. The Infectious Disease Society of America (IDSA) recommends plain film radiograph initially to determine the presence of osteomyelitis (7). More advanced imaging, usually MRI is then used in the setting of an abnormal radiograph or no improvement with antibiotic therapy (7).

Grade 1 and 2 ulcers should be treated with antibiotic therapy. The most common agents causing infection in diabetic lower extremity wounds with <2 cm of surrounding inflammation are Staphylococcus aureus (S. aureus), methacillin resistant Staphylococcus aureus (MRSA), group B Streptococcus (GAS) and Streptococcus pyogenes (8). If the inflammation is >2cm surrounding the affected area with extension into the fascia, coliforms should also be suspected (8). Less extensive infection can be treated with oral trimethoprim/sulfamethoxazole (Bactrim) plus second generation cephalosporins or amoxicillin-clavulanate (Augmentin) (8). If there is extensive soft tissue involvement and systemic signs and symptoms, anaerobic bacteria should be covered in therapy (8). This would require intravenous (IV) vancomycin plus a beta lactam antibiotic (8). Other therapy for grade 1 and 2 ulcers may include chemical or mechanical wound debridement, casting to relieve pressure on the ulcer and therapeutic shoes to help prevent recurrence (6).

Grade 3 ulcers are deep with cellulitis or abscess formation and often have associated osteomyelitis (6). Signs and symptoms may include those associated with grade 1 and 2 ulcers. Osteomyelitis is a much more severe infection. However, symptoms are frequently indistinguishable from a less serious infection and pain may or may not be present in a diabetic due to peripheral neuropathy. Osteomyelitis is much more difficult to diagnose and should be suspected if lesions are greater than 2 cm x 2 cm, deeper than 3mm and erythrocyte sedimentation rate (ESR) is greater than 70mm/h (7). Other laboratory findings may be similar to grade 1 and 2 ulcers. MRI can assist in diagnosing osteomyelitis, abscess or soft tissue masses (7). However, the diagnosis of osteomyelitis can be made definitively only through bone biopsy (7).

Treatment for grade 3 ulcers requires incision and drainage of abscess if present. IV antibiotic coverage is the same as extensive tissue involvement of grade 1 and 2 ulcers. Osteomyelitis in the lower extremity of diabetic patients is commonly poly-microbial including gram positive cocci, gram negative bacilli, aerobic and anaerobic bacteria (8). If osteomyelitis is suspected, no empirical antibiotic therapy is necessary unless the patient is acutely ill with symptoms of local infection (8). In the case of acute illness secondary to osteomyelitis, broad spectrum antibiotic therapy is indicated. Otherwise, surgical debridement, bone biopsy, if possible and total contact casts with non weight bearing instructions for the patient is the ideal treatment until specific microbials are determined (8). However, bone biopsy may be difficult to achieve without amputation and many times patients with osteomyelitis are treated empirically with IV antibiotics in clinical practice (7).

Grade 4 ulcers have localized gangrene, while grade 5 ulcers have extensive gangrene involving the entire foot (6). Early signs of gangrene include dull pain and pallor of the affected area. These necrotizing infections should be suspected when subcutaneous gas, purple or black discoloration, bullae formation and malodorous smell is present (7). Systemic signs and symptoms including fever, chills and tachycardia may or may not be present in grade 4 and 5 ulcers.

Grade 4 and 5 ulcers are much more difficult to treat, often fail antibiotic therapy and typically require amputation. Alternative options in treating wounds with associated osteomyelitis include a platelet-derived growth factor dressing, skin grafts, topical oxygen therapy and hyperbaric oxygenation therapy (7).

Hyperbaric oxygenation (HBO) has been used and studied for centuries; however, it is only in the last century that scientific research has been done to show its therapeutic benefits. HBO therapy was founded in 1662 by Henshaw, who built the first chamber called the ‘domicilium' (9). By the 1870's, HBO therapy was being used in multiple settings in surgery and for decompression sickness. In the 1900's, Cunningham discovered a correlation with HBO therapy and improvement of circulation (9). Collaboratively, he built a hyperbaric hospital called the Steel Ball Hospital in 1927, but was unable to provide sufficient evidence that HBO benefited patients in this hospital and it was closed (9). Military research during WWII provided some evidence of the therapeutic benefits of HBO (9). In the 1950's, HBO was being used to treat radiotherapy effects, prolonged circulation arrest during surgery, anaerobic infections, carbon monoxide poisoning, dementia, emphysema and arthritis (9).

Undersea Medicine or what is now known as the Undersea and Hyperbaric Medical Society (UHMS) began in 1967.

This society was founded to provide research evidence for HBO and its medical indications (9). The UHMS still exists today and continues to research and publish articles on HBO.

HBO therapy involves multiple treatment intervals of 100% oxygen inhaled at pressures greater than sea level. The physiology of HBO involves scientific concepts which relate to the changes that occur as a patient drops below sea level within the chamber. Below sea level pressure increases causing changes in gas concentration. The major gas laws that are involved in hyperbaric medicine include Dalton's Law, Henry's Law and Pascal's principle (9).

Dalton's law can be used to explain the increases in oxygen concentration below sea level. This law states that in a "mixed gas each element exerts a pressure proportional to its fraction of the total volume or partial pressure" (9).

"Henry's law states that the amount of gas dissolved in a liquid or tissue is proportional to the partial pressure of that gas in contact with the liquid or tissue" (9). Pascal's principle is defined as "a force applied to part of a confined liquid or gas is uniformly distributed to all portions of the liquid or gas" (10). Together these laws explain the increased rate of oxygen perfusion into tissue.

At sea level or normobaric conditions, pressure is considered to be 0 atmospheres or 760 mmHg or 1 ATA. With room air, oxygen is carried in blood by hemoglobin at a 97% saturation rate (9). Arterial oxygen tensions are about 100 mmHg and tissue oxygen tensions are approximately 55 mmHg (9). Normobaric conditions typically allow 3mL of oxygen to be carried within 1L of blood (9).

In an HBO chamber a patient goes below sea level, typically between 2 and 3 ATA and receives additional 100% oxygen delivered within the chamber (9). This increased pressure increases the concentration of oxygen as described in Dalton's Law and increases the amount of solution delivering oxygen to tissues as described in Henry's Law. Arterial oxygen tensions can increase to as much as 2000 mmHg and tissue oxygen tensions to 500 mmHg while undergoing therapy (9). At 3 ATA, the oxygen to blood ratio increases to 6mL/L (9). The oxygen perfusion rate is sufficient enough to maintain oxygenation to tissues at rest even if hemoglobin is not present. Areas in which red blood cells are not able to reach or damaged areas of tissue that no longer have normal vasculature can be supplied with oxygen under hyperbaric conditions (9).

There are two types of HBO chambers: monoplace chambers and multiplace chambers. A monoplace chambers is designed for one patient. This chamber allows the patient to breathe 100% oxygen simultaneously as he/she experiences pressurized oxygen below sea level, up to 3 atmospheres (9). Multiplace chambers are intended for multiple occupants and oxygen is delivered to the patients via face mask.

HBO is FDA approved for various conditions. HBO helps reduce the amount of carboxyhemoglobin in a patient with carbon monoxide poisoning and may prevent associated neurocognative deficits. Scuba divers with decompression sickness and air embolism can undergo HBO to reduce symptoms. Wagner grade 3 or higher non-healing wounds are treated with HBO to increase oxygenation saturation and revascularization in hypoxic tissue. Other conditions approved for HBO therapy include: chronic refractory osteomyelitis, osteonecrosis, soft tissue radionecrosis, compromised skin grafts, progressive necrotizing infections, acute peripheral arterial insufficiency or ischemia, actinomycosis, crush injuries of limbs, gas gangrene, gas embolism and cyanide poisoning (11). Diving parameters are determined by the diagnosis.

HBO therapy for non-healing wounds was approved by the FDA in 1988. This allows wounds that are Wagner Grade 3 or higher after at least 30 days of standard wound care to be treated with adjunctive hyperbaric oxygenation therapy (10). Treatment includes 70 to 90 minute intervals of HBO at 2.0 to 2.5 ATM for about 30 days (11). Length of therapy is usually determined by insurance coverage.

HBO works to promote the natural healing process and does not accelerate healing. Normal tissue oxygen tension in the extremities is > 40mmHg which is needed for adequate oxygenation and immunological response in tissues (10). Diabetic wounds often have oxygen tensions < 20mmHg causing hypoxia and an impaired ability to generate an immune response to that area (10). During treatment HBO oxygen plasma concentration levels are increased 10-15 fold as pressure increases causing tissue oxygenation tensions to increase and the vascular supply of damaged tissue to have greater oxygen perfusion (10). Increasing vascular supply supports collagen, an important structure in oxygenation allowing oxygen to diffuse more readily into capillaries (10).

HBO is a considerably safe therapy and side effects are rare. However, there are some complications associated with HBO. Boyles Law states that "at a constant temperature, the

pressure and volume of gas are inversely proportional" (9). This concept defines the slight temperature increase below sea level and the "squeeze" that some patients may experience during HBO. A squeeze occurs when there is a disparity between outside pressure and pressure inside any enclosed air filled chamber such as the ear. The difference between the pressure outside and inside the ear may result in inner ear pain, most often occurring with eustachian tube dysfunction. Other complications that may occur because of this law include arteriole gas embolism and pneumothorax; however these side effects are uncommon (9).

Other more serious complications relate to oxygen toxicity. Central nervous system (CNS) oxygen toxicity can occur in patients taking CNS stimulants, epinephrine, corticosteroids and patients with hyperthyroidism or a history of seizure disorder, increasing the risk of seizure while undergoing HBO. Pulmonary oxygen toxicity is rarely seen in HBO. Symptoms of pulmonary oxygen toxicity include shortness of breath, substernal chest pain and dyspnea. Chest pain typically resolves in 2 to 4 hours after exposure while shortness of breath can last for weeks (10). Ocular oxygen toxicity may cause transient hyperoxic myopia (9). Acceleration of malignant growth has been suggested as a complication, but not yet studied (9).

Relative contraindications to HBO therapy include high fever, sinusitis, upper respiratory infection, emphysema, known seizure disorder, history of spontaneous pneumothorax, history of otosclerosis and history of optic neuritis (10). Risks and benefits must be assessed before initiating therapy for patients with relative contraindications. Absolute contraindications include untreated pneumothorax and patients taking adriamycin, bleomycin, cis-platinum, disulfiram and sulfamylon (10). In order to prevent a fire, patients must remove all jewelry, electronic devices and any metals before entering the HBO chamber. Hospital gowns should be worn into the chamber and a patient must not take anything in with them.

HBO may be an effective way to manage non-healing diabetic wounds that fail traditional therapy. Although this treatment may not be curative, it may prolong the need for more aggressive and invasive procedures and subsequent amputation. However, HBO therapy is a controversial issue. Its efficacy is not clearly defined in the research, and it can be very costly and may not be covered under health insurance. This emphasizes the importance of defining its benefit in the treatment of non-healing wounds in diabetic patients.

METHODS

An article by Davis, described in numerous literatures as the foundation for the FDA approval of HBO for diabetic non-healing wound therapy, was specifically sought out. However, after a thorough search, the original article couldn't be found, but it is referenced heavily in the other articles chosen to be reviewed.

Studying the benefits of HBO therapy for diabetic non-healing wounds poses a question of prognosis. It is best answered using studies with high levels of evidence such as a meta-analysis and systemic reviews using non-randomized controlled clinical trials and cohort studies. It is impossible to perform a blind or double blind study in this case due to the equipment needed in HBO therapy.

Two sources (12,13) were found on Pubmed/Medline, a database provided by Pinnacle Health, through a Mesh search using key words "Hyperbaric oxygenation" and "diabetic foot". No limits were set during the search.

Two other sources (14, 15) were referenced in an article by Wang et al. entitled "Hyperbaric Oxygen for Treating Wounds". Sources were found using the Undersea and Hyperbaric Medical Society database called the Rubicon Foundation using the author search tab by searching the author listed on the article by Wang et al. in the reference section.

Inclusion criteria consisted of articles in English at any level of evidence relating to hyperbaric oxygen therapy and non-healing wounds of diabetic patients. Exclusion criteria consisted of other disease states FDA approved for hyperbaric oxygenation, scientific mechanism of hyperbaric oxygenation and studies relating to hyperbaric therapy complications or side effects. Article relevance was determined by content in the abstract. Both articles that oppose and support the topic were included in this paper. Articles were chosen to review data that has helped formed guidelines in treating non-healing wounds with HBO.

DISCUSSION OF ARTICLES

STUDY #1

A systematic review by Wiedmann, et al. entitled "Systemic review of hyperbaric oxygen in the management of chronic wounds" evaluated data on HBO therapy used to treat four common chronic wound types: diabetic foot ulcers, venous

leg ulcers, arterial leg ulcers and pressure ulcers (12). Inclusion criteria consisted of: 1) studies performed that compared the used of adjunctive HBO therapy with no HBO therapy, 2) studies where allocation of treatment was randomized, 3) treatment of chronic wounds which have failed standard wound therapy and 4) associated with diabetes, arterial disease, venous disease or wounds that result from external pressure. Articles were also included based on one of the following clinical outcomes: 1) wound size reduction, 2) proportion healed, 3) risk of major and minor amputation, 4) pain, 5) recurrence rate after healing, 6) quality of life, 7) transcutaneous oxygen tension changes. Exclusion criteria included: 1) animal studies, 2) topical oxygenation therapy, 3) previous treatment with HBO. Only six articles met criteria during search: five relating to diabetic foot ulcers and one concerning venous ulcers.

Results were difficult to assess due to the variation between the studies. Two of the five diabetic ulcer related articles reported increased healing rates but collectively did not reach significant healing levels when compared to control groups. Another study showed significant wound healing in patients who received HBO but did not account for subjects dropping out and amputation rates. A trial measuring wound size reported immediate significant data suggesting benefits of HBO therapy, but did not show the same significance in long-term follow up of subjects. Three of the studies also observed major amputation rates 1 year post treatment and concluded that the risk for amputation was in fact reduced by HBO therapy. However, two other trials reported the risk for minor amputations was actually slightly increased in HBO. The studies that monitored transcutaneous oxygen tensions showed significant increases in tissue oxygen tension measurements while undergoing HBO therapy; however, there was not a significant increase in oxygen tensions from the beginning to the end of the study. The study assessing HBO treatment in venous ulcers was based on wound size reduction and did not show a significant benefit of therapy.

The articles collectively did not support the long term effects in wound healing using HBO therapy. However, there was a significant reduction in amputation rates. Also, HBO seemed to benefit wound healing in the short term setting. This systemic review provides a helpful overview of the most recent studies challenging the benefit in HBO therapy.

This systemic review included multiple studies that observed the effects of HBO. However, the details pertaining to how many subjects were used in each study, the demographics of the subjects, the severity of the wounds and the amount of HBO therapy the subjects received varied greatly. This review only compares studies done using HBO to treat lower extremity wounds but doesn't reflect actual similarity in the method of the study. In spite of this, significant evidence that HBO benefits in short term effects of healing and reduces the amount of major amputation secondary to diabetic non-healing wounds has been shown in multiple studies. This systemic review is a valuable study in supporting the use of HBO therapy.

STUDY #2

An article by Kessler, et al. entitled “Hyperbaric Oxygenation Accelerates the Healing Rate of Nonischemic Chronic Diabetic Foot Ulcers” is a prospective randomized study performed on diabetic patients with Wagner 1 to 3 stage ulcers (13). The control period included 28 DM-I and DM-II patients admitted to the facility from January 1999 to January 2000. The study period included 28 DM-I and DM-II patients that were hospitalized for 2 weeks at which time they received HBO therapy in multiplace chambers for two 90 minute sessions, 5 days per week. Chambers were pressurized at 2.5 ATA and 100% oxygen was administered via face mask. Transcutaneous oxygenation tensions and ulcer surface area were measured during the study to determine progress. The results demonstrated that HBO therapy doubled healing rates in non-ischemic diabetic ulcers.

The study was approved by an ethics committee and examined only diabetic patients. During the study period all patients were monitored in an inpatient setting, glucose control was implemented and orthopedic devices to reduce pressure on the wound were given to all subjects. Transcutaneous oxygen tension and ulcer size were measured systematically during the study to ensure accuracy.

Multiple details about the methods of the study were left out of the article. The inclusion and exclusion criteria were not provided. There was no reference to where this study was performed, the type of institution that the subjects were tested at nor whether all subjects were accountable for at the end of the study. Wagner grade 1 and 2 ulcers, which were evaluated in this study, are less severe and can be treated with more conservative therapy such as IV antibiotics and routine wound care; these stages are not even FDA approved for treatment with HBO. Therapy was initiated two times per day, which is not the typical treatment for non-healing wounds. This could have increased the success of the

subjects in the trial but does not specifically show the benefit in clinical practice. The investigator did not disclose information regarding skipped or missed sessions by the subjects in the study. Due to the lack of information relating to the methods of this study, it is difficult to say whether the results are valid.

STUDY #3

An article by WA Zamboni et al. entitled "Evaluation of hyperbaric oxygen for diabetic wounds: a prospective study" was published in a journal by the UHMS (14). The control group consisted of five insulin dependant diabetic (IDDM) patients that did not participate in adjunctive HBO therapy. The study group was made up of five IDDM patients who underwent HBO therapy with 100% oxygen inhalation at 2 ATM for 120 minutes per day, 5 days per week for a total of 30 days. Inclusion criteria for the study group consisted of: 1) diabetics with >10 years of insulin dependence, 2) chronic lower extremity wounds (14). Subjects underwent surgical debridement of the wound before beginning the study. Transcutaneous oxygen tension and wound surface area were measured to evaluate progress during the study.

The results of the study showed a significant reduction in wound surface area in patients using HBO. Eighty percent of the control group had persistent non-healing of lower extremity wounds while 80% of the study group had spontaneous healing of lower extremity wounds.

Informed consent was obtained from all subjects participating in the study. HBO therapy was not withheld from the subjects in the control group; the subjects that made up the control group refused HBO therapy. Surgical debridement with identical wound dressings were done initially, allowing for consistent wound care and healing stages at the start of the study. The individuals measuring the progress of the wounds were blinded during the study allowing wound measurement to be free of bias. Patients were re-evaluated at 7 weeks and between 4 and 6 months after HBO therapy. During the study glucose control was maintained in the subjects with the assistance of an endocrinologist. All subjects were accountable at the end of the study.

This study was executed in a systematic way and supports the use of HBO therapy in treating diabetic non-healing wounds. However, the study sample is small and it only evaluates the short term effects of HBO therapy. Also, the demographics of the subjects and how subjects were chosen was not provided. The investigator did not disclose the severity of the wounds nor the exact locations of the wounds on the lower extremity. The study may show a false benefit if the wounds of the subjects were less severe than FDA approved HBO non-healing wounds. This data is valuable in HBO therapy and should be repeated evaluating more subjects designed to include long term effects. Possible bias should not be excluded due to the fact that this study was published in a journal owned by UHMS. No reference or relation to UHMS was mentioned in the literature.

STUDY #4

An article entitled "Hyperbaric Oxygen Therapy in Diabetic Gangrene" by G Oriani, et al is non-randomized control study performed in Milano, Italy in 1982 (15). All subjects were affected with diabetic gangrene. The control group consisted of 18 subjects that were treated with daily curettage to remove necrotic tissue without HBO therapy. The study group had 62 participants that underwent daily curettage and HBO therapy at 2.5-2.8 ATM, six days per week until the wound healed. Total healing time was estimated as 72 sessions with a margin of 28 sessions. The results showed a decrease in amputations in patients being treated with HBO, without statistical significance.

This article is relatively abbreviated and does not give much information relating to the methods of the study. Inclusion and exclusion are not included in the article. The study does not disclose how progress was measured in the subjects, nor does it discuss how the severity of gangrene affected data. Information relating to the demographics of the subjects, how the subjects were chosen and if the subjects were accountable at the end of the study was not provided. The study group was much larger than the control group which may show a false benefit due to error in analyzing the data. This study is likely outdated and bias cannot be ruled out due to the fact that it is published in a UHMS sponsored journal.

CONCLUSION

According to the evidence presented, there does not seem to be a significant long-term benefit in using HBO in non-healing diabetic foot wounds. Most patients will inevitably continue to have issues with chronic lower extremity wounds and may eventually need to have a limb amputated. However, there is data that suggests a significant increase in short term healing rates and a reduction in amputation rates. This is an important factor in assessing the quality of life of

the patient. HBO is a non-invasive method to prolong the need for amputation. I think that it is justifiable to use HBO in specific diabetic patients who suffer from chronic non-healing wounds in order delay the need for amputation and improve their quality of life.

HBO may also show a benefit in decreasing costs on the healthcare system. By decreasing the amount of amputations relating to diabetic lower extremity wounds, patients may be able to work longer, have shorter hospitalizations and undergo fewer complicated surgeries.

The conflicting research further explains the controversy in using HBO. More non-bias research should be performed to clearly show how HBO benefits diabetic non-healing wounds. By establishing more evidence as to if and how HBO works for this patient population, it may be more available to those who may benefit from it.

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Author Information

Carla Novaleski
King's College Physician Assistant Program