



TO DETERMINE THE ACCEPTABILITY AND TOLERANCE OF THE PATIENTS RECEIVING HBOT THERAPY.

General Medicine

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ABSTRACT

Aim & Objectives: The main aim of this Study is to determine the acceptability and tolerance of the patients receiving H.B.O.T. therapy. **Materials And Methods:** Our study included 31 patients with diabetic foot ulcers who were offered H.B.O.T. **Conclusion:** Hyperbaric Oxygen therapy, based on its principle and evidence around its beneficial impact on improving tissue oxygenation and neovascularization, comes across as an acceptable modality to be used as an adjunctive therapy tool for diabetic foot ulcers. It may also help alleviate the neuropathic symptoms in the other foot. While the procedure does cause certain side effects, these are reversible – making the whole process well-tolerable, too. More extensive studies are needed to reinforce the adoption of this novel mode of treatment for diabetic foot ulcers to address this issue for patients with diabetes.

KEYWORDS

INTRODUCTION

Diabetic foot ulcer (D.F.U.) is the presence of an ulcer in the lower limb associated with neuropathy and peripheral arterial disease in a patient with diabetes. In due course of time, the D.F.U.s may get infected and develop multi-drug resistance (M.D.R.), turning into non-healing wounds – leading to amputations and mortality. Diabetic foot ulcers (D.F.U.s) are indeed one of the tricky complications that hold primary responsibility for raised morbidity and mortality in patients with diabetes globally. Despite a clearly charted standard of care (SoC) for the D.F.U.s, the barely satisfactory outcomes indicate the need for newer approaches to add to the SoC in this condition. Amidst the various newer trends, Hyperbaric Oxygen Therapy (H.B.O.T.) is one of the interesting leads that has shown promising results in multiple countries, such as the United States and Europe.¹

India has 77 million patients living with diabetes and diabetic foot ulcers remain one unaddressed problem as of today, even globally. Implications of DFU range from as minor as infection and morbidity to as major as amputation and potential life risk, not to mention the overall downhill impact on the quality of life of the family.

REVIEW OF LITERATURE

Hyperbaric oxygen therapy (HBOT) is a modality of treatment that involves breathing 100% oxygen in a specialized pressure chamber – called a 'hyperbaric' chamber.¹ While the HBOT has been used for various medical conditions (approved for 13 medical conditions by USFDA, including DFU), such as decompression sickness, carbon monoxide poisoning, wound healing, and infection control, we would focus on its use as an adjunctive therapy for managing chronic DFUs. Patients with DFUs are usually prescribed HBOT sessions, lasting 80-90 minutes each, once daily for a minimum of 5 days a week for up to 6-8 weeks, depending on the severity of their ulcer. The pressure applied is usually between 2.0-2.5 ATA (10-15 m below sea surface). The principle of HBOT is to provide oxygen at high pressures to restore abnormal tissue oxygen via basic physics gas laws.^{1,2,3}

The basic physics fundamental of hyperbaric oxygenation is a consequence of three main factors: (1) Breathing in 100% O₂ creates a positive gradient which stimulates diffusion of hyper oxygenated lungs to hypoxic tissues; (2) As per Henry's Law, the high-pressure causes the O₂ concentration in the blood to rise (the amount of dissolved gas within a liquid is directly proportional to its partial pressure) and (3) As a next step, there is a decrease in the size of gas bubbles in the blood due to Boyle-Marriott Law and Henry's Law. To summarise, creating a hyperbaric environment with pure oxygen brings about a significant increase in the oxygen supply to blood

(hypoxemia) as well as to the tissues (hyperoxia) with no role in hemoglobin. Thus, HBOT, through the listed virtues, provides multiple positive effects in an organism and could be potentially used to correct tissue hypoxia and chronic hypoxemia and to aid in the clinical management of different pathological processes, including wound healing, necrosis or reperfusion injuries (Figure.1).^{1,2,3}

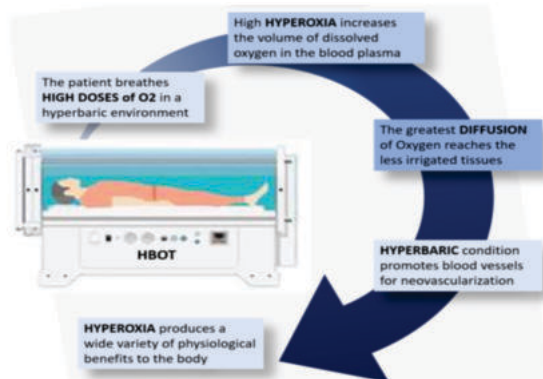


Figure 1: Physics behind Hyperbaric Oxygen Therapy

HBOT can have beneficial effects on the body, such as increasing oxygen delivery, reducing inflammation, and stimulating tissue repair. However, HBOT can also have some potential risks, such as ear injuries, lung collapse, seizures, and temporary near-sightedness. Hence, the need for the right patient selection and more evidence generation in this line is warranted.^{4,5,6}

In India, neuropathy accounts for about 80% of DFUs, with neuro-ischemia being the root cause in the remaining 20% of cases. In one of the studies, DFU was reported in 4.5% of the newly diagnosed population with diabetes. Comparatively lower proportions of DFU in India are attributed to under-reporting, lack of awareness, negligence, and other such factors. The prevalence of peripheral vascular disease (PVD) is 3.2% in diabetic patients <50 years, but it increases to 33% in patients >80 years – thus confirming the association with age as well as duration of diabetes. In fact, DFU stands out as one of the most frequent reasons for hospitalizations (30%) globally in patients with diabetes. Talking about clinical outcomes in India, 25% of patients with diabetes develop DFUs, of which 50% get infected, requiring hospitalization while 20% need amputation. These DFUs contribute to approximately 80% of all non-traumatic amputations in India

annually. On a mortality scale, patients with DFU have a 40% higher 10-year death rate than those without DFU.^{7,8,9}

Evidence has shown that beyond effectiveness, the acceptability of interventions is more critical for keeping away anxiety disorders in evidence-based practice. Given this background, we decided to analyze the acceptability and tolerance of HBOT as an adjunctive therapy for DFU in our subset of patients with diabetes.

Rationale Of The Study

India as a country has 77 million people living with diabetes – a very fast-growing burden and equally increasing prevalence of diabetic foot ulcers and related morbidity and mortality. DFUs call for the maximum need for hospitalization for a patient with diabetes, thus bringing in a loss of productivity and incremental expenditure from personal patient pockets toward medical care. Despite the available standard of care approaches, DFU outcomes remain unsatisfactory. Thus, there is a need to evaluate and adopt novel tools and approaches that may be beneficial for this subset of patients. HBOT is one such widely used non-surgical modality that has promising potential in the management of DFU. However, for any medical procedure, the acceptability and tolerance of the patient need to be taken into consideration for successful application at a mass level. Acceptability decides the adherence and drop-out rates for any and every intervention in the medical field.

Aim & Objective Of The Study

The main aim of this Study is to determine the acceptability and tolerance of the patients receiving HBOT therapy.

METHODS

Study Design and Recruitment

Patient population with DFU being treated at the prana HBOT center were interviewed telephonically post-completion of their prescribed no of sessions of HBOT. The interview consisted of questions from a survey form that was filled out for later analysis. The Survey form was adopted based on the Treatment Acceptability/Adherence Scale (TAAS) developed by Irena Milosevic, Hannah C. Levy, Gillian M. Alcolado & Adam S. Radomsky (2015). It was slightly modified to suit our study purpose and modality. PRANA center, located in Mumbai, Maharashtra, India, has all the requisite certifications and registrations required by the local authority in Mumbai to carry out HBOT.

Study Tool

Treatment Acceptability/Adherence Scale (TAAS) is a survey developed by Irena Milosevic, Hannah C. Levy, Gillian M. Alcolado & Adam S. Radomsky (2015). This scale aimed to help analyze psychometric properties on the acceptability of the therapy under question. This would help clinicians to assess the effectiveness of interventions and thereby build more robust interventions for clinical practice. In this study, we utilized the TAAS questionnaire framework and modified the questions to evaluate their opinion about HBOT and their experience during the procedure. The interview has been taken after the patients have completed the prescribed HBOT sessions.

Study participants:

The Study included 31 patients with diabetic foot ulcers who were offered HBOT with the following inclusion & Exclusion Criteria.

RESULTS

Around 31 patients of T2DM with neuropathy with a foot ulcer for more than three months were advised varying prescriptions of HBOT based on their DFU. Among the 21 males and 10 females, most patients, 22, were aged 50-75 years, while six were less than 50 years, and 3 were more than 75 years. In terms of duration, the majority had diabetes for > 10 years (Figure 2).

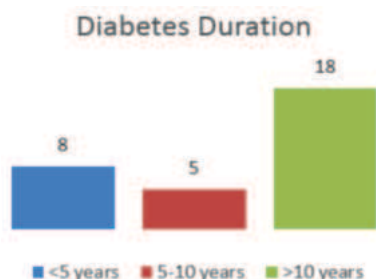


Figure 2: Diabetes duration of the study population

Of the 31 patients, 100% were aware of their neuropathy, and 55% of patients mentioned having severe neuropathy, followed by 29% and 16% having moderate and mild neuropathy, respectively (Figure 3). As the literature suggests, the severity of neuropathy showed a clear association with the duration of diabetes. Verifying Doppler studies, ten patients had evidence of PVD, while 18 had no evidence of PVD. For three patients, doppler reports were unavailable.

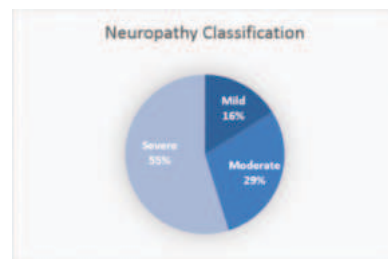


Figure 3: Severity of Neuropathy within study population

In context with Diabetes control, 55% of the population had optimal glucose control with their HbA1c between 7-8 %, 35% had A1c between 8-9%, and around 10% had poor control with HbA1c >9% (Figure 4).

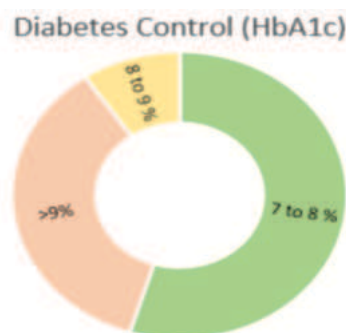


Figure 4: Diabetes Control within the study population as depicted by HbA1c

The procedure in our Study was associated with a few side effects, such as Ear pain/pressure, Fatigue, hypoglycemia, headache, and dizziness. While 35% of patients did not have any side effects, the commonest side effect was ear pain/pressure – 57% of the patient population. Approximately 4 and 6 patients, respectively, mentioned having reversible complaints such as fatigue/hypoglycemia and dizziness/headache (Figure 5).

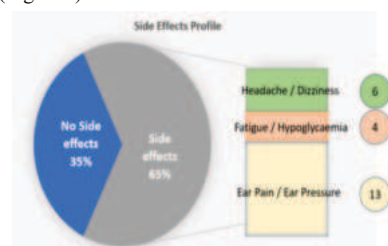


Figure 5: Side Effects seen with HBOT at PRANA HBOT centre, Maharashtra, India

Based on the survey form, questions were segregated into buckets, determining acceptance and tolerance of the modality in question – HBOT. Except for two questions that overlapped, most of the questions had a clear propensity toward the two parameters (Table 1).

Almost the majority of patients showed acceptance towards the novel approach of HBOT, posing positive responses to questions under this segment. 100% of subjects completed the Study with no fallouts.

Table 1: Question Segregation for Analysis

Questions in Survey Form for Interview	Acceptance	Tolerance
When you hear about the treatment, do you feel that you would be able to complete it fully and successfully?		

When you heard about the treatment, did you feel that you would be able to adhere to this treatment (Cope with it)		
Did you find this treatment Exhausting?		
Was It distressing to Participate in this treatment?		
Did you find this treatment intrusive?		
Were there any efforts before the session to make it comfortable and with less fear/ anxiety?		
How was the experience during the session compared to surgery in the OPD/OT		
Would you prefer HBOT instead of surgical treatment?		
Would you recommend this treatment to a friend with a similar problem of DFU?		
Did you at any time feel that you would drop this treatment midway? If yes, why?		
Were you happy & satisfied with this modality of treatment?		
Do you feel that both feet are benefited in terms of Symptoms of Neuropathy after HBOT?		

The questions under the banner of tolerance were simulated together based on their experience with the procedure, their satisfaction with the overall process, and their preference for HBOT in comparison to alternate treatment measures, be it medicines or surgery. Data was then analyzed and put together to show a clear predilection when it comes to satisfaction. However, the experience was an inconclusive finding, which is the standard opinion of patients for anything new. Side effects – while reversible, may have influenced these outcomes.

Also, while 100% of the study population agreed to recommend the new procedure to their family and friends with similar conditions of DFU – the preference for HBOT over surgery showed a higher bend towards being inconclusive. This follows every new modality that launches in any market, especially in the medical field (Figure 6).

We also found 100% agreement in response to whether patients felt HBOT benefitted both their feet. This observation points towards HBOT's potential for improvement in neuropathy symptoms.

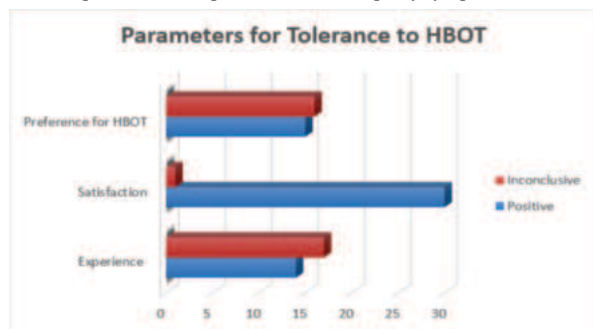


Figure 6: Tolerance to HBOT basis Telephonic Interview using a standard questionnaire in T2DM with DFUs

DISCUSSION

All 31 patients with diabetic foot ulcers >3 months who were subjected to HBOT as an adjunctive therapy successfully completed their sessions as prescribed based on the severity of their DFU. 100% of patients showed good recovery of their foot ulcers with positive opinions about their satisfaction with the procedure. Patients agreed that HBOT benefits neuropathy symptoms of both feet – that is, both feet with an ulcer and the other foot without an ulcer.

Acceptability was a clear win among patients with good adherence rates, too – No drop-outs from the sessions at any point in time.

While side effects were seen in 65% of the study population, anticipatory education and counseling of patients done prior to HBOT sessions helped alleviate any fear/anxiety in patients' minds. Also, the majority of these side defects were reversed post-HBOT sessions. These factors tend to raise the acceptability of newer treatment modalities.

Talking about the patient perspective, a positive inclination was clearly seen toward the adoption of HBOT as captured under 'Satisfaction' for

the management of DFUs. The experience of HBOT was compared to choosing a surgical intervention. This question was not commented on well by 16 patients and was hence termed inconclusive. Sometimes, new procedures may be overwhelming and, hence, difficult for patients to opine about.

Upon conducting an online literature search, most studies on HBOT have been done on clinical outcomes determining the efficacy of HBOT on DFUs – long-term outcomes, i.e., major and minor amputations.^{6,10,11} There is no documentation on patient perspectives for this novel approach. However, when it comes to a country like India, where the patient pays out-of-pocket, acceptance and tolerance of any and every modality claims prime importance. Also, as stated earlier, acceptance of any intervention largely influences its outcomes.

Strength & Limitations

This study was done on a small scale and should be considered only as a stepping stone to larger randomized control trials for evaluating HBOT's impact on neuropathy and human life. The results obtained cannot be broadly applied. Additionally, the efficacy of HBOT in terms of wound control, amputations, morbidity, and mortality has not been accommodated in this Study. However, this study sets a strong hypothesis for the possibility of future research on this acceptable and well-tolerable treatment modality, given its fundamental potential to improve DFU outcomes in India.

CONCLUSION

Hyperbaric Oxygen therapy, based on its principle and evidence around its beneficial impact on improving tissue oxygenation and neovascularization, comes across as an acceptable modality to be used as an adjunctive therapy tool for diabetic foot ulcers. It may also help alleviate the neuropathic symptoms in the other foot. While the procedure does cause certain side effects, these are reversible – making the whole process well-tolerable too. Larger studies are needed to reinforce the adoption of this novel mode of treatment for diabetic foot ulcers to address this issue for patients with diabetes.

REFERENCES

- Ortega MA, Fraile-Martinez O, García-Montero C, Callejón-Peláez E, Sáez MA, Álvarez-Mon MA, García-Hondurilla N, Monserrat J, Álvarez-Mon M, Bujan J, Canals ML. A General Overview on the Hyperbaric Oxygen Therapy: Applications, Mechanisms and Translational Opportunities. *Medicina (Kaunas)*. 2021 Aug 24;57(9):864. doi: 10.3390/medicina57090864. PMID: 34577787; PMCID: PMC8465921.
- New Evidence-based Therapies for Complex Diabetic Foot Wounds | Compendia | American Diabetes Association (diabetesjournals.org)
- HBOT for Diabetic Foot Ulcer – An Overview (woundreference.com)
- Diabetic Foot Ulcers: Appraising Standard of Care and Reviewing New Trends in Management: American Journal of Clinical Dermatology (springer.com)
- Can Hyperbaric oxygen therapy treat diabetic foot ulcers? (medicalnewstoday.com)
- <https://www.fda.gov/consumers/consumer-updates/hyperbaric-oxygen-therapy-get-facts>
- Das A, Pendsey S, Abhyankar M, Malabade R. Management of Diabetic Foot in an Indian Clinical Setup: An Opinion Survey. *Cureus*. 2020 Jun 15;12(6):e8636. doi: 10.7759/cureus.8636. PMID: 32685305; PMCID: PMC7364422.
- Kale, DS; Karande, GS; Dathkile, KD1., Diabetic Foot Ulcer in India: Aetiological Trends and Bacterial Diversity. *Indian Journal of Endocrinology and Metabolism* 27(2):p 107-114, Mar–Apr 2023. [DOI: 10.4103/ijem.ijem.458_22]
- Ghosh P; Valia R; Burden of Diabetic Foot Ulcers in India: Evidence Landscape from Published Literature; DOI: <https://doi.org/10.1016/j.jval.2017.08.489>
- A.L. Gill, C.N.A. Bell, Hyperbaric oxygen: its uses, mechanisms of action and outcomes, *QJM: An International Journal of Medicine*, Volume 97, Issue 7, July 2004, Pages 385–395, <https://doi.org/10.1093/qjmed/hch074>
- Thom SR. Hyperbaric oxygen: its mechanisms and efficacy. *Plast Reconstr Surg*. 2011 Jan;127 Suppl 1(Suppl 1):131S-141S. doi: 10.1097/PRS.0b013e3181f8e2bf. PMID: 21200283; PMCID: PMC3058327.