Original Paper

Urologia Internationalis

Urol Int 2018;101:206–211
DOI: 10.1159/000490356

Received: March 28, 2018
Accepted after revision: May 20, 2018
Published online: August 8, 2018

The Effect of Hyperbaric Oxygen Therapy on Erectile Functions: A Prospective Clinical Study

Mehmet Oguz Sahin[a] Volkan Sen[a] Erhan Eser[b] Evin Koc[c] Umit Gumus[a] Cengiz Karakuzu[c] Oktay Ucer[d]

[a]Department of Urology, Manisa State Hospital, Manisa, Turkey; [b]Department of Public Health, Celal Bayar University School of Medicine, Manisa, Turkey; [c]Department of Underwater and Hyperbaric Medicine, Neoks Hyperbaric Oxygen Therapy Center, Izmir, Turkey; [d]Department of Urology, Celal Bayar University School of Medicine, Manisa, Turkey

Keywords
Erection · Erectile dysfunction · Hyperbaric oxygen therapy · International index of erectile function

Abstract
Introduction: We aimed to evaluate the effects of hyperbaric oxygen therapy (HBOT) on erectile function in patients who had no cavernosal or urethral injury by using International Index of Erectile Function (IIEF) questionnaire. ***Materials and Methods:*** The male patients who were treated by HBOT for several diseases between July 2017 and September 2017 were examined. All patients filled the IIEF questionnaire form before the first day and after the last day of HBOT and a questionnaire including demographic characteristics and medical history. The effects of demographic characteristics and risk factors on erectile function were evaluated, and the IIEF domain scores of patients in first day and last day of HBOT were compared. ***Results:*** Totally, 50 patients were included in the study between July 2017 and September 2017 and the mean age was 59.38 ± 13.77. The mean post-HBOT IIEF-EF score of patients was significantly higher than the mean pre-HBOT IIEF-EF score of patients (15.74 ± 10.52 vs. 19.50 ± 10.91; $p < 0.001$). The mean post-HBOT IIEF scores of other domains including intercourse satisfaction, orgasmic function, sexual desire, and overall satisfaction were also significantly higher than pre-HBOT scores. ***Conclusions:*** HBOT may be a good alternative treatment or adjunctive treatment for erectile dysfunction.

Introduction

Erectile dysfunction (ED) is defined as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance [1]. It is a common problem in men worldwide, and has major impact on the quality of life [2]. The prevalence of ED increases with age, and it is estimated to affect 25–52% of men in the age-group of 40–70 years [3–5]. Common risk factors for ED include aging, metabolic syndrome, diabetes mellitus, obesity, lack of exercise, and smoking [1, 6].

E-Mail karger@karger.com
www.karger.com/uin

Volkan Sen, MD, FEBU
Department of Urology
Manisa State Hospital
TR–45125 Manisa (Turkey)
E-Mail sen_volkan@yahoo.com

ED may be classified as anatomical, neurogenic, vasculogenic, drug-induced, hormonal, and/or psychogenic. While various treatments are available for ED, permanent cure is only possible in ED due to hormonal deficiency, post-traumatic arteriogenic ED in young patients, and psychogenic ED. First-line treatment of ED is usually with oral phosphodiesterase type 5 inhibitors. Intracavernous injections constitute second-line treatment, and surgical implantation of penile prosthesis comprises third-line therapy. In addition, there are new treatment modalities that have become popular in recent years; these include low-intensity extracorporeal shock wave therapy and hyperbaric oxygen therapy (HBOT) [7–9]. In HBOT, the patient is made to breathe 100% oxygen at pressures greater than normal atmospheric (sea level) pressure (>1 atm). This increases oxygen tension and the dissolved oxygen in blood, and results in increased oxygen delivery to tissues [10]. Over the past 50 years, HBOT has been used in several diseases, including urological conditions such as interstitial cystitis, radiation-induced hemorrhagic cystitis, and Fournier gangrene [10, 12–14]. In the first report on the effect of HBOT on erectile function, Müller et al. [8] showed that HBOT could improve erectile function in the rat cavernous nerve (CN) injury model. Later, in 2010, Yuan et al. [11] showed that HBOT could improve erectile function in patients undergoing posterior urethral reconstruction.

In the present study, we aimed to evaluate the effect of HBOT on erectile function in patients without cavernosal or urethral injury by using the International Index of Erectile Function (IIEF) questionnaire.

Methods

Participants

Male patients treated by HBOT for different diseases (foot wound, avascular necrosis of the femoral head, sudden hearing loss, and sudden loss of vision) between July 2017 and September 2017 at our institution were consecutively enrolled in this prospective study. Patients were eligible for inclusion if they (1) were ≥18 years old, (2) heterosexual, and (3) were not using phosphodiesterase type 5 inhibitors, intracavernosal injections, or any other treatment for ED during the study period. Patients were excluded if they (1) had history of persistent spinal cord or (2) brain disease or (3) of drug abuse or (4) did not have a regular sexual partner.

Data on demographic characteristics and past medical history were collected using questionnaires. ED was assessed using the IIEF questionnaire, which was filled in by each patient before the first day and after the last day of HBOT. Table 1 shows the IIEF scoring algorithm.

Approval for the study was obtained from the local ethics committee. All participating patients gave written informed consent.

Table 1. Scoring algorithm for IIEF

Domain	Items	Range	Max score
Erectile function	1–5, 15	0–5	30
Orgasmic function	9, 10	0–5	10
Sexual desire	11, 12	0–5	10
Intercourse satisfaction	6–8	0–5	15
Overall satisfaction	13, 14	0–5	10

IIEF, international index of erectile function.

HBOT Procedure

HBOT was applied using a multiplace hyperbaric chamber (Hyperbot Model 101, 2005, Turkey), with which up to 10 patients can be treated at a time. The chamber was first pressurized up to 2.4 atmospheres absolute with 100% oxygen for 15 min. Patients were then made to breathe this oxygen through a mask. Each treatment session lasted 120 min; this included the initial 15 min for compression, 3 oxygenation periods of 25 min each (total 75 min), three 5-min air breaks (total 15 min), and 15 min for decompression of the chamber. The HBOT sessions were repeated once daily for 6 days a week. Each patient received a total of 30 sessions of HBOT.

The relationship of demographic and medical factors with erectile function was evaluated, and the IIEF scores before and after HBOT were compared. Social class of the family was evaluated by Boratav's Social Classification of Turkey [15].

Statistical Analysis

SPSS 21.0 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. Statistical significance was at $p \leq 0.05$. The paired t test was used to compare pre- and post-HBOT IIEF domain scores, and the independent samples t test was used to examine the significance of differences in the IIEF scores between subcategories of the covariates. The differences between the pre-HBOT and post-HBOT IIEF domain scores and the covariates' subcategory IIEF score comparisons were also presented as Cohen's effect size [16]. Cohen's effect size is calculated as the difference between mean scores divided by the pooled standard deviation. Effect sizes of 0.20, 0.50, and 0.80 indicate small, medium, and high effects, respectively. Independent categorical variables were compared by the chi-square test or Fisher's exact test. Type 1 error of 0.05 was considered acceptable.

Results

A total of 58 patients who received HBOT between July 2017 and September 2017 were initially enrolled. However, 8 patients did not complete therapy, and so only 50 patients were included in the final analysis. The mean age of the 50 participants was 59.38 ± 13.77 years. The reasons for administration of HBOT were foot wound in 30 of 50 (60%) patients, avascular necrosis of the femo-

Table 2. Demographic characteristics of the patients

	Mean ± SD, *n* (%)
Age, years	59.38±13.77
BMI*	26.17±4.02
Education level	
Primary and secondary school	24 (48)
High school	11(22)
College and higher education	15 (30)
Social classification of the family**	
High-medium social class family	40 (80)
Low social class family	10 (20)
Operation history	
Urological operation	24 (48)
Non-urological operation	9 (18)
No operation	17 (34)
Comorbidities	
Diabetes mellitus	26 (52)
Hypertension	20 (40)
Coronary artery diseas	13 (26)
Thyroid diseases	1 (2)
Chronic obs. pulmonary disease	2 (4)
Smoking	
Yes	30 (60)
No	20 (40)
Alcohol use	
Yes	26 (52)
No	24 (48)

* BMI, body mass index; ** Boratav's social class classification.

ral head in 4 of 50 (8%) patients, sudden hearing loss in 10 of 50 (20%) patients, and sudden loss of vision in 6 of 50 (12%) patients. The most common comorbidities were diabetes mellitus and hypertension (52 and 40% patients; respectively). Table 2 presents the demographic characteristics and medical history of all patients.

Of the 50 patients, 42 of 50 (84%) were married, 5 of 50 (10%) were single, and 3 of 50 (6%) were divorced. According to the pre-HBOT IIEF-EF scores, 18 of 50 (36%) patients had severe ED, 7 of 50 (14%) had moderate ED, 8 of 50 (16%) had mild to moderate ED, 6 of 50 (12%) had mild ED, and 11 of 50 (22%) had no ED. The mean post-HBOT IIEF-EF score was significantly higher than the mean pre-HBOT IIEF-EF score (19.50 ± 10.91 vs. 15.74 ± 10.52; $p < 0.001$). The mean post-HBOT IIEF scores for specific domains (orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction) were also significantly higher than the respective pre-HBOT scores (Table 3).

Table 4 presents the association between HBOT and ED risk factors including age, body mass index, comorbidities, smoking, alcohol use, and so on. Smoking was found to be an effect modifier variable for HBOT; the other variables were neither confounders nor effect modifiers in this study (Table 4).

Discussion

HBOT was first applied in medicine by Behnke and Shaw in 1937 for the treatment of decompression sickness [17]. The modern form of HBOT by the inhalation of oxygen in a pressure chamber was introduced only in the 1950s [18]. HBOT is presently used as the primary treatment modality for selected diseases or as an adjunct to surgical or pharmacologic interventions. Treatment is administered in a monoplace or a multiplace hyperbaric chamber. In the monoplace chamber, only 1 patient can be treated at a time; the patient is placed in the pressurized chamber and breathes the ambient oxygen directly. With the multiplace chamber, 2 or more patients can be treated at a time; the patients enter the pressurized chamber and breathe 100% oxygen via masks, endotracheal tubes, or head hoods. All patients in the present study were treated in a multiplace hyperbaric chamber.

HBOT has been used previously in the treatment of urological disorders such as interstitial cystitis and radiation-induced hemorrhagic cystitis [12, 14, 19, 20]. Increase in tissue oxygenation during HBOT is believed to stimulate angiogenesis, leukocyte activity, collagen formation, and fibroblastic proliferation. HBOT has been shown to be effective in the treatment of hypoxic tissues [12, 19, 20].

HBOT has also been used in the treatment of Fournier gangrene, a life-threatening disease; however, its use in this condition is controversial [21–24]. Rosa et al. [21], Mehl et al. [22], and Li et al. [23] reported lower mortality rates in Fournier gangrene when conventional treatment was combined with HBOT than when only conventional treatment was used. The authors suggested that the benefits of HBOT were likely due to improvement in neutrophil function, neutralization of anaerobic organisms, and promotion of angiogenesis. However, the benefit with HBOT has not been consistently demonstrated. Shupak et al. [24], for example, did not find any decrease in the mortality of Fournier gangrene patients with the use of adjunctive HBOT. There are only a few reports on the effect of HBOT on erectile function [8, 11]. Müller et al. [8] evaluated the effects of HBOT on erectile function and cavernosal tissue in a rat CN injury model. They separated rats into 4 groups: rats with bilateral CN crush

Table 3. Comparison of pre-HBOT* and post-HBOT IIEF domain scores (n = 50)

IIEF domains	ED category	Pre-HBOT Score, mean ± SD	Post-HBOT Score, mean ± SD	p value†	ES‡
Erectile function: **IIEF-EF	Severe (n = 18)	16.44±10.58	20.06±11.31	<0.01††	0.33
	Mild-moderate (n = 15)	11.80±9.13	16.13±10.43	0.005††	0.45
	Overall (n = 50)	15.74±10.52	19.50±10.91	<0.001†	0.35
Intercourse satisfaction	Severe (n = 18)	7.77±5.16	9.16±5.30	<0.01††	0.25
	Mild-moderate (n = 15)	5.26±4.41	7.13±4.94	0.007††	0.41
	Overall (n = 50)	7.40±5.14	8.90±5.31	<0.001†	0.29
Orgasmic function	Severe (n = 18)	6.55±4.21	7.11±4.12	>0.05††	0.13
	Mild-moderate (n = 15)	4.46±4.08	5.53±3.87	0.027††	0.27
	Overall (n = 50)	6.14±4.11	6.84±3.91	<0.01†	0.17
Sexual desire	Severe (n = 18)	5.83±2.12	6.55±2.66	<0.05††	0.30
	Mild-moderate (n = 15)	4.93±2.46	6.13±2.35	0.026††	0.50
	Overall (n = 50)	5.60±2.31	6.66±2.51	<0.001†	0.44
Overall satisfaction	Severe (n = 18)	6.11±3.17	6.77±3.37	<0.05††	0.21
	Mild-moderate (n = 15)	4.26±3.19	5.33±3.59	0.023††	0.31
	Overall (n = 50)	5.48±3.27	6.44±3.43	<0.001†	0.29

* HBOT, hyperbaric oxygen therapy.
** IIEF-EF, international index of erectile function – erectile function.
† Paired t test.
†† Wilcoxon signed rank test.
‡ Cohen's effect size.
ED, erectil dysfunction.

Table 4. The association between HBOT* and the demographic characteristics and erectile dysfunction risk factors (n = 50)

Covariate	Category	Pre-HBOT (mean IIEF** score)	Post-HBOT (mean IIEF score)	p value†	ES‡
Age	<60	21.27±8.67	24.92±7.00	<0.001	0.46
	>65	15.74±10.52	19.50±10.91	<0.001	0.35
BMI	<25	17.29±11.25	21.18±11.54	<0.001	0.34
	≥25	14.94±10.22	18.64±10.66	<0.001	0.36
Education level	Primary and secondary school	19.11±10.55	22.80±9.54	<0.001	0.37
	High school	12.08±9.38	15.91±11.36	<0.001	0.38
Smoking	No	17.70±12.92	19.70±12.79	0.017	0.16
	Yes	14.43±8.56	19.36±9.70	<0.001	0.54
Alcohol drinking	No	16±11.34	19.79±11.94	<0.001	0.33
	Yes	15.50±9.92	19.23±10.11	<0.001	0.37
Comorbidities	Absent or just one	18.93±10.15	22.52±10.25	<0.001	0.35
	At least two	11.33±9.59	15.33±10.66	<0.001	0.39

* HBOT, hyperbaric oxygen therapy.
** IIEF-EF, international index of erectile function – erectile function.
† Paired t test.
‡ Cohen's effect size.

injury that were treated with HBOT (C+/H+); rats with bilateral CN crush injury and no HBOT (C+/H–); rats with no CN crush injury and no HBOT (C–/H–); and rats with no CN crush injury but with HBOT (C–/H+). Outcomes in the 4 groups were examined by calculating the maximal intracavernosal pressure/mean arterial pressure ratios. Corporal tissue changes were evaluated by immunohistochemical staining for nerve growth factor (NGF), endothelial nitric oxide synthase (eNOS), and cluster of differentiation molecule (CD31). The authors found that C+/H+ rats had significantly better recovery in intracavernosal pressure/mean arterial pressure ratio than C+/H– rats (55 vs. 31%; $p = 0.005$). C+/H+ rats also had significantly higher NGF and eNOS staining densities than C+/H– rats. The higher staining density for NGF antibodies after HBOT supports the theory that HBOT has a neuroprotective effect, while the higher staining density for eNOS suggests that improvement in erectile function is mediated by increased eNOS expression. The authors concluded that HBOT could be a useful and reliable treatment to preserve or recover erectile function after CN injury, and that the mechanism of action was probably via increase in expression of neurotrophic and endothelial factors [8].

Yuan et al. [11] evaluated the effect of HBOT on recovery of erectile function after posterior urethral reconstruction. Preoperative and postoperative erectile function was evaluated with IIEF scores. They found that patients receiving HBOT after posterior urethral reconstruction had significantly higher total IIEF, IIEF-EF, IIEF-OS, and IIEF-IS scores than those not receiving HBOT, and concluded that HBOT could be used to improve erectile function recovery after posterior urethral reconstruction [11]. The improvement in erectile function may be associated with increase in tissue oxygenation, eNOS expression, and angiogenesis following HBOT.

Unlike in previous studies, our patients did not have cavernosal nerve or urethral injury; nevertheless they too showed improvement in all IIEF domains. This suggests that HBOT can be beneficial even when ED is not due to tissue damage. However, it should be noted that a recent study by Chiles et al. [25] did not find any improvement in IIEF scores after HBOT in prostate cancer patients treated with nerve-sparing robotic radical prostatectomy. They randomized the patients as sildenafil 50 mg daily + HBOT and control group (sildenafil 50 mg daily + normal air) after nerve-sparing robotic radical prostatectomy. Hereby, all participants had used sildenafil 50 mg daily. The effect of HBOT might be better compared with control group if both of the groups did not use sildenafil therapy. The HBOT procedure of their study included 10 sessions; however, 30 sessions were performed on our patients. The different results can also be connected to the HBOT procedures.

In our study, HBOT improved IIEF scores regardless of the presence of risk factors. Of all the risk factors, only smoking seemed to act as an effect modifier for HBOT. The hypoxia following inhalation of cigarette smoke has been documented to last ~1 h in human volunteers and is attributed to nicotine-induced peripheral vasoconstriction. Hyperbaric oxygen exposure appears to magnify the effects of hyper-oxygenation in smokers [26, 27].

This study has some limitations; there was no control group in our study and the patient sample was heterogeneous in terms of HBOT indications. Further studies including control groups and more homogeneous patient samples can be designed. Psychiatric conditions of patients might be evaluated at the beginning and end of the HBOT with a scale. Laboratory analyzes used for identifying ED including serum testosterone can be performed in novel studies.

To conclude, the study results suggest that HBOT may be a good alternative treatment or adjunctive treatment for ED. However, our findings need to be confirmed in larger studies.

Acknowledgment

None declared.

Disclosure Statement

The authors have no conflict of interest to disclose.

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