



## The Role of Hyperbaric Oxygen Therapy in Andrology

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### Abstract

Hyperbaric oxygen (HBO) therapy is a supplemental treatment, in addition to the conventional approach, for patients with an underlying ischemic process. In Andrology, HBO is a therapeutic approach supplemental to surgical and medical options for some patients, mainly reported in the treatment of perineal necrotizing fasciitis (Fournier's gangrene). There were also case reports of successful management using the HBO therapy for posttraumatic ischemic injury, infertility caused by varicocele, hydrocele, testicular torsion, and erectile dysfunction.

### Keywords

Hyperbaric oxygen, Andrology, Treatment

## Introduction

Hyperbaric oxygen (HBO) therapy is considered a supplemental treatment to medical and surgical care. It is a treatment alternative for patients with an underlying ischemic process unresponsive to conventional therapy. Optimal tissue oxygenation, with HBO therapy, potentiates or restores the host's bactericidal mechanisms and wound healing activity in patients who suffered from serious synergic aerobic and anaerobic infections of the cutaneous and subcutaneous tissues. Furthermore, HBO therapy has a direct toxic effect on anaerobic bacteria [1]. Specific factors which may influence patient selection of HBO therapy include cancer and absolute contraindications of active viral disease, intercurrent pneumothorax and treatment with doxorubicin or cisplatin [2]. In Urology, the use of HBO for the management of hemorrhagic cystitis has been extensively reported with positive results in the majority of studies [2,3]. In Andrology, the effectiveness of HBO has been reported in treating peno-scrotal necrotic lesions, infertility related to varicocele, penile ischemia caused by injury, testicular torsion, and hydrocele.

### Peno-Scrotal Necrotic Lesion

The most commonly reported peno-scrotal necrotic lesion being treated with HBO is Fournier's gangrene (FG), which is a very aggressive necrotizing fasciitis involving subcutaneous fat and skin of the scrotal and perineal regions. It is a rare but very serious condition which, regardless to aggressive treatment, can lead to a lethal outcome in up to 20-30% of patients [4-22]. The principles of treatment include improving the general condition of a patient, debridement

of wound, excision of necrotic tissue, combined antibiotic therapy, HBO therapy, and reconstructive procedures [4-22].

Hounnasso, et al. [10] analyzed the epidemiological, diagnostic, and therapeutic aspects of peno-perineo-scrotal gangrene of subjects in a university hospital in a developing African country. The frequency of this disease was low, and most patients (about 72%) were between the ages of 40 to 70 years. The authors identified urethral stricture (31.25%) and idiopathic causes as the main predisposing factors, and many pathogenic bacteria, including *P. mirabilis*, *P. aeruginosa*, *S. aureus*, *K. pneumoniae* etc., as decisive factors. The treatment of peno-perineo-scrotal gangrene must be both medical and surgical. In addition to the medical treatment performed in their department, the authors would like to combine HBO therapy and, as in Japan, the use of argatroban to accelerate wound healing.

Eke, et al. [11] reviewed literature reports on FG from January 1950 to September 1999. They were able to identify 1726 cases for study. Most reported cases have occurred in the USA and Canada. The major sources of sepsis were the local skin, colon, anus, and rectum, and the lower urinary tract. Colonic, anal, and rectal sources carry the worst prognosis. Diabetes mellitus is important in aetiological terms. Rare causes include vasectomy and circumcision. They concluded that early aggressive treatment of FG and underlying conditions is essential, but HBO therapy and honey as treatment modalities have yet to be universally adopted.

Bejany, et al. [23] reported 3 cases of gangrene of the penis after penile prosthesis implantation. All 3 patients had insulin-dependent diabetes mellitus. Amputation was required in 2 patients. Aggressive debridement in conjunction with HBO therapy prevented amputation in the third patient.

Soft tissue necrosis is reported in up to 26% of patients undergoing radiotherapy for penile cancer. Gomez-Iturriaga, et al. [24] reported 7 of 43 men treated with penile brachytherapy for squamous carcinoma developed refractory soft tissue necrosis and were treated with HBO. All 7 experienced an excellent response, with healing of the necrosis and resolution of symptoms, although 3 required an additional course, 2 for consolidation of healing, and 1 for a relapse four months later. No patient was submitted to penectomy.

In summary, most studies reported positive results of HBO as a supplementary therapy for peno-scrotal necrotic lesions. These include controlling infection, promoting healing and improving cosmetic outcome, and reducing the mortality [1-11,13-27]. However,

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there were also several studies suggesting that routine HBO in the treatment of FG may not or less indicate. Verit, et al. [12] reviewed reports of FG in the English language. The clinical characteristics of FG have been changing; atypical locations of necrotizing fasciitis, e.g., in the head and neck, and the incidence of patients with FG without predisposing factors, have been increasing. While the role of anaerobic bacteria in FG is decreasing, and that of atypical organisms is increasing; they postulated that HBO therapy will probably cease to be a common treatment. They also speculated that FG will not be as likely to cause death in the future. Mindrup, et al. [28] reviewed records of patients with the hospital discharge diagnoses of FG from 1993 to 2002. A total of 42 patients were identified and followed for a median of 4.2 years. Of these patients, 16 underwent surgical debridement and antibiotic therapy alone, and 26 were treated with HBO, surgery, and antibiotics. Overall, disease specific mortality was 21.4%, which is 12.5% in the non-HBO group and 26.9% in the HBO group. Three or more complications occurred in 13% of non-HBO and in 19% of HBO cases, of which the most common was myocardial infarction. The skin graft failure rate was 6% (non-HBO) and 8% (HBO). A statistically significant difference was noted in average daily hospital charges in non HBO vs. HBO cases. There was a trend toward higher morbidity and mortality in the HBO group, even though the HBO treatment may have been given to patients who were more ill.

## Penile Injury

Zhong, et al. [29] reported a case with successful engraftment and function by combining a microsurgical procedure and postoperative supplemental care. Hyperbaric oxygen therapy was used to accelerate the healing process. Similar success was reported by Landström, et al. [30] for a case of penile reimplantation complicated by a pseudomonas wound infection, and by Faydacı, et al. [31] for a case of glans penis amputation as a rare circumcision complication.

Mydlo, et al. [18] described their experience with treating a series of 40 penile injuries, including 2 gunshot wounds, 1 stab wound, 1 zipper injury and 34 penile fractures, of which 29 were corrected surgically and 5 were managed conservatively, as well as 2 cases of glandular gangrene at 3 large medical centers over a 12-year period of time. Distal amputation in patients with localized glandular gangrene may result in sloughing and further complications. However, HBO and local wound care may be adequate if there is no progression of gangrene.

Acute ischemia of the glans penis could occur after a circumcision and successful outcomes with HBO therapy were reported [32-34]. Tzeng, et al. [32] reported a 33-year-old male receiving dorsal penile nerve block (DPNB) for circumcision, exhibited a postoperative ischemic change over the glans penis. The patient was treated with intravenous pentoxifyllin and HBO. A total reversal of the ischemia was observed. Acute ischemia of the glans penis could also be a medication-induced complication [35]. In a case report of a 26-year-old man who experienced severe glans ischemia due to buprenorphine injection into the deep dorsal vein of the penis, combination of ilomedin with HBO therapy and anticoagulant and antiplatelet drugs resulted in clinical improvement of the lesions with no functional complications [35].

A significant number of people are bitten by the brown recluse spider (BRS) each year. Medical treatment regimens are sometimes unsatisfactory and surgical intervention is often necessary to debride the necrotic wound. In a case report of a 19-year-old patient who suffered a BRS bite to the glans penis, patient received immediate medical attention and was started on intravenously administered diphenhydramine, methylprednisolone, calcium gluconate, and famotidine. Oral dapsone treatment was begun in the emergency room. Within 24 hours after his injury, the patient received his first HBO treatment, which was continued twice daily for 5 days. Skin necrosis was avoided; the patient did not require any surgical intervention [36].

## Testicular Torsion

Experimental studies on rats have shown that HBO therapy plays a role in treating testicular ischemia/reperfusion injury [37,38], may

through blockade of oxidative stress, suppression of inflammation, and reduction of nitric oxide formation [38]. In a case report of a 13-year-old boy who had prolonged right testicular ischemia. Despite surgery, the color of the testis remained poor. He underwent a post-operative course of 10 HBOT sessions over 8 days, with restoration of blood flow on color Doppler and reduction of edema. At 4-month follow-up, the testis appeared normal on ultrasonography [39]. Despite of these encouraging experimental and clinical case reports, the possibility of spontaneous detorsion should be ruled out [40-42].

## Infertility

To explore the therapeutic effects of combination of varicocelectomy with HBO therapy in treating infertile patients with varicocele (VC), Zheng, et al. [43] reported a study of 96 patients who were randomly divided into two groups: 40 patients in group A treated by varicocelectomy with HBO, and 56 in group B treated by solitary varicocelectomy. They found that varicocelectomy with HBO can more effectively regulate reproductive hormone, improve semen quality, sperm penetration assay index, and pregnant rate than solitary varicocelectomy and can markedly shorten the pregnant time.

To study the mechanism of male infertility caused by VC by evaluating the effects of HBO therapy on the testicular tissue morphology and function of rabbit model with VC, Guo, et al. [44] carried out a study in which 24 mature male rabbits were randomly divided into three groups: pseudo-operation, VC model, and VC model administered by HBO. Experimental VC was induced by partial ligation of the left "lumbotesticular" trunk vein in rabbits. HBO was administered to one of the two groups of VC model rabbits after the operation. Weight and volume of testes, parameters of seminal fluid, and histological changes of testicular tissues, MTDs, TFI, and Sertoli cell index (SI) of seminiferous tubules were studied. They found that HBO can effectively alleviate, even eliminate, chronic ischemia, anoxia, and microcircular dysfunction in testicular tissues with VC, and thus protect the structure and functions of testes.

Mitrović, et al. [45] carried out a study to evaluate the effect of HBO treatment to the vigilance of spermatozooids. The sperm samples were obtained from the patients (n = 10) with diagnosed oligospermia. The motility of spermatozooids in tested samples was not lower than 30% but it did not exceed the critical proportion of 50%. Three groups of samples were formed, with respectively 10 samples in each group. All of them were exposed to HBO conditions of 2.5 ATA for 90 minutes. The obtained results suggested that the acute exposure of the sperm samples to HBO has favorable impact to functional capacity of spermatozooids in view of their better motility.

Metelev, et al. [46] performed a study to explore the potential of HBO for reduction of sperm DNA fragmentation level and reactive oxygen species (ROS) in semen. The study included 90 men with idiopathic infertility. Patients of the treatment group (n = 60) underwent HBO before the vitro fertilization (IVF) procedure. In the control group (n = 30) IVF was carried out without prior course of HBO. HBO treatment resulted in a significant decrease in the mean level of sperm DNA fragmentation from  $33.2 \pm 7.5$  to  $11.9 \pm 5.9\%$ , and the median ROS in sperm from 0.89 to 0.39 mV/s. Pregnancy after IVF occurred in 63.3% of sexual partners of the treatment group men and in 36.7% of the control group.

## Hydrocele

Dellis, et al. [47] reported a unique case in which a male patient with decompression illness affecting inner ear and spinal cord presented a worsened unilateral hydrocele synchronously with the neurological pathology. Hyperbaric oxygen treatment had not been used for the treatment of hydrocele, but disappearance of the hydrocele occurred during the time he was treated with HBO for decompression illness. It is unclear what the exact mechanism is but we need more case reports to certify the treatment role of HBO in hydrocele.

## Erectile Dysfunction

Müller, et al. [48] conducted a study to define the effects of HBOT on erectile function (EF) and cavernosal tissue in the rat cavernous

nerve (CN) injury model. Four groups of rats were studied: rats with bilateral CN crush, HBOT treated (Crush+/HBOT+); bilateral CN-crush/no HBOT (C+/H-); no crush/no HBOT (C-/H-); and no crush/HBOT (C-/H+). HBOT following a CN injury improved EF preservation in this model, supporting the cavernosal oxygenation concept as a protective mechanism for EF. The effects appear to be mediated via preservation of neurotrophic and endothelial factor expression. In a clinical study with 24 male patients with posterior urethral reconstruction and without erectile dysfunction (ED) before urethral stricture, 12 of them were assigned to HBOT group that received HBOT, and the others comprised the control group. The total IIEF scores and scores in two domains of IIEF (EF and overall satisfaction (OS) domains) were significantly lower than the preoperative baseline scores in HBOT group. Meanwhile, a significant decrease in the total IIEF scores as well as scores in three domains of IIEF (EF, OS and intercourse satisfaction (IS) domain) was observed in control group. However, at 3 months postoperatively, the total IIEF scores, and scores in three domains of IIEF after HBOT were significantly higher in HBOT group than in control group [49].

## Conclusions

In summary, HBO is a therapeutic approach supplemental to the surgical and medical options for some patients with FG or other peno-scrotal necrotic lesions. There were also case studies showing its efficacy on infertility related to varicocele, penile ischemia caused by injury, testicular torsion, hydrocele, and ED with evidences from limited case numbers.

## Conflict of Interests

The author declares that there is no conflict of interest regarding the publication of this paper.

## References

- Pizzorno R, Bonini F, Donelli A, Stubinski R, Medica M, et al. (1997) Hyperbaric oxygen therapy in the treatment of Fournier's disease in 11 male patients. *J Urol* 158: 837-840.
- Capelli-Schellpfeffer M, Gerber GS (1999) The use of hyperbaric oxygen in urology. *J Urol* 162: 647-654.
- Al-Waili NS, Butler GJ, Lee BY, Carrey Z, Petrillo R (2009) Possible application of hyperbaric oxygen technology in the management of urogenital and renal diseases. *J Med Eng Technol* 33: 507-515.
- Rosa I, Guerreiro F (2015) Hyperbaric Oxygen Therapy for the Treatment of Fournier's Gangrene: A Review of 34 Cases. *Acta Med Port* 28: 619-623.
- Li C, Zhou X, Liu LF, Qi F, Chen JB, et al. (2015) Hyperbaric Oxygen Therapy as an Adjuvant Therapy for Comprehensive Treatment of Fournier's Gangrene. *Urol Int* 94: 453-458.
- Pastore AL, Palleschi G, Ripoli A, Silvestri L, Leto A, et al. (2013) A multistep approach to manage Fournier's gangrene in a patient with unknown type II diabetes: surgery, hyperbaric oxygen, and vacuum-assisted closuretherapy: a case report. *J Med Case Rep* 7: 1.
- Devaney B, Frawley G, Frawley L, Pilcher DV (2015) Necrotising soft tissue infections: the effect of hyperbaric oxygen on mortality. *Anaesth Intensive Care* 43: 685-692.
- Shaw JJ, Psinios C, Emhoff TA, Shah SA, Santry HP (2014) Not just full of hot air: hyperbaric oxygen therapy increases survival in cases of necrotizing soft tissue infections. *Surg Infect (Larchmt)* 15: 328-335.
- Milović N, Bancević V, Campara Z, Kosević B, Zoranović U (2008) Fournier's gangrene. *Vojnosanit Pregl* 65: 775-778.
- Hodonou R, Houmesso PP, Gbessi DG, Akpo C (2000) Penile-perineal-scrotal gangrene. Epidemiologic, diagnostic, and therapeutic features. Report of 32 cases. *Prog Urol* 10: 271-276.
- Eke N (2000) Fournier's gangrene: a review of 1726 cases. *Br J Surg* 87: 718-728.
- Verit A, Verit FF (2007) Fournier's gangrene: the development of a classical pathology. *BJU Int* 100: 1218-1220.
- Gürdal M, Yücebas E, Tekin A, Beysel M, Aslan R, et al. (2003) Predisposing factors and treatment outcome in Fournier's gangrene. Analysis of 28 cases. *Urol Int* 70: 286-290.
- Sherman J, Solliday M, Paraiso E, Becker J, Mydlo JH (1998) Early CT findings of Fournier's gangrene in a healthy male. *Clin Imaging* 22: 425-427.
- Vick R, Carson CC 3rd (1999) Fournier's disease. *Urol Clin North Am* 26: 841-849.
- Cuccia G, Mucciardi G, Morgia G, Stagno d'Alcontres F, Gali A, et al. (2009) Vacuum-assisted closure for the treatment of Fournier's gangrene. *Urol Int* 82: 426-431.
- Fan H, Zhu D, Liu F, Wang H, Liu L (2006) Rebuilding of scrotum in gangrene. *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi* 20: 235-237.
- Mydlo JH, Harris CF, Brown JG (2002) Blunt, penetrating and ischemic injuries to the penis. *J Urol* 168: 1433-1435.
- Dahm P, Roland FH, Vaslef SN, Moon RE, Price DT, et al. (2000) Outcome analysis in patients with primary necrotizing fasciitis of the male genitalia. *Urology* 56: 31-35.
- Hollabaugh RS Jr, Dmochowski RR, Hickerson WL, Cox CE (1998) Fournier's gangrene: therapeutic impact of hyperbaric oxygen. *Plast Reconstr Surg* 101: 94-100.
- Benizri E, Fabiani P, Migliori G, Chevallier D, Peyrottes A, et al. (1996) Gangrene of the perineum. *Urology* 47: 935-939.
- Monge Mirallas JM, Portillo Martín JA, Martín García B, Hernández Rodríguez R, Correas Gómez MA, et al. (1992) Our caseload in Fournier's disease. *Arch Esp Urol* 45: 993-996.
- Bejany DE, Perito PE, Lustgarten M, Rhamy RK (1993) Gangrene of the penis after implantation of penile prosthesis: case reports, treatment recommendations and review of the literature. *J Urol* 150: 190-191.
- Gomez-Iturriaga A, Crook J, Evans W, Saibishkumar EP, Jeziorski J (2011) The efficacy of hyperbaric oxygen therapy in the treatment of medically refractory soft tissue necrosis after penile brachytherapy. *Brachytherapy* 10: 491-497.
- Paty R, Smith AD (1992) Gangrene and Fournier's gangrene. *Urol Clin North Am* 19: 149-162.
- Wessells H (1999) Genital skin loss: unified reconstructive approach to a heterogeneous entity. *World J Urol* 17: 107-114.
- Baykal K, Albayrak S, Inal H, Elbuken E, Dündar K, et al. (1996) Fournier's disease: adjunctive hyperbaric oxygen therapy to classic therapy. *Int J Urol* 3: 161-162.
- Midrup SR, Kealey GP, Fallon B (2005) Hyperbaric oxygen for the treatment of fournier's gangrene. *J Urol* 173: 1975-1977.
- Zhong Z, Dong Z, Lu Q, Li Y, Lv C, et al. (2007) Successful penile replantation with adjuvant hyperbaric oxygen treatment. *Urology* 69: 983.
- Landström JT, Schuyler RW, Macris GP (2004) Microsurgical penile replantation facilitated by postoperative HBO treatment. *Microsurgery* 24: 49-55.
- Faydacı G, Ugur K, Osman C, Sermin S, Bilal E (2011) Amputation of glans penis: a rare circumcision complication and successful management with primary anastomosis and hyperbaric oxygen therapy. *Korean J Urol* 52: 147-149.
- Tzeng YS, Tang SH, Meng E, Lin TF, Sun GH (2004) Ischemic glans penis after circumcision. *Asian J Androl* 6: 161-163.
- Migliorini F, Bianconi F, Bizzotto L, Porcaro AB, Artibani W (2016) Acute Ischemia of the Glans Penis after Circumcision Treated with Hyperbaric Therapy and Pentoxyfylline: Case Report and Revision of the Literature. *Urol Int*.
- Pepe P, Pietropaolo F, Candiano G, Pennisi M (2015) Ischemia of the glans penis following circumcision: case report and revision of the literature. *Arch Ital Urol Androl* 87: 93-94.
- Brecheteau F, Grison P, Abraham P, Lebdai S, Kemgang S, et al. (2013) Successful medical treatment of glans ischemia after voluntary buprenorphine injection. *J Sex Med* 10: 2866-2870.
- Broughton G 2nd (1996) Management of the brown recluse spider bite to the glans penis. *Mil Med* 161: 627-629.
- Kolski JM, Mazolewski PJ, Stephenson LL, Texter J, Grigoriev VE, et al. (1998) Effect of hyperbaric oxygen therapy on testicular ischemia-reperfusion injury. *J Urol* 160: 601-604.
- Zhang Y, Lv Y, Liu YJ, Yang C, Hu HJ, et al. (2013) Hyperbaric oxygen therapy in rats attenuates ischemia-reperfusion testicular injury through blockade of oxidative stress, suppression of inflammation, and reduction of nitric oxide formation. *Urology* 82: 489.
- Alp BF, Cebi G, Özdemir A, Irkılıta HC, Uzun G (2014) Hyperbaric oxygen treatment for unilateral testicular torsion in a child. *Diving Hyperb Med* 44: 161-162.
- Al-Kandari AM, Kehinde EO, Khudair S, Ibrahim H, ElSheemy MS, et al. (2017) Intermittent Testicular Torsion in Adults: An Overlooked Clinical Condition. *Med Princ Pract* 26: 30-34.

41. Ugwumba FO, Okoh AD, Echetabu KN (2016) Acute and intermittent testicular torsion: Analysis of presentation, management, and outcome in South East, Nigeria. *Niger J Clin Pract* 19: 407-410.
42. Eaton SH, Cendron MA, Estrada CR, Bauer SB, Borer JG, et al. (2005) Intermittent testicular torsion: diagnostic features and management outcomes. *J Urol* 174: 1532-1535.
43. Zheng RQ, Wang XS, Wang PT (2006) Effect of varicocelectomy with hyperbaric oxygenation in treating infertile patients with varicocele. *Zhonghua Nan Ke Xue* 12: 46-49.
44. Guo YL, Zhou SW, Zhang XP (2003) Effects of hyperbaric oxygenation on rabbits' testes with varicocele. *Zhonghua Nan Ke Xue* 9: 443-446.
45. Mitrović A1, Brkić P, Jovanović T (2011) The effects of hyperbaric oxygen treatment on vigility of spermatozooids: preliminary report. *Acta Physiol Hung* 98: 85-90.
46. Metelev AY, Bogdanov AB, Ivkinl EV, Mitrokhin AA, Vodneva MM, et al. (2015) Hyperbaric oxygen therapy in the treatment of male infertility associated with increased sperm dna fragmentation and reactive oxygen species in semen. *Urologii*: 74-76.
47. Delis AE, Skolarikos A, Vavasis P, Spyropoulos E, Kalentzos VN (2010) Spontaneous hydrocele resolution after hyperbaric oxygen treatment: a clinical case report. *Undersea Hyperb Med* 37: 199-201.
48. Müller A, Tal R, Donohue JF, Akin-Olugbade Y, Kobylarz K, et al. (2008) The effect of hyperbaric oxygen therapy on erectile function recovery in a rat cavernous nerve injury model. *J Sex Med* 5: 562-570.
49. Yuan JB, Yang LY, Wang YH, Ding T, Chen TD, et al. (2011) Hyperbaric oxygen therapy for recovery of erectile function after posterior urethral reconstruction. *Int Urol Nephrol* 43: 755-761.