



The Effectiveness of Adjuvant Hyperbaric Oxygen Therapy in Adults who Underwent Hypospadias Surgery

Erişkinlerde Hipospadias Cerrahisi Sonrası Uygulanan Hiperbarik Oksijen Tedavisinin Etkinliği

Hypospadias and Hyperbaric Oxygen Therapy

Önder Kara¹, Ercan Malkoç², Furkan Dursun², Mesut Mutluoğlu³, Zeki Aktaş², Ali Memiş³, Hasan Soydan², Ferhat Ateş²
¹Üroloji Anabilim Dalı, Amasya Üniversitesi Tıp Fakültesi, Amasya,
²Üroloji Servisi, Gülhane Askeri Tıp Akademisi, Haydarpaşa Eğitim Hastanesi, İstanbul,
³Sualtı Hekimliği ve Hiperbarik Tıp Servisi, Gülhane Askeri Tıp Akademisi, Haydarpaşa Eğitim Hastanesi, İstanbul, Türkiye

Çalışmamız 23. Ulusal Üroloji Kongresinde poster bildiri olarak sunulmuştur (7 Ekim 2014)

Özet

Amaç: Hipospadias tedavisi amacıyla bukkal mukoza ile tüp üretroplastisi yapılan erişkin hastalarda hiperbarik oksijen tedavisi (HBO2T)'nin rolünü değerlendirmek. **Gereç ve Yöntem:** Çalışmaya hipospadiası olan 16 erişkin hasta dahil edildi. Kısa üretra ve penil kurvaturu olan hastalar iki aşamalı tedavi edildi (ortoplasti+bukkal mukoza ile tüp üretroplastisi). Tüp üretroplastisi için alınan mukoza 16 Fr. nelaton kateter etrafında tübularize edilerek üretral meatus ile glans penis arasına yerleştirildi. Hastaların 13'üne ameliyat sonrası birinci günden itibaren hafta içi günlerde toplam 10 seans HBO2T uygulandı. **Bulgular:** Hastaların ortalama hasta yaşı 21(±1,23) ve takip süresi 10.1(±2.1) aydı. HBO2T uygulanan 13 hastanın 6(%46)'sinde iki aşamalı (ortoplasti+bukkal tüp mukoza grefti) onarım gerçekleştirildi ve ortalama greft uzunluğu 5.4(±1,23) cm idi. Bu gruptaki hastalarda hipospadias ameliyatı sonrası %54(7/13) oranında başarı sağlanırken, ikincil işlem (internal üretrotomi ve/veya fistül onarımı) sonrası başarı oranı %84.6 (11/13) olarak izlendi. HBO2T uygulanmayan 3 hastanın 1(%33)'inde iki aşamalı onarım gerçekleştirildi ve ortalama greft uzunluğu 8(±5) cm idi. Bu gruptaki hastalarda hipospadias ameliyatı sonrası başarı sağlanamazken ikincil işlem sonrası başarı oranı %33(1/3) olarak izlendi. **Tartışma:** Hiperbarik oksijen tedavisinin bukkal mukoza ile tüp üretroplastisi cerrahisiyle kombine edilmesi başarıyı arttırmaktadır. Bu konuda daha geniş, prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler

Erişkin Hipospadias; Bukkal Mukoza; Hiperbarik Oksijen Tedavisi

Abstract

Aim: To evaluate the role of hyperbaric oxygen therapy (HBO2T) with buccal mucosal tube urethroplasty in adult patients with hypospadias. **Material and Method:** Sixteen adult patients with hypospadias were included in our study. Patients with a short urethra and penile curvature were treated in two stages (orthoplasty+buccal mucosal tube urethroplasty). Buccal mucosa was taken and prepared for tube urethroplasty around a 16 French (Fr) nelaton catheter and the urethral tube was introduced between the urethral meatus and glans penis. Beginning the 1st postoperative day (HBO2T) was applied for 10 sessions during weekdays in 13 patients. **Results:** The mean age was 21 (±1.23) years and mean follow-up time was 10.1 (±2.1) months. In the group who received HBO2T postoperatively (n=13), a two-stage (orthoplasty+buccal mucosal tube urethroplasty) procedure was performed in 6 (46%), and the mean length of graft was 5.4 (±1.23) cm. In this group of 13 the success rate without any additional manipulations (urethrotomy intern, fistula repair) was 54% (7/13). After additional manipulations, complete healing was achieved in 11 out of 13 patients (84.6%). In the group who did not receive HBO2T postoperatively (n=3), a two-stage procedure was performed in 1 patient (33%), and the mean length of graft was 8 (±5) cm. In this group of 3, complete healing was not achieved in any of these patients as a result of the hypospadias surgery. However, after the additional manipulations, complete healing was achieved in 1 patient (33%). **Discussion:** Given the promising rates of surgical success, postoperative HBO2T might be considered as a supportive treatment modality for adult patients with hypospadias who undergo buccal mucosal tube urethroplasty. Randomized controlled studies are needed.

Keywords

Adult Hypospadias; Buccal Mucosa; Hyperbaric Oxygen Therapy

DOI: 10.4328/JCAM.4691

Received: 15.06.2016 Accepted: 17.07.2016 Printed: 01.01.2017 J Clin Anal Med 2017;8(1): 60-3

Corresponding Author: Önder Kara, Üroloji Polikliniği, Amasya Üniversitesi Tıp Fakültesi Eğitim Araştırma Hastanesi, 05100, Amasya, Türkiye.

GSM: +905332374067 E-Mail: onerkara@yahoo.com

Introduction

Hypospadias is one of the most frequently seen congenital anomalies in boys. Its occurrence is reported in the literature to be 1/300 [1]. Tubularized Incised Plate Urethroplasty (TIPU) is the most common procedure used for distal hypospadias. It is being used effectively for mid and proximal hypospadias, primary adults, and the patients who require re-operations [2, 3]. Additionally, the dorsal onlay or inlay methods for oral mucosa graft urethroplasty surgeries have been proven effective and are widely applied in the treatment of hypospadias [1]. The aim of the hypospadias repair is to provide a penis that is cosmetically and functionally normal. The most important factor that may affect the outcomes of the surgery is age. Hypospadias repair has been recommended between 6 and 12 months. However, in the developing countries most births are conducted at home, with corresponding lack of recognition of congenital deformities [4]. Patient and social factors such as lack of knowledge and difficulties accessing health units lead patients to be presented late and operated on after the age of two, or maybe even after childhood as adults [5]. While the majority of the patients, in adolescent and adult life, require surgical repair for cosmetic reasons, uncorrected hypospadias patients are at risk of urethral problems including urethral stricture and lichen sclerosus [6]. In previous publications it has been shown that when compared to those in infancy, urethral complications were higher in adulthood after primary repair (10-50%) [6, 7]. Additionally, the outcomes of tube grafts performed after puberty are poor [6, 8]. Therefore, two-stage urethroplasty is the option preferred by surgeons for adult patients [9].

The use of hyperbaric oxygen therapy (HBO2T), which is based on increasing the dissolved oxygen level in the tissues, has been successfully demonstrated in urology for the treatment of chronic pelvic pain, interstitial cystitis, Fournier's gangrene, and radiation-induced cystitis [10]. In our study we aimed to evaluate the role of (HBO2T) with buccal mucosal tube urethroplasty in adult patients with hypospadias.

Material and Method

After approval from our institutional ethics and review board and receipt of informed consents signed by the patients, our study included 16 (n=9 proximal, n=7 mid penile) consecutive adult patients who had undergone hypospadias repair with buccal mucosal tube urethroplasty at our center between 2009 and 2014. Four experienced surgeons (FA, HS, ŞB, KK) performed all the surgical procedures.

Surgical Technique:

The surgery was completed in all patients with general anesthesia. After placing the 16 French (Fr) catheter into the urethra, a complete circumferential incision and de-gloving procedure was performed. Orthoplasty was applied for the patients

if required after the determination of chordee by administering an artificial saline injection. Patients with short urethra and penile curvature were treated in two stages. In the first stage, an inlay (dorsal) buccal graft was applied to extend the urethral plate. In the second stage, buccal mucosal tube urethroplasty was performed. Buccal mucosa was harvested and prepared for tube urethroplasty around a 16 Fr. nelaton catheter. The graft, usually of width 10-12 mm, was introduced between the urethral meatus and glans penis. Buccal mucosal graft (n=7 (44%)) and lower limb mucosal graft (n=9 (56%)), with or without buccal mucosa) were used. Subcutaneous tissue was used to prepare a local flap, which with the skin was closed over the tube. The penis was wrapped with an elastic bandage and immobilized for 10 days. The Foley catheter was withdrawn on the 10th day.

HBO2T procedure:

Within the first day of the surgery HBO2T was applied on 13 out of 16 patients (81%) for 10 sessions during weekdays. Treatment consisted of exposure to HBO2T at 2.4 ATA for 130 minutes [11].

Internal urethrotomy and/or fistula repair were performed 3 months after hypospadias repair to those who developed post-operative urethral stricture or fistula.

Results

The mean age was 21 (± 1.23) years and mean follow-up time was 10.1 (± 2.1) months. In the group who received HBO2T postoperatively (n=13), a two-stage (orthoplasty+buccal mucosal tube urethroplasty) procedure was performed in 6 (46%) patients, and the mean length of graft was 5.4 (± 3.83) cm. In this group of 13 the success rate without any additional manipulations (internal urethrotomy, fistula repair) was 54% (7/13). After additional manipulations, complete healing was achieved in 11 out of 13 patients (84.6%) (Table 1).

In the group who did not receive HBO2T postoperatively (n=3), a two-stage procedure was performed in 1 (33%), and the mean length of graft was 8 (± 5) cm. In this group, complete healing was not achieved in any of these patients as a result of hypospadias surgery. However, after the additional manipulations (internal urethrotomy, fistula repair) complete healing was achieved in 1 (33%) patient (Table 1).

With regard to the entire group of 16, complete healing after the first stage was achieved in 7 (43%) patients without any complication. However in 9 (56%) patients, fistula development (n=5), slough (n=2), urethral stenosis (n=1), or fistula with urethral stenosis (n=1) occurred. After the second manipulations, complete healing was achieved in 12 (75%) patients but 4 (25%) patients required additional surgical procedures (Table 2). No wound infection was seen in the surgical areas, and during the follow-up time none of the patients had any oral complications.

Table 1. Patients' characteristics and results

HBO2T	N	Age	Primer/Redo	Orthoplasty +/-	Buccal/Lower limb +/- buccal	Graft (cm)	1st stage success	2nd stage success
Yes	13	21.1	5/8	6/7	6/7	5.4	54% (7/13)	84.6% (11/13)
No	3	20.6	1/2	1/2	1/2	8	0	%33% (1/3)
Total	16	21	6/10	7/9	7/9	5.9	43.8% (7/16)	%75% (12/16)

HBO2T: Hyperbaric Oxygen Therapy

Table 2. Details of complications after 1st stage operations

	HBO2T (Yes)	HBO2T (No)	Total
Fistula formation (n)	3	2	5
Slough (n)	1	-	1
Urethral stricture (n)	1	-	1
Fistula + stricture (n)	1	1	2

Discussion

Due to surgical, psychological, and cosmetic reasons the consensus recommendation of pediatricians for the optimal hypospadias repair period is postpartum 6-12 months [4]. However, in developing countries hypospadias is not considered a serious disease. Repair is mostly deferred to adulthood due to lack of knowledge by parents and by the patients. The majority of these adult patients request to be treated in the pre-marriage period [12]. In our study, the patient mean age was 20, confirming this reason and corresponding to the patients' pre-military service period. Among the patients who received HBO2T, after additional manipulations (internal urethrotomy, fistula repair) complete healing was achieved in 11 out of 13 patients (84.6%). However, in the group who did not receive HBO2T, the success rate was only 33%. Although complete healing rates were different between the two groups, the low sample size of our study does not allow us to reach statistically significant results. Additionally, the difference between the lengths of grafts among the groups should be taken into consideration. In previously reported series, Hensle et al., Nuininga et al., and Dodson et al. reported higher complication rates in adults when compared to those in infancy (52.3%, 54%, 54% respectively) [6, 7, 13]. Bhat et al. reported 20% complication rates in >15 year old patients who underwent hypospadias repair [14]. In contrast to all these studies, Snodgrass et al. reported similar complication rates for hypospadias repairs performed in adults when compared to children [15]. However, all these cases were performed by a single highly-experienced surgeon; therefore results may not be generalizable to less experienced surgeons. In our study, overall complete healing rates for the group who received HBO2T and for the whole cohort are 85% and 75% respectively, showing promising results in patients who underwent buccal mucosa graft urethroplasty when compared with results in the current literature. In a recently published study, two-stage repair of complex and re-operated cases was associated with a success rate of approximately 56%. However, the remaining boys required further surgeries [16].

Extra-genital tissues are usually required for the cases of failed hypospadias surgeries. With the advantages of buccal mucosa grafts such as ease of harvest, quality of substrate, and low complication rates, this treatment has become more popular in the repair of hypospadias [17]. Hairless, highly-vascularized lamina propria and non-keratinized epithelium of buccal mucosa provide excellent substrates for the reconstruction [18]. The use of buccal mucosa grafts in children with proximal hypospadias was first reported by Burger et al. in 1992 [19] and has gradually been popularized. In our study, buccal mucosal graft (n= 7 (44%)) and lower limb mucosal graft (n=9 (56%)), with or without buccal mucosa) were used, and none of the patients had oral complications during the follow-up period. Zhao et al.

reported a series of 57 adults with a history of failed hypospadias in whom they performed tubularized buccal mucosa graft. In this study, there was no graft loss. There were 8 fistulas, of which 6 were healed [20]. In our study, at the first stage, complete healing was achieved in 7 (43%) patients without any complication. However in 9 (56%) patients fistula development (n=5), slough (n=2), urethral stenosis (n=1), or fistula with urethral stenosis (n=1) occurred. After the second manipulations, complete healing was achieved in 12 (75%) patients but 4 (25%) patients required additional surgical procedures.

Wound healing is a dynamic and complex process of replacing damaged tissue [21]. The surgical interventions such as urethroplasty and hypospadias repair that we use to repair defects of the urinary tract have to provide functional wound healing [22]. Insufficient wound healing may cause urethra-cutaneous fistula or urethral strictures. The phases of urethral healing are similar to dermal healing; however, the duration of each phase is longer than for the skin [23]. Given the high potential of complication rates after the hypospadias repair in adults, in order to improve the outcomes, we used perioperative HBO2T to optimize tissues threatened by ischemia. The primary rationale of HBO2T is that it increases the dissolved oxygen level in the tissues when it is provided at higher pressures. This improves the anti-inflammatory process, protects the tissues from reperfusion injury, increases the bacterial permeability to antibiotics, and promotes wound healing. Successful tissue healing relies on satisfactory oxygenation in the zone that surrounds the fresh wound [24, 25]. HBO2T, which has been used in urology previously [10], has the potential to improve outcomes in adult patients who undergo buccal mucosa graft urethroplasty for the treatment of hypospadias. The cost of HBO2T may be one of the most important concerns in the treatment decision. HBO2T is recognized by Social Security Institution in the Turkey as reimbursable for approved conditions. A 130 min. session costs 60 Turkish liras (TL); the total overall cost of the HBO2T (10 sessions) treatment with health insurance coverage is 600 TL. The occurrences of a fistula or urethral stricture inevitably require secondary manipulations and/or prolong the hospitalization, and thus are costly both for the patient and the health economy.

The limitations of our study include its small sample size, retrospective nature, and short follow-up. The promising outcomes in our preliminary series for one of the most challenging areas of urology suggest that larger prospective randomized trials are warranted.

Conclusion

Hypospadias surgery has unfavorable results due to fistula formation and scarring of penile tissue, so many surgical methods have been developed to increase the success rate of this surgery. HBO2T is an important and effective treatment modality in wound healing, especially of tissues with insufficient vascular support. HBO2T can be considered as a supportive treatment modality for hypospadias patients who undergo buccal mucosal tube urethroplasty. Larger sample sizes and prospectively randomized studies are required to confirm.

Competing interests

The authors declare that they have no competing interests.

References

1. Roberts J. Hypospadias surgery past, present and future. *Curr Opin Urol* 2010;20:483-9.
2. Snodgrass W. Tubularized, incised plate urethroplasty for distal hypospadias. *J Urol* 1994;151:464-5.
3. Steckler RE, Zaontz MR. Stent-free Thiersch-Duplay hypospadias repair with the Snodgrass modification. *J Urol* 1997;158:1178-80.
4. Bhat A, Bhat M, Kumar V, Kumar R, Mittal R, Saksena G. Comparison of variables affecting the surgical outcomes of tubularized incised plate urethroplasty in adult and pediatric hypospadias. *J Pediatr Urol* 2016;12:108.
5. Bhat A. Extended urethral mobilization in incised plate urethroplasty for severe hypospadias: a variation in technique to improve chordee correction. *J Urol* 2007;178:1031-5.
6. Hensle TW, Tennenbaum SY, Reiley EA, Pollard J. Hypospadias repair in adults: adventures and misadventures. *J Urol* 2001;165:77-9.
7. Nuininga JE, RP DEG, Verschuren R, Feitz WF. Long-term outcome of different types of 1-stage hypospadias repair. *J Urol* 2005;174:1544-8.
8. Secrest CL, Jordan GH, Winslow BH, Horton CE, McCraw JB, Gilbert DA, et al. Repair of the complications of hypospadias surgery. *J Urol* 1993;150:1415-8.
9. Bracka A. Hypospadias repair: the two-stage alternative. *Br J Urol* 1995;76 Suppl 3:31-41.
10. Pasquier D, Hoelscher T, Schmutz J, Dische S, Mathieu D, Baumann M, et al. Hyperbaric oxygen therapy in the treatment of radio-induced lesions in normal tissues: a literature review. *Radiother Oncol* 2004;72:1-13.
11. Kindwall EP. Creating a hyperbaric oxygen treatment unit in a major medical center: a personal experience. *Ann Plast Surg* 1992;29:543-9.
12. Bhat A. General considerations in hypospadias surgery. *Indian J Urol* 2008;24:188-94.
13. Dodson JL, Baird AD, Baker LA, Docimo SG, Mathews RI. Outcomes of delayed hypospadias repair: implications for decision making. *J Urol* 2007;178:278-81.
14. Bhat A, Sabharwal K, Bhat M, Saran R, Singla M, Kumar V. Outcome of tubularized incised plate urethroplasty with spongioplasty alone as additional tissue cover: A prospective study. *Indian J Urol* 2014;30:392-7.
15. Snodgrass W, Villanueva C, Bush N. Primary and reoperative hypospadias repair in adults are results different than in children? *J Urol* 2014;192:1730-3.
16. Faure A, Bouty A, Nyo YL, O'Brien M, Heloury Y. Two-stage graft urethroplasty for proximal and complicated hypospadias in children: A retrospective study. *J Pediatr Urol* 2016: doi: 10.1016/j.jpuro.2016.02.014.
17. Castagnetti M, Longo R, Tocco A, Berrettini A, Rigamonti W. Long-term (>5 years) donor site outcome after mandibular labial mucosa graft harvesting for urethral reconstruction in children. *J Pediatr Urol* 2008;4:442-4.
18. Holzle F, Mitchell DA, Rau A, Palisaar J, Loeffelbein DJ, Noldus J, et al. Assessment of the perfusion and morbidity of the buccal mucosal donor site for grafting of urethral strictures. *J Craniomaxillofac Surg* 2012;40:47-50.
19. Burger RA, Muller SC, el-Damanhoury H, Tschakaloff A, Riedmiller H, Hohenfellner R. The buccal mucosal graft for urethral reconstruction: a preliminary report. *J Urol* 1992;147:662-4.
20. Zhao M, Li Y, Tang Y, Chen W, Yang Z, Li Q, et al. Two-stage repair with buccal mucosa for severe and complicated hypospadias in adults. *Int J Urol* 2011;18:155-61.
21. Ninan N, Muthiah M, Bt Yahaya NA, Park IK, Elain A, Wong TW, et al. Antibacterial and wound healing analysis of gelatin/zeolite scaffolds. *Colloids Surf B Biointerfaces* 2014;115:244-52.
22. Karakus OZ, Ates O, Tekin A, Hakguder G, Olguner M, Akgur FM. Tubularized incised plate urethroplasty for the treatment of penile fistulas after hypospadias repair. *J Pediatr Urol* 2014;10:455-8.
23. Sahinkanat T, Ozkan KU, Ciralik H, Ozturk S, Resim S. Botulinum toxin-A to improve urethral wound healing: an experimental study in a rat model. *Urology* 2009;73:405-9.
24. Fitzpatrick DT, Murphy PT, Bryce M. Adjunctive treatment of compartment syndrome with hyperbaric oxygen. *Mil Med* 1998;163:577-9.
25. Myers RA. Hyperbaric oxygen therapy for trauma: crush injury, compartment syndrome, and other acute traumatic peripheral ischemias. *Int Anesthesiol Clin* 2000;38:139-51.

How to cite this article:

Kara Ö, Malkoç E, Dursun F, Mutluoğlu M, Aktaş Z, Memiş A, Soydan H, Ateş F. The Effectiveness of Adjuvant Hyperbaric Oxygen Therapy in Adults who Underwent Hypospadias Surgery. *J Clin Anal Med* 2017;8(1): 60-3.