

Effect of Hyperbaric oxygen and Honey in the management of Fournier's gangrene

Fournier gangreninde hiperbarik oksijen tedavisinin ve balın yeri

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Abstract

Background: Fournier's gangrene is an extensive fulminant infection of the genitals, perineum, or the abdominal wall. The aim of study is to investigate retrospectively the efficacy of surgery, antibiotic treatment, honey application and hyperbaric oxygen treatment.

Methods: Records of patients with the diagnosis of Fournier's gangrene were reviewed retrospectively. Patients were divided into three groups. Group I patients (n=17) were treated with broad-spectrum triple antimicrobial therapy and broad debridement. Group II patients (n=20) were treated with broad-spectrum triple antimicrobial therapy alone without debridement. And the wound was dressed with topical unprocessed honey after cleaned with saline. Group III patients (n=12) were treated with hyperbaric oxygen treatment (2.5 ATA, 90 minutes, daily) in addition to the treatment of group I.

Results: The source of the gangrene was mostly urinary. The most encountered predisposing factor was diabetes mellitus. The mean duration of hospital stay was 41 (28-72) days. Response to treatment and alleviation of morbidity were faster in group II, III than group I.

Conclusions: Treatment of Fournier's Gangrene is based on aggressive debridement, broad-spectrum antibiotics and intensive supportive care. Besides, unprocessed honey and hyperbaric oxygen treatment may revolutionize the treatment of this dreadful disease by reducing cost, morbidity and mortality.

Key words: Fournier's Gangrene, Necrotizing Fasciitis, Hyperbaric Oxygen, Unprocessed Honey

Özet:

Amaç: Fournier gangreni, genital organları, perineyi veya karın duvarının derin ve şiddetli bir enfeksiyonudur. Bu çalışmanın amacı cerrahinin, antibiyotik tedavisinin, bal uygulamasının ve hiperbarik oksijen tedavisinin etkinliğinin geriye dönük olarak incelenmesidir.

Materyal ve Metod: Fournier gangreni tanısı alan hastaların kayıtları geriye dönük olarak incelendi. Hastalar üç grup altında toplandı. Grup I deki hastalar (n=17) geniş spektrumlu üçlü antibiyotik ile tedavi edildi ve geniş debritleme yapıldı. Grup II deki hastalar (n=20) debritleme yapılmadan sadece geniş spektrumlu üçlü antibiyotik tedavisi aldı. Ve yara salin ile temizlendikten sonra topical olarak bal ile örtüldü. Grup III teki hastalar (n=12) grup I deki tedaviye ilave olarak Hiperbarik oksijen tedavisi (2.5 ATA, günde 90 dakika) ile tedavi edildi.

Bulgular: Gangrenin kaynağı genellikle ürinerdi. En sık rastlanan yatkınlık sebebi diabetes mellitus idi. Hastanede kalış süresi 41 gündü (28-72). Grup II ve grup III te tedaviye yanıt ve hastalığın hafiflemesi grup I e göre daha hızlıydı.

Sonuç: Fournier gangreninin agresif debritleme, geniş spektrumlu antibiyotik tedavisi ve yoğun destek tedavisi ile edilir. Bunlardan başka olarak, işlenmemiş bal ve hiperbarik oksijen tedavisi bu kötü hastalığın tedavisinde maliyeti, morbiditeyi ve mortaliteyi azaltarak bir yenilik getirebilir.

Anahtar kelimeler: Fournier gangreni, bal, hiperbarik oksijen tedavisi

Introduction

Fournier's gangrene (FG) is a necrotizing fasciitis of the genitalia that progresses from erythema to necrosis. Gangrene can occur within hours and the mortality rate changes from 15% to 50%. Mostly after trauma, a bacterial infection spreads quickly from the urinary tract and anorectal area and causes gangrene due to thrombosis of small blood vessels below the skin. The disease is commonly seen in adults but also occur in children from infancy to adolescence following events such as insect bites, trauma, burns, perirectal diseases and infections. Predisposing factors are diabetes, immunodeficiency and corticosteroid use (1). Treatment involves surgically debridement of the infected and necrotic tissues and administration of triple antibiotics. Additional use of hyperbaric oxygen therapy (HBOT) and administration of topical unprocessed honey are alternative

methods (2, 3, 4)

Honey decreases inflammatory edema, hastens sloughing of devitalized tissue, attracts macrophages which cleanse the wound, provides a local cellular energy source, and protectively covers the wound. As well as having an antibacterial action, honey also provides rapid autolytic debridement, deodorizes wounds, and stimulates the growth of wound tissues to hasten healing and start the healing process in dormant wounds. The mechanism of action is thought to be its chemical pH and osmotic effects (5).

In this study we analyzed our experience on FG to define the etiologic factors, surgical treatment and the effect of HBOT and unprocessed honey treatment on wound healing and patient survival.

Materials and methods

The medical records of 49 consecutive patients admitted to the departments of General surgery, Urology and Plastic Surgery of Gulhane Military Medical Faculty and Urology Department of Firat University Medical Faculty during a 16-year period between January 1990 and December 2005 were retrospectively reviewed. The diagnosis Fournier's gangrene was established clinically on the basis of the patient's history and physical examination. Patients with a simple scrotal or perirectal abscess without necrotizing infection were not included in this series. Patient's age, etiology and predisposing factors, microbiological findings, duration of hospital stay, surgical procedures, use of colostomy, determined bacterial agents and treatment and outcome were analyzed. Additional colostomy was performed in patients with conditions consisting high risk of contamination such as rectal perforation, anal sphincter insufficiency and pelvic fistula. Additional debridements were performed in cases in which tissue necrosis progressed. First 17 patients (Group I) were treated with broad-spectrum triple antimicrobial therapy (Targocid 400mg flk 2x1 IV, Flagyl 500 mg 2x1 IV, Sulperazon 1 g IV 2x1), broad debridement, exhaustive cleaning, and then underwent split-thickness skin grafts or delayed closure as needed (Figure 1). Second group 20 patients (Group II) were treated with local application of unprocessed honey (20 ml daily) and broad-spectrum triple antimicrobial therapy without debridement. These patients (group II) had a localized disease at presentation. Their wounds cleaned with saline and then dressed with topical unprocessed honey, with the wounds inspected and the honey reapplied daily after cleansing with normal saline, and then their scrotum and penis were covered with their own new scrotal skin. Scrotal skin was closed by secondary suturing (Figure 2). Group III (n=12) received the same treatment as in Group I and additionally HBO treatment at the Department of Sea and Underwater Medicine, Gulhane Military Medical Faculty in single rooms and at 2,5 ATA pressure for 90 minutes, postoperatively (Figure 3).

Results

Group I was the conventional treatment group. This group was including 17 patients, 13 males and 4 females. Mean age in this group was 57 (range 34-71) years. Group II (honey group) was including 20 patients. There were 18 males and 2 females. Mean age in this group was 49 (range 23-61) years. Group III (HBO group) was including 12 patients consisting of 9 males and 3 females. Mean age in this group was 56.5(21-78) years.

The source of the gangrene in the first group was local trauma in 1, perianal abscess in 8, ischio-rectal abscess in 1, scrotal frunculosis in 4, idiopathic in 2 and basal cell carcinoma in one patient. In the second group, the etiological factors were mostly of urological origin (12), other reasons were trauma in 3 and scrotal frunculosis in 2 patients. In 3 patients, the reason was not clear (idiopathic). Etiological factors in group III were as follows; perianal abscess in 8, hemorrhoidectomy in 2, rubber band ligation of hemorrhoids in one and giant condyloma acuminata exicion in one patient. Predisposing factors included diabetes mellitus in 14 patients (28,5%), alcoholism in 10 patients (20,4%), malnutrition in 9 patients (18,3%), medical immune suppression in 4 (chemotherapy, steroids, 8,1%) patients, and malignancy in 1 patient (2%). Of the lesions 59,2% (n=29) were located at the penis and scrotum, and 81,6% (n=40) involved the scrotum and perineum. Presenting symptoms included scrotal edema in 18 patients (36,7%), scrotal pain in 22 patients(44.8%) crepitations in 19 patients(38,7%), feculent odor in 49 patients (100%) and fever

> 38°C in 11 patients(22,4%),. All patients except five had leukocytosis at presentation. The diagnosis of primary necrotizing fasciitis (Fournier's gangrene) was established clinically on the basis of the patient's history and physical examination and by radiological imaging in selected cases. Radiological evaluation was used for FG patients to detect a possible focus of infection or abscess. This was done with transrectal ultrasonography (TRUS) and Computed Tomography (CT) and especially in FG patients with perianal or perirectal origin. The most used diagnostic modality was TRUS and used in 13 patients. CT was used in 9 patients. TRUS revealed perianal abscess in 6 and perianal and perirectal inflammation and swelling 4 patients. CT was more useful could present the perianal inflammation and abscess focus in 7 patients. CT could also demonstrate inflammation and subcutaneous free air at the gangrene area in all patients (9 patients).

The mean number of surgical debridement daily was three (range 2-5) in groups I and III and no surgical debridements were performed in patients in group II. In group II the foul odor, edema subsided within 1 week of topical application of honey.

The median hospital stay was 41 (28-72), 41(14-54) and 32(21-46) days for groups I,II and III, respectively. Fourteen patients died from severe sepsis in group I and 3 in group III. The mortality rates in group I and III were the same (33.3%). There were no mortalities in group II. The clinical and cosmetically results were better in group II and III than group I. Four (8,1%) patients were diverted via suprapubic cystostomy. The demographical features of the patients and etiological factors are shown at table I and II, respectively.

Discussion

The incidence of Fournier's gangrene has been reported between % 0,01 - % 0,05 in different studies (6, 7). Although the mean age of patients appears to be between 40 years to 50 years , this disease may affect a wide age range from neonates to the very elderly5. Mean age of our patients was 54.1 years and the female/male ratio is reported to be 1/10, but we found it 9/49 in our study (8).

The epidemiologic features of FG determines a close relationship between the initial insult (traumatic, urogenital or anorectal pathology), host immunity and the organisms present at the affected site. Rapid tissue destruction and gangrene are clinical and pathognomic characteristics of the disease and are promoted and widened with the contribution of various bacteria and the combined effects of their virulence (9).

The initial infection may be of anorectal or urogenital origin. Our patients had mostly anorectal infections (75.51% vs. 24.49%). Ischiorectal, perianal and intersphincteric abscesses or urethral strictures, traumatic catheterization, urethral calculi and prostate biopsy are some kind of anorectal or urogenital infection which can result with FG (10). In our study, some reasons of the gangrene were rubber band ligation in one, basal cell carcinoma arising from pilonidal sinus in one, hemorrhoidectomy in one and condyloma acuminata in one patient. It is reported that infections after routine procedures can cause FG (11).

Like the other necrotizing infections, FG is also caused by either a monobacteriolar or mixed synergistic flora (12). Less frequently anaerobes, mostly aerobes are isolated, but both are invariably present. The isolated species are mostly enterobacteria, particularly *Escherichia coli*, followed by *Bacteroides* and streptococcal species. *Staphylococci*, *Peptostreptococci* and *Clostridia* are also frequently identified. A mean of four different organisms is cultured from each patient (13). These organisms are normal flora of the lower gastrointestinal tract and perineum.

It is reported that the impairment of the immune system predisposes FG. Immun-compromised patients; especially patients with diabetes mellitus and alcoholism are predisposed for FG.

Alcohol abuse has been reported in 20% to 60% of FG patients (14, 15). In our patients diabetes mellitus was 29%; alcoholism was 20%; malnutrition was 18% and medical immune suppression was 1%.

Common complaints were perianal and scrotal swelling, pain, crepitus and fever, and 24.6% of the lesions were evident initially in the penis and scrotum and 75.36% started from the perianal area. It is reported that the most common presenting features of FG are pain, pale erythema, swelling of the scrotum and cyanosis, blistering or bronzing of the skin. These symptoms are often associated with fever. Crepitus can be seen in 50-62% of cases and, obvious cutaneous necrosis may be evident when dermal gangrene develops. In the early stages, patients often have systemic symptoms of sepsis which appear disproportionate to the appearance of the scrotal skin. Shock, intestinal ileus and delirium are common (16).

Although the principal evaluation techniques FG cases are Ultrasonography and Magnetic resonance imaging (MRI) for presenting the occurrence of free air at the subcutaneous tissue, thickening at the scrotal tissue and fluid collection we used them for the diagnosis of perianal lesions mostly. The diagnosis in our cases was mostly established with the clinical appearance of the case. Free air at the imaging studies, loss of tissue tension and crepitus at the examination are findings which remind and anaerobic infections(1).

The principles of management are urgent and aggressive surgical debridement administration parenteral broad-spectrum antibiotics, and hemodynamic stabilization. The surgical removal of devitalized tissue is the main step of the treatment. All frankly necrotic tissue and that with doubtful viability should be carefully debrided and excised. Testes and spermatic cords and also deep fascia and muscular layers are generally not affected by the disease, since they maintain an adequate and independent blood supply (17). Repeated debridements are applied if necessary. The debridements can made under general anesthesia or as small debridements at bedside. Some authors suggest minimal debridement and drainage for gangrene of the scrotum and part of the perineum to decrease morbidity and shortening hospital stay and eliminate the need for reconstructive surgery (18). Antibiotics are routinely used and hemodynamic stabilization is necessary for the completion of the treatment.

Adjuvant therapies such as the irrigation of wounds with hydrogen peroxide to generate nascent oxygen to destroy the anaerobic organisms or the use of hyperbaric oxygen (HB) have all been tried with sound reasons and justifiable results. HBO therapy is a kind of treatment in which the patient breaths 100% oxygen at a pressure over 1 atmosphere absolute (ATA). Tissues require 60 ml/L oxygen/L blood flow to maintain adequate cellular metabolism. At normal atmosphere pressure plasma oxygen concentration is only 3ml/L and O₂ is delivered to tissues mainly by hemoglobin. If the inspired oxygen concentration is increased to 100%, the amount dissolved in the plasma will increase to 20 ml/L. At a hyperbaric pressure of 3 atmosphere absolute (ATA) the dissolved plasma oxygen increases to 70 ml/L, which exceeds the resting tissue oxygen requirements and does not require a contribution from hemoglobin 31,32. Macroscopically, HBO decreases tissue edema through vasoconstriction and thus improves local tissue swelling. It also leads to increased tissue oxygen tension, which is critical for local defense mechanisms. Tissue hyper oxygenation may optimize neutrophil function and inhibit anaerobic growth, and also reduces the systemic inflammatory response by decreasing the plasma levels of proinflammatory

cytokines and tumor necrosis factor alpha (19, 20).

Hyperbaric oxygen treatment remains controversial in the treatment of FG (1). Previous series have shown mixed results regarding the effects of HB on outcome in the treatment of FG (21). Some groups attributed a very low mortality rates (0% mortality rate) or decreased mortality rates to the administration of HBO (22). These studies showed that HBO treatment reduces systemic toxicity, prevents extension of the necrosis, narrows the demarcation line and provides a better prognosis when combined with surgery and wide spectrum antibiotherapy (19). Other reported that they found the mortality rate slightly higher in the HBO group with no statistical difference (21). We found that the mortality rates were the same in both groups I and III. But there was a significant difference in the hospitalization time. It was shorter in HBO group. This leads us to think that HBO shortens the treatment period. Like this the cosmetic results in group III were better than in group I. We think that these results can be attributed to the effects of HBO on wound healing.

Another treatment option with positive effects on wound healing is application of topical unprocessed honey. It has also antibacterial properties which first described by Van Ketel (23). The antibacterial properties of honey are attributed to its low pH and high osmolarity. However, it has been shown that wounds infected with *Staphylococcus aureus* are quickly rendered sterile by honey. Honey also contains enzymes, which digest dead and necrotic tissue. It also stimulates growth and multiplication of epithelial cells at the wound edges (1, 2). Studies in animal models have demonstrated that honey reduces inflammation, compared with various controls, in deep and superficial burns and in full-thickness wounds (24). Unprocessed honey has been used to treat infections in a wide range of wound types (25).

Some studies were performed to evaluate the effect of topical honey (6, 14). In these studies honey was administered with or without debridements. The positive effects of honey to the healing process and to the removal of necrotic tissue are demonstrated at these studies. In our study first thirty-seven patients (group I) were treated with broad-spectrum triple antimicrobial therapy, broad debridement, exhaustive cleaning, and then underwent split-thickness skin grafts or delayed closure as needed. However 20 patients (group II) who have localized FG were treated with only topical unprocessed honey and broad spectrum antibiotics. The cosmetic results were better than the other groups. The mean hospitalization time was longer than group III.

As conclusion necrotizing fasciitis of the perineum and genitalia is a severe condition with a high morbidity and mortality. Unfortunately we couldn't standardize the patients in our study. It could helpful to use the FG index. Therefore the low mortality rate in Group II couldn't have a definitive significance. But we were able to present that the hospitalization time can be reduced and cosmetic results can be improved with both the use of topical unprocessed honey and HBO treatment.

Table 1: Demographic properties of the cases

	Group I	Group II	Group III
Male/Female	13/4	18/2	9/3
Mean of age	57 (34-71)	49 (23-61)	56,5 (21-78)
Hospital Stay	41 (28-72)	41 (14-54)	32 (21-46)
HBOS	-	-	15 (2-22)
Mortality	8	0	3
Colostomy	13	-	5
Necessity for triple antibiotic therapy	14/17	7/20	4/12

Table 2:Etiologic factors

Etiologic Factors	Group I	Group II	Group III
Trauma	1	3	-
Perianal abscess	8	-	8
Ischiorectal abscess	1	-	-
Hemorrhoidectomy	-	-	2
Rubber tape ligation	-	-	1
Condyloma accuminata excision	-	-	1
Urogenital lesions	-	12	-
Scrotal Froncul	4	2	-
Basal Cell carcinoma	1	-	-
Idiopathic	2	3	-

Table 3:Predisposing factors

	Group I	Group II	Group III
Diabetes Mellitus	7	1	6
Alcoholism	7	2	1
Malnutrition	6	1	2
Medical immune suppression	2	-	2
Malignancy	1	-	-

Table 4: Microbiologic Characteristics of Groups

	Group I (n=17)	Group II (n=20)	Group III (n=12)	Total (n=49)	%
E. Coli	5	7	4	16	33
Peptostreptococcus	2	5	1	8	16
Pseudomonas	2	2	-	4	8
E.Coli, Bacteroides	1	1	1	3	6
S. Aureus, Bacteroides	1	2	1	4	8
Enterococcus, Bacteroides	2	1	-	3	7
Entereococcus, S.Aureus	-	2	-	2	4
Serratia, Bacteroides	1	-	1	2	4
S.Aureus, E.Coli, Entereococcus	-	-	1	1	2
No Growth	1	-	1	2	4
Morganella	1	-	1	2	4
Klebsiella	1	-	1	2	4

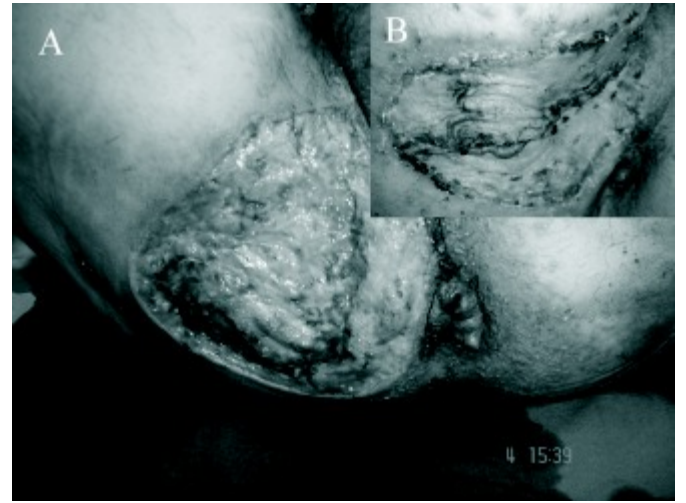


Figure 1: A: The appearance after debridements which belongs to a case of group I, B: The appearance after infection controlled and skin graft applied also belongs to the case of group I.

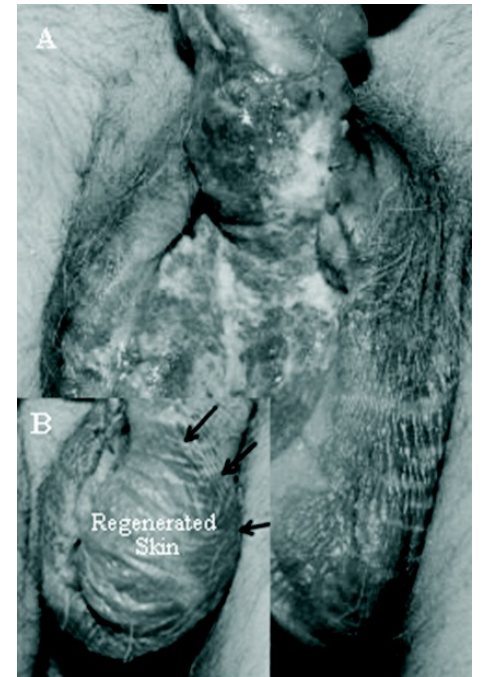


Figure 2: A: The appearance of the tissue after desquamation of necrotic parts since the honey applicated on the scrotum. B: The regenerated appearance of skin which honey is applied on. (A case of Group II)

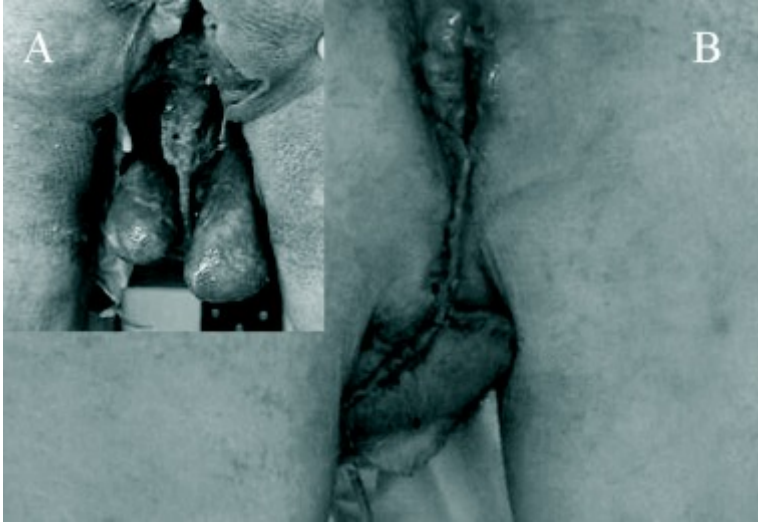


Figure 3: Appearance of a patient before (A) and after (B) HBOT (A case of Group III)

Yazarlarla ilgili bildirilmesi gereken konular (Conflict of interest statement) : Yok (None)

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