



ORIGINAL ARTICLE

Hyperbaric oxygen therapy adjunctive to surgical debridement in management of Fournier's gangrene: Usefulness of a severity index score in predicting disease gravity and patient survival[☆]

A. Janane^{a,*}, F. Hajji^a, T.O. Ismail^a, J. Chafiqui^a, M. Ghadouane^a,
A. Ameer^a, M. Abbar^a, A. Albouzi^d

^a Departamento de Urología, Hospital Militar Universitario, Facultad de Medicina Mohamed V, Rabat, Morocco

^b Departamento de Patología, Hospital Militar Universitario, Facultad de Medicina Mohamed V, Rabat, Morocco

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KEYWORDS

Fournier's gangrene;
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Abstract

Introduction: Hyperbaric oxygen therapy (HBOT) concomitant to surgery has been reported to reduce Fournier's gangrene (FG) mortality compared to exclusive surgical debridement. Most report from centers with relatively few patients using only surgical procedure. To assess efficiency of aggressive debridement with adjunctive HBOT. To evaluate Fournier's gangrene severity score index (FGSI) predictive value.

Material and methods: 70 Fournier's gangrene (FG) treated by surgical debridement and HBOT. Data were evaluated for physical examination findings, admission and final laboratory tests, surgical debridement extent, and antibiotic used. Patients had adjunctive (HBOT). FGSI, developed to assign a score describing the acuity of disease, was used. This index presents patients' vital signs and metabolic parameters (sodium, potassium, creatinine, and bicarbonate levels, and white blood cell count) and computes a score related to the severity of disease at that time. Data were assessed accordingly whether the patient survived or died. All patients underwent surgical debridement. Wound debridement was regularly performed in the postoperative period.

Results: Of 70 patients, 8 died (11.4%) and 62 survived (88.5%). Difference in age between survivors (median age, 50.0 yr) and non-survivors (median age, 54.5 yr) was not significant ($p=0.321$). Median extent of body surface area involved in necrotizing process in patients who survived and did not survive was 2.4% and 4.9%, respectively ($p=0.001$). Except for albumin,

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* Corresponding author.

E-mail address: a.janane@yahoo.fr (A. Janane).

PALABRAS CLAVE

Gangrena de Fournier;
Terapia de oxígeno hiperbárico;
Desbridamiento quirúrgico;
Puntuación del índice de gravedad

no significant differences were found between survivors and non-survivors. Median admission FGSI scores for survivors and non-survivors were 2.1 ± 2.0 and 4.2 ± 3.8 ($p = 0.331$).

Conclusion: FGSI score did not predict disease severity and the patient's survival. Metabolic aberrations and extent of disease seemed to be important risk factors for predicting FG severity and patient survival.

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Terapia de oxígeno hiperbárico complementaria al desbridamiento en el control de la gangrena de Fournier: utilidad de la puntuación de un índice de severidad en la predicción de la gravedad de la enfermedad y la supervivencia del paciente

Resumen

Introducción: La terapia de oxígeno hiperbárico (TOHB) concomitante con la cirugía ha demostrado una mejora en la reducción de la mortalidad por gangrena de Fournier (GF) en comparación con la aplicación exclusiva de desbridamiento quirúrgico. La mayoría de los datos se provienen de centros con un número relativamente reducido de pacientes, y en los que se emplea el procedimiento quirúrgico. El objetivo planteado consistía en evaluar la eficiencia del desbridamiento agresivo con TOHB complementaria, así como evaluar el valor predictivo del índice de puntuación de gravedad de la gangrena de Fournier (IGGF).

Material y métodos: 70 gangrenas de Fournier (GF) tratadas con desbridamiento quirúrgico y TOHB. Los datos evaluados fueron los resultados de las exploraciones físicas, los análisis de laboratorio tanto en el momento del ingreso como los finales, la extensión del desbridamiento quirúrgico y el antibiótico utilizado. Los pacientes recibieron TOHB complementaria. Se desarrolló un IGGF con el fin de adjudicar una puntuación que describiese la gravedad de la enfermedad. Este índice tiene en cuenta las constantes vitales de los pacientes, los parámetros metabólicos (niveles de sodio, potasio, creatinina y bicarbonato, así como recuento de linfocitos) y calcula una puntuación relativa a la gravedad de la enfermedad en ese momento. Se evaluaron los datos en función de la supervivencia o no del paciente. Todos los pacientes fueron sometidos a desbridamiento quirúrgico, realizándose el desbridamiento de la herida de forma periódica en el periodo postoperatorio.

Resultados: De un total de 70 pacientes, fallecieron 8 (el 11,4%) y sobrevivieron 62 (el 88,5%). La diferencia de edad entre los supervivientes (edad media 50,0 años) y no supervivientes (edad media 54,5 años) no fue significativa ($p = 0,321$). La extensión media del área del cuerpo afectada por el proceso de necrosis en los pacientes que sobrevivieron y en los que no sobrevivieron era del 2,4% y del 4,9%, respectivamente ($p = 0,001$). Excepto en lo referente a la albúmina, no se encontraron diferencias significativas entre supervivientes y no supervivientes. Las puntuaciones medias en el IGGF en el momento del ingreso de los supervivientes y de los no supervivientes fueron de $2,1 \pm 2,0$ y de $4,2 \pm 3,8$ ($p = 0,331$).

Conclusión: La puntuación del IGGF no resultó ser un factor de predicción de la gravedad ni de la enfermedad ni de la supervivencia del paciente. Sin embargo, tanto las alteraciones metabólicas como la extensión de la enfermedad aparecieron como factores significativos de riesgo en cuanto a predicción de la gravedad de la GF y la supervivencia del paciente.

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Introduction

A life-threatening necrotizing fasciitis, concerning the male genitourinary tract-perineum region, was first described by Jean-Alfred Fournier in 1883.¹ When the disease extends to the abdominal wall, it is also called Melenay's gangrene.² A current review³ indicates that Fournier's gangrene (FG) tends to affect older men, based on predisposing medical conditions, and has mostly an identifiable etiology.

Despite the development of knowledge regarding the etiology, diagnosis, treatment, and intensive care techniques, the mortality rate of FG is still approximately 10–50%.^{3,10} Laor et al. first described important factors for survival or death and then they described the Fournier's Gangrene Severity Index (FGSI) for predicting the severity of the disease.⁴ In this study, measurable pathophysiologic data between survivors and non-survivors of FG were compared to the FGSI score.

In the present study, we reviewed our 10-yr experience with 70 patients treated for FG to identify the etiologic

Table 1 The Fournier's Gangrene Severity Index.⁴

Variables	High abnormal values					Low abnormal values			
	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature, °C	>41	39–40.9		38.5–35.9	35–38.4	34–35.9	32–33.9	30–31.9	<29.9
Heart rate	>180	140–179	110–139		70–109	–	55–69	40–54	<39
Respiration rate	>50	35–49		25–34	12–24	10–11	6–9		<5
Serum Na, mmol/l	>180	160–179	155–159	150–154	130–149		120–129	111–119	<110
Serum K ⁺ , mmol/l	>7	6–6.9	–	5.5–5.9	3.5–5.4	3–3.4	2.5–2.9	–	<2.5
Serum creatinine, mg/100 ml, 2× for acute renal failure	>3.5	2–3.4	1.5–1.9	–	0.6–1.4	–	<0.6	–	–
Hematocrit, %	>60	–	50–59.9	46–49.4	30–45.9	–	20–29.9	–	<20
White blood cell count, total/mm ³ 1000×	>40	–	20–39.9	15–19.9	3–14.9	–	1–2.9	–	<1
Serum bicarbonate, venous, mmol/l	>52	41–51.9	–	32–40.9	22–31.9	–	18–21.9	15–17.9	<15

factors and discuss the validity of FGSI for predicting the disease severity and patient survival.

Patients and methods

Patients

Seventy consecutive male patients with a median age of 63.5 yr (range = 35–76 yr) who were treated for FG at our university department between January 2000 and August 2009 were included in the study. Data were collected about their medical history, symptoms, physical examination findings, and vital signs. The patients were followed up with daily biochemical and hematologic tests. The results of all biochemical, hematologic, and microbiologic tests were recorded at admission and final evaluation. The criteria for the onset of the symptoms were fever >38 °C, scrotal erythema or swelling, purulence or wound discharge, and fluctuation or crepitus.

Methods

The extent of gangrene was calculated for modified body surface area monograms routinely used to assess the extent of burn injuries: the penis, scrotum, and perineum accounted for 1% surface area each, every ischiorectal fossa 2.5% and so forth.

All culture samples were transported without delay to the clinical microbiology laboratory. The material was routinely streaked into two plates (eosin-methylene blue (EMB) agar and plain blood agar). The two plates were incubated in air at 37 °C for 24 h for aerobic microorganisms. Another EMB agar and plain blood agar plates were sealed in a Ziploc plastic bag to maintain the increased CO₂ atmosphere at 37 °C during 24 h for anaerobic microorganisms. Until the culture results and sensitivity tests were available, double parenteral antibiotic treatment with third-generation cephalosporin (ceftriaxone 4g/d)

and metronidazole 1.5 g/d was administered. During the postoperative period, wound debridement was regularly performed twice a day at the bedside for all patients. In the bedside debridement procedure, all infected and necrotic tissues were resected. The wound was covered by gauze impregnated with antimicrobial agents (povidone iodine plus nitrofurazone). The debridement was usually performed under local anesthesia (Prilocaine 2%) and the majority of the patients tolerated the procedure. Sedative analgesia (midazolam + fentanyl citrate) was administered.

The use of adjunctive hyperbaric oxygen therapy (HBOT) was based on a number of physiological principals. Patients were brought to the hyperbaric unit. They received 100% of oxygen at 2.5 atmospheres of pressure (2.5 ATA) in a monoplace hyperbaric unit, for 90–120 min.

FGSI was used in our study (Table 1). The index has been developed in an attempt to assign a numerical score that describes the severity of the FG. In the FGSI, nine parameters are measured, and the degree of deviation from normal is graded from 0 to 4. The sum of the individual values is then tallied to arrive at the FGSI score. These parameters are temperature, heart rate, respiratory rate, serum sodium, potassium, creatinine levels, bicarbonate levels, hematocrit, and leukocyte count. The data were assessed according to whether the patient survived or died.

Statistical analysis

Statistical analysis was performed with the Statistical Package for Social Science (SPSS) for Windows, version 8.0 software. A comparison of the median age and the median admission time, the median extent of the body surface area involved in the necrotizing process, and admission and final metabolic parameters was performed between survivors and non-survivors

with the Mann–Whitney U test. The admission and final parameters in each group were compared by Wilcoxon signed rank test. A $p < 0.05$ was considered significant.

Results

Of the evaluated 70 patients, 8 died (11.4%) and 62 survived (88.5%). The difference in age between survivors (median = 50.0 ± 12.9 yr; range = 37–64 yr) and non-survivors (median = 54.5 ± 6.5 yr; range = 48–66 yr) was not significant ($U = 30.000$; $p = 0.321$).

Patients were evaluated with the onset of the symptoms. The first symptom had appeared in the scrotum in 60 survivors and 6 non-survivors and in the perineum in 2 patients in each group. The median extent of the body surface area involved in the necrotizing process in patients who survived and did not survive was 2.3% and 4.8%, respectively ($p = 0.001$). The median admission time was 5.8 d (range = 2–11 d). No significant difference was found in terms of duration of symptoms before presentation between patients who survived (4.0 ± 1.3 days) and did not survive (4.8 ± 1.4 days) ($U = 29.500$; $p = 0.134$).

All the patients underwent HBOT adjunctive to radical surgical FG debridement. Necrotizing tissues were completely removed and abscess drainage was performed when necessary. During surgery, the pathology was found to be localized to the genital region in 41/62 survivors and 4/8 non-survivors, whereas it had spread beyond the genital region to the umbilicus in 21/62 survivors and 4/8 non-survivors. Moreover, orchiectomy (in no survivors and 4/8 non-survivors, unilateral in 2/62 survivors and in no non-survivors) and scrotoectomy (bilateral in 41/62 survivors and all non-survivors, unilateral in 21/62 survivors) were performed. Among those who died, 6/8 patients underwent a diverting colostomy. Cystostomy was needed in 37/62 survivors and 3/8 non-survivors.

Positive cultures from the necrotic tissue revealed *Staphylococcus aureus* in 42 patients (60%), coagulase-negative *Staphylococcus aureus* in eight (11.4%), *Acinetobacter calcoaceticus* in seven (10%), *Enterococcus* in seven (10%) and *Klebsiella oxytoca* in six patients (8.5%). Anaerobes were not harvested in our patients.

The median admission FGSI scores for survivors and non-survivors were 2.1 ± 2.0 and 4.2 ± 3.8 , respectively ($p = 0.331$). However, the median final FGSI scores for survivors and non-survivors were 1.0 ± 0.9 and 6.0 ± 3.3 , respectively ($p = 0.017$).

A comparison of the admission and final laboratory parameters in the survivors and non-survivors is shown in Table 2. Except for the albumin level, no significant differences were found between survivors and non-survivors in other admission laboratory parameters. At the end of the treatment, serum urea, creatinine, alkaline phosphatase levels, and FGSI score significantly decreased, and albumin levels significantly increased in the survivors ($p = 0.030$, $p = 0.004$, $p = 0.084$, $p = 0.001$, $p = 0.005$, respectively).

Discussion

Fournier's gangrene is also described as dermohypodermatitis of the perineal, genital or perianal regions. The etiology of this disease has not been completely elucidated.^{1,2} In the present study, the median age of our patients was 52.5 yr, consistent with the literature.

Various results have been published about mean age of the survivors and non-survivors. In a study by Clayton et al., surviving patients were significantly younger than non-survivors.³ This result was also confirmed by Laor et al.⁴ Conversely, in another current study, no statistical difference was found between survivors and non-survivors.⁵ In our analysis, no significant difference in terms of age between the survivors and non-survivors was noticed.

There is a consensus that despite the advances in medical therapy and intensive care procedures, FG still remains a serious medical condition due to the progressive disease leading to death. The mortality rate remains high (16.8–50%).^{6,7}

Two studies from Turkey revealed that FG mortality rates were 7% and 23%, respectively.^{8,9} In our department, despite the development of treatment options (adjunctive HBOT to radical surgical debridement, wound debridement in the postoperative period regularly performed twice a day at the bedside for all patients) and antibiotic therapy, our mortality rate was 11.4%. This low death rate could be due to the young age of our patients (85.8% < 54 years), also the beneficial role of adjuvant HBOT used in our experience.

Our good results could be explained by both the relative young age of our patients and, especially, the systematic use of HBOT. The suggested potential role of adjunctive HBOT in the treatment of Fournier's gangrene is based on a number of physiological principles. Phagocytic leucocytes provide a primary defense against bacterial infections. In order to provide effective bacterial killing, they require oxygen for the production of high energy radicals. In the necrotic wound, the availability of oxygen is severely limited. In the diabetic, microangiopathy further limits tissue oxygenation in the surrounding, potentially viable tissues. The supplemental oxygen provided by hyperbaric therapy effectively provides for enhanced white cell killing function by elevating the tissue PO₂.^{10,11}

In the presence of anaerobic bacteria, hyperbaric oxygen has direct antibacterial effect. Lacking endogenous catalases and peroxydases, these bacteria cannot exist in the normoxic/hyperoxic environments created by the hyperbaric chamber. In certain clostridial species, the liberation and activity of endotoxins are diminished in the presence of elevated tissue oxygen.¹²

To influence the evolution of the patients and to improve the prognosis in the recovery phase of the disease, HBOT plays an important role in the promotion of wound healing. Angiogenesis, essential for the development of granulation tissue and subsequent reepithelialization, requires the presence of actively dividing fibroblasts. Hypoxia suppresses their growth. Return of tissue oxygen levels to normal or higher ameliorates this problem.¹³

Table 2 Serum admission and final parameters for survivors and non-survivors.

Variable	Survivors (n=62) Median \pm SD (min-max)	Non-survivors (n=8) Median \pm SD (min-max)	p-Value
Age, yr	60.0 \pm 12.9 (35-75)	64.5 \pm 6.5 (58-76)	0.321
Time to consult, d	4.0 \pm 1.3 (2-6)	4.8 \pm 1.4 (3-8)	0.134
Body surface, %	2.3 \pm 1.2 (1-4.8)	4.8 \pm 1.6 (2-6.4)	0.001
Urea, mg/dl			
Admission	48.0 \pm 39.0 (12-142)	59.0 \pm 62.7 (35-195)	0.248
Final	31.5 \pm 20.4 (7-92)	46.2 \pm 68.0 (20-192)	0.302
Creatinine, mg/dl			
Admission	1.2 \pm 0.5 (0.6-2.2)	1.8 \pm 1.5 (0.5-4.9)	0.934
Final	0.8 \pm 0.2 (0.5-1.3)	1.2 \pm 0.7 (0.4-2.5)	0.934
Hematocrit, g/dl			
Admission	35.6 \pm 10.8 (22.1-68.5)	31.3 \pm 3.7 (26.6-36.5)	0.161
Final	30.2 \pm 13.7 (22.8-35.4)	28.6 \pm 7.0 (20.0-38.9)	0.804
WBC, g/dl			
Admission	12,400 \pm 7312 (3130-27,500)	15,850 \pm 1067 (10,800-39,500)	0.322
Final	7725 \pm 3909 (4980-18,500)	12,430 \pm 5797 (5570-20,700)	0.564
Sodium, mmol/l			
Admission	137.0 \pm 4.3 (129-145)	136.0 \pm 3.1 (130-139)	0.589
Final	138.5 \pm 3.0 (132-142)	136.5 \pm 5.8 (132-HG)	0.739
Potassium, mmol/l			
Admission	4.2 \pm 0.6 (3.2-5.4)	4.1 \pm 1.0 (2.4-5.2)	0.650
Final	4.1 \pm 0.5 (2.9-4.7)	3.6 \pm 0.8 (2.6-4.8)	0.057
Total protein, g/dl			
Admission	58.5 \pm 8.6 (44-71)	54.0 \pm 8.4 (40-65)	0.283
Final	55.4 \pm 11.2 (39-79)	53.6 \pm 6.9 (50-68)	0.361
Albumin, g/dl			
Admission	28.6 \pm 6.5 (20-44)	24.1 \pm 4.6 (19-30)	0.022
Final	32.5 \pm 6.2 (22-47)	28.0 \pm 5.3 (21-36)	0.136
FGSI score			
Admission	2.1 \pm 2.0 (0-9)	4.2 \pm 3.8 (0-13)	0.331
final	1.0 \pm 1.7 (0-5)	6.0 \pm 3.3 (0-9)	0.017

WBC, white blood cell count; FGSR, Fournier's Gangrene Severity Index; SD, standard deviation; min, minimum; max, maximum.

The recommended hyperbaric treatment schedule for Fournier's gangrene is twice daily at 2.0 ATA to 2.5 ATA for 90-120 min until the patient's condition stabilizes.¹⁴ These conditions allow a complete efficiency based on physiological principals to improve the patient's prognosis.^{12,14} Treatments are then given once daily. This is the treatment profile that we followed in our series.

FG is a surgical emergency. Many patients may present with only minor skin lesions in the early stages of the disease. The majority of our patients (88.5%) were admitted at this stage. Previous reports have shown that delay in the first debridement of a necrotizing tissue infection worsens outcome.^{14,15} We have concluded through our 10-years experience that early admission, rapid diagnosis, and effective treatment are crucial components in achiev-

ing a successful outcome. In our study, the first symptom was observed in the scrotum in 90% of the patients and median admission time was 3.4 days. Moreover, the median extent of the body surface area involved in the necrotizing process was significantly lower in patients who survived than that in those who died. In a study by Spimak et al., a greater extent of the disease was associated with a greater mortality rate for patients who had more frequent operations.^{16,17} We found that the extent of body surface area involved in the necrotizing process was significantly higher in the non-survivors. We believe that this is one of the most important risk factors for mortality in patients with FG.

The various etiologic risk factors for FG include perianal disease, urethral stricture, local trauma, diabetes mellitus, malignancy, hemorrhoids, urinary tract infections, and

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