

Significance of Hyperbaric Oxygenation in the Treatment of Fournier's Gangrene: A Comparative Study

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Keywords

Necrotizing fasciitis · Fournier's gangrene · Necrotomy · Soft tissue infection · Hyperbaric oxygenation

Abstract

Introduction: Hyperbaric oxygenation (HBO), in addition to anti-infective and surgical therapy, seems to be a key treatment point for Fournier's gangrene. The aim of this study was to investigate the influence of HBO therapy on the outcome and prognosis of Fournier's gangrene. **Patients and Methods:** In the present multicenter, retrospective observational study, we evaluated the data of approximately 62 patients diagnosed with Fournier's gangrene between 2007 and 2017. For comparison, 2 groups were distinguished: patients without HBO therapy (group A, $n = 45$) and patients with HBO therapy (group B, $n = 17$). The analysis included sex, age, comorbidities, clinical symptoms, laboratory and microbiological data, debridement frequency, wound dressing, antibiotic use, outcome and prognosis. The statistical analysis was performed with GraphPad Prism 7[®] (GraphPad

Software, Inc., La Jolla, USA). **Results:** Demographic data showed no significant differences. The laboratory parameters C-reactive protein and urea were significantly higher in group B (group B: 301.7 vs. 140.6 mg/dL; group A: 124.8 vs. 54.7 mg/dL). Sepsis criteria were fulfilled in 77.8 and 100% of the patients in groups A and B respectively. Treatment in the intensive care unit (ICU) was therefore indicated in 69% of the patients in group A and 100% of the patients in group B. The mean ICU stay was 9 and 32 days for patients in groups A and B respectively. The wound debridement frequency and hospitalization stay were significantly greater in group B (13 vs. 5 debridement and 40 vs. 22 days). Initial antibiosis was test validated in 80% of the patients in group A and 76.5% of the patients in group B. Mortality was 0% in group B and 4.4% in the group A. **Conclusion:** The positive influence of HBO on the treatment of Fournier's gangrene can be estimated only from the available data. Despite poorer baseline findings with comparable risk factors, mortality was 0% in the HBO group. The analysis of a larger patient cohort is desirable to increase the significance of the results.

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Introduction

Fournier's gangrene is defined as necrotizing fasciitis of the external genitals (as shown in Figs. 1a, b), which usually affects male patients. Fournier's gangrene is a rare and serious disease with high morbidity and mortality and was first described by Baurienne in 1764. One century later, the French venereologist Fournier described this condition as a special type of soft tissue infection localized to the scrotum, penis, perineum, and anterior abdominal wall [1]. Key points for the successful treatment of Fournier's gangrene are immediate surgical debridement accompanied by forced antibiotic therapy and, usually, intensive medical management [2–4]. Fournier's gangrene usually causes local tissue hypoxia. Hyperbaric oxygen (HBO) therapy has a bactericidal effect on anaerobic infections. HBO improves tissue perfusion, promotes angiogenesis, increases the oxygen level in tissues, and inhibits the production of toxins. Therefore, HBO therapy is widely used to treat mixed infections [5, 6].

The aim of the following investigation was to compare differences in clinical parameters, morbidity, mortality, and prognosis between Fournier patients treated with or without HBO therapy in consideration of the risk factors.

Patients and Methods

In the present multicenter, retrospective observational study (Department of Urology, Asklepios Clinic, Hamburg, Germany; Department of Urology and Kidney Transplantation, Martin Luther University, Halle [Saale], Germany; Department of Urology and Paediatric Urology, St. Antonius Hospital, Eschweiler, Germany and Department of Internal Medicine, University Medicine Greifswald, Hematology-Oncology-Transplant Center, Greifswald, Germany), we evaluated the data of approximately 62 patients diagnosed with Fournier's gangrene between 2007 and 2017. We analyzed the following parameters: sex, age, comorbidities, clinical symptoms, laboratory and microbiological data, debridement frequency, wound dressing, antibiotic use, outcome, and prognosis. To compare the efficacy of HBO, the patients were divided into 2 groups (group A, without HBO, $n = 45$; group B, with HBO, $n = 17$). Furthermore, the data were stratified by outcome. The statistical analysis was performed with GraphPad Prism 7[®] (GraphPad Software, Inc., La Jolla, USA). Time-dependent changes between the 2 groups are presented as the mean \pm SD and range and were evaluated by the Man-Whitney U test. Categorical data are presented as the count and percentage and were evaluated by the chi-square test or Fisher's exact test. Statistical significance was considered at $p < 0.05$.

Results

Of the 62 patients, 45 (72.6%) were treated with standard therapy: urgent surgical debridement and parenteral broad-spectrum antibiotics (group A, non-HBO). The other group, with 17 (27.4%) patients, was additionally treated with a hyperbaric procedure (group B, HBO).

There were no significant differences between the groups regarding the demographic data or preexisting diseases. All patients in both groups were male (Table 1). The infection parameters measured in the blood at the beginning of the inpatient stay are listed in Table 2. There were significantly higher values C-reactive protein values (301.7 vs. 140.6 mg/dL) and urea values (124.8 vs. 54.7 mg/%) in the HBO group than in the non-HBO group ($p < 0.001$). There was a positive trend regarding leukocytes (22.9/nL, group B; 17.1/nL, group A; $p = 0.06$). No significant difference was observed concerning the mean level of thrombocytes (225.2/nL, non-HBO; 270.2/nL, HBO; $p > 0.21$).

The original points of infection are presented in Table 3. In most cases, the infection originated in the scrotal, perineal, or both regions (33 patients, 73.4%, group A; 15 patients, 88.2%, group B). There were 5 patients with a penile origin of infection (5 patients, 11.1%) in the non-HBO group, while no patients in the HBO group were affected in this way. Only some patients showed a rectal (4 patients, 8.9%, non-HBO; 1 patient, 5.9%, HBO), inguinal (2 patients, 4.4%, non-HBO), urethral (1 patient, 5.9%, HBO), or renal (1 patient, 2.2%, non-HBO) origin of infection, as shown in Table 3.

There were significant differences in the therapeutic parameters and clinical outcomes. The median hospital stay was 22.5 days in the non-HBO group and 40.3 days in the HBO group ($p < 0.008$). Treatment in the intensive care unit (ICU) was necessary for 31 patients (69%) in the non-HBO group and for 17 patients (100%) in the HBO group. Furthermore, the ICU stay differed significantly between the groups (9 days, non-HBO; 32 days, HBO; $p < 0.001$). A total of 77.8% of the patients in the non-HBO group met the sepsis criteria (35 patients), as did all 17 patients in the HBO group ($p = 0.025$). Septic shock affected 9 of 45 patients (20%) in the non-HBO group and 12 of 17 patients (70.5%) in the HBO group ($p < 0.001$).

In the non-HBO and HBO groups, 80% (36 patients) and 76.5% (13 patients) of the patients were administered test-appropriate first-line antibiotic ($p = 0.680$). The incidence of 3MRGN was 13.3% (6/45) in the non-HBO group and 17.6% (3/17) in the HBO group ($p = 0.347$). In



Fig. 1. **a** Clinical appearance of Fournier's gangrene with the involvement of the left groin in an obese patient; case and photo from the Department of Urology and Pediatric Urology, St. Antonius Hospital, Eschweiler, Germany. **b** Typical findings of a Fournier's gangrene with primary scrotal manifestation of the same patient.

this context, there was no difference in the ICU stay between patients with or without test-appropriate first-line antibiotic treatment ($p < 0.753$). Vacuum therapy (VAC) was administered to 18 patients (40%) in the non-HBO group and to 16 patients (94%) in the HBO group ($p < 0.001$). The number of surgical wound debridement sessions varied significantly between the groups, with an average of $4.8 (\pm 2.9)$ debridement sessions in the non-HBO group and $13.3 (\pm 6.3)$ debridement sessions in the HBO group ($p < 0.001$).

Inpatient mortality was 4.5% (2/45) in the non-HBO group and 0% in the HBO group (0/17).

Discussion

While HBO therapy is an additional treatment after surgical debridement and antibiotic therapy in cases of soft tissue infection (potential benefits are shown in Fig. 2), the benefits of adjuvant HBO therapy remain controversial for necrotizing fasciitis [7]. Nevertheless, the positive effects on soft tissue affected by an infection with aerobic, and especially anaerobic bacteria, are well understood [8–10]. There are bactericidal and bacteriostatic effects of increasing the oxygen supply to the cellular level.

Table 1. Demographic data and physical conditions of patients

	Non-HBO	HBO	<i>p</i> value
Number of patients	45	17	
Mean age	60	58	>0.55
Gender, male, <i>n</i> (%)	45 (100)	17 (100)	
BMI	28.4	30.1	>0.73
Diabetes melitus, <i>n</i> (%)	23 (50.0)	9 (52.9)	>0.89
Alcoholism, <i>n</i> (%)	14 (31.1)	5 (29.4)	>0.89
HIV, <i>n</i> (%)	1 (2.2)	0 (0)	>0.67
Colon carcinoma, <i>n</i> (%)	2 (4.4)	1 (5.9)	>0.81

HBO, hyperbaric oxygenation; BMI, body mass index.

Table 2. Blood parameters before the beginning of therapy

	Non-HBO	HBO	<i>p</i> value
Leucocytes/nL	17.1	22.9	0.06
Thrombocytes/nL	225.2	270.2	>0.21
CRP, mg/%	140.6	301.7	<0.001
Urea, mg/%	54.7	124.8	<0.001

HBO, hyperbaric oxygenation.

Table 3. Clinical parameters of patients

	Non-HBO	HBO	<i>p</i> value
Median days stay	22.5	40.3	<0.008
Number of ICU, <i>n</i> (%)	31 (69)	17 (100)	0.009
Median days ICU	6.13	32	<0.001
Number wound debridements, mean	4.8	13.3	<0.001
VAC, <i>n</i> (%)	18 (40)	16 (94)	
First antibiotics appr., <i>n</i> (%)	36 (80)	13 (76.5)	0.680
3-MRGN, <i>n</i> (%)	6 (13.3)	3 (17.6)	0.347
Sepsis (criteria), <i>n</i> (%)	35 (77.8)	17 (100)	0.025
Septic shock, <i>n</i> (%)	9 (20)	12 (70.5)	<0.001
Mortality, % (<i>n</i>)	4.5 (2)	0 (0)	0.204

HBO, hyperbaric oxygenation; ICU, intensive care unit; VAC, vacuum-therapy.



Fig. 2. Granulated wound after necrotomy and hyperbaric oxygenation (HBO) therapy in a patient with Fournier's gangrene due to a necrotizing rectal carcinoma with the involvement of the left groin; case and photo from the Department of Urology and Kidney Transplantation, Martin Luther University, Halle (Saale), Germany.

Angiogenesis is promoted, and collagen synthesis is doubled; both processes are important for the wound-healing process. Furthermore, the production of alpha-toxin is reduced, and antibiotic therapy is more effective in the presence of higher oxygen concentrations [6]. Nevertheless, the use of HBO therapy has not been comprehensively established. The main reason for this fact is its availability in only a few centers in Germany, leading to the prolonged and dangerous transportation of patients who

are likely septic. Another important factor is the tremendous expense of this treatment, ranging from approximately 8,000–25,000 EUR per patient, which is not reimbursed by health insurance [4].

Additionally, the results of HBO therapy in cases with soft tissue infection, such as Fournier's gangrene, vary in the literature. Earlier studies have reported the mortality rate to be up to 43% [11]. Recent trials have presented better results, with 13% for conventional treatment and 27% for HBO therapy [5]. In contrast to these data, Pizzorno et al. [12] reported approximately 0% mortality without HBO therapy, while other studies have reported approximately 3 and 9% [13–15]. The mortality rate in our series was 4.5% without HBO, with incidences of mortality resulting from heart attack and septic shock. While no patients in the HBO group died during the hospital stay, there was no significant difference in mortality between the groups. The better results in the HBO group compared with the results mentioned in the literature, and the non-HBO group in our series could be attributable to the excellent availability of HBO therapy and reduced dangerous and onerous transportation of patients in poor physical conditions. It is known that a delay of 24 h in the initial surgical treatment may lead to a tenfold greater mortality rate [3, 4]. Experience is an additional important factor affecting mortality in the treatment of patients with Fournier's gangrene: seeing more than 1 patient per year had an adjusted 42–84% lower mortality rate ($p < 0.0001$) [15, 16]. Another key point for improving patient outcome is the immediate start of treatment with a broad antibiotic [2, 18] and intensive care therapy [18–20].

Regarding the poorer physical conditions of patients in the HBO group compared to the condition of pa-

tients in the non-HBO group (70.5 vs. 20% with septic shock), the inclusion of worse infectious parameters could explain the only marginally better results in this study [18, 19].

Regarding the total hospital stay (22.5 days non-HBO vs. 22.9 days HBO), there was no difference between the groups, which highlights the positive impact of HBO therapy.

The limitations of this study are the retrospective nature of the data, the heterogeneous patient sample, and the multidisciplinary and multicenter approach.

Conclusion

The positive influence of HBO therapy on the treatment of Fournier's gangrene is going to be difficult to measure. This nonrandomized retrospective study presents opposite findings. Despite poorer baseline findings with comparable risk factors, there was a 0% mortality in the HBO group. This could be a sign of positive influence of the HBO-treatment. In contrast, the mean ICU-stay differed significantly in favor of the non-HBO group. With this observation, the accelerating effect on tissue re-

generation and general convalescence of HBO-therapy is not precisely verifiable. To summarize, there are comparable problems as found in other studies on this subject of retrospective nature: Prospective investigations with larger patient samples are desirable and necessary to clear these findings.

Ethics Statement

Formal consent was provided by the patients to participate in this study.

Disclosure Statement

The authors declare that they have no conflicts of interest to disclose.

Authors Contribution

P.A. and S.M. were responsible for protocol development, data collection, analysis, and manuscript writing. J.K. and L.S. were responsible for data collection and manuscript editing. J.S. and P.F. were in charge of protocol development and manuscript editing.

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