Efficiency of Hyperbaric Oxygen Therapy Combined with Negative-Pressure Wound Therapy in the Treatment Strategy of Fournier's Gangrene –A Retrospective Study

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Purpose: Fournier's gangrene (FG) is a serious, aggressive, and often fatal multi-organism infection that affects the soft tissues of the perineum, rectum, and external genitalia. This study aimed to analyse the treatment's strategies of FG.

Materials and Methods: This was a retrospective study of 35 patients with a diagnosis of FG admitted between 2016 and 2021. The diagnosis of FG was established on a clinical basis. Data on patient's age, sex, comorbidities, laboratory results (C-reactive protein (CRP), white blood cell (WBC), hematocrit (HCT), platelets (PLT), sodium, potassium, creatinine, procalcitonin, international normalized ratio (INR), and gangrene culture), extent of resection, antibiotics used, and hospitalisation time were obtained. The extent of resection was assessed on a scale of 1–5.

Results: The study group consisted of all men (n=35) aged 24–85 (mean, 58) years. In 13/35 (37%) patients, hyperbaric oxygen therapy (HBOT) combined with negative-pressure wound therapy (NPWT) was used as a treatment for wound healing in Fournier's syndrome (group 1), and in 22/35 (63%) patients, open standard wound care was used (group 2). There were no fatalities in group 1, but four deaths (18%) were noted in group 2. The median extent of resection was 3 in group 1 and 2 in group 2. There was a correlation between the extent of resection and the use of HBOT combined with NPWT. The hospitalisation time was much shorter in group 2 (mean, 23 days) than in group 1 (mean, 26 days).

Conclusion: HBOT and NPWT (group 1) showed advanced wound healing with a high efficiency rate. The longer median hospitalisation time in this group may be related to the severity of the injury.

Keywords: Fournier Gangrene; treatment; wounds

INTRODUCTION

Fournier's gangrene (FG) is a serious, aggressive, and often fatal multi-organism infection that affects the soft tissues of the perineum, rectum, and external genitalia. It is an anatomical subcategory of necrotising fasciitis with a similar aetiology and treatment strategy. This disease was first described by Jean Alfred Fournier, who described five cases in young men. FG is 10 times more common in men than in women and can occur at any age.(1) It usually causes painful swelling of the scrotum or perineum with sepsis. Physical examination revealed small areas of necrotic skin with erythema and swelling. In the more advanced stage of the disease, there is a foul-smelling discharge. Mortality increases due to risk factors such as immunosuppression, diabetes, alcoholism, arteriosclerosis, malnutrition, recent urethral or perineal surgery, HIV infection, liver disease, leukaemia, and obesity.(2)

Insidious onset of the disease occurs in 40% of cases, and unrecognised pain causes a delay in treatment. FG can be caused by trauma, insect bites, or unsafe sexual practices.(3) Computed tomography or magnetic resonance imaging may contribute to the assessment of the degree of rectal involvement.(3) The degree of internal necrosis is usually higher, as indicated by the external symptoms. Surgical debridement should be performed within 24 h, as delayed or incorrect surgery may result in increased mortality. Immediate initiation of empiric broad-spectrum parenteral antibiotic therapy, which provides adequate protection against all likely microorganisms, is recommended. The suggested regimen usually includes a broad-spectrum penicillin or a third-generation cephalosporin (in combination with a beta-lactamase inhibitor), gentamicin, metronidazole, and clindamycin.(3)

Hyperbaric oxygen therapy (HBOT) is increasingly used in the treatment of severe soft tissue infections, especially FG. The use of HBOT supports the main components of treatment, i.e. surgical intervention and broad-spectrum antibiotic therapy.(4) The interdisciplinary treatment of FG consists of a combination of surgical and urological interventions, antibiotic therapy, negative-pressure wound therapy (NPWT), HBOT, and plastic reconstructive procedures.

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Table 1. Comparison of group 1 hyperbaric oxygen therapy + negative-pressure wound therapy and group 2 open standard wound care in DM, hypertension, neoplasm, and mortality.

	Group 1 HBOT + NPWT (n=13)		Group 2 open standard wound care (n=22)		Test Chi-2	
	N	%	N	%	Chi-2	*p*
DM (n)	4	31%	7	32%	0.004	0.948
HT (n)	7	54%	7	32%	1.652	0.199
Neoplasm (n)	1	8%	6	27%	1.958	0.162
Mortality (n)	0	0%	4	18%	2.669	0.102

Wound healing methodologies can remain classically driven but have also evolved with advances over time. One of the ongoing sea changing currents is the use of NPWTs. In many ways, NPWTs and all their variants share similar mechanisms of action and challenges to their usage, as we see in HBOTs.[5]
This study aimed to analyse the treatment's strategies of FG.

MATERIALS AND METHODS

Study Population

This was a retrospective study of 35 patients with a diagnosis of FG admitted between 2016 and 2021. The data were collected from the analysis of medical records at the Department of Urology and Oncological Urology, Praski Hospital, and the Department of Urology, Military Institute of Medicine in Warsaw, Poland. The study participants were from Mazovia Province, 33 were Polish, 1 Ukrainian and 1 Indian.
All patients signed the informed consent that their medical data might be used in the future as part of a retrospective study. The datasets analyzed during the current study were anonymised before we used it for the purpose of current study.
The diagnosis of FG was established on a clinical basis. Data on patient's age, sex, comorbidities, laboratory results (C-reactive protein (CRP), white blood cell (WBC), hematocrit (HCT), platelets (PLT), sodium, potassium, creatinine, procalcitonin, international normalized ratio (INR), and gangrene culture) extent of resection, antibiotics used, and hospitalisation time were obtained. The extent of resection was assessed on a scale of 1–5 as follows: 1, lesion only on the scrotum; 2, scrotum + perineum; 3, scrotum + perineum + buttocks; 4, scrotum + perineum + buttocks + orchidectomy; and 5, scrotum + perineum + buttocks + orchidectomy + lower abdomen + thighs.

Inclusion and exclusion criteria

The inclusion criteria were: inflammatory infiltration, swelling of the perineum and / or urogenital area and / or external genitalia and skin necrosis, the patient's condition requiring immediate resection of affected lesions + systemic inflammatory response syndrome (SIRS). The exclusion criteria were: inflammatory infiltration, edema of the perineum and / or urogenital area and / or external genital organs without elevation of inflammatory parameters , a testicular abscess, and scrotal abscess.
In this study, all patients with FG were divided into two groups: group 1 (n=13), HBOT and NPWT, and group 2 (n=22), open standard wound care.

Statistical Analysis

Data analysis was performed using IBM Statistical Package for the Social Sciences (IBM SPSS Statistics Corp.; Armonk, NY, USA) version 26 for Windows. Univariate analyses (chi-square test and Student's *t*-test) were used for comparison. Statistical significance was set at $p < 0.05$. Descriptive data are presented as parametric and nonparametric data.

RESULTS

The study group consisted of all men (n=35) aged 24–85 (mean, 58) years. In 13/35 (37%) patients, HBOT combined with NPWT was used as a treatment for wound healing in Fournier's syndrome (group 1), and in 22/35 (63%) patients, open standard wound care was used (group 2). There were no fatalities in group 1, but four deaths (18%) were noted in group 2 (**Table 1**).
Table 1 compares the groups in terms of the incidence of diabetes, hypertension (HT), cancer, and mortality. The numbers and percentages of the aforementioned phenomena in each of the groups were presented and using the chi-square test, it was established whether there were statistically significant differences between the groups. As it turned out, no statistically significant differences were found in terms of diabetes, HT, cancer, and deaths. It is worth noting, however, that a significantly higher percentage of deaths and neoplasms occurred in group 2 than in group 1. In turn, a clearly greater percentage of patients with arterial HT occurred in group 1 than in group 2.
Among the comorbidities, diabetes mellitus (DM) was noted in four patients in group 1 and seven in group 2. In contrast, there were seven patients in group 1 and seven patients in group 2 who had arterial HT. In both groups, seven neoplasms, including kidney cancer, bladder cancer, prostate cancer, colorectal cancer, brain cancer, and lung cancer, were noted. Group 2 had six cases of cancer, while group 1 had one case (**Table 1**).
Escherichia coli, Pseudomonas aeruginosa, and En-

Table 2. Comparison of group 1 hyperbaric oxygen therapy + negative-pressure wound therapy and group 2 open standard wound care in age, hospitalisation time, and extent of resection.

	Group 1 HBOT + NPWT (n=13)	Group 2 open standard wound care (n=22)	U Mann -Whitney test	
	Me	Me	Z	*p*
Age (median age)	53	61.5	-1.059	0.29
Hospitalization time (days)	26	23	-0.803	0.422
Extent of resection (median)	3	2	-2.989	0.003*

Table 3. Analysis of previous studies on FG management.

Reference	Study design	Intervention	Primary endpoint	Secondary endpoint	Number of patients	Limitation
Hung et al. [1]	Retrospective observational study	Adjuvant HBOT	Mortality	Septick shock survival	60	Retrospective design. Insufficiency of some data within the registry. Inability to access all data.
Schneidewind et al. [2]	Systematic review (all types of study designs were included)	Adjuvant HBOT	Mortality rate or overall survival	Duration of inpatient treatment. Duration of intensive care treatment. Number of surgical debridement. Quality of life	376	Only English and German publication included. Heterogeneous data. Retrospective design of included publication.
Li et al. [8]	Retrospective observational study	Adding HBOT to conventional therapy	Mortality	Number of surgical debridement. Indwelling drainage tube time. Curative time	28	Retrospective design. Small sample size.
Tutino et al. [9]	Retrospective observational study	HBOT	Length of hospital stay	Mortality	23	Retrospective design. Small sample size
Assenza et al. [10]	Retrospective observational study	VAC therapy (1 pt. with HBOT)	Reducing in number of dressing	Lengh of hospital stay	6	Retrospective design. Small sample size
Cuccia et al. [11]	Retrospective observational study	Treatment algorithm with VAC therapy and HBOT	Reducing in the number of surgical debridement	-	6	Retrospective design. Small sample size. Lack of control group.
Balli et al. [12]	Retrospective observational study	VAC therapy	Mortality rate	Hospitalisation time. Re-debridement rate. Reconstruction rate.	33	Retrospective design. Small sample size.

terococcus faecalis are usually detected in cultures of gangrene. Antibiotic therapy included, in particular, the use of metronidazole, vancomycin, clindamycin, meropenem, tazocin, and linezolid. The median extent of resection was 3 in group 1 and 2 in group 2. There was a correlation between the extent of resection and use of HBOT combined with NPWT. The hospitalisation time was much shorter in group 2 (mean, 23 days) than in group 1 (mean, 26 days) (**Table 2**).

Table 2 compares the groups in terms of age (in years), length of hospital stay (in days), and extent of resection (on a scale of 1–5). The medians were presented separately in each group and were established using the Mann–Whitney *U* test to determine whether there were statistically significant differences between the groups. No significant differences were noted between the groups in terms of age and length of hospital stay. Patients in group 2 had a clearly higher median age than those in group 1. On the other hand, a significantly greater range of resections occurred in group 1 than in group 2.

DISCUSSION

FG was first characterised as a rapidly progressing idiopathic infection, including necrotising infection of the external genitals and perineum in both sexes.[6] Despite aggressive wide-spectrum antibiotic treatment, aggressive surgical debridement, intensive care, and anaesthesia, the mortality rates are reported to be as high as 43% in some series. In addition, diabetes plays a key role, as approximately 60% of patients with FG have diabetes.[6]

The treatment process for FG should be initiated as early as possible. The gold standard for decreasing mortality is early and aggressive debridement and the use of wide-spectrum antibiotics.[7] In this study, we applied the interdisciplinary treatment of FG consisting of a combination of surgical and urological interventions, antibiotic therapy, NPWT, HBOT, and plastic reconstructive procedures.

Li et al. showed the beneficial influence of HBOT on the survival rate in patients with FG in a shock status. The authors indicated the key role of adjuvant HBOT in promoting the bactericidal effect. HBOT improves tissue perfusion and promotes angiogenesis and fibroblast proliferation In addition, it causes an increase in collagen synthesis and oxygen levels in tissues (**Table 3**).

The results of the study by Li et al. showed that patients who received HBOT had a significant improvement in survival (100%) compared with those who did not receive HBOT(66.7%).[8] In our study, there were no fatalities in group 1 (HBOT therapy + NPWT), but four deaths were noted in group 2 (18%)

In a study by Tutino et al., mortality was not associated with the adjunction of HBOT to surgical debridement plus antibiotic therapy. It is claimed that the only factor that adversely affects prognosis is a delay between admission and surgical debridement.[9]

Assenza et al. analysed six male cases of FG and concluded that NPWT is a time-saving method. They confirmed the high efficiency of NPWT, including a decrease in hospitalisation time, number of medications, and improvement of quality of life.[10]

Similarly, Cuccia et al. assessed the results of NPWT within postoperative wound therapy in six cases with a very extensive FG (mean FGSI, 10.5). NPWT was evaluated as an effective treatment strategy for wound cleaning. This therapy contributed to decreasing hospitalisation time.[11]

Another study showed similar results in the hospitalisation time and reconstruction rate between NPWT and standard wound therapy of FG. However, the most important role of NPWT is to decrease the re-debridement rates and dressing frequency.[12]

In this study, the median extent of resection was 3 in group 1 and 2 in group 2. There was a correlation be-

tween the extent of resection and use of HBOT combined with NPWT. The study limitations were a low availability of HBOT and a hospitalization time.

CONCLUSIONS

HBOT and NPWT (group 1) showed advanced wound healing with a high efficiency rate. Specialists should consider implementing these treatment strategies in their practices to manage difficult wounds as either separate or combined strategies. The longer median hospitalisation time in this group may be related to the severity of injury.

CONFLICT OF INTEREST

There is no conflict of interest.

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