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Original Research

Microbiological aspects of Fournier's gangrene

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HIGHLIGHTS

- Treatment of Fournier's gangrene (FG) starts with empirical antibiotic therapy. However, empirical therapy in FG has not been updated in recent years.
- All institutes should evaluate their own culture results and then choose the best empirical antimicrobial therapy regimen.
- Future large studies are necessary to find out the most accurate empirical antibiotherapy for FG.

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ABSTRACT

Background: Fournier's gangrene (FG) is a devastating disease that is characterized by necrotizing fasciitis of the perineal, genital, or perianal region. Broad-spectrum antibiotics are the key component of its treatment. However, there is paucity of data regarding the optimal empirical antibiotherapy for FG.
Materials and methods: Data from patients who underwent surgery for FG between January 2007 and December 2012 were retrieved from a prospectively collected departmental FG database. Demographics, clinical characteristics, causative pathogens and drug susceptibility/resistance were evaluated.
Results: Fifty patients with a median age of 58.5 (22–83) years were included. The perianal origin (58%) was most commonly affected. A positive growth was found in specimen cultures of 48 (96%) patients. The median number of bacterial strains that grew in the cultures was 3 (0–10). Amikacin was the antibiotic with the highest frequency of sensitivity (74%), while the highest resistance was observed against ampicillin-sulbactam (64%). *Escherichia coli* was the most common microorganism (72%). *Acinetobacter baumannii* and *Klebsiella pneumonia* were significantly more common in patients who required mechanical ventilation. The mortality rate was 26%. An Uludag Fournier's Gangrene Severity Index (UFGSI) score of >9.5 and ventilatory support requirement were factors associated with an increased rate of mortality. *Acinetobacter baumannii* was the only microorganism which was associated with an increased mortality rate.
Conclusion: Causative pathogens in FG appeared to be shifting; thus, empirical antibiotic treatment for this disease should be modified. We recommend 3rd-generation cephalosporin, metronidazole and amikacin for empirical therapy.

1. Introduction

Fournier's gangrene (FG) is a disease that is characterized by necrotizing fasciitis due to synergistic polymicrobial infection of the perineal, genital or perianal region [1,2]. The highly virulent, usually polymicrobial infection causes disease leading to rapid and widespread tissue injury [3]. Treatment of FG includes fluid resuscitation, regulation of electrolyte balance, aggressive debridement of necrotic tissues, and parenteral broad-spectrum antibiotic therapy [4,5]. The accepted and recommended empirical antibiotic therapy consists of gentamicin, clindamycin and ampicillin-sulbactam/3rd-generation cephalosporin [6]. However, some studies have recommended metronidazole instead of clindamycin, and other aminoglycosides as well as fluoroquinolone-group antibiotics instead of gentamicin (which is also an aminoglycoside) [6,7].

Studies examining the pathogens associated with FG and their susceptibility/resistance to antibiotics have been scarce despite ongoing changes in human bacterial flora due to increasing and inappropriate use of antibiotics, particularly in recent years, and effects of environmental factors.

The present study aimed to identify pathogens whose growth was associated with FG and their antibiotic susceptibility/resistance

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based on bacterial culture; in additional, this study investigated the relationship between causative pathogens and prognostic factors and mortality.

2. Materials and methods

Prospectively collected data on patients who were treated in our department for FG between January 2007 and December 2012 were retrospectively evaluated. Patients with a solitary abscess of the perineal-perianal region were not included in the study. Fluid resuscitation began in all these patients at the time of hospital admission, and empirical 3rd-generation cephalosporin, metronidazole and amikacin were administered. The patients then underwent radical debridement of devitalized necrotic tissues within the first 12 h. The patients were treated with VAC (vacuum assisted closure; Kinetic Concepts, Inc., San Antonio, TX) dressing, and they underwent re-exploration once every 48–72 h. The debridement was continued whenever necessary. Tissue cultures were obtained from the patients during each debridement. Appropriate antibiotic therapy was started based on tissue culture results. Patients with negative results for tissue culture and patients without clinical evidence of infection were discharged home after the defects had healed via gradual tertiary wound closure or skin grafts. Anaerobic cultures could not be carried out due to technical reasons. Colonizing or contaminating pathogens which were observed in the cultures were not considered to be among the pathogens associated with FG.

Demographic data on the cases, co-morbid diseases, time to symptom onset, etiology, ventilator requirement, UFSGI (Uludag Fournier's Gangrene Severity Index) score and mortality were evaluated, and their relationship with causative pathogens, as well as their impact on antibiotic susceptibility and resistance patterns, were investigated.

Statistical analysis was performed using The Statistical Package for Social Sciences (SPSS®) for Windows Ver.10.0 (SPSS, Chicago, IL, USA). Data were presented as mean (±standard error) or median (min-max) as necessary. Comparison of the means between the groups for the various variables was performed using the Pearson chi-square test or the Kolmogorov-Smirnov test, whereas comparison of the magnitude of values between the groups was performed using the Mann-Whitney *U* test. The level of statistical significance was $p < 0.05$.

3. Results

Of the 50 patients treated for FG in our clinic between January 2007 and December 2012, the median age was 58.5 (22–83) years, and 27 patients (54%) were female. Twenty-five (50%) patients were referred from an external center, whereas 15 (30%) patients were transferred to us while they were an in-patient of another hospital, and 10 (20%) patients were hospitalized after they were seen in our emergency room. Diabetes mellitus (DM) was the most common comorbidity (64%). The median time to onset of symptoms was 7 (2–15) days, and the median duration of hospital stay was 22 (4–65) days. The perianal origin (58%) was the most commonly affected region, followed by decubitus ulcers (12%) and Bartholin's abscesses (10%). Ventilator requirement was required in 15 (30%) patients. The median UFGSI score was 9.5 (3–15). The overall mortality rate was 26%.

A positive growth was found in the tissues of 48 (96%) patients, whereas no growth was observed in 2 (4%) patients. The median number of bacteria that grew in the cultures was 3 (0–10). The culture was monomicrobial in 20% of patients and polymicrobial in 76% (n = 38). *Escherichia coli* was the most commonly identified microorganism (72%), followed by *Enterococcus sp.* (62%) and *Acinetobacter baumannii* (30%) (Table 1).

Amikacin was the antibiotic which had the highest frequency of bacterial sensitivity (74%), followed by imipenem (58%), meropenem (56%) and vancomycin (52%). The highest bacterial resistance was observed against ampicillin-sulbactam (64%), followed by ciprofloxacin and levofloxacin (44%) and cefazolin (42%) (Table 2).

Mechanical ventilation support was required in 30% of patients, and the mortality rate was higher in patients who required ventilatory support ($p = 0.0001$). When microorganisms which were isolated from the patients with and without ventilator requirement were compared, Acinetobacter baumannii ($p = 0.0005$) and Klebsiella pneumonia ($p = 0.0240$) were significantly more commonly found in patients who required mechanical ventilation.

The mortality rate was 26% (13 patients). A UFGSI score of >9.5 ($p = 0.046$) and ventilatory support ($p = 0.0001$) were factors associated with an increased rate of mortality. When microorganisms between the patients with and without mortality were compared, Acinetobacter baumannii was the only microorganism which was associated with an increased mortality rate ($p = 0.0108$).

4. Discussion

The present study is the largest study aiming to identify the causative pathogens in FG and their associated patterns of antibiotic susceptibility/resistance. The prevalence of resistant pathogens increased with inappropriate treatment of FG, which was typically a polymicrobial infection related to environmental factors. A positive growth of *Klebsiella pneumonia* and *Acinetobacter baumannii* increased in patients who required mechanical ventilation for bacterial pneumonia. The mortality rate was influenced by a UFGSI score >9.5, ventilator requirement and positive growth of *Acinetobacter baumannii.*

Although anaerobic culture was not performed in the present study, the median number of microorganisms that grew in the cultures was 3 (0–10). The most common pathogens identified included *Escherichia coli, Bacteroides sp., Staphylococcus aureus, Proteus, Streptococcus, Pseudomonas and Enterococci* strains [8]. Although *Escherichia coli* and *Enterococci* were the most prevalent pathogens identified in the present study, a positive growth of *Acinetobacter* which has not been reported in the literature, as well

Table 1
Distribution of causative pathogens.

	n	%
Polymicrobial	38	76
Monomicrobial	10	20
None	2	4
Gram positive		
Enterococcus sp.	31	62
MRSE	5	10
Streptococcus anginosus	3	6
Staphylococcus aureus	2	4
Corynebacterium cytriatum	1	2
Gram negative		
Escherichia coli	36	72
Acinetobacter baumannii	15	30
Pseudomonas aeruginosa	9	18
Protesus mirabilis	7	14
Klebsiella pneumoniae	5	10
Morganella morganii	4	8
Citrobacter youngae	2	4
Burkholderia gladioli	2	4
Serratia fonticola	1	2
Candida albicans	6	12

sp; species, MRSE; Methicilin-resistant staphylococcus epidermidis.

Table 2
Antibiotics, sensitivity and resistance.

	Sensitivity (%)	Resistance (%)
Ampicillin	42	26
Ampicillin-Sulbactam	24	64
Piperacillin-tazobactam	40	14
Cefazolin	22	42
Cefepime	34	28
Imipenem	58	18
Meropenem	56	16
Ciprofloxacin	22	44
Levofloxacin	48	44
Moxifloxacin	26	18
Amikacin	74	16
Vancomycin	52	20
Gentamycin	20	40
Daptomycin	12	22
Teicoplanin	46	16
Colymicin	28	6

as a high rate of *Pseudomonas sp*., which has rarely been reported, and low rates of *Staphylococcus and Streptococci* are interesting findings of this study. In particular, the high number of patients who were referred from other medical centers to us might explain the high culture growth rates of *Acinetobacter, Pseudomonas and Klebsiella sp*., which are resistant and opportunistic pathogens. All these findings suggested that empirical treatment of hospitalized patients with FG should include antimicrobial therapy against these opportunistic pathogens.

The generally accepted and recommended empirical antibiotic therapy includes gentamicin, clindamycin and ampicillin-sulbactam/3rd-generation cephalosporin [6]. However, some studies have recommended metronidazole instead of clindamycin, as well as other aminoglycosides or fluoroquinolone-group antibiotics instead of gentamicin (which is also an aminoglycoside) [6,7]. In our clinical practice, ceftriaxone and a combination of metronidazole and amikacin are used for empirical therapy. Although this is the largest study to investigate antibiotic resistance/susceptibility in FG, the roles of clindamycin/penicillin derivatives in empirical antibiotic treatment should be explored in future studies with larger numbers of patients given the limited number of cases with streptococcal infection in the present study. Amikacin, which is used in our clinical practice to treat Gram-negative bacterial infections, should routinely be used due to the high susceptibility rates. A high rate of susceptibility to carbapenem antibiotics (imipenem, meropenem) is remarkable. The routine use of ampicillin-sulbactam [6] and fluoroquinolone [7] group antibiotics, which have been recommended for empirical antibiotic therapy, should be reviewed in larger studies given their high rates of bacterial resistance in our study.

The positive growth of *Acinetobacter baumannii* and *Klebsiella pneumonia* in patients with ventilator-associated pneumonia is consistent with the results of previously reported studies which used relevant methodology [9]. Our study revealed that empirical use of high-susceptibility carbapenem antibiotics (*Klebsiella pneumonia*) as well as high-susceptibility amikacin and colistin (*Acinetobacter baumannii*) was more appropriate in FG for patients who developed ventilator-associated pneumonia.

While the mortality rate has been reported to be 3–45% in the medical literature [1,2,10,11], the mortality was 26% in the present study. A UFGSI score >9.5 and ventilator requirement increased mortality. The increased rate of ventilator-associated mortality can be explained by development of ventilator-associated pneumonia, which was diagnosed by a significant growth of *Klebsiella pneumonia* and *Acinetobacter baumannii* [9,12]. In the present study, *Acinetobacter baumannii* was the only pathogen which was associated with an enhanced mortality rate in FG. Given the increased prevalence of *Acinetobacter baumannii* in recent years, there may also be an increasing prevalence of *Acinetobacter baumannii* in FG. The high rate of *Acinetobacter* among the causative pathogens of FG in our study in patients with a history of hospitalization is particularly striking. Although no study has specifically examined the relationship between FG and *Acinetobacter baumannii*, the fact that a positive growth of *Acinetobacter baumannii* enhanced ventilator-associated mortality has also been reported in a meta-analysis by Siempos et al. [13] which showed the mortality rate in ventilator-associated pneumonia caused by *Acinetobacter baumannii* to range between 30% and 70% [9,12,13].

The prospectively collected data stored in our departmental FG database is the major strength of the present study. The major limitations are unavailability of anaerobic culture data for technical reasons and retrospective design of the study.

In conclusion, antibiotic therapy for treatment of FG should be modified based on culture and antibiogram results. It is important to make alterations in empirical therapy based on changes in bacterial flora and relationship between poor prognostic factors and mortality and causative pathogens in FG. Institutes should evaluate their own culture results and choose their best empirical antimicrobial therapy regimen. Based on the findings of this study, larger further studies are necessary to find out the most accurate empirical antibiotherapy for FG.

The authors declare that there is no conflict of interest regarding the publication of this paper.

Ethical approval

This study was approved by the Institutional Review Board of Uludag University School of Medicine.

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Author contribution

Tuncay Yilmazlar: design, data analysis, writing, critical review.
Baris Gulcu: data collection, data analysis, writing.
Ozgen Isik: data collection, data analysis, writing, critical review.
Ersin Ozturk: data collection, data analysis, writing, critical review.

Conflicts of interest

None.

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