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3차 의료기관의 최근 10년간 성인 부고환염의 원인균주의 항생제 저항성의 변화

박종진, 김종욱, 배재현, 문두건, 오미미

고려대학교 구로병원 비뇨기과

Changes of Bacterial Resistant Pattern in Adult Acute Epididymitis at a Tertiary Hospital in Recent Ten Years

Jong Jin Park, Jong Wook Kim, Jae Hyun Bae, Du Geon Moon, Mi Mi Oh

Department of Urology, Korea University Guro Hospital, Seoul, Korea

Purpose: We conducted a retrospective study to investigate causative bacteria of adult epididymitis and their characteristics and resistance in the recent 10 years at a tertiary hospital.
Materials and Methods: We reviewed the medical records of 121 patients who were diagnosed with acute epididymitis from 2002 to 2012. Diagnosis was based on symptoms, physical examination, and ultrasonography. We analyzed causative organisms and changes of antibiotic resistance pattern according to time course in the recent 10 years.
Results: The most commonly detected bacteria were *Pseudomonas aeruginosa* and *Escherichia coli*. Fluouroquinolone resistance has emerged since 2006 and 50% of the patients have resistance to fluouroquinolones.
Conclusions: Quinolone resistance composes a major proportion of the causative organism. Therefore, while according to the guidelines, fluoroquinolone may be the first response for elderly men, we recommend that antibiotic resistance should be considered if fever persists, and other antibiotics could be included.

Keywords: Epididymitis; Drug resistance, microbial

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Correspondence to: Mi Mi Oh
Department of Urology, Korea University Guro Hospital, 148, Gurodong-ro, Guro-gu, Seoul 152-703, Korea
Tel: +82-2-2626-1310, Fax: +82-2-2626-3203
E-mail: mamah77@paran.com

INTRODUCTION

Traditionally, acute epididymitis is known as result from the spread of infection from the bladder, urethra, or prostate into the epididymis. Although viral or fungal infection, tuberculosis, and urinary obstruction can cause epididymitis, the most common cause of acute epididymitis is bacterial infection.[1] In sexually active younger men, the most common causative organisms of epididymitis are the urethritis-causing bacteria such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. In elderly men, benign prostate hypertrophy (BPH) and associated urine stasis, urinary tract

Table 1. General characteristics of the patients

Variable	Value
Age (y)	46.1±5.6
Culture positive (n)	21 (17.3)
Hospitalization (d)	6.8±4.9
Intravenous treatment (d)	6.2±4.9
Fever (n)	30 (24.8)
Peak fever (°C)	38.2±0.8
WBC ($\times10^3$/μL, peak level)	11.6±5.7
ANC ($\times10^3$/μL, peak level)	9.0±5.8
ESR (mm/h, peak level)	33.2±28.2
CRP (mg/L, peak level)	67.4±46.9
Prostate total volume (g)	46.9±8.4
Prostate TZZ volume (g)	15.9±3.38
UA micro RBC (>5, n)	28 (23.1)
UA micro WBC (>5, n)	41 (33.9)

Values are presented as mean±standard deviation or number (%).
WBC: white blood cell, RBC: red blood cell, ANC: absolute neutrophil count, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, TZZ: transitional zone, UA: urine analysis.

infection (UTI), and catheterization are the most common causes of epididymitis. The most common causative microorganisms in the elderly are the coliform bacteria that cause bacteriuria.[2,3] Additionally, recent data has shown that antibiotic-resistant bacteria such as fluoroquinolone-resistant bacteria and extended-spectrum β-lactamase-producing (ESBL) *Escherichia coli* also appeared more frequently than previous.[4-6] However, there is insufficient recent research about recent causative bacteria of epididymitis.

In this study, we conducted a retrospective study to investigate pathogen, antibiotic resistances of acute epididymitis in recent 10 years at tertiary hospitals.

MATERIALS AND METHODS

From June 2002 to June 2012, we reviewed 121 adults hospitalized for acute epididymitis in our hospital. They had been examined and diagnosed with acute epididymitis based on abrupt scrotal pain and tenderness on physical examination and epididymal enlargement on scrotal ultrasonography regardless of fever.[7-9] Patients less than 18 years old and with chronic epididymitis, recurrent epididymitis and who had history of antibiotic treatment before hospitalization due to acute epididymitis, viral epididymitis were excluded from analysis.

We analysed causative organisms and changes of antibiotic resistance pattern according to time course in recent 10 years.

Table 2. Frequency of isolates causing acute epididymitis

Bacterial strains	n (%)
Pseudomonas aeruginosa	8 (38.1)
Escherichia coli	8 (38.1)
Klebsiella pneumonia	2 (9.5)
Neisseriae gonorrhoae	1 (4.8)
Enterococcus faecalis	1 (4.8)
Streptococcus agalactiae	1 (4.8)
Total	21

All values are expressed as the mean±standard deviation. IBM SPSS Statistics 19.0 (IBM Co., Armonk, NY, USA) was used to evaluate the data. For all tests, $p<0.05$ was considered to indicate statistical significance.

RESULTS

The mean age of the 121 patients was 46.1±5.6 years, and the mean hospitalization duration was 5.8±0.4 days. Twenty-one men (17.35%) were culture positive (Table 1).

When the component bacteria were categorized, the most common was *Pseudomonas aeruginosa* (8/21) and *E. coli* (8/21). *Klebsiella pneumonia* was detected in 2 samples (Table 2).

Quinolone resistant strain increased since 2006 composing near 50% of culture positive strains. The most susceptible antibiotic was meropenem (19/21) followed by piperacillin/tazobactam (18/21), imipenem (18/21), and amikacin (17/21). Near 50% of the patients with fluoroquinolone resistant epididimitis showed co-resistance to ampicillin, amoxicillin/clavulanic acid, cefotaxime, gentamycin and trimethoprim/sulfamethoxazole. ESBL positive strain first emerged in 2012 (Table 3).

When we try to compare the antibiotic resistance on a separate group every two years, quinolone resitant strain was increased to 2006-2007 year group, but it tended to decrease again in recent years. And 1 ESBL positive strain incubated at 2010-2012 (Fig. 1).

DISCUSSION

Recent data has shown that antibiotic-resistant bacteria such as fluoroquinolone-resistant bacteria and ESBL *E. coli* also appeared more frequently than previous as the cause of UTI.[4-6] Therefore, the causative organism of acute epididymitis and changes of bacterial resistance to

Table 3. Antibiotics susceptibility of cultured organisms

	Total (n=21)			Fluoroquinolone resistance (n=10)			ESBL positive
	Susceptible	Resistant	Indeterminate	Susceptible	Resistant	Indeterminate	Susceptibility
Ampicillin	6	14	1	2	7	1	R
Amoxicillin/clavulanic acid	15	6	0	4	6	0	R
Amikacin	17	3	1	6	3	1	S
Cefotaxime	12	9	0	4	6	0	R
Ceftazidime	15	2	4	4	2	4	R
Cefepime	15	5	1	4	5	1	R
Cefoxitin	16	5	0	5	5	0	R
Imipenem	18	2	1	7	2	1	S
Meropenem	19	2	0	8	2	0	S
Gentamicin	12	9	0	4	6	0	R
Piperacillin/tazobactam	18	3	0	7	3	0	R
Trimetho/sulfamethoxazole	10	11	0	5	5	0	S
Ciprofloxacin	10	10	1	0	10	0	R
ESBL positive		1			1		

ESBL: extended-spectrum β-lactamase-producing.

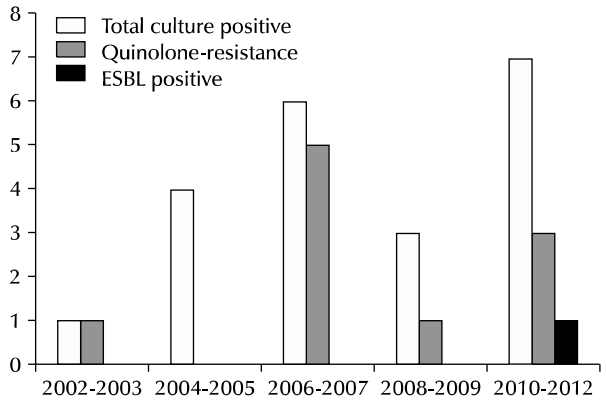

Fig. 1. Comparison of bacteria and laboratory data by 2 years. ESBL: extended-spectrum β-lactamase-producing.

antibiotics should be identified.

Acute epididymitis has been known to result from the spread of UTI or sexually transmitted disease (STD). The most common cause is bacteria, but viruses, fungi, and BPH can cause acute epididymitis. *P. aeruginosa* and *E. coli* were the most common organism causing acute epididymitis in our study. Holmes et al.[2] reported that *E. coli* and *C. trachomatis* were the most commonly detected bacteria in acute epididymitis. As the patients in our study were older than that of previous studies, the epididymitis from UTI was less likely to stem from an STD.

The traditional treatment approach suggests tetracycline or erythromycin with fluoroquinolone or azalide.[10] Recent empirical antibiotic treatment consists of ceftriaxone plus doxycycline for sexually transmitted pathogens, or fluoroquinolone for enteric organisms.[11,12] Our study showed high rate of quinolone resistance (10/17) and also quinolone resistant culture showed co-resistance to to ampicillin, amoxicillin/clavulanic acid, cefotaxime, gentamycin and trimethoprim/sulfamethoxazole. It is well known that quinolone resistance consist major proportion of antibiotic resistance in UTI in South Korea. Owing to these advantages, empirical treatment with fluoroquinolones has been a standard treatment for UTI in Korea.[13] Concurrently and perhaps consequently, UTIs due to fluoroquinolone-resistant bacterial strains have continued to increase at an alarming rate in Korea.[14,15] A study of antimicrobial resistance in community acquired UTI using Korean antimicrobial monitoring system reported 24.6% of quinolone resistance which is higher than the resistance rate of the United States of America.[15] Even higher rate of quinolone resistance are noted in acute epididymitis. Study by Lee[14] demonstrated near 50% resistance rate to levofloxacin, ciprofloxacin and norfloxacin. His report suggests that ciprofloxacin is no longer a recommended therapy for *Enterococcus faecalis* from complicated UTI. The author emphasized that quinolone resistance is higher than we expected. Our result showed similar results. 10 of 21 bacteria detected (47.6%) were fluoroquinolone-resistant, and were resistant to other antibiotics as well.

Additionally 1 ESBL positive strain incubated in the 2010-2012 year group. This result may indicate the era of newer and more advanced antibiotic resistance causing acute epididymitis came nearby. ESBL positive strain is a more challenging problem than quinolone resistance.

ESBLs are plasmid-encoded β-lactamases that confer significant resistance to a wide range of β-lactam antibiotics, including all extended-spectrum cephalosporins, except carbapenem and cephamycin. Furthermore, ESBL-encoding plasmids frequently carry resistance genes for additional antibiotic classes, such as quinolones, aminoglycosides, and trimethoprim/sulfamethoxazole.[6] Carbapenem is considered the treatment of choice for invasive infections caused by ESBL-producing bacteria.[6] Because of the emergence of carbapenem resistance among the Gram-negative bacteria worldwide, the increasing rate of multidrug resistant infection has caused the dilemma whether to use meropenem as the first line therapy or not. To overcome this dilemma, the empirical treatment of carbapenem can be suggested only for the patients who present with severe sepsis or septic shock due to UTI or intra-abdominal infections.[16] Besides meropenem, amikacin can be an alternative option for empirical therapy when ESBL production is a concern is still low.[17-19] However, the efficacy of amikacin against ESBL producers has not yet been evaluated much and this needs further evaluation.[16]

In previous studies of the causative bacteria of acute epididymitis, a quarter of epididymitis patients had positive urine bacterial cultures.[20] But in our study, 21 patients (17.4%) had positive urine bacterial cultures. Our study was a retrospective data review and compared a small sample size. For this reasons, our results appear lower than that of previous studies.

Prospective randomized clinical trials with a larger number of cases are required to classify the bacteria cultured and the characteristics of epididymitis. Despite these limitations, our study is important in that we identified antibiotic resistance pattern in recent 10 years and emphasized the importance of quinolone resistance in acute epididymitis patient as well.

CONCLUSIONS

Therefore, while according to the guidelines, fluoroquinolone may be the first response for elderly men, we recommend that antibiotic resistance should be considered if fever persists, and other antibiotics could be included.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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