Effects of an Initial Single Dose of Intravenous Antibiotics on Emergency Department Revisits Among Elderly Patients with Urinary Tract Infections

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ABSTRACT

Purpose: Urinary tract infection (UTI) is the second most common infectious disease among older adults. It is important that the treatment strategy used for older patients with UTIs in the emergency department (ED) be adequate. The effectiveness of an initial single dose of intravenous antibiotics in the ED for treating UTIs has not been extensively studied. Therefore, we investigated the clinical outcomes of single-dose intravenous antibiotic administration before discharge from the ED in elderly patients with UTIs.

Materials and Methods: This retrospective study was conducted among patients who visited two academic tertiary hospitals in Seoul, South Korea. We included all patients older than 65 years of age with UTI who visited the ED and were directly discharged between 1 January and 31 December 2019 (n = 429). The patients were divided into two groups according to whether they received a single dose of intravenous antibiotics before ED discharge.

Results: Patients who received intravenous antibiotics had a higher 72-hour revisit rate (43 [15.4%] vs 10 [6.7%], $p = .009$) and a longer mean duration of therapy (total days of antibiotics use) (11 [4.00 – 15.00] vs 5 [3.00 – 11.00], $p < .001$) than patients who received only oral antibiotics. However, the rate of admission after revisits did not differ significantly between the groups (27 [62.8%] vs 5 [50.0%], $p = .492$).

Conclusion: Older patients with severe UTIs were prescribed intravenous antibiotics in the ED. Decisions on admission or discharge should be made carefully for older patients with UTIs who are prescribed intravenous antibiotics in the ED.

Keywords: administration, intravenous; older adults; anti-bacterial agents; emergency department; infusions, intravenous; infusions, parenteral; urinary tract infection

INTRODUCTION

Urinary tract infection (UTI) is the second most common infection among older patients, and UTIs account for approximately 5% of all emergency department (ED) visits in the United States each year [(1)]. The clinical presentation of UTI varies from asymptomatic bacteriuria to severe sepsis. UTIs in older patients who are asymptomatic or who present with mild symptoms can easily be managed with antibiotics, but these infections can develop into severe sepsis if treatment is delayed [(2)]. Therefore, a sufficient understanding of the spectrum of UTIs and the choice of appropriate treatment plans are crucial, especially for older patients with UTIs.

Antibiotics should be used promptly when patients in the ED are diagnosed or suspected of having UTIs. According to the severity of the infection, patients are admitted or discharged by emergency physicians. Patients identified with severe conditions usually undergo empiric broad-spectrum intravenous antibiotic therapy. In the case of patients who are to be discharged from the ED, oral antibiotics may be prescribed after the administration of intravenous antibiotics in the ED. Conversely, oral antibiotics may be prescribed without the administration of intravenous antibiotics. According to the 2018 Korean guidelines for UTI, for patients with acute pyelonephritis not requiring hospitalization, a single dose of intravenous antibiotics should be administered, followed by oral antibiotics, until culture results are obtained [(3)]. Although the recommendation grade is strong, this recommendation is based on expert opinion with limited evidence [(4)]. The effectiveness of an initial single dose of intravenous antibiotics for patients with UTIs in the ED has been studied, and the results are varied. In one study of adult patients with UTIs, intravenous antibiotic use was associated with a decrease in ED revisits [(5)]. However, in a study of children with UTIs, intravenous antibiotic use in the ED had no benefit on clinical outcomes [(6)]. No study has assessed the effects of intravenous antibiotic use for older patients with UTIs. Therefore, we investigated the clinical outcomes of older patients with UTIs in the ED according to the use of single-dose intravenous antibiotic

administration before ED discharge.

MATERIALS AND METHODS

Study design and population

This retrospective study was conducted among patients who visited two academic tertiary hospitals in Seoul, South Korea. Electronic Registry data were collected from the National Emergency Department Information System (NEDIS), managed by the National Emergency Medical Center. NEDIS is a prospective database of the demographic and baseline clinical characteristics of patients from all emergency healthcare facilities in the Republic of Korea. The sample size for was measured by using the G*Power program. Considering power of 0.80, alpha level of 0.05 and confidence interval 95%, we found the required sample size was 342. The total number of patients who presented to the two study EDs between 1 January and 31 December 2019 was 94,803 (**Figure 1**). Patients who visited the ED for trauma and non-medical reasons and those under 65 years old were excluded. Codes from the International Classification of Diseases 10th revision (ICD-10) for UTI, cystitis (ICD-10 N30, N39.0), and pyelonephritis (N10, N15.1, N16) were used to identify UTI diagnoses. Patients diagnosed with UTIs and directly discharged from the ED were included. Individuals who had been admitted to the ward, were transferred to other hospitals, were discharged against medical advice, had previous visits for UTI in the previous 30 days, or had received multiple doses of intravenous antibiotics were excluded. After exclusions, 429 patients were enrolled in this study. The enrolled patients were divided into two groups: the single intravenous antibiotics group (those who received a single dose of intravenous antibiotics in the ED and were directly discharged with oral antibiotic prescriptions) and the only oral antibiotics group (those who were prescribed only oral antibiotics without intravenous antibiotics). The single intravenous antibiotics group had 279

(65%) patients, whereas the only oral antibiotics group had 150 (34.9%) patients. This study was approved by the relevant institutional review board (IRB No. 2022-05-005). Due to the study's retrospective design and the use of anonymized patient data, the requirement for informed consent was waived.

Baseline characteristics

Study variables included patient demographics (such as age and sex), initial vital signs (pulse rate, respiratory rate, and body temperature), systolic blood pressure, diastolic blood pressure, mental status, quick Sequential (Sepsis-related) Organ Failure Assessment (qSOFA) score, and Korean Triage and Acuity Scale (KTAS) level. The Korean Triage and Acuity Scale (KTAS) was developed as a triage tool and comprises five acuity levels: level 1 (resuscitation), level 2 (emergency), level 3 (urgent), level 4 (less urgent), and level 5 (non-urgent), in which lower numbers indicate a higher level of urgency. Data on cultured strains, antibiotic types, and antibiotic susceptibility profiles were also included.

Clinical outcomes

The primary outcome was the 72-hour ED revisit rate, and the secondary outcome was admission following a 72-hour ED revisit and duration of therapy. The duration of therapy was defined as the total duration of antibiotic use. Additionally, symptoms related to the reasons for revisits were recorded.

Statistical analysis

Categorical variables are expressed as counts and percentages, and continuous variables are expressed as mean ± standard deviation. For continuous variables, the independent t-test was used for normally distributed data, and the Mann–Whitney U test was used for skewed data. The Pearson chi-square test or the Fisher exact test was used for nominal variables; in particular, the Fisher exact test was applied when more than 20% of cells had expected frequencies less

than 5. Continuous variables are expressed as the mean ± standard deviation or median (interquartile range), and categorical variables are expressed as counts and percentages. Logistic regression was used to investigate the clinical factors associated with revisits. Differences with $p < .05$ were considered statistically significant. All statistical analyses were performed using SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Baseline characteristics

There was no statistical difference between the two groups regarding age or sex (**Table 1**). The single intravenous antibiotics group had a significantly lower mean systolic blood pressure at ED admission. The mean respiratory rate and body temperature at ED admission were significantly higher in the single intravenous antibiotics group. The single intravenous antibiotics group had a significantly larger proportion of patients categorized as KTAS levels 2 (emergency) and 3 (urgent) and a lower proportion categorized as level 4 (less urgent).

Clinical outcomes

The proportion of 72-hour revisits was significantly higher in the single intravenous antibiotics group (**Table 2**). However, there was no significant intergroup difference in the rate of admissions after revisits. The duration of therapy was significantly longer in the intravenous antibiotics group.

In the univariate analysis, only single intravenous antibiotics were associated with revisits (**Table 3**).

Fever, urinary symptoms, dyspnoea, and poor oral intake were the symptoms associated with reasons for revisits most commonly identified in the single intravenous antibiotics group (**Table**

4). In the only oral antibiotics group, the reasons for revisits were fever, urinary symptoms, general weakness, and poor oral intake. There was no statistical differences were observed regarding reasons of revisit symptoms.

Urinary tract infection pathogens

The most frequently identified bacterium in both groups was *Escherichia coli*, followed by *Enterococcus* species, *Klebsiella pneumoniae*, and *Proteus mirabilis*. In 45 cases, urine culture yielded no bacterial growth. In 25 cases, no culture test was performed, and in six cases, the samples were contaminated (**Table 5**). In the single intravenous antibiotics group, the most commonly identified pathogen was *Escherichia coli*, followed by *Enterococcus species*, *Klebsiella pneumoniae*, and *Proteus mirabilis*. There was no growth in 23 cultures in the single intravenous antibiotics group, whereas culture was not performed in nine cases, and three samples were contaminated in this group. In the only oral antibiotics group, the most identified pathogen was *Escherichia coli*, followed by *Streptococcus* species, *Staphylococcus* species, and *Citrobacter freundii*. There was no growth in 22 cultures, cultures were not performed in 16 cases, and three samples were contaminated in this group.

Antibiotic types and susceptibility

Third-generation cephalosporins were the most prescribed antibiotic category in both groups, followed by fluoroquinolones (**Table 6**). The total sensitivity was 60.7% in the single intravenous antibiotics group and 74.3% in the only oral antibiotics group. Specifically for third-generation cephalosporins, the sensitivity rates were 63.6% and 76.9% in the single intravenous antibiotics and only oral antibiotics groups, respectively. For fluoroquinolones, the sensitivity rates were 57.1% in the single intravenous antibiotics group and 65.5% in the only oral antibiotics group.

DISCUSSION

In the present study, older patients with UTIs treated with single intravenous antibiotics before ED discharge had a higher 72-hour ED revisit rate and longer duration of antibiotic treatment. Moreover, single-dose intravenous antibiotic administration before ED discharge was the only clinical factor associated with revisits (**Table 3**). However, there were no differences between the groups in admission rates following ED revisits (**Table 2**) or reasons for revisits (**Table 4**). Although the groups were not compared in terms of disease severity, the single intravenous antibiotics group had a lower mean systolic blood pressure, higher mean respiratory rate, higher mean body temperature, and lower mean KTAS level (which indicated more urgency) at the time of ED presentation (**Table 1**). Although ED physicians tend to prescribe intravenous antibiotics for patients with more severe disease, it is difficult to determine whether this tendency affected the final treatment plan.

Generally, ED physicians use intravenous antibiotics assuming that quickly raising the blood concentration of antibiotics will benefit patients' clinical outcomes. In a previous investigation of UTIs in patients aged 29 days to 2 years, patients who received parenteral antibiotics before discharge from the ED had a higher rate of 72-hour revisits [(6)]. In contrast, in adult patients with UTIs aged over 18 years, intravenous antibiotic use before ED discharge has been associated with fewer ED revisits within 72 hours of discharge [(5)]. These conflicting study results make it difficult to determine the administration of intravenous antibiotics in the ED.

In this study, the patients in the intravenous antibiotics group were older and had a higher heart rate and lower systolic and diastolic blood pressure than those in the only oral antibiotics group. Therefore, the group that received intravenous antibiotics had signs of worse disease severity at initial ED presentation, which aligns with our results. Thus, ED physicians could have prescribed intravenous antibiotics to patients with relatively severe UTIs.

UTIs are among the commonest diagnoses in patients with ED revisits [7]. Moreover, patients aged over 65 years have been shown to make significantly more return visits to the ED [8]. Therefore, quick diagnoses and appropriate antibiotic management are important for older patients with UTIs visiting the ED. A high proportion of older patients show asymptomatic bacteriuria and are less likely to show typical clinical features of UTI, making diagnosis difficult [9]. The diagnostic challenges could result in delayed treatment for UTIs, leading to ED revisits. Additionally, prescribing resistant antibiotics is known to increase ED revisit rates [8]. However, in the ED setting, since it takes time to obtain culture results, antibiotics are administered without considering microbiological information, despite the prevalence of increasing antibiotic resistance. To the best of our knowledge, no published study has investigated the effects of intravenous antibiotics on older patients with UTIs in the ED.

The most common pathogen causing UTI in this study was *Escherichia coli* (58.5%, **Table 5**), followed by *Enterococcus* species, *Klebsiella pneumoniae,* and *Proteus mirabilis*, which are similar results to those of a previous study [10]. According to a report on the antibiotic susceptibility of *Escherichia coli* in community-acquired UTIs from 2008 to 2017 in Korea, the susceptibility to ciprofloxacin decreased from 79.5% (2008) to 58.6% (2017), whereas that to cefotaxime decreased from 95.5% (2008) to 68.0% (2017) [11]. Although susceptibility was not assessed for the same condition, the results were similar in the previous study. In our study, the susceptibilities to fluoroquinolone in the intravenous and oral-only groups were 57.1% and 65.5%, respectively. For third-generation cephalosporins, the susceptibility was 63.6% in the intravenous antibiotics group and 76.9% in the without intravenous antibiotics group (**Table 6**). These high rates of antibiotic resistance imply the necessity of further evaluation of domestic antibiotic resistance.

Due to increasing antibiotic resistance, an update of the domestic guidelines that includes predicting antibiotic-resistant organisms and selecting the types, optimal doses, routes, and

durations of antibiotic regimens based on a local antibiogram is necessary. In this study, the revisit rate and total treatment duration were higher in the single intravenous antibiotics group, but there was no significant intergroup difference in admission rates. Our findings suggest that, in the case of older patients with UTIs in the ED prescribed intravenous injections, decisions between admission or discharge should be made more carefully and that the worsening of symptoms should be explained in more detail to patients discharged from the ED.

This study had several limitations. First, the study was conducted in two academic tertiary hospitals in the capital of South Korea; therefore, this study may not have represented the health behaviour of the entire older population in the country. Second, due to the study's retrospective nature, there may have been a selection bias while selecting the two groups. Third, the enrolled patients were not classified by severity, and the effect of single-dose intravenous antibiotics before ED discharge could not be compared in patients with the same severity. Finally, as UTI treatment was started before the culture result was obtained in the ED setting, this study included every older patient diagnosed with or was clinically suspected of having UTI regardless of the culture result. Moreover, patients with inappropriate urine culture results (not performed, contaminated sample, no growth of microorganisms) were included. Thus, patients without UTIs could have been included, which may have affected the results.

CONCLUSIONS

Older patients with UTIs who received initial single intravenous antibiotics before ED discharge had more revisits to the ED and longer durations of antibiotic treatment than patients who received only oral antibiotics. Older patients with UTIs with relatively severe symptoms were prescribed intravenous antibiotics in the ED. Decisions on admission or discharge should be made more carefully in older patients with UTIs prescribed intravenous antibiotics in the

ED.

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CONFLICT OF INTEREST

No conflict of interest to declare.

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Figure Legends

Figure 1. Inclusion and exclusion flow diagram

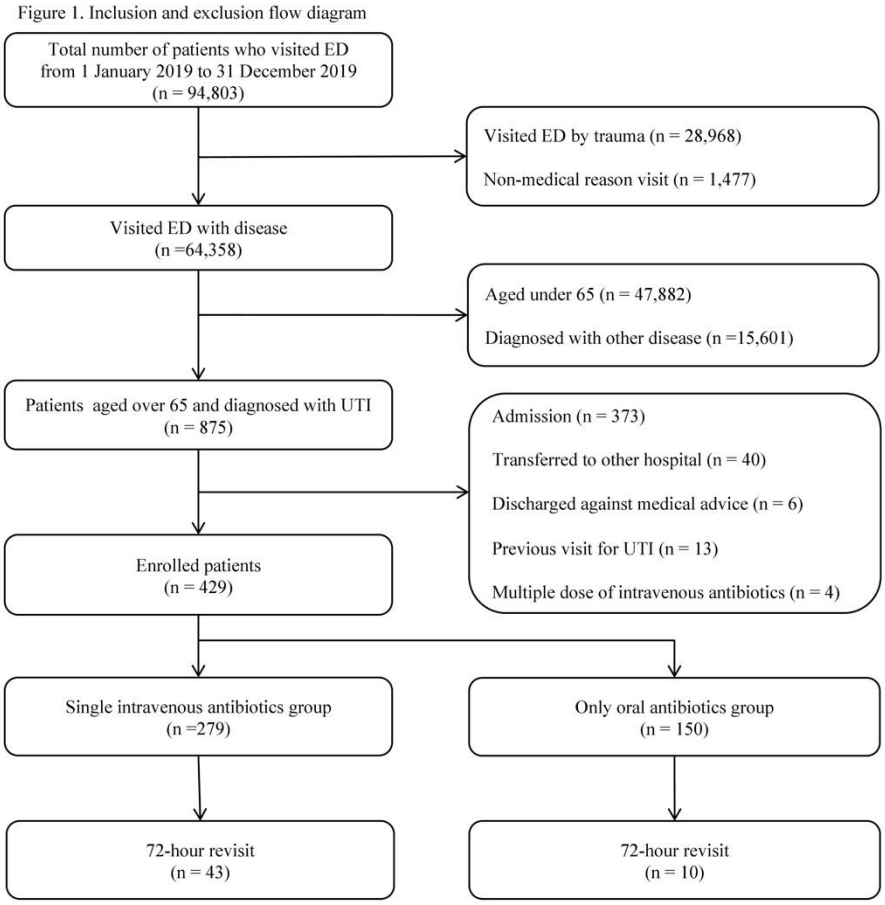

Table 1. Baseline characteristics of enrolled patients

Variables	Single-dose Intravenous Antibiotics (n = 279)	Only Oral Antibiotics (n = 150)	*p*-value
Age (y) [a]	78.27 ± 7.66	77.62 ± 8.16	.420
Sex[b]			.679
Male	73 (26.1)	36 (24.0)	
Female	206	114	
Vital signs[a]			
Systolic blood pressure (mmHg)	135.44 ± 24.51	142.85 ± 25.70	.004
Diastolic blood pressure (mmHg)	72.91 ± 15.74	75.98 ± 16.74	.061
Pulse rate (beats/min)	92.42 ± 16.11	90.38 ± 18.83	.262
Respiratory rate (breath/min)	20.05 ± 1.42	19.68 ± 0.96	.001
Body temperature (°C)	37.56 ± 1.10	36.87 ± 0.81	<.001
Mental status[b]			.315
Alert	269 (96.4)	148 (98.6)	
Verbal response	7 (2.5)	2 (1.3)	
Painful response	3 (1.0)	0	
Unresponsive	0	0	
qSOFA ≥2[b]	4 (1.4)	1 (0.6)	.480
KTAS Triage category[b]			<.001
Level 1 Resuscitation	0	0	
Level 2 Emergent	13 (4.6)	3 (2.0)	
Level 3 Urgent	186 (66.7)	82 (54.6)	
Level 4 Less urgent	69 (24.7)	63 (42.0)	
Level 5 Non urgent	11 (3.9)	2 (1.3)	

[a]Values are given as mean ± standard deviation

[b]Values are given as number (%)

Abbreviations: KTAS, Korean Triage and Acuity Scale; LOS, length of stay; qSOFA, quick Sequential (Sepsis-related) Organ Failure Assessment

Table 2. Clinical outcomes of urinary tract infections among older individuals

Variable	Single Intravenous Antibiotics (n = 279)	Only Oral Antibiotics (n = 150)	*p*-value
72-hour ED revisits[a]	43 (15.4)	10 (6.7)	.009
Admissions after 72-hour ED revisit[a]	27 (62.8)	5 (50.0)	.492
Duration of therapy (days)[b]	11 (4.00 – 15.00)	5 (3.00 -11.00)	<.001

[a]Values are given as number (%)

[b]Values are given median (IQR)

Abbreviation: ED, emergency department

Table 3. Logistic regression analysis of revisit predictors

Variable	Univariate analysis			Multivariate analysis		
	Non-72-hour ED Revisit	72-hour ED Revisit				
	n = 376	**n = 53**	*p*-value	**OR**	**B**	***p*-value**
Age (y)[a]	77.84 ± 7.87	79.49 ± 7.31	.149			
Sex; Male[b]	90 (23.9)	19 (35.8)	.062			
Systolic blood pressure (mmHg)[a]	137.89 ± 25.73	134.83 ± 29.08	.426			
Diastolic blood pressure (mmHg)[a]	74.10 ± 16.23	71.17 ± 18.73	.229			
Pulse rate (beats/min)[a]	91.29 ± 17.21	92.72 ± 20.65	.582			
Respiratory rate (breaths/min)[a]	19.88 ± 1.26	19.75 ± 3.28	.779			
Body temperature (°C)[a]	37.28 ± 1.04	36.85 ± 5.42	.566			
Altered mental status[b]	12 (3.2)	0	.187			
qSOFA ≥2[b]	5 (1.3)	0	.398			
KTAS category ≤3[b]	244 (64.9)	39 (73.6)	.211			
Single intravenous antibiotics[b]	236 (62.8)	43 (81.1)	.009	2.551 (1.243 – 5.236)	0.936	.011

[a]Values are given as mean ± standard deviation

[b]Values are given as number (%)

Table 4. Reasons for revisits

Variable	Single Intravenous Antibiotics (n = 43)	Only Oral Antibiotics (n = 10)	*p*-value
Reason of revisit symptoms			.146
Fever	21 (48.8)	4 (40.0)	
Dyspnoea	7 (16.3)	0	
General weakness	0	1 (10.0)	
Urinary symptoms	8 (18.6)	4 (40.0)	
Poor oral intake	5 (11.6)	1 (10.0)	
Flank pain	2 (4.7)	0	

Values are given as number (%)

Table 5. Common pathogens associated with urinary tract infections

Rank	Name	Total n (%)	Single Intravenous Antibiotics (n = 279)	Only Oral Antibiotics (n =150)
1st	*Escherichia coli*	251 (58.5)	178 (63.8)	73 (48.7)
2nd	*Enterococcus species*	20 (4.6)	17 (6.1)	3 (2.0)
3rd	*Klebsiella pneumoniae*	17 (3.9)	15 (5.4)	2 (1.3)
4th	*Proteus mirabilis*	15 (3.5)	12 (4.3)	3 (2.0)
5th	*Citrobacter freundii*	14 (3.3)	8 (2.8)	6 (4.0)
6th	*Streptococcus species*	13 (3.0)	5 (1.8)	8 (5.3)
7th	*Staphylococcus species*	13 (3.0)	5 (1.8)	8 (5.3)
8th	*Pseudomonas aeruginosa*	10 (2.4)	4 (1.4)	6 (4.0)
	No growth	45 (10.5)	23 (8.2)	22 (14.7)
	Culture not performed	25 (5.8)	9 (3.2)	16 (10.6)
	Contamination	6 (1.4)	3 (1.1)	3 (2.0)

Values are given as number (%)

Table 6. Antibiotic types and susceptibility

Antibiotics used	Single Intravenous Antibiotics (n = 279)	Sensitivity (%)	Only Oral Antibiotics (n =150)	Sensitivity (%)
Total antibiotics used	244	60.7	109	74.3
Third-generation Cephalosporin	140 (57.3)	63.6	78 (52)	76.9
Fluoroquinolone	84 (34.4)	57.1	29 (19.3)	65.5
Carbapenem	17 (6.0)	64.7	0	-
Fosfomycin	0	-	2 (1.3)	100
Piperacillin/Tazobactam	3 (1.0)	0	0	-
Excluded data				
No growth	23 (8.2)	-	22 (14.6)	-
Culture not performed	9 (3.2)	-	16 (10.6)	-
Contamination	3 (1.0)	-	3 (2.0)	-

Values are given as number (%)