# EFFICACY OF INTRAVESICAL INSTILLATION OF NETILMICIN ON MANAGING UTI

# <sup>1</sup>Praba, Barry Arief; <sup>2</sup>Utomo, Trisula.

Department of Urology, Faculty of Medicine/Indonesia University, Cipto Mangunkusumo General Hospital, Jakarta. Division of Urology/Department of Surgery, Faculty of Medicine/Gadjah Mada University, Sardjito General Hospital, Yogyakarta.

# **ABSTRACT**

Objectives: To evaluate the efficacy of instilled netilmicin in indwelling-urinary-catheter-associated nosocomial urinary tract infection (UTI) patients. Material & method: In a prospective clinical trial performed in the Urologic Ward of Sardjito General Hospital, Yogyakarta, Indonesia, we studied 56 patients who had indwelling urethral catheters for more than 4 days. Patients were divided into two groups. In group 1 (28 patients) one-time intravesical instillation of netilmicin 25 mg was administered, and in group 2 (28 patients) none were given any treatment. Urinalysis was evaluated before and after instillation of netilmicin. Statistical data and results were studied using descriptive statistics as median (minimum and maximum). To compare the response to treatment, Chi-Square test was used in two groups. Consequently, the data were analyzed using the SPSS 17 software. Results: Urinalysis were evaluated in two groups 4 days after intravesical instillation of 50 mg netilmicin. The patients we studied, the median age 59 years old (min 29; max 81). In the first group we found 22 (78.5%) patients still without UTI, 6 (21.5%) patients with UTI, in the second group we found 4 (14.3%) still without UTI, 24 (85.7%) patients with UTI. The difference was statistically significant (p = 0.0001). Conclusion: Intravesical instillation of netilmicin on patients with indwelling urethral catheter was effective in preventing catheter-related UTI.

**Keywords:** Urinary tract infection, indwelling catheter, netilmicin, intravesical antibiotic instillation.

## ABSTRAK

Tujuan: Menilai efektivitas instilasi antibiotik aminoglikosida, netilmisin, intravesika terhadap angka terjadinya infeksi saluran kemih (ISK) nosokomial akibat penggunaan kateter uretra menetap. Bahan & cara: Sebuah studi klinis prospektif yang dilakukan di Bangsal Urologi RSU Dr. Sardjito Yogyakarta, kami mempelajari pasien yang terpasang kateter uretra menetap. Pasien dibagi kedalam 2 kelompok. Pada kelompok pertama (28 pasien) dilakukan sekali pemberian instilasi Netilmicin 25 mg intravesika, pada kelompok kedua (28 pasien) tidak diberikan instilasi Netilmicin. Dilakukan urinalisis sesaat sebelum pemasangan kateter uretra dan 4 hari pasca pemasangan kateter. Dilakukan pemeriksaan urinalisis sebelum dan sesudah instilasi netilmisin. Data dan hasil dianalisis secara statistik deskriptif. Digunakan uji Chi square untuk membandingkan kedua kelompok. Penelitian ini menggunakan perangkat lunak SPSS 17. Hasil: Dilakukan analisis pada urinalisis kedua kelompok yang diambil 4 hari pasca instilasi netilmisin 25 mg. Pasien yang diteliti, median usia adalah 59 tahun (min 29; maks 81 tahun). Pada kelompok pertama, 22 pasien (78.5%) tetap tidak terdapat ISK, 6 pasien (21.5%) menderita ISK. Pada kelompok kedua kami dapatkan 4 pasien (14.3) tetap tanpa ISK, 24 pasien (85.7%) menderita ISK. Perbedaan pada kedua kelompok berbeda secara statistik (p = 0.0001). Simpulan: Instilasi netilmisin intravesika efektif untuk manajemen infeksi saluran kemih pada pasien dengan kateter menetap.

Kata kunci: Infeksi saluran kemih, kateter menetap, netilmisin, instilasi antibiotik intravesika.

Correspondence: Praba, Barry Arief; c/o: Department of Urology, Faculty of Medicine/Indonesia University, Cipto Mangunkusumo General Hospital Jakarta. Jl. Diponegoro 71, Jakarta 10430. Office: (021) 3152892, 3923631–32; Fax: (021) 3145592. Email: barry.a.praba@gmail.com.

#### INTRODUCTION

Nosocomial infections are significant sources of morbidity and mortality. They also

augment health care costs due to the prolonged duration of hospitalization and also additional needs during the hospitalization. In United States, nosocomial infections occur in 5% of patients admitted to public hospitals. Nosocomial urinary tract infection (UTI) remains as an important contributor in the prevalence or incidence of all nosocomial infections. The infection affect 2 in 100 patients who were treated in public hospitals in United States or more than 0.8 million patients each year. Therefore, the measures taken to prevent and control nosocomial infections have been performed for a long time.<sup>1</sup>

Indwelling urethral catheter is an important predisposing factor of the incidence of nosocomial UTI and bacteremia. Approximately 80% of nosocomial UTIs are associated with the use of indwelling urethral catheter. Most nosocomial UTI caused minimal impact, although 30-40% may result in systemic bacteremia due to negative gram bacteria as a complication. Therefore, studies to determine new steps to prevent nosocomial UTI due to indwelling urethral catheter are needed to reduce the morbidity and mortality rate. One of the steps used to reduce the incidence of nosocomial UTI is the instillation of intravesical antibiotics.

#### **OBJECTIVE**

The study was performed to assess the effectiveness of intravesical antibiotic instillations using an aminoglycosides, netilmicin, to prevent the incidence of nosocomial UTI due to the use of indwelling urethral catheter.

#### **MATERIAL & METHOD**

We performed a prospective clinical study to compare between the levels of UTI incidences in patients using indwelling urethral catheter with intravesical netilmicin instillation and without the instillation (control group). The study was conducted in the Urology Ward of Sardjito General Hospital, Yogyakarta, during the period of September 2011 until March 2012. Sampling was performed consecutively. We included all patients who were urologic patients using indwelling urethral catheter from latex material. Patients using double-J stent, gross hematuria, irrigated indwelling catheter, those who were allergic to aminoglycosides, and who refused the antibiotic instillations were excluded from the study. The patients were then allocated into two groups. The first group received the intravesical instillation using 25 mg of netilmicin, while the second group did not receive the netilmicin instillation.

Immediately after the catheter was installed, urine samples were taken for urinalysis and netilmicin instillation. The solution used for the instillation is a mixture of 25 mg/1 ml of netilmicin (in the 25 mg/1 ml Hypobhac® preparation) in 50 ml of 0.9% NaCl. Aseptically, the solution was inserted retrogradely through an outlet catheter. It was left for 15 minutes, and then flowed passively into the urine bag. A second urinalysis is performed on day 4 since the installation of indwelling urethral catheter. To measure the effectiveness of intravesical netilmicin instillation, parameters of infections in urinalysis including nitrite levels, leukocyte esterase, and leukocyte and bacterial counts in urine sediments.

Data analysis in this study was performed using Chi Square test to assess the relationship between intravesical netilmicin instillation and the incidence of urinary tract infection in patients with indwelling catheter. The software used in statistical analysis was SPSS Statistics 17.0.

#### **RESULTS**

During the study period, 56 patients were equally allocated into the experimental group (with instillation) and control group (without instillation). The majority of patients (96.4%, 54 patients) were male, while two patients were female. Urinary retention due to benign prostate hyperplasia (BPH) was the most frequent reported diagnosis, represented by 32 cases or 57.1% of all cases. The second most common diagnosis was prostate carcinoma, reported in seven cases (12.5%). The age of patients ranged between 20 to 77 years old, with the mean of 58.9% years old (SD±11.39).

In the control group, there were 21 UTI patients at catheter installation and 7 patients without UTI. On day 4 of catheter use, the 21 patients who had UTI at onset still had UTI and three patients who previously did not have UTI contracted the infection. In the experimental group, there were 19 patients with UTI and 9 patients without UTI on the onset of urethral catheter installation. On day 4 after catheter installation plus netilmicin instillation, the number of UTI patients at onset of installation was reduced to 3 patients, while 3 patients who were previously UTI-free contracted the infection (Table 1).

From the data in table 1, statistical analysis was performed to assess the relationship between intravesical netilmicin instillation and the rate of UTI measured through urinalysis. The samples used in the study were unpaired samples. Non-parametric

Group	UTI	Number of patients	Rate of UTI	
			Still (+)/Increased	Still (-)/ Decreased
Control $(n = 28)$	(+)	21	21	0
	(-)	7	3	4
Instillation $(n = 28)$	(+)	19	3	16

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**Table 1.** Urinalysis results on day 4 since catheter installation and antibiotic instillation.

test was used in the analysis because 1). The scale used here is categorical, 2). The data distribution was not normal, and 3). Data variance similarities were not observed. Using the Pearson Chi-Square method for hypothesis test of two unpaired categorical groups, p value of < 0.005 was observed.

(-)

#### **DISCUSSION**

In this study, urinary retention due to benign prostate hyperplasia (BPH) was found to be the most common diagnosis, as shown in 32 cases or 57.1% of all cases. The second most common diagnosis was prostate carcinoma, found in seven cases (12.5%). The age range of patients was 20 to 77 years old, with the mean of 58.9 years old (SD + 11.39). These findings are in accordance to those found by Presti et al, suggesting that prostate is the most common organ in men to suffer stroma disorder, either benign or malignant. The most common benign disorder of the prostate is benign prostate hyperplasia (BPH). The incidence of BPH depends on the age of the patient, where among men aged 55 years old, approximately 25% would suffer from voiding disorders.2

The tests to assess significance showed that there is a significant association between the instillation of netilmicin and the incidence of UTI. This result is in accordance with the study of Hooton et al (2010), which suggested that antibiotic-irrigated catheter may delay the onset of bacteriuria. It is also in agreement with the study by Agarwal (2008) and Wan et al (2004), suggesting that antibiotic instillation, in this instance amino-

glycosides, may reduce the incidence of recurrent UTI in patients using indwelling catheter. 4,5

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Some weaknesses of the study include 1). Larger sample size is required to gain a more-representative result for the population, 2). Contamination during urinalysis sampling may occur, resulting in less accurate results, 3). There could be a bias due to the use of systemic antibiotics in the study subjects.

#### **CONCLUSION**

Intravesical instillation using 25 mg of netilmicin in 50 mL of 0.9% NaCl is effective for the management of UTI in patients with indwelling urethral catheter.

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