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Efficacy and safety of preventing catheter-associated urinary tract infection by inhibiting catheter bacterial biofilm formation: a multicenter randomized controlled trial

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Abstract

Background Catheter-associated urinary tract infection (CAUTI) remains the most significant challenge among hospital-acquired infections (HAIs), yet still unresolved. The present study aims to evaluate the preventive effectiveness of JUC Spray Dressing (name of U.S. FDA and CE certifications, while the medical device name in China is Long-acting Antimicrobial Material) alone for CAUTI without combining with antibiotics and to evaluate the impact of bacterial biofilm formation on CAUTI results on the inserted catheters of patients.

Methods In this multicenter, randomized, double-blind study, we enrolled adults who suffered from acute urinary retention (AUR) and required catheterization in 6 hospitals in China. Participants were randomly allocated 1:1 according to a random number table to receive JUC Spray Dressing (JUC group) or normal saline (placebo group). The catheters were pretreated with JUC Spray Dressing or normal saline respectively before catheterization. Urine samples and catheter samples were collected after catheterization by trial staff for further investigation.

Results From April 2012 to April 2020, we enrolled 264 patients and randomly assigned them to the JUC group ($n=132$) and the placebo group ($n=132$). Clinical symptoms and urine bacterial cultures showed the incidence of CAUTI of the JUC group was significantly lower than the placebo group ($P<0.01$). In addition, another 30 patients were enrolled to evaluate the biofilm formation on catheters after catheter insertion in the patients' urethra (10 groups, 3 each). The results of scanning electron microscopy (SEM) showed that bacterial biofilm formed on the 5th day in the placebo group, while no bacterial biofilm formed on the 5th day in the JUC group. In addition, no adverse reactions were reported using JUC Spray Dressing.

Conclusion Continued indwelling urinary catheters for 5 days resulted in bacterial biofilm formation, and pretreatment of urethral catheters with JUC Spray Dressing can prevent bacterial biofilm formation by forming

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a physical antimicrobial film, and significantly reduce the incidence of CAUTI. This is the first report of a study on inhibiting bacterial biofilm formation on the catheters in CAUTI patients.

Keywords Urinary tract infection, Catheters, Bacterial biofilm on patient catheters, Physical antimicrobial film, Hospital-acquired infections

Introduction

Acute urinary retention (AUR) is an emergency caused by mechanical or dynamic factors that lead to difficulty in urination in men, usually resulted from prostate hyperplasia or urethral stones [1]. Indwelling catheters can help patients with urinary retention urinate, but may cause urinary tract infections (UTIs) due to catheterization operations and opening of the urethral orifice [2]. Catheter-associated urinary tract infection (CAUTI) has become one of the most common hospital-acquired infection, accounting for approximately 40% of all hospital-acquired infections, second only to respiratory infections in terms of incidence [3, 4]. It has been shown that bacterial biofilm formation on the inserted urethral catheter is a key reason for the high incidence and difficulty in treating CAUTI [5]. There are currently reports of in vitro bacterial biofilm tests on catheters and animal in vivo bacterial biofilm tests on catheters [6–8]. However, to our knowledge, there are currently no reports of in vivo bacterial biofilm formation tests on catheters inserted into the patient's urethra. This trial is different from the reported trial of JUC Spray Dressing (name of U.S. FDA and CE certifications, while the medical device name in China is Long-acting Antimicrobial Material) inhibiting biofilm formation on the catheter in vitro [9], and is the first report of an in vivo bacterial biofilm formation test on the catheters inserted into the patient's urethra. JUC Spray Dressing in this study is a product of an international patented technology of 'physical antimicrobial method' (Patent No. ZL201210271421.9), composed of 2% organosilicone double long chain diquaternary ammonium salt and 98% deionized water. When sprayed on objects and body surfaces, it forms a positively-charged antimicrobial film (antimicrobial nanofilm). The negatively charged pathogenic microorganisms are electrostatically killed, thereby achieving physical antimicrobial purpose [10–14].

This study aimed to evaluate the effectiveness of JUC alone in preventing CAUTI without the combination use of antibiotics, and to evaluate the impact of bacterial biofilm formation on CAUTI results on the inserted catheters of patients.

Methods

Patients

This study recruited male patients aged 50–80 years old who required indwelling urethral catheterization for more than 7 days, from April 2012 to April 2020 in 6 hospitals in China. A total of 465 male patients were recruited to determine eligibility. Only 294 patients (aged 50–80 years old) were eligible, and the average age of the placebo group and JUC group was 67.8 and 69.6 years old, respectively. Out of these patients, 264 were assessed for CAUTI. They were randomly assigned to either the JUC group ($n=132$) or the placebo group ($n=132$) (Flowchart of the study see Fig. 1). Additionally, 30 were assessed for catheter biofilm and were also randomly divided into JUC ($n=15$) and placebo ($n=15$) groups. All patients were catheterized due to AUR. Participants were excluded if they had any of the following conditions: (1) body temperature > 38.5 °C; (2) white blood cell count > 5 per high power field; (3) have used urinary catheters in the last 2 weeks; (4) patients with intermittent self-catheterization; (5) patients with suprapubic / percutaneous nephrostomy; (6) patients who received antibiotic treatment in the last 7–14 days; (7) psychiatric disorders; (8) other immunosuppressive diseases. The patients should be excluded if one of the above exclusion criteria was present. The trial was approved by the Chinese Ethics Committee of Registering Clinical Trials at the WHO International Clinical Trials Registry Platform (approval number: ChiECRCT-2012021), registered at the Chinese Clinical Trial Registry of WHO International Clinical Trials Registry Platform (registration number: ChiCTR-TRC-12002562, 26/06/2012). All procedures were conducted in accordance with the latest version of the Declaration of Helsinki, and all participants signed an informed consent form before participating.

Procedure

Grouping

According to a randomization table, the 294 enrolled patients were randomly assigned in a 1:1 ratio to either the JUC Spray Dressing group (JUC group) or the normal saline (placebo group). Among these patients, 30 underwent a biofilm test.

JUC

JUC Spray Dressing is a spray-type medical liquid dressing registered as a Class III medical device Long-acting Antimicrobial Material in China, produced by NMS Technologies Co., Ltd., and also registered with the U.S. FDA and EU CE. There is also report of an in vitro study on biofilm formation on catheters and a CAUTI clinical study [15].

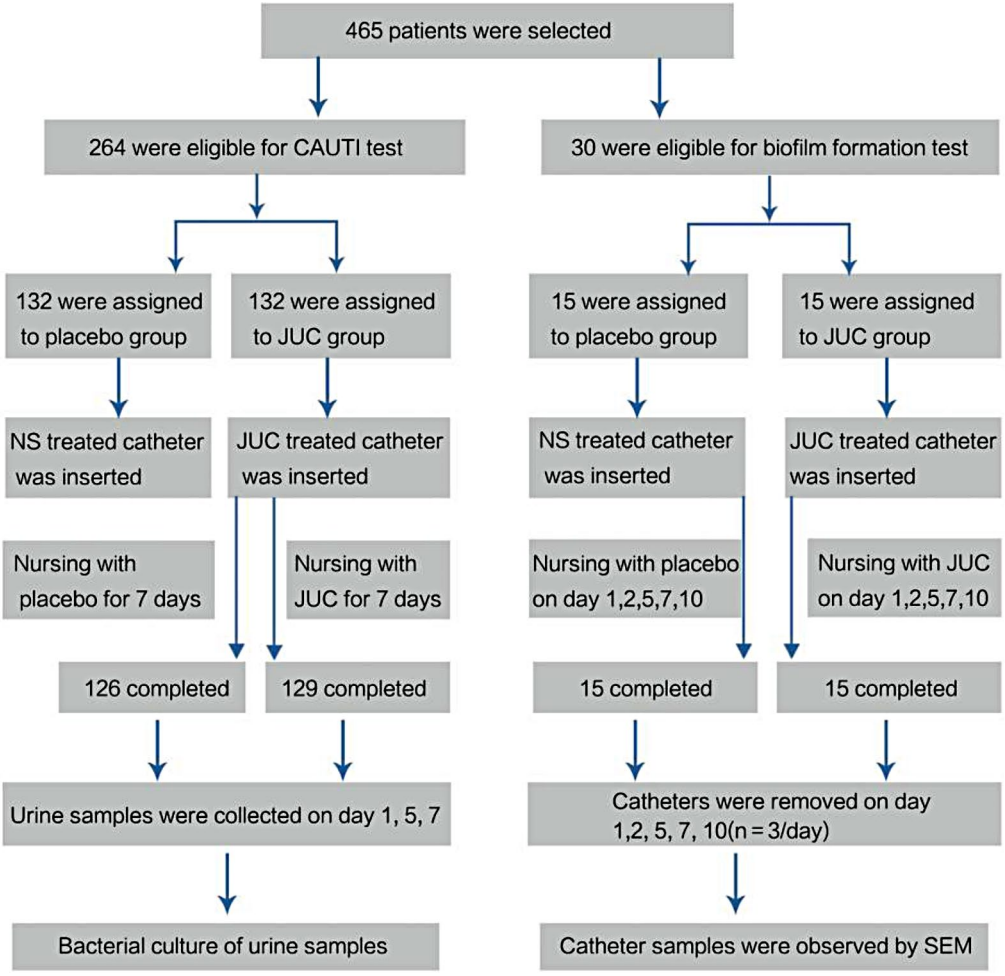

Fig. 1 Flowchart of the study

Blind method

JUC Spray Dressing and placebo (normal saline, NS) were packaged in the same way. All test reagents (JUC and placebo) were consistent in appearance, smell, and skin feel properties. JUC and the same amount of placebo were put into completely identical bottles and sterilized by a high-pressure sterilizer. (From a study safety standpoint, the spray dressing and placebo containers in this study required sterilization. However, it is not necessary when the product enters regular clinical use.) All subjects used catheters with the same brand, and JUC and placebo of the same amount were marked according to a random table. Only the person responsible for packaging knew and recorded the randomization code. Patients and medical staff participating in the trial did not know whether the patient received JUC or placebo. The person responsible for marking could make it unblind only after the study was completed and the Case Report Forms were collected.

Surface treatment of catheters with antimicrobial film

Before catheterization, all external surfaces of all catheters were sprayed with 3 mL JUC or placebo, and the interior surfaces were irrigated with 5mL sterile normal saline or JUC using a sterile syringe. Sterility was maintained during catheterization.

Care

During the post-catheterized care, the perineum, skin and mucous membranes around the urethra were cleaned with saline cotton swabs, and other standard-of-care urinary catheter maintenance measures such as keeping the collection bag below the patient and avoiding dependent catheter tubing loops are regularly recorded, and equally implemented in both study arms. And then JUC or placebo was sprayed on the perineum, catheter surface, and catheter-drainage junction. The distance between the spray nozzle and the skin or catheters was 10–15 cm. All patients were treated with 3–5 sprays each time, twice a day for seven consecutive days.

CAUTI test

UTIs, allergies, and discomfort symptoms were recorded on days 1, 5, and 7 after catheterization, and urine samples were collected aseptically for bacterial culture on days 1, 5, and 7. Bacteria were cultured on MacConkey agar and blood agar. The number of colonies was counted after culturing the urine bacteria. During the trial, if the patient developed an aggravation of infection, allergy, etc., the catheter was removed immediately, systemic antibiotics were given, and the patient was withdrawn from the study.

Biofilm test

To record the formation of bacterial biofilm on the catheter inserted into the patient's urethra. On days 1, 2, 5, 7 or 10 after catheterization, 6 patients' catheters were removed respectively. Each catheter was cut into 3 parts from the bladder segment, urethral segment and extracorporeal segment, and each segment was further divided into 2 parts (one to assess the biofilm on the interior surface of the catheter and the other to assess the biofilm on the exterior surface). A total of 180 pieces were obtained from the 30 catheters and were analyzed by scanning electron microscopy at 2000x magnification (test method see Fig. 2), to visualize bacterial biofilm formation on catheters over time.

Indicator evaluation

According to the definitions of the Infectious Diseases Society of America and the U.S. Centers for Disease Control and Prevention, CAUTI is defined by the presence of microbiological indicators and symptoms or signs compatible with UTI:

1. Patients with indwelling catheterization for more than 48 h.
2. Presence of at least one bacterial species ≥ 10 colony-forming unit (CFU)/mL in the urine.
3. Presence of at least one of the following symptoms or signs compatible with UTI in the patients:

1) >38 °C; 2) suprapubic tenderness; 3) costospinal angle pain or tenderness; 4)urinary urgency; 5) urinary frequency; 6) chills; 7) dysuria; 8) acute hematuria; 9) pelvic discomfort.

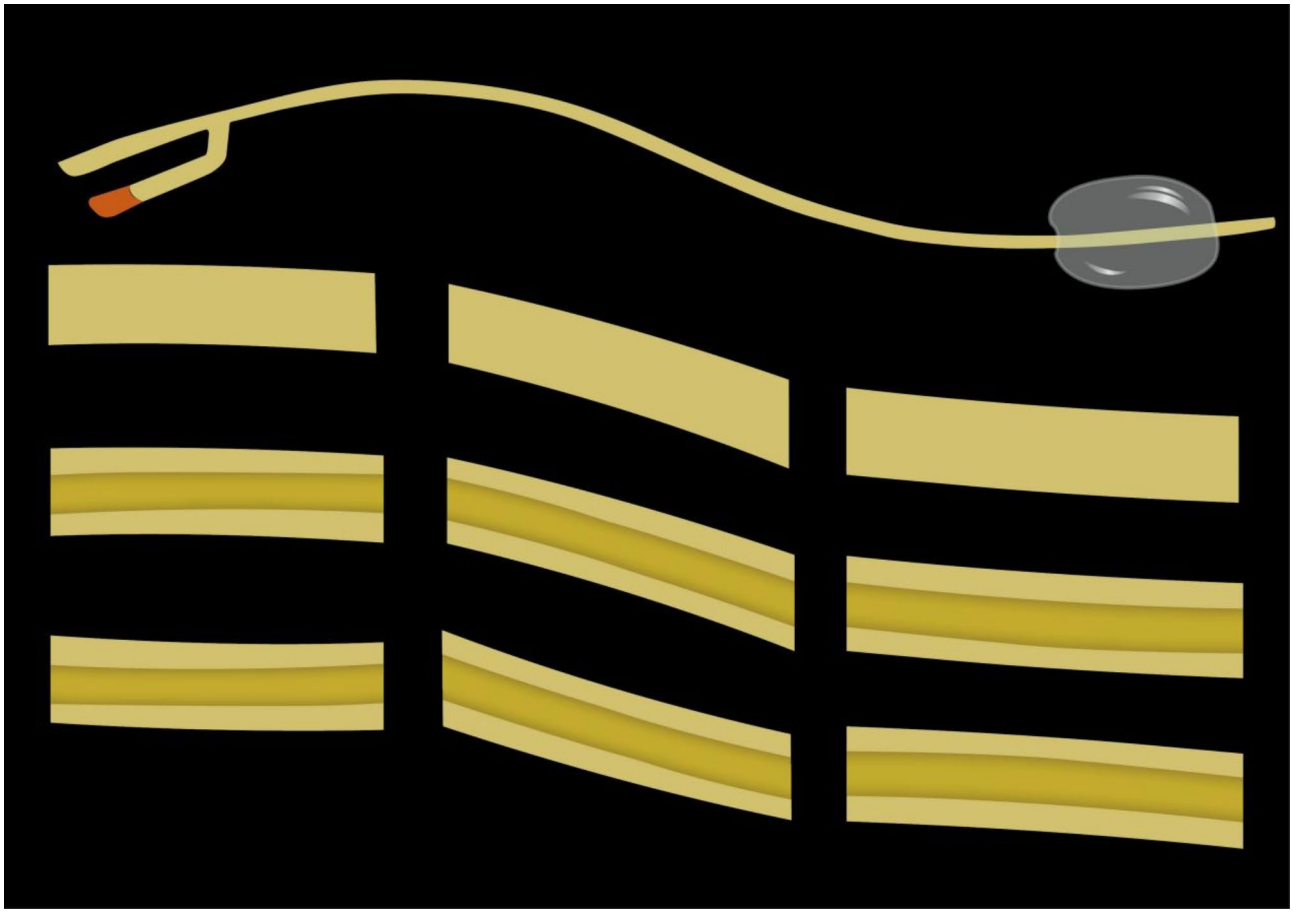

Fig. 2 Biofilm test method

Table 1 Common bacterial typing detected in urine samples

Bacterial species	Day 5 (number of cases, %)		Day 7 (number of cases, %)	
	Control group	Treatment group	Control group	Treatment group
Escherichia Coli	19(15.08%)	2(1.55%)	40(31.75%)	9(6.98%)
Enterococcus faecalis	4(3.17%)	0	1(0.79%)	1(0.78%)
Klebsiella pneumoniae	2(1.59%)	1(0.78%)	3(2.38%)	2(1.55%)
Pseudomonas aeruginosa	1(0.79%)	0	1(0.79%)	0
Staphylococcus epidermidis	3(2.38%)	0	6(4.76%)	1(0.78%)
Staphylococcus aureus	0	0	1(0.79%)	0

The primary efficacy indicator is CAUTI (including microbiological indicators and symptoms or signs).

Secondary outcomes were bacterial biofilm formation on the catheters and adverse reactions in patients. After filling out the case report form by visiting, statistical analysis can be performed on the above indicators.

Statistical analysis

All results were analyzed using the SPSS statistical analysis software. Based on the 20% absolute incidence of CAUTI, the number of patients in this study would provide the study with 80% statistical power, a two-sided type I error rate of 5% and a type II error rate of 10%. A non-adherence rate of 10% was also set based on previous investigations. The proportions of patients with primary outcome were compared by conducting a chi-square test and secondary outcome with time-to-event analysis.

Results

Study patients for CAUTI

Complete follow-up data were obtained for 255 participants (126 in the placebo group and 129 in the JUC group) who participated in the CAUTI assessment. Five patients (4 in the placebo group and 1 in the JUC group) were lost to follow-up due to UTI on day 1. Besides, there was one instance of catheter dislodgement (JUC group); Self-removal of the catheter in 3 patients (2 in the placebo group and 1 in the JUC group). $p>0.05$, there was no statistical difference between the two groups. Among the patients who participated in the biofilm assessment, the catheters were removed on days 1, 2, 5, 7, and 10 after catheterization in both the JUC group and the placebo group (3 patients/group/time, removing the catheter would not affect the treatment, this was to observe the bacterial biofilm, just insert another catheter). $p>0.05$, there was no statistical difference between the two groups.

Table 2 Comparison of urinary tract infection after catheterization between two groups (number of cases, %)

Group	Number of cases	Day 1	Day 5	Day 7
Treatment group	129	0	4 (3.10%)	15 (11.63%)
Control group	126	0	30 (23.81%)	55 (43.65%)
P value			$p<0.01$*	$p<0.01$**

Notes *$\chi^2=23.66$, $p<0.01$, in the comparison of urinary tract infection rate between two groups on day 5, there was extremely significant differences

**$\chi^2=32.81$, $p<0.01$, in the comparison of urinary tract infection rate between two groups on day 7, there was extremely significant differences

Incidence of UTI

Detailed results of bacterial cultures were shown in Table 1. On the 5th day, there were 3 cases of bacteriuria in the JUC group, including 2 cases of *Escherichia coli* and 1 case of *Klebsiella pneumoniae*. The bacteriuria rate was 2.33%. In the placebo group, 29 cases of bacteriuria occurred, including 19 cases of *Escherichia coli*, 4 cases of *Enterococcus faecalis*, 2 cases of *Klebsiella pneumoniae*, 1 case of *Pseudomonas aeruginosa*, and 3 cases of *Staphylococcus epidermidis*. The bacteriuria rate was 23.02%. On the 7th day, urine was collected for bacterial culture before extubation. There were 13 cases of bacteriuria in the JUC group, including 9 cases of *Escherichia coli*, 1 case of *Enterococcus faecalis*, 2 cases of *Klebsiella pneumoniae*, and 1 case of *Klebsiella pneumoniae*. The bacteriuria rate was 10.08%. In the placebo group, there were 52 cases of bacteriuria, including 40 cases of *Escherichia coli*, 1 case of *Enterococcus faecalis*, 3 cases of *Klebsiella pneumoniae*, 1 case of *Pseudomonas aeruginosa*, 6 cases of *Staphylococcus epidermidis*, and 1 case of *Staphylococcus aureus*. The bacteriuria rate was 41.27%. On the 5th day after catheterization, the UTI rate was 4% in the JUC group and 23.81% in the placebo group. The UTI rate was significantly lower in the JUC group compared with the placebo group ($p<0.01$). On the 7th day, UTI rate (11.63%) was also significantly lower in the JUC group compared with the placebo group (43.65%, $p<0.01$) (Table 2). Patients with UTI had 9 UTI symptoms within 7 days. In the placebo group, 10 patients (18.2%) had fever, 10 patients (18.2%) had chills, and 9 patients (16.4%) had hematuria. In the JUC group, there were 2 cases of fever (13.3%), 2 cases of chills (13.3%), and 2 cases of hematuria (13.3%).

Study of bacterial biofilm in catheterized patient's urethra

In one of the hospitals where the patients were studied, 30 patients underwent a catheter bacterial biofilm test. The results are listed in Table 3. Figure 3 is the SEM image of the interior of the bladder segment catheter. The placebo group started to form bacterial biofilms from day 5. In the JUC group, no bacterial biofilm was formed, and the formation of an antimicrobial film was seen. Almost no bacterial debris was seen on days 7 and 10 in the JUC group. In addition, as can be seen from Table 3,

Table 3 Number of bacteria on the catheter

Time points	Catheter segments	Control group		Treatment group	
		Interior surface	Exterior surface	Interior surface	Exterior surface
Day 1	Intravesical	-	-	-	-
	Urethral	+	+	-	-
	Extracorporeal	+ +	-	-	-
Day 2	Intravesical	+	+	-	-
	Urethral	+ +	++	+	-
	Extracorporeal	+ + +	+	+	+
Day 5	Intravesical	+ + +	+	-	+
	Urethral	+ +	+ +	+	+
	Extracorporeal	+ + +	+	+	+
Day 7	Intravesical	+ + +	++	+	+
	Urethral	+ + +	++	+	+
	Extracorporeal	+ + +	-	+	+
Day 10	Intravesical	+ + +	+ + +	+	-
	Urethral	+ + +	+++	-	-
	Extracorporeal	+ + +	+	-	-

-: No bacteria (negative); + and ++: colony counting $< 10^5$ CFU/ml; +++: colony counting $\geq 10^5$ CFU/ml

in the placebo group, there were more bacteria on the interior surface of the catheter than on the exterior surface. According to previous literature, due to the lack of immune cells on the interior surface of the catheter for the bacteria, or rich nutrition of the urine, for catheterized patients, it's easier to have more bacteria on the interior surface of the catheter than on the exterior surface [16].

Safety assessment

No symptoms of itching, allergies, or irritation associated with JUC group or placebo group occurred during the follow-up period.

Discussion

The inclusion criteria for this study were adults suffering from acute urinary retention (AUR) who require catheterization. Urinary retention is commonly observed in males and is often caused by benign prostatic hyperplasia. In the actual study process, all patients who met the criteria for inclusion were male. We aimed to determine whether JUC Spray Dressing is effective in reducing CAUTI without the need to use antibiotics at the same time. The results of scanning electron microscopy (SEM) demonstrated that bacterial biofilm began to form in the placebo group on the 5th day, but no bacterial biofilms were formed in the JUC group on the 5th day. From a clinical point of view, and taking into account previous reports [17, 18], we believe that our results are valid and feasible, and are in line with patient treatment interests. Bacterial biofilm formation on the catheter is the most important cause of CAUTI [19]. In vitro biofilm models on abiotic surfaces have allowed for investigations into biofilm formation [20], and in vivo study on animal models have confirmed biofilm formation in living bodies [6]. This study was the first report through catheter in vivo to demonstrate that bacterial biofilm can appear on indwelling catheters in 5 days. At the same time, this study is the first report to validate an effective method that can prevent the formation of bacterial biofilm in vivo. World Health Organization (WHO) pointed out that systemic prophylactic antibiotics, bladder irrigation or saline/antibiotic infusion, and application of sterile drainage bags cannot prevent CAUTI [21]. In Tambyah's study, the patients were catheterized with nitrofurantoin-impregnated silicone catheters, silver polyurethane hydrogel catheters, or control catheters. Between medicated catheters and control catheters, there were no significant differences in the incidence of UTI [10]. In the present study, the antimicrobial nano-film formed on catheters was confirmed by SEM. Even 10 days after the application, the antimicrobial nano-film still existed on the interior surfaces of the catheters, and successfully prevented the formation of bacterial biofilm, significantly reducing the incidence of CAUTI.

Due to the limited scale of the trial and limited available resources, we were unable to verify whether participants who did not receive antibiotic prescriptions reported CAUTI after discharge from the hospital. There is also no data on how to treat patients after the study period. Furthermore, this study is limited to elderly men with acute urinary retention, and the findings may not be applicable to other situations in which urinary catheter use is more common and prolonged. In the future, more multicenter and well-designed research should be conducted to further confirm our results.

Conclusion

This study was the first to report on the formation test of bacterial biofilms on catheters of CAUTI patients in the human urethra in vivo, as well as tests aimed at inhibiting the formation of these biofilms. The test results of bacterial biofilm and of using JUC Spray Dressing alone without the use of antibiotics significantly reduces the incidence of CAUTI shows the consistency between these two results. It explores innovative approaches to address the challenge of treating infections caused by bacterial biofilm resistance in the human body, especially treating chronic inflammatory infections, and providing effective and feasible solutions for clinicians to combat drug resistance.

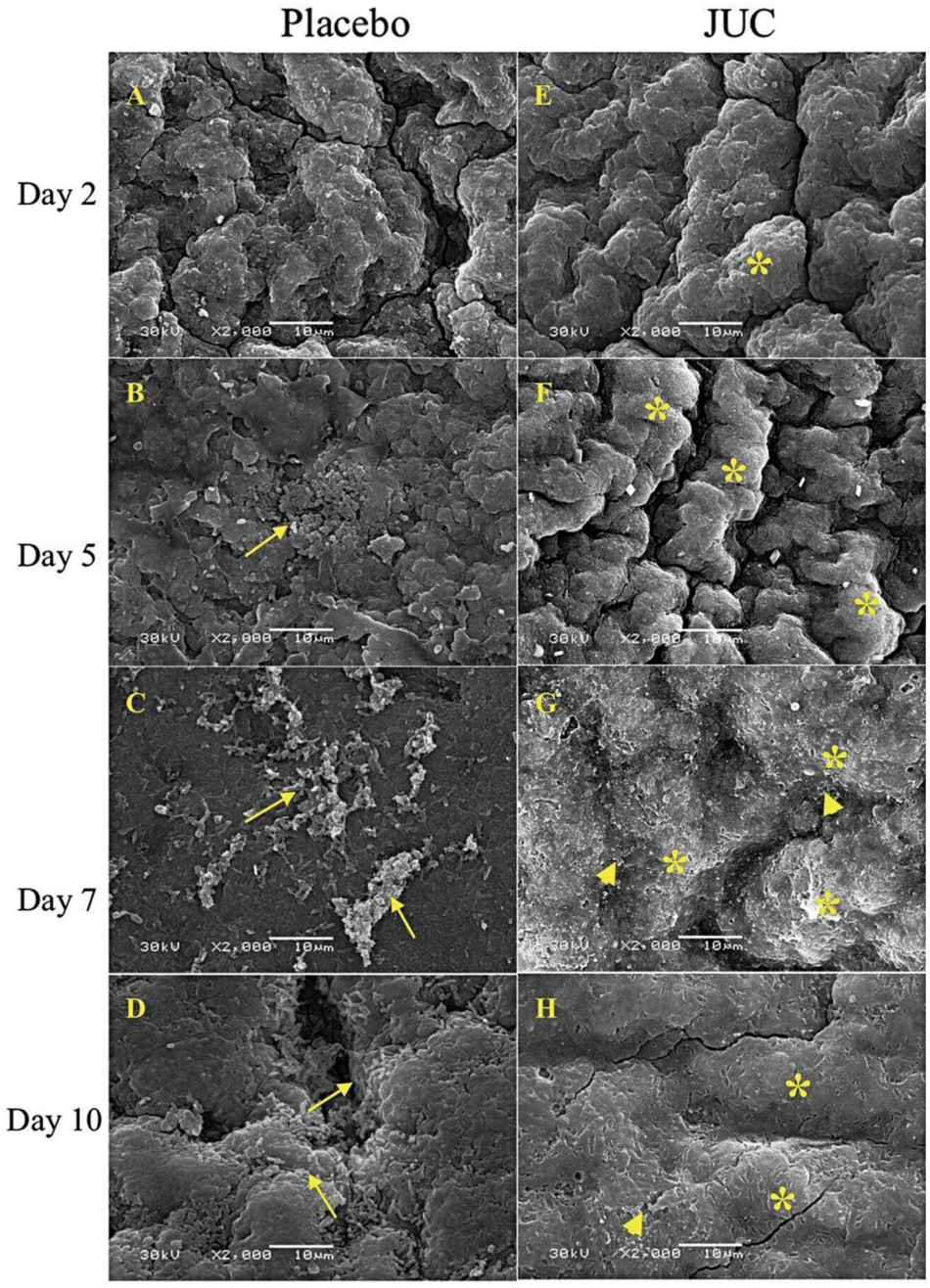

Fig. 3 Scanning electron microscopy (SEM) images of bacterial biofilms and antimicrobial film formed on interior surfaces of the intravesical slices of catheters. **A**-**D**: In the placebo group, from day 5, a layer of bacterial biofilm formed (indicated by arrowheads) and a large number of bacillus grew in the bacterial biofilm. **E**-**H**: The antimicrobial film formed in all JUC groups (indicated by asterisks), yet no bacterial biofilm formed, only very few bacterial debris was seen on day 7 and day 10 (indicated by triangles). Scale bars = 10 μm

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Author contributions
HW, MP, LL, WD, LX, and WX designed the study, participated in data collection, analysis, and drafting of the manuscript. WZ, ZY, GQ, ZY, and CR participated in the study design, data analysis, and critically reviewed the manuscript. All authors have read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Registration number and name of trial registry.
The trial was approved by the Chinese Ethics Committee of Registering Clinical Trials at the WHO International Clinical Trials Registry Platform (approval number: ChiECRCT-2012021), registered at the Chinese Clinical Trial Registry of WHO International Clinical Trials Registry Platform (registration number: ChiCTR-TRC-12002562, 26/06/2012).

Competing interests
The authors declare no competing interests.

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References

1. Bengtsen MB, Farkas DK, Borre M, Sørensen HT, Nørgaard M. Acute urinary retention and risk of cancer: population based Danish cohort study. BMJ. 2021;375:n2305.
2. Chenoweth CE, Urinary Tract I. 2021 Update. Infect Dis Clin North Am. 2021;35(4):857–70.
3. Mong I, Ramoo V, Ponnampalavanar S, Chong MC, Wan Nawawi WNF. Knowledge, attitude and practice in relation to catheter-associated urinary tract infection (CAUTI) prevention: a cross-sectional study. J Clin Nurs. 2022;31(1–2):209–19.
4. Clarke K, Hall CL, Wiley Z, Tejedor SC, Kim JS, Reif L, Witt L, Jacob JT. Catheter-Associated urinary tract infections in adults: diagnosis, treatment, and Prevention. J Hosp Med. 2020;15(9):552–6.
5. Ch'ng JH, Chong KKL, Lam LN, Wong JJ, Kline KA. Biofilm-associated infection by enterococci. Nat Rev Microbiol. 2019;17(2):82–94.
6. Saini H, Vadekeetil A, Chhibber S, Harjai K. Azithromycin-ciprofloxacin-impregnated urinary catheters avert bacterial colonization, Biofilm formation, and inflammation in a murine model of Foreign-Body-Associated urinary tract infections caused by Pseudomonas aeruginosa. Antimicrob Agents Chemother. 2017;61(3):e01906–16.
7. Ionescu AC, Brambilla E, Sighinolfi MC, Mattina R. A new urinary catheter design reduces in-vitro biofilm formation by influencing hydrodynamics. J Hosp Infect. 2021;114:153–62.
8. Vargas-Cruz N, Rosenblatt J, Reitzel RA, Chaftari AM, Hachem R, Raad I. Pilot Ex vivo and in Vitro evaluation of a Novel Foley catheter with Antimicrobial Periurethral Irrigation for Prevention of Extraluminal Biofilm Colonization Leading to Catheter-Associated urinary tract infections (CAUTIs). Biomed Res Int. 2019;2019:2869039.
9. Barford JM, Anson K, Hu Y, Coates AR. A model of catheter-associated urinary tract infection initiated by bacterial contamination of the catheter tip[J]. BJU Int. 2008;7(1):67–74.
10. Yuen J, Chung T, Loke A. Methicillin-Resistant Staphylococcus aureus (MRSA) contamination in bedside surfaces of a hospital ward and the potential effectiveness of enhanced disinfection with an antimicrobial polymer surfactant. Int J Environ Res Public Health. 2015;12:3026–41.
11. Tam B, Chow S. A preliminary report on the effectiveness of Nanotechnology Anti-microbial Spray Dressing in preventing tenckhoff catheter exit-site infection. Periton Dialysis Int. 2014;34:6.
12. Wan KA, Ng MY, Wong YT. New horizon on community-acquired methicillin resistant Staphylococcus aureus (CA-MRSA) skin and soft tissue infection: nanotechnology antimicrobial spray.Hong Kong j. Emerg. Med. 2011;18(6):432–6.
13. Li W, Ma X, Peng Y. al.Application of a nano-antimicrobial film to prevent ventilator-associated pneumonia: a pilot study. Afr J Biotechnol. 2011;10(10):1926–31.
14. Yuen J, Yung J. Medical implications of antimicrobial coating polymers-organosilicon quaternary ammonium chloride. Mod Chem Appl. 2013;1:3.
15. He W, Ye Z, Wang D. Application a nanotechnology antimicrobial spray to prevent lower urinary tract infection: a multi urology centers trial[J]. J TRANSL MED. 2012;10(Suppl 1):S14.
16. Marks LR, Reddinger RM, Hakansson AP. Biofilm formation enhances fomite survival of Streptococcus pneumoniae and Streptococcus pyogenes. Infect Immun. 2014;82:1141–6.
17. Yan J, Bassler BL. Surviving as a community: antibiotic tolerance and persistence in bacterial biofilms. Cell Host Microbe. 2019;26(1):15–21.
18. Razdan K, Garcia-Lara J, Sinha VR, Singh KK. Pharmaceutical strategies for the treatment of bacterial biofilms in chronic wounds. Drug Discov Today. 2022;27(8):2137–50.
19. Lin Y, Chen J, Zhou X, Li Y. Inhibition of Streptococcus mutans biofilm formation by strategies targeting the metabolism of exopolysaccharides. Crit Rev Microbiol. 2021;47(5):667–77.
20. Lusardi G, Lipp A, Shaw C. Antibiotic prophylaxis for short-term catheter bladder drainage in adults. Cochrane Database Syst Rev. 2013;7:CD005428.
21. David JS. Bacterial biofilms in patients with indwelling urinary catheters. Nat Clin Pract Urol. 2008;11(5):598–608.

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