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INTRODUCTION AND OBJECTIVES: Long-term indwelling urinary catheters are susceptible to blockage due to formation of crystalline biofilms by urease-producing microorganisms such as Proteus mirabilis. An in vitro catheter biofilm model CBM was developed to compare current methods for maintaining urinary catheter patency. We compared various bladder irrigation solutions or antimicrobial-coated urinary catheters, versus a novel anti-microbial catheter irrigation solution containing auriclosene (N,N-dichloro-2,2-dimethyltaurine; formerly designated NVC-422).

METHODS: CBM units were fed artificial urine at 0.5 mL per min. The artificial bladder chamber was inoculated with 10^8 colony forming units (CFU) of Proteus mirabilis and biofilm was allowed to establish for 48 hours before daily treatments commenced. A single treatment consisted of two sequential irrigations of 50 mL. Aspirate was collected into the catheter for 15 min and then drained, with a 30-min washout period between the two irrigations. Experiments were conducted for up to 10 days or until catheter blockage. The pH of the effluent, CFU counts in the bladder chamber and the time to catheter blockage were recorded. The area of catheter encrustation was measured using Stereo Zoom imaging.

RESULTS: Inoculation of the CBM reactor with 10^8 CFU of P. mirabilis resulted in 100% biofilm formation of the urinary catheter within one day. As artificial urine or nitrates-free-coated catheters did not extend the period of catheter patency, P. mirabilis irrigated with 0.25% acetic acid, 10 mM acetic acid-buffered saline or isotonic saline blocked at the same rate as untreated catheters. Catheter irrigation with a citrate-buffered formulation of 0.2% auriclosene resulted in complete eradication of P. mirabilis biofilm within one treatment day. In contrast, daily irrigations of infected catheters with P. mirabilis in 0.25% auriclosene in 10 mM acetic acid-buffered saline (at pH 4) or Renacidin® Irrigation Solution had no effect on P. mirabilis colonization of the bladder chamber, even though catheter patency was maintained throughout 10-day studies.

CONCLUSIONS: Irrigation with the rapidly bactericidal antimicrobial auriclosene in a buffered acetic formulation – termed Auriclosene Irrigation Solution – significantly enhanced catheter patency in vitro versus other irrigation solutions and antimicrobial-coated urinary catheters. Clinical evaluation of Auriclosene Irrigation Solution is ongoing.

Materials and Methods

Methods

P. mirabilis

Auriclosene Irrigation Solution Prevents Encrustation by Crystalline Biofilm of Proteus mirabilis in an In Vitro Urinary Catheter Patency Model

**Abstract**

Patients with long-term indwelling bladder catheters often face bacterial colonization causing encrustation and subsequent catheter blockage. Among the many urinary pathogens, urine-positive Proteus mirabilis is the most common culprit. These urine-producing bacilli catalyze the hydrolysis of urea to ammonia, thus creating alkaline conditions. As the urinary pH elevates, calcium and magnesium phosphates precipitate out of solution as struvite and hydroxyapatite crystals, respectively (1). The continued formation of crystalline biofilms blocks the normal flow of urine from the bladder, leading to incontinence (2) and increased risks of developing bacteriuria, pyelonephritis, bacteremia, and sepsis, respectively (3). There are currently no suitable treatment protocols for controlling catheter encrustation and blockage (2).

In the present study, we utilized an in vitro catheter biofilm model that closely mimics the crystalline biofilm found in prostate cancer patients, uterine cancer patients, or patients with ovarian cancer. Similar studies were performed in laboratory models, where catheterization-related bacteria were isolated and inoculated with the appropriate ATCC bacteria. Various bladder irrigation solutions and other control solutions were incorporated into the catheterized biofilm model following protocols to simulate clinical irrigation and drainage regimen.

In vitro catheter biofilm studies were performed, in which catheters were left untreated until blockage. Antimicrobial-coated catheters blocked at the same rate as all-silicone catheters. The experimental study, but the irrigation had no effect on P. mirabilis colonization. Catheters irrigated with 0.2% auriclosene in 10 mM acetic acid buffered acidic formulation – termed Auriclosene Irrigation Solution – significantly enhanced catheter patency in vitro versus other irrigation solutions and antimicrobial-coated urinary catheters. Clinical evaluation of Auriclosene Irrigation Solution is ongoing.

**Results**

**Fig. 1.** In vitro catheter biofilm model

**Fig. 3.** Stereo Zoom images of all-silicone catheters irrigated daily. (A) Saline pH 7 (10 mM acetic acid-buffered saline, pH 4 (C) 0.25% acetic acid (D) Renacidin® (E) 0.2% auriclosene in 10 mM acetic acid saline (F) 0.2% auriclosene in 6.6% citrate buffer

**Table 1.** Catheter blockage time

**Fig. 2.** Stereo Zoom images of untreated catheters. (A) All-silicone (B) Silver-alloy (C) Nitrouricuso Strata-NF (D) Nitroruricuso Relassa-NF

**Fig. 4.** Daily measurement of the colony forming units of P. mirabilis per mL before irrigation. 0.2% auriclosene in 6.6% citrate buffered saline P. mirabilis interferes with the limit of detection by one treatment day. Irrigation with 0.2% auriclosene in 10 mM acetic acid reduced P. mirabilis counts. All other irrigation solutions (Renacidin® 0.25% acetic acid, 10 mM acetic acid, and isotonic saline) did not reduce P. mirabilis counts. The limit of detection was 400 CFU/mL.

**Conclusions**

- **In irrigation with 0.2% auriclosene in 6.6% citrate buffer resulted in complete eradication of P. mirabilis biofilm within one treatment day**
- **In irrigation with isotonic saline, 0.25% acetic acid and 10 mM acetic acid saline resulted in catheter blockage within 4 to 6 days**
- **Catheters irrigated with Renacidin® or 0.2% auriclosene in 10 mM acetic acid maintained patency throughout the study but P. mirabilis colonization was not reduced**
- **Clinical evaluation of 0.2% auriclosene solution is ongoing**

**References**


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