

A Preliminary Report on the Effectiveness of Nanotechnology Anti-Microbial Spray Dressing in Preventing Tenckhoff Catheter Exit-Site Infection

For most patients receiving peritoneal dialysis (PD), there is evidence showing that their satisfaction and quality of life have been increasing (1). However, the Tenckhoff catheter (TC) can become a potential source of infection and peritonitis. If exit-site infection (ESI) is not well managed it can lead to peritonitis or require removal of the TC (2). Peritonitis is a well-known cause of mortality in PD patients (3). Consequently, suspending treatment due to access failure may affect patients' overall health status. The purpose of routine care of the exit site is to prevent ESI. There is a large volume of information focused on the prevention of ESI, with different approaches being proposed. The practice guidelines and protocols from institutions are varied and have not been adequately evaluated, although large volumes of data have been published on the prevention of ESI (4).

Several recent trial studies show that the application of JUC Physical Antimicrobial Spray Dressing (NMS Technologies Company Limited, Nanjing, Jiangsu Province, China), has proven to be effective in the prevention of lower urinary tract infection where the spray was applied on the surface of the catheter and the urethral orifice (5,6), treatment of post-operative infection for oral cancer (7), open wound treatment in

emergency clinics (8), and managing radiation-induced acute skin reactions (9). It is also an alternative to antibiotic treatment on wound management for patients with methicillin-resistant *Staphylococcus aureus* (MRSA) infection (10). JUC spray dressing was developed in China in 2002 and registered as a dressing product by the United States Food and Drug Administration in 2006. The spray consists of 2% organosilicon quaternary ammonium salt and 98% distilled water, and is safe for application, even for contact with eyes and mucous membranes. It is composed using nano-manufacture technology, yet the antibacterial mechanism is not fully understood. Some proposed mechanisms relate to the physical structure of the nanoparticles while others relate to the enhanced release of antibacterial metal ions from nanoparticle surfaces which interact with and penetrate into the bacteria (11).

Proper exit-site care is of paramount importance in reducing TC-associated infection and subsequent catheter loss. In current practice, patients who have a TC are usually advised to use the traditional antiseptic 0.05% chlorhexidine in exit-site care. Previous studies suggest that 0.05% chlorhexidine is able to reduce the bacterial load in the wound and promotes cell growth (12). In this study, JUC spray was applied to the TC exit site to compare the incidence of ESI with the usual standard care. In addition to ESI, the existence of skin allergy, catheter damage, and time spent on exit-site dressing were examined.

METHODS

The study was carried out through a randomized controlled trial. Patients were recruited from the renal unit of a 1,700-bed acute-care, general regional hospital in Hong Kong. Those patients who did not receive oral or external antibiotics and who had a TC in place for at least 3 months were recruited sequentially. Patients presenting with signs and symptoms of exit-site infection and poor healing of exit site were excluded. There were 121 patients assessed for eligibility and 47 subjects were excluded. The reasons for exclusion were patients not meeting the inclusion criteria or refusing to participate. To compute the sample size, we referred to Li *et al.* (10) on the effectiveness of JUC spray to prevent ventilator-associated pneumonia. To have 80% power, $\alpha = 0.05$, to detect a 27.9% reduction in the incidence of bacterial colonization in the pharyngeal cavity in the experimental group compared with the control group, a sample size of 35 subjects for each group was required. The catheter was inserted surgically by open surgical incision. It was well secured with a dressing and PD was started 4 weeks

after insertion. A 47-cm Argyle Peritoneal curl catheter with double cuff (Covidien, Mansfield, MA, 02048 USA) was used for both groups of patients.

A total of 78 patients were randomized into study or comparison group by the researcher using computer-generated numbers. Baseline data were collected before randomization with masking of treatment allocation. It was a single-blinded study as the patients were not blinded to the group assignment while the data collector was blinded to group allocation. The study group patients used JUC spray dressing while the comparison group used 0.05% chlorhexidine dressing daily for standard wound care. Coaching was provided by the nurses to ensure that the patients were able to perform the procedures correctly. The study team called the patients on the first 3 days and they were instructed to report any abnormalities they noticed to the nurses, such as signs and symptoms of infection, skin allergy, and TC damage. The patients were treated with a full course of antibiotics prescribed by the physician if diagnosed for ESI and they continued with the study after full recovery from treatment. Clinical efficacy was assessed for a period of 6 months after implementation of intervention.

According to the study unit protocol, the presence of 2 out of 3 equivocal signs and symptoms of ESI was diagnosed as acute ESI. Signs and symptoms included red

color around the exit site, with 3 – 4 mm measurement from the edge or purulent discharge.

RESULTS

A total of 74 patients, 37 each in the study and comparison groups, were included in the final analysis. Continuous variables are expressed as median (range) and were analyzed using Mann-Whitney U-test. Categorical variables were analyzed using Chi-square test or Fisher's Exact test. The demographic and clinical information was examined and no significant difference was found between the 2 groups except age. See Table 1 for details.

Exit-site infection developed in 2 patients (5.4%) in the study group and 9 patients (24.3%) in the comparison group. The results were significant ($p = 0.02$) for the 2 groups. Among the 9 patients in the comparison group, ESI occurred twice during the 6-month period in 2 patients. The 2 patients who developed ESI in the study group were 45 and 65 years of age, ages of individual patients in the comparison group were: 50, 1; 58, 2; 61, 1; 73, 1; 75, 1; 80, 2; and 82, 1. There was 1 patient in the comparison group who reported damage to the catheter, having a small crack near the distal part of the TC as confirmed by the physician of the study unit. No allergic

TABLE 1
Demographic Data and Clinical Characteristics of the Study Population ($n=74$)

	Study Group ($n=37$)	Comparison Group ($n=37$)	p -value
Age ^a	56 (47.5–74)	72 (60–75.5)	0.01 ^c
Duration of TC insertion (month) ^a	25 (11–46)	17 (10.5–54.3)	0.94
Gender ^b			0.34
Male	18 (48.6%)	14 (37.8%)	
Female	19 (51.4%)	23 (62.2%)	
Diabetes ^b			0.32
Yes	10 (27%)	14 (37.8%)	
No	27 (73%)	23 (62.2%)	
Normal albumin ^b			0.10
Yes	14 (37.8%)	21 (56.8%)	
No	23 (62.2%)	16 (43.2%)	
Previous ESI ^b			0.81
Yes	16 (43.2%)	15 (40.5%)	
No	21 (56.8%)	22 (59.5%)	

TC = Tenckhoff catheter; ESI = exit-site infection.

^a Continuous variables are expressed as median (25th–75th percentile).

^b Categorical variables are expressed as count (column %).

^c $p < 0.05$.

TABLE 2
Results at Six Months Post-Intervention

	Study Group (n=37)	Comparison Group (n=37)	p-value
Allergy ^a			—
No	37 (100%)	37 (100%)	
Exit site infection ^a			0.02 ^c
Yes	2 (5.4%)	9 (24.3%)	
No	35 (94.6%)	30 (75.7%)	
TC damage ^a			1
Yes	0 (0%)	1 (2.7%)	
No	37 (100%)	36 (100%)	
Time used for dressing (minutes) ^b	2 (1–8)	10 (2–15)	<0.001 ^c
Treatment cost (HK\$)	0.50	3.00	

TC = Tenckhoff catheter; HK\$ = Hong Kong dollars.

^a Categorical variables are expressed as count (column %).

^b Continuous variables are expressed as median (range).

^c $p < 0.05$.

reactions were reported for either group of patients. Time spent on TC dressing was significantly shorter in the study group (median: 2 minutes) than in the comparison group (median: 10 minutes). The study group patients were all satisfied with the new treatment. The cost for chlorhexidine dressing was HK\$3.00 (equivalent to US\$0.38) per dressing, while the cost for JUC spray was HK\$0.50 per application. See Table 2 for results.

Eleven samples were taken for bacteria analysis from the infected exit sites of both groups and the results confirmed bacteria growth. Coagulase-negative *Staphylococci*, *Diphtheroid bacillus*, *Pseudomonas aeruginosa* and *Streptococcus salivarius* were found mostly in the wounds of the comparison group. *Acinetobacter* spp and *Pseudomonas* spp were found in the JUC group.

DISCUSSION

Proper exit-site care is of paramount importance to reducing TC-associated infection and subsequent catheter loss. Adequate immobilization of the catheter and daily exit-site care are the significant issues to be investigated. Our study demonstrated that JUC spray can replace traditional disinfectants for exit-site care as it does not cause adverse effects and can counter the problem of drug resistance. The results demonstrated that the incidence of ESI in the treatment group was significantly lower than in the comparison group. Although it is difficult to draw definite conclusions about the relative efficacy given the much younger

average age of the treatment group, the data suggest that the JUC spray is at least as effective as standard chlorhexidine protocol.

JUC physical antimicrobial dressing is considered a new method for safely and effectively preventing the onset of ESI. In the application of JUC, the easy-to-use treatment also reduced the time spent on daily TC exit-site care. The procedure is convenient and facilitates wound inspection. Once JUC is sprayed on the skin surface, it dries within 30 seconds, thus reducing the time, effort, and discomfort of exit-site care. It is actually invisible and does not cause uncomfortable feelings to the patients or cause damage to the PD catheter. Patients enjoy better quality of life, as daily exit-site care is no longer a burden. However, our results on time savings need to be interpreted with caution as patients in the study group were significantly younger; and the younger patients may perform faster in daily activities than older patients, depending on the nature and severity of their respective conditions. Antibiotic resistance may be the result of extensive use of antibiotics for end-stage renal failure patients with compromised immune systems. The use of JUC spray can play a role in exit-site management for patients who may be sensitive to chlorhexidine and/or antibacterial agents. Medical expenses in public hospitals in Hong Kong are heavily subsidized by the Hong Kong government. The use of JUC spray to replace traditional dressing materials and methods could reduce the financial burden on Hong Kong's healthcare system by reducing medication expenses.

CONCLUSION

JUC spray is a simple, safe and sustainable technique for TC care. Further studies are required using a larger sample size to investigate the applicability of JUC in exit-site care for patients from multiple age categories residing in hospital renal units and in the community.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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纳米抗微生物喷雾敷料用于 预防 Tenckhoff 导管出口部 位感染有效性的初步报告

对于大多数接受腹膜透析（PD）的患者而言，有证据显示，患者满意度和生活质量得到持续提高（1）。然而，Tenckhoff 导管（TC）可成为感染和腹膜炎的一个潜在来源。如没有处理好出口部位感染（ESI），可导致腹膜炎或者需要拔除 TC 管（2）。腹膜炎是腹膜透析患者死亡的一个众所周知的原因（3）。因此，因透析通路失败而导致的治疗暂停可能会影响患者的整体健康状况。出口部位常规护理的目的是为了预防出口部位感染。针对出口部位感染的预防有大量的资料，推荐了多种不同的方法。各机构的实践指南和治疗方案各有不同，且没有得到充分评估。然而已有大量关于出口部位感染预防的资料出版。（4）。

最近几项试验研究证明了应用 JUC 物理抗微生物喷雾敷料（南京神奇科技开发有限公司，江苏南京）的疗效：喷洒在导管表面和尿道口可以有效预防患者下尿路感染（5，6），治疗口腔癌术后感染（7）、急诊科开放性伤口（8）、以及处理放射性急性皮肤损伤（9）。它也可替代抗生素治疗耐甲氧西林金黄色葡萄球菌感染患者的伤口（10）。JUC 于 2002 年在中国发明，2006 年被美国食品和药物管理局注册为敷料产品。该喷雾剂由 2% 的有机硅季铵盐和 98% 蒸馏水构成，即使在与眼睛和粘膜接触的时候也可以安全应用。其成分使用了纳米制造技术，但其抗菌机理尚未完全弄清楚，一些提出的机理涉及纳米粒子的物理结构，而其他机理涉及抗菌金属离子从纳米粒子表面增强释放，与细菌产生相互作用并渗透（11）。

正确的出口部位护理对于降低 TC 管相关感染和后续导管破损是至关重要的。在目前的实践中，通常建议患者在出口部位护理时使用传统的抗菌剂，0.05% 洗必泰。之前的研究显示，0.05% 的洗必泰能减少伤口中的细菌量，并促进细胞生长（12）。在这项研究中，将 JUC 喷雾剂应用于 TC 管出口部位，和常规护理的出口部位感染的发生率进行比较。除了出口部位感染以外，检查出口部位皮肤过敏情况，导管损伤及更换敷料所需时间。

方法

本研究采用一项随机对照试验。从香港一家拥有 1700 个急诊护理床位的地区综合性医院肾病科招募受试者。按顺序招募未接受口服或外用抗生素、插入 TC 管至少 3 个月的患者。排除存在出口部位感染症状、体征、出口部位愈合不良的患者。评估 121 位患者的资格，排除了 47 人。排除的原因是病人未达到入选标准或拒绝参加。为了计算样本量，参考 Li 等人（10）有关 JUC 喷雾剂预防呼吸机相关性肺炎疗效的论文。要达到 80% 的检验效能， $\alpha=0.05$ ，要达到与对照组相比，研究组的咽部细菌定植率有 27.9% 的减少，需要每组 35 个受试者的样本量。通过开放性手术切口插入腹膜透析管。用敷料固定，插导管 4 周后开始腹膜透析。两组患者均使用 47cm 的 Argyle 腹膜透析双气囊卷曲管（Covidien, Mansfield, MA, 02048 美国）。

研究人员用电脑生成的号码将 78 例患者随机分入研究组或对照组。在用隐藏的治疗分配进行随机分配之前收集基线数据。这是一个单盲实验，患者了解分组，但数据收集者不了解分组。研究组患者使用 JUC 喷雾敷料，而对照组每天使用 0.05% 洗必泰敷料进行标准的术后护理。护士提供指导，以确保患者能正确执行程序。研究团队在头三天打给患者，指导他们如有异常情况（如感染的症状、体征、皮肤过敏和 TC 管损坏）需报告给护士。如被确诊为出口部位感染，由医生对患者进行全套的抗生素治疗。完全康复后继续本研究。干预实施后 6 个月评估

临床疗效。

根据研究单位的临床方案，如存在三分之二的出口部位感染可疑症状和体征，则被诊断为急性出口部位感染。症状和体征包括出口部位周围 3-4mm 红肿，或排脓。

结果

总共 74 例患者，最终的分析包含研究组和对照组每组 37 例患者。连续变量表示为中位数（范围），并使用曼-惠特尼 U 检验进行分析。采用卡方检验或费雪正确性检定分析分类变量。检查人口统计学和临床资料，两组间除了年龄未发现显著差异。详情见表 1。
出口部位感染在研究组发生 2 例（5.4%），

对照组发生 9 例（24.3%）。两组结果有显著性差异（ $P=0.02$ ）。对照组 9 名病人当中，在 6 个月内，出口部位感染在 2 例患者身上发生了两次。研究组 2 名出口部位感染患者分别为 45 岁和 65 岁，在对照组中各病人的年龄为：50、1；58、2；61、1；73、1；75、1；80、2；82、1。对照组有 1 例患者报告导管损坏，TC 管远端部分附近有小裂纹，且经研究单位医师证实。两组患者中没有过敏的报道。关于更换 TC 管敷料所花费的时间，研究组（平均：2 分钟）对比对照组（平均：10 分钟）有显著缩短。研究组患者均满意新疗法。费用为每个洗必泰敷料 3.00 港币（相当于 0.38 美元），而 JUC 喷雾剂应用一次的成本为 0.5 港币。请见表 2 的结果。

表 1 研究人群（n = 74）的人口统计学资料和临床特点

	研究组 (n=37)	对照组 (n=37)	p-值
年龄 ^a	56 (47.5 – 74)	72 (60 – 75.5)	0.01 ^c
插入 Tenckhoff 导管的时间(月) ^a	25 (11 – 46)	17 (10.5 – 54.3)	0.94
性别 ^b			0.34
男	18 (48.6%)	14 (37.8%)	
女	19 (51.4%)	23 (62.2%)	
糖尿病 ^b			0.32
是	10 (27%)	14 (37.8%)	
否	27 (73%)	23 (62.2%)	
正常白蛋白 ^b			0.10
是	14 (37.8%)	21 (56.8%)	
否	23 (62.2%)	16 (43.2%)	
之前有出口部位感染 ^b			0.81
是	16 (43.2%)	15 (40.5%)	
否	21 (56.8%)	22 (59.5%)	

^a连续变量表示为中位数（25 - 75%）。

^b分类变量表示为计数（列%）。

^c $P < 0.05$

表 2 干预后 6 个月的结果

	研究组 (n=37)	对照组 (n=37)	p-值
过敏 ^a			---
否	37 (100%)	37 (100%)	
出口部位感染 ^a			*0.022
是	2 (5.4%)	9 (24.3%)	

否	35 (94.6%)	30 (75.7%)	
TC管损坏 ^a			1
是	0 (0%)	1 (2.7%)	
否	37 (100%)	36 (100%)	
更换敷料所用时间(分钟) ^b	2 (1 – 8)	10 (2 – 15)	<0.001 ^c
治疗费用 (港币)	0.50	3.00	

^a分类变量表示为计数 (列%)。

^b连续变量表示为中位数 (范围)。

^c P < 0.05

从两组患者感染的出口部位采集了 11 份样本用于细菌分析, 检验结果证实了细菌的生长。凝固酶阴性葡萄球菌、类白喉棒状杆菌、绿脓杆菌、葡萄球菌、唾液链球菌和假单胞菌大多出现在对照组的伤口中。在 JUC 组, 检出了不动杆菌和假单胞菌。

讨论

恰当的出口部位护理是非常重要的, 能减少 TC 管相关感染和随后的导管破损。充分固定导管和出口部位日常护理是需要研究的重要问题。我们的研究表明, JUC 喷雾可以取代传统的消毒剂进行出口部位护理, 因为它不会造成不良反应, 并能避免耐药性问题。结果表明, 研究组的出口部位感染发生率较对照组显著降低。考虑到研究组的平均年龄要小得多, 关于相对疗效很难得出确切的结论, 数据显示, JUC 喷雾剂至少和标准的洗必泰方案一样有效。

JUC 物理抗菌敷料被认为是安全有效预防出口部位感染的新方法。应用 JUC 后, 方便易用的治疗方法也减少了每日用于 TC 管出口部位护理的时间。程序方便、有利于伤口检查。一旦喷洒在皮肤表面, JUC 在 30 秒内干燥, 从而减少出口部位护理的所需的时间、精力和不舒适感。它实际上是隐形的, 所以不会给患者带来不舒服的感觉, 也不会给腹膜透析管带来损坏。患者会享受更好的生活质量, 日常出口部位的护理将不再是一种负担。然而, 我们在节省时间方面的

结果需要进行谨慎解读, 因为研究组中的患者在年龄上显著更年轻, 年轻患者通常会在进行日常活动时, 会比老年人速度更快, 具体视各人体质和病情严重程度而定。抗生素耐药性可能是在免疫系统受损的终末期肾衰竭患者中大量使用抗生素的结果。对于那些对洗必泰和/或抗菌药物过敏的患者来说, 使用 JUC 喷雾剂可以在出口部位处理中发挥作用。香港公立医院的医疗费用由政府进行了大量补贴。使用 JUC 喷雾来取代传统敷料和方法, 通过减少用药支出费用, 能减轻香港医疗保健系统的财务负担。

结论

JUC 喷雾剂是一种简单、安全、可持续的 TC 管护理技术。需要使用更大的样本量进行进一步研究, 以充分调查在医院肾科和社区环境的各年龄段患者中间, JUC 对出口部位护理的适用性。

披露

各作者没有要公布的财务利益冲突。

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