New horizon on community-acquired methicillin resistant *Staphylococcus aureus* (CA-MRSA) skin and soft tissue infection: nanotechnology antimicrobial spray

由社區感染的抗甲氧苯青黴素金黃葡萄球菌(CA-MRSA)導致的皮膚及軟組織發炎的新前景：納米科技抗菌噴霧劑

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The prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in community and hospital is increasing. The development of drug resistance may be attributed to the extensive use of antibiotics. Nanotechnology antimicrobial spray (NTAS), a physical antibacterial agent, is an alternative to antibiotic treatment on wound management. We report a case of MRSA associated skin abscess using NTAS in the wound management. NTAS possesses potent, broad spectrum antibacterial effect while carrying no risk of resistance and minimal adverse effect. Moreover, NTAS facilitates home wound management, thus reducing dependency on public health resources. Further studies are indicated to explore the clinical role of NTAS in an attempt to reduce the use of antibiotics. (Hong Kong j.emerg.med. 2011;18:432-436)

抗甲氧苯青霉素金黃葡萄球菌在社區和醫院的流行率有上升趨勢。抗藥性的產生可能與廣泛使用抗生素有關。作為一種物理性的抗菌劑，納米科技抗菌噴霧劑（NTAS）是一種另類的傷口處理抗菌方式。我們在此報告一個使用NTAS治療受MRSA感染的皮膚膿腫病例。NTAS擁有強力和廣譜的抗菌效力，且不會導致抗藥性及極少副作用。再者，NTAS能促進家居傷口護理，因而減少對公共健康資源的依賴。NTAS在減少使用抗生素方面的臨床角色值得更深入研究。

Keywords: Abscess, antibacterial agents, drug resistance, wound infection

關鍵詞：膿腫、抗菌劑、抗藥性、傷口感染

Introduction

Since the first antibiotic, penicillin, was discovered several decades ago, antibiotics have played an important role in the treatment and prevention of diseases caused by microorganisms. Penicillin was once a very effective antibiotic against *Staphylococcus aureus*. However, due to the extensive use of antibiotics, drug-resistant strains emerges as a result of natural selective pressure to antibiotic exposure. The first penicillinase-producing strain was found in 1944.[1] It was followed by methicillin-resistant *Staphylococcus aureus* (MRSA).[2,3] MRSA was first discovered in 1960s. Initially it was found in health care setting and involved patients with risk factors. Over the following four decades, MRSA has become a major community health problem as it spreads in the community and involves healthy individuals with no risk factor for MRSA infection. The prevalence of MRSA in both hospital and community setting is increasing.[4]

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Newer generation antibiotics and guidelines on proper use of antibiotics have been developed to overcome the problem of drug resistance and to reduce the misuse of antibiotics. Despite these efforts, drug-resistant strains continue to develop. One example is the vancomycin-resistant *Staphylococcus aureus* (VRSA), after the use of vancomycin to combat MRSA infection. Moreover, the newer generation antibiotics may be associated with adverse effects and higher treatment cost.

Skin and soft tissue infection (SSTI) is one of the most common clinical conditions encountered in the daily practice of emergency physicians. The use of nanotechnology antimicrobial spray (NTAS) may be a breakthrough in medicine, while scientists are inventing powerful antibiotics against drug-resistant bacteria.

We have successfully managed more than ten cases of MRSA associated skin abscess by incision and drainage followed by JUC (one kind of NTAS). We here report one of these cases.

Case

A 55-year-old gentleman suffered from a painful swelling over the scalp for five days. He had unremarkable past medical history and no history of MRSA infection. There was no history of hospitalisation, surgery or catheterisation prior to this episode of SSTI. On examination a scalp abscess measuring 3 cm in diameter was revealed. Incision and drainage was done under aseptic technique. The abscess cavity was swabbed and the specimen was sent for culture and sensitivity testing. Initially daily wound packing and saline dressing were done in General Outpatient Clinic. Three days after the incision and drainage, culture result confirmed the presence of MRSA associated with positive Panton-Valentine Leukocidine gene and type IV SCCmec typing. Community acquired MRSA (CA-MRSA) infection was confirmed. He was followed up on the same day. The wound condition was satisfactory with scanty discharge and there was no clinical evidence of wound infection (Figure 1). He was educated on using JUC spray for wound care at home and the procedure was demonstrated once. Standardised, self-explanatory leaflets were given to enhance the patient's compliance and confidence. The patient was instructed to use JUC three times per day. Before each application, the patient cleaned the wound simply with ordinary soap or shampoo. Then the wound was dried with clean gauze. JUC was subsequently sprayed into the wound cavity. In general, one or two sprays were adequate but more sprays were necessary for larger abscess cavity initially. Spray nozzle and packing gauze were provided because of the presence of deep cavity and discharge. No other form of treatment including antibiotic was involved. Follow up on post-operative day nine and thirteen showed satisfactory wound healing, and repeat wound swab yielded no bacterial growth (Figures 2 and 3). He was satisfied with the convenience of wound care by himself, and he could manage to apply JUC on his scalp wound in front of the mirror.

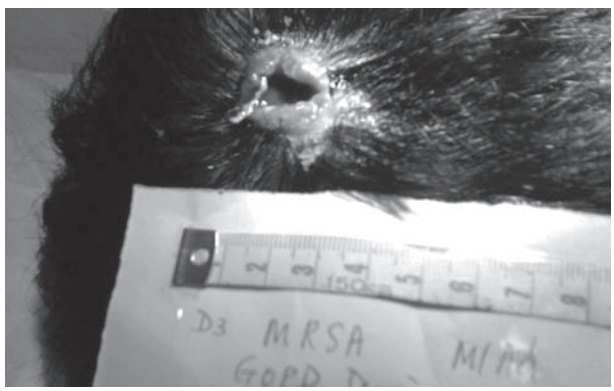

Figure 1. Post-operation day 3.

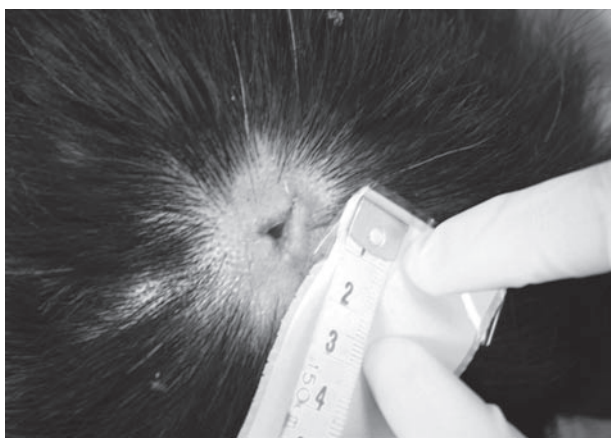

Figure 2. Post-operation day 9.

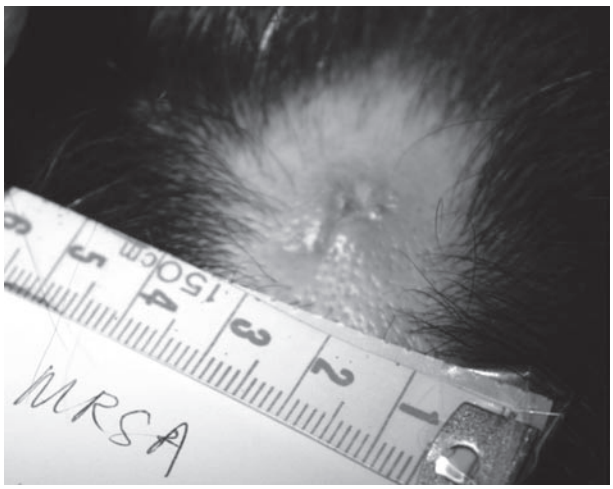

Figure 3. Post-operation day 13.

Discussion

JUC has been introduced into our department for wound care since one year ago. It was first produced in 2002, and has been registered as a dressing product for use in general and plastic surgery by the United States Food and Drug Administration. It is made of organosilicon quaternary ammonium salt and distilled water. JUC is made through Nano-Manufacture Technology, with nano-cations on the nano-scale molecular structure produced and then prepared in water-soluble spray. JUC achieves antibacterial action on skin and wound surface by physical mechanisms and hence they can be regarded as physical antimicrobial agents.[5]

Bacteria are unicellular microorganisms. It has been found that these microorganisms are negatively charged. NTAS is made of nanometer cations that adsorb microorganisms by the electrostatic force between the positively charged nanometer cations and negatively charged microorganisms. This electrostatic force causes destruction of cell membrane and interferes with the mitochondrial enzyme to achieve broad-spectrum physical bactericidal effect. NTAS has been shown effective in vitro in eradicating bacteria such as *Staphylococcus aureus*, *Enterobacteriaceae* and *Pseudomonas aeruginosa*. When NTAS is sprayed and adheres onto the skin, mucosa or wound surface, it solidifies to form an invisible antibacterial layer. The antibacterial film can kill the bacteria and prevent the bacteria from invading the skin or wound surface.[5]

Initially JUC was prescribed to those patients who suffered from second-degree burn. Subsequently, because of the broad-spectrum antibacterial effects, JUC has been used on infected wounds and MRSA associated skin abscess after incision and drainage. The antibacterial effect of JUC lasts for eight hours, which is longer than the ordinary antiseptics.[5] These patients are given JUC for wound care at home. They are educated to clean the wound with ordinary soap prior to the application of JUC. After the wound is dried properly, the JUC bottle is held about seven inches above the skin or mucous membrane, and the content is sprayed onto the surface directly. In general, one or two sprays will be adequate but more sprays may be necessary for larger abscess cavity. If the abscess cavity is deep, spray nozzles are also provided and the patients are educated on wound packing technique. They are also advised on proper personal hygiene and bathing as usual. JUC can be used two to three times every day. Follow up appointments at A&E should be arranged in order to monitor the compliance to treatment, to check the wound management technique and to assess the wound healing.

Apart from treatment of MRSA infection, NTAS may have a role in prevention of disease transmission. Colonisation of wounds by MRSA represents a significant threat in cross-infection and spread of MRSA in the community. Infection may be spread with contact of contaminated wound dressing, towel or human hands. The basic interventions for preventing spread of MRSA include hand washing, proper wound management and good hygiene. Using NTAS to eradicate MRSA on the wound and other carrier sites may be useful in controlling spread of MRSA in the community.

The Centers for Disease Control and Prevention recommends decolonisation in individuals with repeated SSTI, after infection control measures.[6] The current decontamination regimen involves 2% mupirocin to nasal nare twice daily for five days

together with 4% chlorhexidine bath daily.[7] However, a Cochrane systemic review of randomised controlled trials between 1966 and 2003 shows that there is insufficient evidence to support the use of antibiotics, either topical or systemic, to eradicate MRSA colonisation. Also there are potentially serious adverse events including the development of drug-resistant strains.[8] Resistance to mucoprin and chlorhexidine has been reported.[6,9] A prospective study has investigated the incidence of nasal carriage of MRSA on admission and the rate of MRSA colonisation during the hospital stay. Nasal carriers were given a five-day course of nasal mupirocin ointment, and daily body wash with 4% chlorhexidine and liquid soap alternatively. Eradication was achieved in nearly 99% patients after one week. However, subsequent recolonisation was common and resistant strain was found.[10] One newer randomised controlled trial showed the effectiveness of nasal mupirocin ointment in decolonisation of *Staphylococcus aureus* in persistent carriers, but the effect declined ninety days later.[11] Selective short-term use of mupirocin for specific patient group may be useful, but needs further investigation of the indications and monitoring of resistant strains.

The two commonly used preparations for hand hygiene and wound management include alcohol and chlorhexidine. However, these agents bear shortcoming in management of MRSA-colonised wound. Alcohol can denature proteins and numerous studies have proven the antimicrobial activity of alcohol.[12] However, alcohol may cause transient tingling discomfort when applied to wound. Chlorhexidine possesses antimicrobial activity to a wide spectrum of bacteria, fungi and virus. However, there may be concentration dependent skin irritation secondary to chlorhexidine, especially the 4% preparation.[13]

On the other hand, NTAS may be an ideal dressing material because it possesses antibacterial property, facilitates easy wound management and inspection, and improves quality of life as the pain associated with conventional wound dressing can be avoided. NTAS causes no serious adverse reaction to patients, and shortens the wound healing by inhibiting the growth of bacteria.[14] Patients are able to perform wound dressing at home, which in turn reduces the attendance to government clinic for wound management and enhances patients' satisfaction. NTAS can be applied to area where traditional dressing may be difficult to perform e.g. axilla, vulva, groin and joint. While systemic antibiotics may create side effects and development of resistant strain, NTAS is not associated with development of resistant strain. NTAS possesses broad-spectrum antibacterial property as the electrostatic interaction between the positive charge of NTAS and negative charge of the microorganism cell membrane are the intrinsic nature and unchangeable. It is a safe, effective and convenient alternative to conventional antibiotic treatment on wound infection. Further prospective randomised controlled studies are necessary to compare the outcome between wound dressing with NTAS and conventional nurse-led wound dressing in order to further delineate the role of NTAS in wound healing and the effectiveness on wound infection.

Moreover, JUC has been shown to promote wound healing and growth of granulation tissue, to decrease wound pain, and to decrease incidence of dermatitis in the peri-colostomy skin.[15,16] A systematic review on the use of antimicrobial urinary catheters to prevent catheter-associated urinary tract infection showed that urinary catheter coated with antimicrobial material could prevent bacteriuria in hospitalised patients during short-term catheterisation.[17] Though NTAS was not included in the studies, a randomised controlled study conducted in the Mainland China has shown the role of JUS (another name of JUC) on prevention of formation of a bacterial bio-film and reduction of the incidence of catheter-associated urinary tract infection.[18]

In summary, NTAS may play a role in reducing the use of antibiotics in wound infection, and combating the development of resistant strains associated with injudicious use of antibiotics. Wound care with NTAS led by patients is feasible and may carry financial implications on healthcare system by reducing the demand on the service of government clinics. Further prospective clinical trials are needed to fully investigate the effectiveness and applicability of NTAS on wound management in hospital and community setting.

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由社区感染的抗甲氧苯青霉素金黄葡萄球菌(CA-MRSA)导致的皮肤及软组织发炎的新前景:纳米科技抗菌喷雾剂

KA Wan 温光安, MY Ng 吴美儿,YT Wong 王友德

抗甲氧苯青霉素金黄葡萄球菌在社区和医院的流行率有上升趋势。抗药性的产生可能与广泛使用抗生素有关。作为一种物理性的抗菌剂，纳米科技抗菌喷雾剂(NTAS)是一种另类的伤口处理抗菌方式。我们在此报告一个使用 NTAS 治疗受 MRSA 感染的皮肤脓肿病例。NTAS 拥有强力和广谱的抗菌效力，且不会导致抗药性及极少副作用。再者，NTAS 能促进家居口护理，因而减少对公共健康资源的依赖。NTAS 在减少使用抗生素方面的临床角色值得更深入研究。

关键词:脓肿、抗菌剂、抗药性、伤口感染

引言

自数十年前第一种抗生素青霉素被发现以来，抗生素在治疗和预防微生物感染中发挥了重要作用。青霉素曾是对抗金黄色葡萄球菌的高效药物，但由于抗生素的过度使用，在自然选择压力下，耐药菌株逐渐出现。1944 年首次发现产青霉素酶菌株[1]，随后出现了耐甲氧西林金黄色葡萄球菌（MRSA）[2,3]。MRSA 于 1960 年代首次被发现，最初仅出现在医疗机构中，且患者多伴有感染风险因素。然而，在接下来的四十年间，MRSA 逐渐成为社区健康问题，感染范围扩展至无风险因素的健康人群。MRSA 在医疗机构和社区环境中的流行率均呈上升趋势[4]。

为应对耐药性问题并减少抗生素滥用，新一代抗生素及用药指南相继推出。然而，耐药菌株仍在不断演变，例如用于对抗 MRSA 的万古霉素后出现的耐万古霉素金黄色葡萄球菌（VRSA）。此外，新一代抗生素可能伴随副作用及更高的治疗成本。

皮肤及软组织感染（SSTI）是急诊医师日常实践中最常见的病症之一。在科学家研发强力抗生素对抗耐药菌的同时，纳米抗菌喷雾剂（NTAS）可能成为医学领域的突破。

我们已通过切开引流联合 JUC（一种 NTAS）成功治疗十余例 MRSA 相关皮肤脓肿病例，本文报告其中一例。

病例

一位 55 岁的先生头皮肿胀五天。他无明显的既往病史，无 MRSA 感染的病史。在此次皮肤和软组织感染之前，无住院治疗、手术或导尿管插入史。检查时发现头皮脓肿尺寸为3厘米。根据无菌术进行切开引流术。用拭子对脓肿腔进行取样，样本被送去进行培养及药敏试验。最初，每天在普通科门诊

进行伤口填塞，并使用生理盐水敷料。切开引流术后三天，培养结果证实存在 MRSA。证实了社区获得性 MRSA （CA-MRSA）感染。同一天进行随访。伤口状况令人满意，有少量分泌物，无伤口感染的临床证据（图 1）。

该患者接受了在家使用JUC喷雾剂用于伤口护理的培训，医护人员向他展示了一次程序。标准化的，一目了然的手册帮助提高患者的依从性和信心。病人被要求每天三次使用JUC。在每次使用JUC之前，患者只需用普通肥皂或香波清洁伤口。然后用干净纱布让伤口干燥。随后将JUC喷到伤口腔中。一般情况下，喷洒一下或两下即可，但如果开始时是较大脓腔，则需喷洒更多下。提供喷雾喷嘴和填塞的纱布是因为深腔和分泌物的存在。无其他治疗形式（包括抗生素）。在手术后第9天和第13天随访，伤口愈合情况令人满意，再次进行伤口取样，未发现细菌生长（图2和图3）。他很满意伤口护理的便利性，他可以在镜子前自行对头皮伤口喷洒JUC。

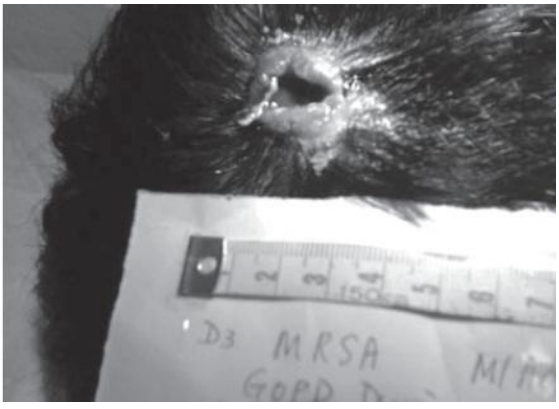

图 1 术后第 3 天

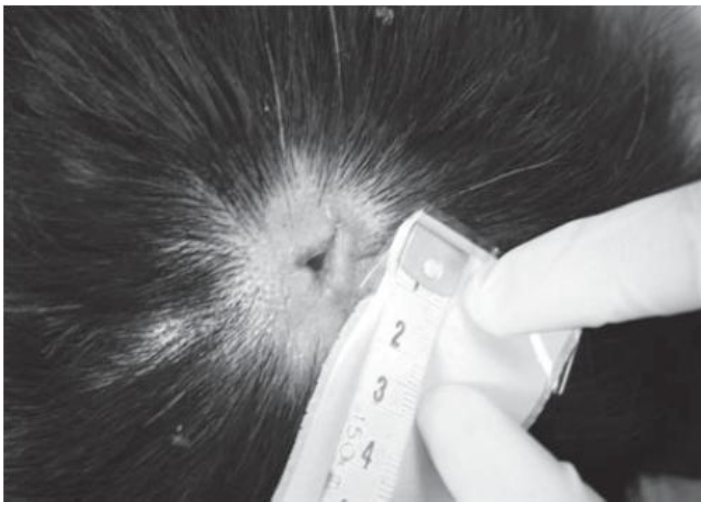

图 2 术后第 9 天

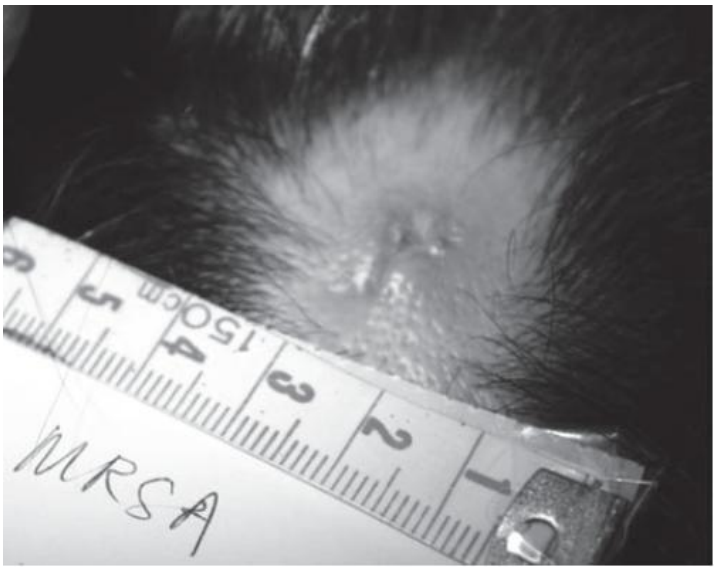

图 3 术后第 13 天

讨论

JUC 作为一种纳米抗菌喷雾剂（NTAS），已在我们科室用于伤口护理一年有余。该产品于 2002 年首次研发，并已通过美国食品药品监督管理局认证，可作为普通外科和整形外科的敷料产品使用。JUC 的主要成分为有机硅季铵盐和蒸馏水，通过纳米制造技术制备而成。其纳米级阳离子结构能溶于水形成

喷雾剂型。JUC 通过物理机制在皮肤和伤口表面发挥抗菌作用，因此可被视为一种物理抗菌剂[5]。

细菌作为单细胞微生物，其表面带有负电荷。NTAS 所含的纳米级阳离子可通过静电吸附作用与带负电的微生物结合。这种静电作用能破坏细菌细胞膜，并干扰线粒体酶活性，从而实现广谱杀菌效果。体外实验已证实 NTAS 对金黄色葡萄球菌、肠杆菌和铜绿假单胞菌等具有显著杀灭作用[5]。当 NTAS 喷洒并附着于皮肤、黏膜或伤口表面时，会固化形成一层看不见的抗菌膜。这层抗菌膜不仅能杀灭细菌，还能防止细菌侵入皮肤或伤口[5]。

JUC 最初用于二度烧伤患者的治疗。后来因其广谱抗菌特性，逐渐应用于感染性伤口及 MRSA 相关皮肤脓肿的切开引流术后处理。JUC 的抗菌效果可持续 8 小时，较普通消毒剂更为持久[5]。这类患者可在家中使用 JUC 进行伤口护理，医护人员会指导他们使用普通肥皂清洁伤口后再喷洒 JUC。待伤口干燥后，将喷雾瓶置于距皮肤或黏膜约 7 英寸（18 厘米）处直接喷洒。一般喷 1-2 次即可，但较大脓肿初期可能需要更多剂量。对于较深的脓腔，还会提供延长喷嘴，并指导患者正确的伤口填塞技巧。同时建议患者保持个人卫生，正常沐浴。JUC 每日可使用 2-3 次。需定期到急诊科复诊，以监测治疗依从性、检查伤口处理技术并评估愈合情况[5]。

除治疗 MRSA 感染外，NTAS 在预防疾病传播方面也可能发挥作用。伤口 MRSA 定植是造成交叉感染和社区传播的重要风险因素。接触受污染的敷料、毛巾或人手都可能导致感染扩散。预防 MRSA 传播的基本措施包括洗手、规范伤口护理和保持良好卫生习惯。使用 NTAS 清除伤口及其他携带部位的 MRSA，可能有助于控制其在社区的传播。

美国疾病控制与预防中心建议，在采取感染控制措施后，对反复发生皮肤软组织感染（SSTI）的个体进行去定植治疗[6]。目前的去定植方案包括：2%莫匹罗星鼻腔涂抹（每日两次，连续 5 天）联合 4%氯己定每日洗浴[7]。然而，一项涵盖 1966 至 2003 年随机对照试验的 Cochrane 系统评价显示，尚无足够证据支持使用局部或全身抗生素来清除 MRSA 定植。此外，这些方法可能导致严重不良事件，包括耐药菌株的出现[8]。已有关于莫匹罗星和氯己定耐药的报道[6,9]。

一项前瞻性研究调查了入院时 MRSA 鼻腔携带率及住院期间定植率。鼻腔携带者接受 5 天莫匹罗星软膏鼻腔涂抹，并交替使用 4%氯己定和普通肥皂洗浴。一周后近 99%的患者实现去定植，但再次定植现象常见，且发现耐药菌株[10]。另一项较新的随机对照试验显示，莫匹罗星软膏对持续携带者的金黄色葡萄球菌去定植有效，但 90 天后效果减退[11]。针对特定患者群体选择性短期使用莫匹

罗星可能有效，但需进一步研究其适应症并监测耐药菌株。

手卫生和伤口护理常用的两种制剂是酒精和氯己定。然而，这些药物在处理 MRSA 定植伤口时存在缺陷。酒精能使蛋白质变性，大量研究证实其具有抗菌活性[12]，但用于伤口时可能引起短暂刺痛感。氯己定对多种细菌、真菌和病毒具有抗菌作用，但可能因浓度依赖性引起皮肤刺激，尤其是4%的制剂[13]。

相比之下，NTAS 可能是理想的敷料选择，因其具有抗菌特性、便于伤口护理和观察，并能提高生活质量（避免传统敷料更换时的疼痛）。NTAS 不会对患者造成严重不良反应，且通过抑制细菌生长加速伤口愈合[14]。患者可自行在家护理伤口，减少到政府诊所换药的次数，提升满意度。NTAS 适用于传统敷料难以处理的部位（如腋窝、外阴、腹股沟和关节处）。全身抗生素可能引起副作用并导致耐药菌株出现，而 NTAS 则无此风险。NTAS 的广谱抗菌特性源于其带正电的纳米阳离子与微生物带负电的细胞膜之间的静电作用，这一机制是固有且不可改变的。NTAS 是安全、有效且便捷的伤口感染治疗替代方案。需进一步开展前瞻性随机对照研究，比较 NTAS 与传统护士换药的疗效，以明确 NTAS 在伤口愈合中的作用及其对伤口感染的效果。

此外，研究显示 JUC 能促进伤口愈合和肉芽组织生长，减轻伤口疼痛，降低造口周围皮炎发生率[15,16]。一项关于抗菌导尿管预防导管相关尿路感染的系统评价表明，涂有抗菌材料的导尿管可短期降低住院患者的菌尿症发生率[17]。虽然这些研究未纳入 NTAS，但中国大陆的一项随机对照试验证实，JUS（JUC 的别称）能预防细菌生物膜形成，降低导管相关尿路感染风险[18]。

总之，NTAS 或能减少伤口感染中的抗生素使用，遏制因抗生素滥用导致的耐药菌株出现。患者主导的 NTAS 伤口护理可行，且通过降低对政府诊所服务的需求，可能对医疗体系产生经济影响。需进一步开展前瞻性临床试验，全面评估 NTAS 在医院和社区伤口管理中的有效性和适用性。

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