

Novel micropore particle technology for spinal cord injury chronic wound healing: a new paradigm?

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ABSTRACT

Current management of chronic wounds involves regular wound cleaning, antiseptic dressings and, when indicated, antimicrobials. Micropore particle technology (MPPT) is a novel concept for wound healing, aiming to bolster the action of the immune system by disrupting the wound biofilm and restoring the microbiome. Amicapsil is the first MPPT product licensed for clinical use. Patients with a spinal cord injury (SCI) are more likely to develop chronic wounds due to downregulation in their immune response increasing the risk of a minor wound, such as pressure sore, developing into large, non-healing wounds. At the Defence Medical Rehabilitation Centre (DMRC) Stanford Hall, patients with SCI often have chronic wounds causing pain, becoming infected and preventing full engagement with effective rehabilitation. We report on the first case of treatment with Amicapsil at the DMRC Stanford Hall and review MPPT as a potential new paradigm for the treatment of wound healing.

INTRODUCTION

Chronic wounds are those which fail to heal within 3 months, having not progressed through the traditional stages of inflammation, proliferation and maturation.¹ This phenomenon, unique to humans, is likely as a result of the multifactorial interaction between bacterial colonisation of the wound, an altered cellular and stress response, repetitive ischaemic-reperfusion injury and local tissue hypoxia.² The current paradigm for managing chronic wounds involves regular wound cleaning and the use of antiseptic dressings—with the addition of antimicrobials when indicated, despite a lack of evidence from systematic reviews and meta-analyses of randomised controlled trials for its efficacy.^{3,4}

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Key messages

- ⇒ Current wound management involve regular cleaning, antiseptic dressing and antimicrobials when indicated despite poor evidence. Micropore particle technology (MPPT) offers an alternative to this.
- ⇒ MPPT works by penetrating and disrupting the biofilm of the wound, enabling the natural immune response to clear the infection and restore the natural microbiome.
- ⇒ Patients with spinal cord injury (SCI) develop reduced immune response and are more likely to develop chronic wounds from minor injuries, restricting rehabilitation and reducing independence.
- ⇒ MPPT has been successfully used at the Defence Medical Rehabilitation Centre Stanford Hall and could potentially improve chronic wound management in patients with SCI there.

Micropore particle technology (MPPT) is a novel concept for wound healing, which aims to bolster the action of the natural immune system. Its mode of action is based on the disruption of the wound biofilm, allowing absorption and evaporation of wound exudate, toxins and harmful enzymes from the wound and the infiltration of immune cells.⁵ This allows the host immune system to work at the wound, clear the inflammatory response and commence the proliferation stage.¹ The first-in-class product Amicapsil (Willingsford, Southampton, UK) has been seen to improve healing rates by 60% compared with existing therapies with no known cytotoxicity.^{6,7}

In the Complex Trauma ward at the Defence Medical Rehabilitation Centre (DMRC) Stanford Hall, patients with spinal cord injury (SCI) and other trauma-related sequelae often have chronic wounds causing pain, becoming infected and preventing full engagement with effective rehabilitation. Amicapsil has the

potential to improve this. We report on the first case of treatment with Amicapsil at DMRC Stanford Hall.

Background

Delayed healing of chronic wounds places a burden on individuals, especially those at high risk, such as patients with SCI, and healthcare systems. It leads to significant discomfort, distress and morbidity to patients. In the UK, there are approximately 2.2 million wounds per annum, costing £5.3 billion a year, of which over a third are chronic.⁵

The microbiome of the skin interacts, and is synergistic with, the immune system. A healthy microbiome is diverse, balanced and constantly changes in response to factors such as environment, health and hygiene.⁵ A microbiome lacking diversity, as a result of indiscriminate or inappropriate use of antiseptics and antibiotics, is at risk of infection, especially if one or two species of bacteria begin to dominate.⁸ Chronic wounds are often caused by persistent or recurrent infection, prolonged by the action of a biofilm nullifying effective treatment.

The formation of a biofilm leads to continued infection and delayed healing. Biofilms are made up of communities of microorganisms, protected by an extracellular matrix of slime in the wound, created during the chronic phase of a wound. This barrier can tolerate the host immune defenses and applied topical antimicrobials and therefore make the treatment of such wounds very challenging.⁹

The current methods of wound treatment, using dressings (including antimicrobial, silver or honey), antiseptic washes and antimicrobial powders, have a poor evidence base and are potentially detrimental to the host immune system while leading to cytotoxic effects and antimicrobial resistance.^{3,5}



Figure 1 3 Oct 2019, before treatment commenced. Length 40 mm, width 10 mm, sinus 40 mm (medial course).



Figure 2 4 Nov 2019. One month after treatment commenced. Sinus healed up. Epithelial tissue evident throughout, dimensions of wound reduced, exudate reduced.

Furthermore, patients who have sustained a SCI are more likely to develop chronic wounds as a result of SCI-induced immune depression syndrome (SCI-IDS).¹⁰ SCI-IDS, caused by loss of neuronal regulation of the immune system below the injury, results in a reduction in the ability to combat infection, delays wound healing and therefore increases the propensity of minor wounds, such as a pressure sore, developing into large, non-healing wounds.¹⁰

Case study

A Service Person in his 30s sustained a complete SCI in 2016. In early 2019, he developed an abscess, requiring incision and drainage. It was packed with Sorbsan ribbon and covered with secondary dressings and began to heal with high levels of wound exudate. In discussion with the plastic surgeons, a further surgical procedure was performed for wound closure in June.

Post surgery, a haematoma formed followed by the wound spontaneously fully reopening. Topical negative pressure wound treatment (TNPWT) was commenced as a second-line treatment. By September, a chronic wound had



Figure 3 8 Dec 2019. Wound decreased in size dramatically.

developed which continued to fail to heal, and the TNPWT was stopped. The wound was subsequently managed with Aquacel ribbon packing, covered with Tegaderm foam or Tielle Lite as a secondary dressing to manage a large amount of exudate. Input was also sought from wound care specialists to assist the nursing staff.

These treatment regimes were unfortunately unsuccessful in wound healing and failed to manage the amount of wound exudate or the strong associated odour. The chronicity of the wound, especially the smell, impacted negatively on the psychological well-being and physical rehabilitation of the patient. He required increased bed rest, reducing his time in the wheelchair, and leading to a dramatic loss of independence.

The patient was offered a trial of Amicapsil therapy commencing in October 2019 (Figure 1). This was initially a twice-daily, non-sterile procedure, with Amicapsil applied by a nurse, after the wound was cleaned with tap water, in the morning and evening. During the application of Amicapsil, the vial was sprinkled over the wound, coating the wound surface and surrounding areas with a thin layer of the powder. After application of Amicapsil, the wound would ideally be left open to air, but if needed for rehabilitation purposes, a thin lint-free gauze, allowing airflow, was applied to manage exudate.

The wound was reviewed daily by nursing staff, weekly on the consultant ward round, and photographs were taken at regular intervals to provide a record of changes in the wound size, shape and exudate production. As part of the trial, representatives of Willingsford also monitored the wound remotely via emails with the patient.

After the first 4 weeks, there was a dramatic improvement in the wound with dimensions and exudate levels substantially reduced and epithelisation visible (Figure 2). Within a week of starting, the wound odour had disappeared. As a result of this improvement, the patient was happy to continue with the trial, especially as the use of an air pump into the gauze dressing allowed wound healing to continue while having the extended periods in his wheelchair. As the wound continued to improve, Amicapsil administration decreased to once daily (Figure 3).

After 3 months, there was a minimal residual open area to the wound with a very low exudate level (Figure 4), and by 6 months, full resolution of the wound was nearly reached with the wound in the remodelling stage (Figure 5). The patient



Figure 4 11 Jan 2020. Residual track present.

encountered no adverse effects as a result of his Amicapsil therapy.

What is MPPT and how does it work?

Amicapsil is the first MPPT product licensed for clinical use by the Food and Drug Administration. It is an inactive, neutral white powder, applied by hand and requires a constant flow of air once applied.⁵ It works in conjunction with the host immune system by disrupting the wound biofilm and helping restore the microbiome. This action occurs by penetrating and perforating the biofilm surface, and allowing the host immune cells (including macrophages, neutrophils and other cells of the inflammatory response) to infiltrate the chronically colonised wound.⁵

The Amicapsil particles draw moisture up through capillary action (mimicking



Figure 5 26 Apr 2020. Wound nearly completely healed.

Table 1 Approximate monthly cost for the different treatments in this patient

Product	Monthly cost (£)
Wound dressing	283.20
Amicapsil (small wound, once daily)	270.00
VAC dressing	878.70
Amicapsil (large wound, twice daily)	1080.00

leukotriene action), drawing the excess fluid up and allowing it to evaporate, hence the need for airflow over the wound site in order to maintain capillary action.⁵ Once the inflammatory response has cleared the colonised bacteria, then micro-biome rebalancing can occur.

The introduction of neutrophils and macrophages into the wound re-triggers the inflammatory phase of wound healing. The former is indicated in chemosignalling, vascular permeability and free radical formation, and the latter is essential in the clearance of debris and bacteria, via phagocytosis, fibroblastic action, and the generation of chemoattractants and other immune cells, before triggering the proliferative phase.¹

For chronic wounds, the proliferative phase is key, as it generates epithelialisation and therefore sets the conditions for healing. Again, macrophages, fibroblasts and their related cells play a key role in the matrix formation, angiogenesis and, eventually, wound contraction with visible remodelling and maturation.¹

A comparative study was performed with 266 patients with acute wounds of different aetiologies, between Amicapsil (n=88), Gentaxan (antibiotic based powder, n=90) and Iodidocerin (antiseptic-based powder, n=88). It demonstrated 60% improved wound healing times, with MPPT taking 3.0±0.9 days compared with 7.0±1.2 for Gentaxan and 8.0±1.1 for Iodidocerin.⁶ This study demonstrates noticeable improvement in wound healing using MPPT compared with antibiotic and antiseptic formulations. Similar findings were seen in a cohort of nine acute dehiscence surgical wounds⁷ and an individual case study of a patient with SCI with a chronic wound.¹¹ The literature also describes much shorter duration of treatment required for acute wounds (days) compared with chronic (months).^{6 7 11}

Implications for military practice

Amicapsil has potential benefit for the patients of DMRC, especially those who have developed SCI-IDS and have chronic, non-healing wounds. These potential benefits include reducing the number and duration of wound-related admissions to

DMRC, earlier commencement of effective rehabilitation, decreased pain and increased patient mobilisation. In complicated wounds requiring surgical input for secondary complications such as osteomyelitis, Amicapsil can be used to prepare for surgery by reducing any concurrent tissue infections.⁵ There is also a potential role for Amicapsil in the treatment of acute wounds to prevent progression into chronicity. Further experience is required with Amicapsil at DMRC to confirm these assumptions.

DISCUSSION

In this single case study, there were benefits seen following use of Amicapsil, professionally, clinically and for the patient. The nurses at DMRC developed knowledge and skills in a new wound care practice. This patient had a chronic wound, unresponsive to traditional treatment for 7 months. After 1 month of Amicapsil, significant improvement was noted, with resolution after 6 months. It has empowered the patient to have increased involvement in his care and fully engage in his overall rehabilitation potential.

Cost estimations can be made, but without formal head-to-head studies between MPPT and existing therapy, no firm cost-benefit analysis can be made. At the time of writing, a vial of Amicapsil costs £78. When the Amicapsil trial commenced, a vial lasted four applications (approximately £19.50/application), but this increased to eight after the first month's treatment and subsequent decrease in wound size (approximately £9.75/application). By way of comparison, the initial wound management routine (packing and gauze), performed twice daily, cost approximately £4.72/application and each daily vacuum-assisted closure (VAC) change cost approximately £29.29/application (dressing and canisters). The approximate monthly cost of each is summarised in table 1.

The comparative study performed by Bilyayeva *et al.* demonstrated that the improvement in wound healing had a correlating reduction in the number of hospital days, with 14.6±5.6 for MPPT, 21.0±10.7 for Gentaxan and 24.0±7.9 for iodine/DMSO.⁶ This has relevance

for inpatient admissions in DMRC Stanford Hall, at approximately £500/night (2010/2011 costing).¹²

This is a single case study, reporting the use of Amicapsil in a new population. Inference has been drawn from similar populations^{6 7 11}; however, there is still limited evidence pertaining to the use of MPPT and further evidence is required.

CONCLUSIONS

Amicapsil has the potential to improve the management of chronic wounds at DMRC with its ability to heal wounds quicker. Patients undergoing rehabilitation will be able to engage fully sooner, with earlier intervention reducing the need for surgical interventions, secondary complications, treatment duration, cost and improve patient quality of life and effective rehabilitation. However, more cases of successful Amicapsil therapy need to be seen showing sustained benefits before practice can be fully changed. A case series of other patients undergoing MPPT treatment at DMRC is planned.

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