Reduced cellular toxicity and clinical performance of Atrauman® Ag

There is currently a wide range of silver-containing dressings available for the treatment of critically colonised and infected wounds. As released silver ions are known to be cytotoxic to human cells, the ideal antimicrobial dressing should balance sustained antimicrobial activity against cytotoxicity. It will also have other desirable features such as minimising trauma on application and removal, and conformability to the wound bed. Atrauman® Ag (Hartmann) non-adherent primary contact wound dressing is one such dressing. Its properties and their supporting evidence will be detailed in this article.

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KEY WORDS
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Clinical efficacy

Silver is well known for its antimicrobial properties and there are now several silver-containing dressings available for the topical management of patients with critically colonised and infected wounds.

This availability is encouraging a wider application of silver-containing dressings in acute and chronic wounds, and now they are used extensively for wound management, particularly in burn wounds (Ross et al, 1993; Caruso et al, 2004), chronic leg ulcers (Karlsmark et al, 2003), diabetic wounds (Hilton et al, 2004) and traumatic injuries.

The extensive use of silver dressings is reflected in the increased NHS expenditure; £25 million or a quarter of the total cost of all dressings in 2006/7 was spent on silver-containing wound dressings (Drug and Therapeutic Bulletin [DTB], 2010).

The increased use of silver-containing dressings is largely attributed to its bactericidal efficacy at low concentration, and its relatively limited toxicity to human cells.

This recent renewed interest possibly arises from advances in impregnation techniques and polymer technologies, coupled with the increase in prevalence of bacterial resistance to antibiotics.

The dressings available vary widely in structure, formulation and concentration of silver used. The carrier dressing component can also differ, and may be made from a variety of materials including nylon, mesh, hydrocolloid or methylcellulose.

The increased use of silver-containing dressings is largely attributed to their bactericidal efficacy at low concentration, and their relatively limited toxicity to human cells. However, efficacy and toxicity can vary between dressings and this should be considered when selecting a product.

The ideal silver-containing dressing should release as many silver ions into the environment as are necessary to produce an effective bactericidal action, while having limited cell toxicity (Ziegler et al, 2006; Madden et al, 1989). It should also:

- Have sustained antimicrobial activity
- Provide a moist wound healing environment
- Allow consistent delivery over the entire surface area of the wound
- Allow monitoring of the wound with minimum interference
- Manage exudate if appropriate
- Be comfortable during wear time
- Conform to the wound bed
- Provide an effective microbial barrier
- Absorb and retain bacteria
- Avoid wound trauma on removal (Malliard and Denyer, 2006).

Figure 1. Atrauman® Ag.

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Atrauman® Ag (Hartmann) is a silver-containing dressing that has these key attributes and is used for the atraumatic treatment of colonised and critically colonised wounds.

Atrauman® Ag

Atrauman Ag is a non-adherent primary contact layer that is impregnated with silver.

The dressing consists of a coarsely woven water repellent polyamide textile, that contains pores that are 1mm in diameter. The pores allow the flow of exudate and air through the dressing into the secondary dressing. The polyester fibres that make up the dressing provide a high degree of conformability, and prevent granulation tissue from penetrating the dressing, thus helping to minimise pain and trauma on removal.

The dressing fabric is also impregnated with neutral triglycerides that enhance its non-adherent properties and keep the wound margins soft and supple, thereby avoiding scar tissue contraction.

Antibacterial properties

The dressing is coated with metallic silver that is chemically bound to the support fabric.

Atrauman Ag is only bactericidal upon direct contact with bacteria. When the dressing comes into contact with wound exudate, Atrauman Ag forms silver ions at the wound-dressing interface, killing bacteria on contact.

The majority of silver ions are kept within the dressing with only small concentrations reaching the wound. Due to this local restriction of silver ion release, the cytotoxicity of Atrauman Ag is low.

A study by Ziegler et al (2006) compared the antimicrobial activity and cellular toxicity of Atrauman Ag with that of two widely used silver-containing dressings, Acticoat® (Smith and Nephew) and Actisorb™ Silver 220 (Systagenix).

Figure 2. Atrauman® Ag non-adherent dressing impregnated with silver.

Atrauman Ag was found to be effective against all bacteria tested, completely eradicating *K. pneumoniae* within two hours of contact with the dressing, *S. aureus* after four hours and all microorganisms within 24 hours.

Antimicrobial activity of the Atrauman Ag was tested against a wide variety of bacteria, including *Staphyloccus aureus,* methicillin-resistant *S. aureus*, *S. epidermidis*, *Klebsiella pneumoniae, Pseudomona aeruginosa, Escherichia coli* and *Bacillus subtilis*. Cytotoxicity of the three different dressings was tested using the human keratinocyte cell line HaCaT.

Atrauman Ag was found to be effective against all bacteria tested, completely eradicating *K. pneumoniae* within two hours of contact with the dressing, *S. aureus* after four hours and all microorganisms within 24 hours. The duration of the antimicrobial efficacy was demonstrated with Atrauman Ag eradicating both *S. aureus* and *K. pneumoniae* despite repeated inoculation with bacteria on the same dressing for nine days.

Low cytotoxicity

In terms of cytotoxicity, Atrauman Ag was found to have the lowest cytotoxic effect with 90% of the keratinocytes remaining viable, compared with 80% for Actisorb Silver 220. Acticoat was the most cytotoxic, eradicating all but a few keratinocytes. Cytotoxicity was correlated with the concentration of silver ions released. Results indicated that Acticoat released 71.4ppm, Actisorb Silver 220 0.38ppm and Atrauman Ag 2.3ppm. The investigators concluded that Atrauman Ag had a superior profile of antimicrobial activity over cellular toxicity (Ziegler et al, 2006).

As with other primary dressings, Atrauman Ag is used in combination with a secondary dressing, and can be used in combination with hydroactive and traditional wound dressings, such as calcium alginates, swabs, foam dressings and absorbent wound dressings. The clinician should select an appropriate secondary dressing depending on the wound's status, and may use the previous wound dressing with Atrauman Ag if it is temporarily indicated.

Wound exudate, dead bacteria and endotoxins pass through the pores of Atrauman Ag and are absorbed by the secondary dressing.

Atrauman Ag is indicated for the

topical treatment of critically colonised or infected, superficial and deep wounds alone, or in conjunction with systemic antibiotics. There are no known contraindications.

The dressing is available in 5x5cm, 10x10cm and 10x20cm sizes.

Clinical evidence for the use of Atrauman Ag

Ziegler et al (2006), as part of their previously described cytotoxicity study, also assessed the clinical performance of Atrauman Ag in 86 patients with traumatic and non-healing wounds of various aetiologies. The wound state was evaluated for three consecutive dressing changes.

The dressing was found to result in an improvement in wound conditions over the course of three dressing changes. The amount of slough present in the wounds was reduced from 59.2–35.8%, granulation tissue increased from 27– 40%, and epithelialisation increased from 12.1–24%. Exudate levels also reduced from 19.5% of wounds to 2.3% after three dressing changes. Patient-reported pain sensation during dressing change decreased from 78–28.7% during the course of the three dressing changes. Of the clinicians involved in the study, 83% reported that in comparison to the initial examination, the condition of the wounds had improved, although surface measurements remained unchanged.

A multicentre clinical observation study in 624 patients also confirmed the efficacy and tolerability of Atrauman Ag (Kopp, 2005).

The wounds treated consisted mostly of chronic wounds, two-thirds of which were infected. Atrauman Ag was applied for an average of 23 days and a marked improvement in wound bed conditions was found following treatment.

There was a reduction in wounds completely and partially covered in necrotic tissue (9–2%, 24.7–0.8%, respectively). The number of wounds covered in slough was also reduced from 27–77%. The number of wounds with moderate, pronounced or complete epithelialisation increased from 4.5% to just below 45%. There was a marked reduction in wound exudate and an increase in granulation tissue. The use of Atrauman Ag also saw an improvement in the reported incidence of pain (17% of patients reported no pain at the start of the study, compared with 53.5% at the end). At the end of the study, 80% of the wounds were free from the clinical signs of infection. The condition of the periwound area also showed marked improvement. Both physicians and patients rated the tolerability of treatment with Atrauman Ag as good or very good.

Conclusion

The availability of silver-containing dressings has significantly improved the management of critically colonised and infected wounds (Landsdown, 2004). The silver ions responsible for the antibacterial action, however, can be toxic cells in the wound. The ideal silver dressing should release only an amount of silver ions to produce an effective bactericidal action (Kopp, 2005). Atrauman Ag was developed with this in mind, and its low toxicity and antibacterial efficacy have been demonstrated in both laboratory and clinical settings (Kopp, 2005; Ziegler, et al, 2006). WUK

Key points

- There are numerous silver-containing antimicrobial dressings available for the treatment of critically colonised and infected wounds.
- Dressings vary in how the silver is formulated, impregnated and released, and in the carrier material used.
- Silver ions can be cytotoxic to wound cells so the perfect dressing must balance antimicrobial activity with cell cytotoxicity.
- Atrauman Ag effectively reduces wound bioburden with a low level of toxicity (Ziegler et al, 2006).
- These findings have been confirmed in a multicentre observation study of 624 patients with chronic, infected wounds who showed a marked improvement in wound condition after an average of 23 days of treatment with Atrauman Ag.

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