Research on wound dressing interface

Introduction

The wound dressing interface represents the zone of contact between the wound surface and the material applied to it. Professionals choose the right dressing after a clinical wound assessment bearing in mind that the interface is of great importance. Pain management, silver ions or nanodelivered particles, control of exudates and bacteriological balance using antimicrobial materials are all factors impacting on the dressing surface. The dressing interface is so important that some medical materials are specifically designed to relieve pain at dressing change, others to deliver medication continuously, or to increase granulation tissue and enhance the stimulation of fibroblasts. The shape of the dressing, the chemical content and adherence to the tissue are important. Mechanical forces imposed on the wound by the dressing are also relevant, like the foam used in negative pressure therapy.

This area is of intense interest to manufacturers who have understood perfectly that moist wound healing was essentially linked to the dressing interface.

Basic physico-chemical principles used for wound dressing interface

Several basic principles drive the wound-dressing interface. These are either very simple, like the mechanical force exerted on the surface of the wound (from absorptive osmotic effect to a permanent assisted suction when using negative pressure therapy), or more sophisticated, as the delivery of active agents (silver, ibuprofen), to the more rarely described biological enzymes coming from salivary glands of maggots or digestive collagenase secretions from krill enzymes.

The first dressing to have demonstrated an effect on absorption was hydrocolloid. Based on the gellification of carboxymethylcellulose (CMC), this material has completely transformed dressing use and was at the origin of the concepts of moist wound healing. The conflict between moist wound healers and conservative users of gauze started there and is still ongoing. Hydrofibre dressing was secondarily created using texturisation of CMC, an original dressing for an optimal regulation of humidity balance. However, odour and leakage are observed and create social difficulties.

The next step was the foam booming. Based on polyurethane technology, its development took place over two decades. Technology became more and more sophisticated, especially in the area of contact. Initially based on differences in the absorptive capacities of three superimposed hydrocellular layers, these medical materials became a source of huge interest when research on wound interface was developed. Silicone coating and safetac technology were steps forward in pain prevention at dressing change; foams progressively became sources of local delivery of agents like silver, ibuprofen or antiseptics. Algaines were also proposed with some changes in their composition, as well as hydrofibres.

Gauzes, size of the mesh and adhesion

Gauzes are regularly accused of provoking pain at dressing change. In recent work conducted by an expert group published in 2007, gauzes presenting large size pores were not considered ideal products, even if their coating prevented them from drying too fast.1 Dry gauzes are strongly adherent to the granulation tissue and it was demonstrated that removing gauzes was a source of trauma to fibroblastic cells, as well as keratinocytes.2 Basic gauzes, where vaseline or grease are just packed over the textile, are more likely to be removed quickly and will cause pain. A new class of dressings, called interface, was introduced, with the manufacture of a non-adherent dressing. This non-adherence is ideal in some products, like silicone dressings, and is linked to the power of loss of coating, following time and reduction of the size of mesh in other products.3-5

• Loss of coating during time is dependant on the local levels of exudate. When applied over dry wounds, the vaseline on hydrocolloid coated dressings will not become too gellified. On the other hand, when a heavy exudation is observed, the coating will quickly disappear and the dry gauze will provoke pain at removal.

• Reduction of the mesh size is technically preferable, and a series of newly developed dressings have a very small mesh, which induces less granulation tissue penetration and less pain when removed.

Hydrocolloid

The amount of gellification of hydrocolloid dressing is directly dependent on the amount of CMC present in the dressing. Thin hydrocolloids are less absorbent than thick hydrocolloids. This dressing is widely indicated and is reimbursed in most of the countries in the world, as its advantages on wound evolution have been fully demonstrated by evidence based medicine (EBM).
Hydrocolloids were demonstrated to be effective in prevention of transmission of germs, mainly due to the complete isolation obtained by adherence to the wound edges. Adherence is linked to the capacity of sticking, dependent on the type and amount of glue present in the material. In the initial period of use, the various used of highly adherent hydrocolloid were debated: they were found to be advantageous when applied to the sacrum or other areas exposed to external forces, but a cause of irritation of the periwound skin and sometimes allergy, whereas mildly adherent hydrocolloids were gentler on the periwound skin but sometimes subject to leakage. One of the remaining difficulties, even when using texturised CMC as in hydrofibres, is the level of saturation caused by exudates making this soft non-adherent dressing dry, sticky and a source of local hyperpressure if kept in place for too long.

**Foams, encapsulation and delivery**

Foam, derived from the chemical industry, arrived on the scene in the late 1980s. Some of the disadvantages observed with the use of hydrocolloids, such as odour and leakage, were not observed with the use of foam. These devices were chemically easier to work with and to use as a source of delivery. The encapsulation technique allows the manufacturer to charge the material with different components that may directly impact on the wound surface. A list of products can now be delivered with these foams.

Silver has been a source of controversy and debate. As the concept of critical colonisation has become more and more difficult to define in term of numbers of germs as well as in term of clinical situations, the antibacterial capacities of silver, even if perfectly demonstrated in vitro, were often unconvincing to clinicians in very different clinical situations in acute or chronic wounds. No highly statistical significance could be obtained with random controlled studies (RCT). It is still difficult to define the amount of silver required for a specific clinical situation: if the silver is maintained in the dressing (germs moving into the dressing to be killed); if the silver goes to the wound surface and kills the germs; or if the silver goes deep into the wound for its activity. There is an absence of strong evidence on the ideal active silver —, free silver ions, active silver ions, or nanocrystalline silver. Some recent works suggest that the main activity of silver could be linked to its anti-inflammatory properties rather than to its antibacterial activity.

There are still a series of unanswered questions concerning wound infection. Theories are numerous concerning biofilms, germ virulence and other factors observed in specific situations. The presence of germs on the wound surface or deeper around capillaries, especially in venous leg ulcers, has been suspected. The wound dressing interface is considered the main field of action for antibacterial or antiseptic agents. The use of systemic antibiotic therapy, too widely prescribed all over the world, is a source of resistance to germs prone to develop ecologic negative consequences.

Antiseptics act at the wound dressing interface, with some limitations — negative side effects on the fibroblasts and keratinocytes are well described. All care givers should know that these antiseptics should not be used at each dressing change, the flora being restored very quickly after elimination of germs by local application of polyvidone iodine or chlorhexidine.

The new generation of antiseptics prevent germ proliferation with highly diluted chlorhexidine, (less than 1%), combined with a surfactant which isolates the wound from contamination. It is thus based on a physical protective layer effect more than a biological effect on cells.

Ibuprofen is a recent source of interest, and has been incorporated into foam dressings. In a recent study it was demonstrated that the ibuprofen-foam dressing provided pain relief and reduced pain intensity without compromising healing or other safety parameters. In other words, ibuprofen locally delivered decreases chronic pain and pain during dressing changes.

**Negative pressure therapy**

When Alard developed a machine to suck on wounds in 1785, nobody could have anticipated the worldwide success of negative pressure therapy some centuries later. The VAC system has established standards of care in modern traumatology, on the battlefield as well as in fractures and loss of tissue from road traffic accidents. An interesting sideline of the system is the possibility of extracting from the wound exudates and their inflammatory corgete of metalloproteases. The other interesting phenomenon is the permanent mechanical effect exerted on the wound surface. This mechanical stimulation is the source of several research papers attempting to answer different related questions:

- How to guarantee that the level of pressure applied on the wound is identical to the one observed at the machine level?
- How does the pressure influence the wound evolution?

Some of the mechanisms were detailed in successive articles. The foam itself, with its specific porosity and the capacity to allow fluids to circulate freely from one side to the other (open porepolyurethane foam), present some changes observed immediately after application of negative pressure. The pores, initially round, become oval when submitted to negative pressure. This mechanical stimulation has direct consequences on cell proliferation and differentiation, leading to a permanent suction all around the foam. These changes were considered very important in producing the clinical effects of VAC therapy. Pain prevention at dressing change may be a problem, and controversies exist on the need to insert a dressing interface between the wound and the foam. When compared to the techniques using gauze as a medium in applying negative pressure therapy, nothing different was described at the cellular level as well as the clinical level. Clinical indications include difficult to heal wounds, mainly trauma and war wounds, but also thoracic wounds, pressure ulcers and abdominal postoperative dehiscences.

**Electrical stimulation**

Physiological electrical current exists over intact skin. When a break is created on the skin surface, the electrical current is changed. When applied over a wound surface, an external electrical current demonstrated an effect of stimulation on cell movements. Cells in the wound move towards the cathode, as observed by some authors. The possibility of applying this modality in a clinical setting is a source of intense speculation (and some confusion). It has been proposed that the use of some dressings (foams) directly applied over the wound surface may act like the negative electrode; other companies propose inserting the electrical source directly into the dressing. Some authors, based on two successive metananalyses,
consider the present level of evidence based medicine (EBM) as very high; others consider that supplementary evidence is needed. Some efficacy has been demonstrated on difficult to heal pressure ulcers, leg ulcers. Clinical trials are in progress.

Chemical mediators: a new era at wound dressing interface?

It has been postulated for over ten years that applying a direct chemical therapeutic factor on a wound recalcitrant to any other treatment (via the normal microvascularisation) may be beneficial. PDGF-BB was evaluated as efficient on difficult to heal leg ulcers and pressure ulcers. Other synthesised growth factors, like b-FGF are under evaluation, some others having not demonstrated enough significant results (KGF, EGF).

Excessive levels of matrix metalloproteinases (MMPs) present in chronic wounds may prevent wound closure. Reducing detrimental components will be key in healing chronic wounds. Some wound dressings have been observed clinically to resolve inflammation and appear to aid healing in acute and chronic recalcitrant wounds (Elta protein).

In a recent publication, Baskevitch et al evaluated the effect of a dressing including proteases on detrimental and beneficial wound healing components such as MMPs, Tissue Inhibitor of Matrix Metalloproteinases (TIMPs), cytokines and growth factors. Standards of pro- and active MMP-2, MMP-9 and chronic wound fluid (CFW) were prepared. Elta Proteases effectively degraded MMP-9 and tumour necrosis factor (TNF-alpha). In contrast, Platelet Derived Growth Factor (PDGF) and interleukin 1 beta were resistant to degradation by Elta Proteases. These results suggest that Elta Protease dressings appear to deactivate detrimental components in CWF, which may reduce wound bed contact with harmful proteins.

Other classical therapies use the chemical capacities of maggot secretion to act on the wound as debrider.

The future

Wound dressing interface as a subject is undergoing intense scrutiny by researchers. Tissue engineering may be one of the key aspects of successfully managing the wound dressing interface. If dressings have a future in term of reimbursement, there is certainly the need for manufacturers to develop a generality of high tech devices where the dressing will be critical to local active therapy. In this direction some recent work on the use of electrospun nanofibers or properties of the dressing allowing it to be used for drug delivery purposes are more than promising. The wound dressing interface should be considered as the front line for pain management, drug delivery and physical force application area.

References

6. Lazareth et al