

Evaluation of a non-adherent, povidone–iodine dressing in a case series of chronic wounds

Here we report a product evaluation for a non-adherent, povidone–iodine (PVP–I) dressing, determining the clinical need for the product, performing a literature review, clinical evaluation and cost-analysis, and developing a recommendation.

This evaluation included 20 patients who experienced dressing pain with the previous antimicrobial dressing. Two patients discontinued the evaluation and four ulcers were non-healing; the remaining wounds closed with the PVP–I dressing.

Patients indicated a preference for the PVP–I dressing, primarily due to lack of dressing pain. The PVP–I dressing was also the most cost-efficient.

antimicrobial dressing; povidone iodine; cost efficiency; wound pain; product selection

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The European Wound Management Association (EWMA) identified iodine as the topical wound antimicrobial with broadest action.¹ Iodine is available as povidone–iodine (PVP–I) or cadexomer iodine; however, a number of studies report that some patients experience transient discomfort with the use of cadexomer iodine,^{2,3} which restricts its use. If an acceptable alternative that causes less discomfort could be identified, the benefits of using the antimicrobial may be realised.

Using a rational, evidence-based product selection process improves wound care, safety and accountability.^{4,5} Clinical experience supported the association between cadexomer iodine dressings and long-lasting dressing pain, with a severity ranging from stinging to intolerable. Therefore, an alternative, a non-adherent, PVP–I dressing (Inadine; Systagenix), stated to decrease dressing pain, was chosen as an appropriate product to evaluate.

Inadine is indicated for the management of suture lines and ulcerative wounds, including diabetic foot ulcers, for the prevention of infection in minor burns and minor traumatic skin loss injuries, and in conjunction with systemic antibiotics in heavily infected wounds. The PVP–I dressing, designed as a non-adherent wound-contact material, consists of a knitted viscose fabric impregnated with a polyethylene glycol (PEG) base containing 10% povidone iodine, equivalent to 1% available iodine, which is released in the presence

of wound exudate. The water-soluble carrier, PEG, allows easy dressing removal.

This article details the process of evaluating the non-adherent, PVP–I dressing as an alternative to cadexomer iodine.

Method

This evaluation was performed because patients frequently reported wound pain with cadexomer iodine and silver wound antimicrobial agents, leading to product discontinuation. A non-adherent, PVP–I dressing (Inadine; Systagenix) was identified as an alternative. The following questions guided the evaluation process:

- Is there a clinical need for the product?
- Does a literature review support the product's efficacy and safety?
- How does the product compare with presently used products in function, utility and cost?
- Should an evaluation of the product be performed to determine wound outcomes, need for staff education and patient feedback?
- Why should the product be accepted or rejected from inventory?

Positive findings for each step justify moving to the next level of inquiry, while negative information may result in discontinuing the evaluation, preventing waste of time and resources.

A literature search was performed for English-language articles in PubMed. The following search terms were used: ['povidone iodine'] AND ['efficacy'

Declaration of interest:

The development of this manuscript was supported by an unrestricted education grant from Systagenix, manufacturers of Inadine. The study itself was performed independently, with no external financial support. The authors have no conflicts of interest to declare with regards to the article or its content.

OR 'safety' OR 'action' OR 'topical' OR 'wound healing' OR 'cost-efficiency']. Articles concerning iodine ingestion, injection or irrigation, and systemic and topical antibiotics were excluded.

Literature review

Multiple systematic reviews demonstrate the lack of randomised controlled trial (RCT) evidence for the use of topical antimicrobial agents in wound care.⁶⁻¹⁴ Several factors contribute to this situation, including the clinical heterogeneity of wounds that may benefit from topical agents, the difficulty in diagnosing wound infection definitively, the diversity of agents and formulations with potentially differing activity, and differences in potential endpoints for such trials.^{5,15}

While a variety of other clinical evidence does support the use of topical antimicrobials, their optimal role remains unclear; a fact that has led to the development of best practice documents, position statements and economic reviews, which attempt to provide recommendations for the use of specific agents.^{1,5,16-18}

Among topical antimicrobials, iodine has the broadest spectrum of activity, with no demonstrated resistance after 150 years of use.¹³ While early formulations were associated with a number of negative side effects and toxicity, modern formulations of iodine, including PVP-I, a stable complex of polyvinylpyrrolidone (povidone [PVP]) and elemental iodine, and cadexomer iodine, comprised of beads of dextrin and epichlorhydrin carrying iodine,¹² have essentially detoxified iodine, providing sustained delivery of low, bactericidal concentrations of iodine.¹⁵ Human studies suggest that iodine reduces bacterial load, decreases infection rates, and promotes healing.¹⁸

Antimicrobial efficacy of iodine

The continuing development of bacterial resistance increases the importance of antimicrobial agents to which resistance does not develop, such as iodine.⁵ Iodine is rapidly microbicidal, with multiple mechanisms of action, including binding to proteins, nucleotides and cell membrane fatty acids, all of which disrupt cell function.¹³ The rapid action of iodine and multiple mechanisms are likely responsible for the lack of resistance.¹⁵ Iodine also has a very broad spectrum of action; it is the only topical antimicrobial agent effective against both Gram-positive and Gram-negative organisms, spores, amoebic cysts, viruses, fungi, protozoa, yeasts and meticillin-resistant *Staphylococcus aureus* (MRSA).¹⁹

A mixed-species biofilm model with bacterial strains isolated from chronic wounds, with *Pseudomonas aeruginosa* and *S. aureus* predominating, has been used to evaluate antimicrobial efficacy against biofilm.²⁰ Hill used this model to test ciprofloxacin,

flucloxacillin, PVP-I and several silver preparations. PVP-I disrupted both 3- and 7-day biofilm. Two silver preparations disrupted 3-day biofilms, but had no effect on 7-day biofilms. No effect was observed with ciprofloxacin and flucloxacillin.²⁰

Effect of iodine on wound healing

A systematic review found 27 RCTs conducted since 1976, including studies of acute and chronic wounds, burns, pressure ulcers and skin grafts.¹⁴ The review evaluated wound healing, bacterial counts and adverse events.¹⁴ Overall, iodine did not significantly change wound healing time compared with other antiseptic wound dressings or agents; however, in individual trials, iodine was superior to other antiseptic agents and non-antiseptic dressings, but inferior to topical antibiotics in reducing bacterial count and/or wound size. There were no differences in the frequency of adverse events reported between iodine and other agents, and no major adverse events or changes in thyroid function were reported.^{13,14} Consultation with the physician responsible for patients with thyroid or renal dysfunction must determine whether the benefits of iodine use exceed the potential risk of toxicity and a monitoring process must be implemented.

Role of topical antimicrobial agents

Although the optimal role of topical agents in wound care remains unclear, topical antimicrobials may have a role in a variety of wound types.²¹ Open wounds have bacterial contamination; in chronic wounds contamination can progress through colonisation to invasive infection, which delays healing.^{17,22} Pathogens delay wound healing by producing inflammatory mediators, metabolic wastes and toxins, and by maintaining neutrophil activation, associated with cytolytic enzymes and free radicals.¹⁸

Poorly-healing wounds with signs suggesting infection may benefit from topical antimicrobial agents, as can wounds with critical colonisation and those at significant risk of infection.²¹ Chronic wounds, which are frequently secondary to neuropathy or vascular insufficiency,^{23,24} may not display the classical signs of infection, rather presenting with increased exudate, friable granulation tissue, wound breakdown, foul odour, and delayed healing.^{5,13,21} Such local infection in compromised patients can be an indication for topical therapy;^{13,21} topical therapy also has a role in treating burns, eradicating bacteria before skin grafting, reducing odour, possibly due to anaerobes,^{13,21} treating non-healing wounds, managing infected ischaemic wounds in patients who cannot undergo revascularisation, removing biofilms, which may be present in persistent infection, preventing development of systemic infection in critically colonised or locally infected wounds, and in conjunction with systemic

antibiotics in treating more invasive infection.^{13,21} In addition, clinical acumen and experience are critical in determining the optimal time to institute topical antimicrobial therapy.

Iodine dressings can be useful in managing pressure ulcers, venous leg ulcers, diabetic foot ulcers, minor burns and superficial skin-loss injuries to prevent infection or recurrence in patients with significantly increased risk of infection, in treating localised infection or suspected infection, and wounds with spreading infection and delayed healing.¹⁵

Comparison with present products

The comparison to products presently used included function, utility and cost. The non-adherent, PVP-I dressing is light and compact, and requires no special storage conditions. Staff education is minimal, as application consists of opening the package and placing the dressing over the wound surface. The PVP-I dressing is also less expensive than both cadexomer iodine and silver products. The non-adherent layer adds value by eliminating the need to apply a protective surface. Any other costs associated with product use may be identified during a clinical evaluation.

Clinical evaluation

The literature review suggested the efficacy, safety and relevance of the PVP-I dressing to our patient population. Thus the evaluation was designed to include patients with chronic wounds of a variety of aetiologies, who reported wound pain associated with the use of cadexomer iodine or other topical antimicrobial dressing, and who agreed to try the PVP-I dressing. Ethics approval was not required as the product is approved by Health Canada as a class II medical device, is a CE-marked product and was not used off-label.

In this context, a chronic wound was defined as 'a wound that fails to progress through an orderly and timely sequence of repair.'⁵ Twenty consecutive patients were entered into the evaluation at the time of a dressing change, after providing verbal, informed consent. Patients with contraindications to the dressing, including known iodine hypersensitivity, use of radio-iodine, pregnancy and breast feeding, were excluded.

Patients were followed for 6 weeks or until wound closure, defined as 100% epithelialisation, whichever came first. Dressings were changed at a frequency determined by individual wound characteristics. After approximately 4 weeks, a patient questionnaire was administered to determine the patients' dressing preference and the reason for that preference.

Outcomes

The outcomes evaluated were wound status (improved, no change, non-healing or discontinuation), self-reported dressing pain, adherence,

Table 1. Patient demographics

No. of patients	20
Male/female	10/10 (50%/50%)
Age (years)	63.3 ± 17.9
• Median (range)	70 (22–88)
Comorbidities (n)	
• Diabetes	11 (55%)
• Peripheral arterial disease	10 (50%)
• Lymphoedema	6 (30%)
Previous topical treatments (n)	
• Cadexomer iodine	18 (90%)
• Silver	18 (90%)

Table 2. Patient outcomes and summary of experience with PVP-I dressing

Wound outcome (n)*	
• No change	0 (0.0%)
• Improved	4 (20%)
• Full epithelialisation	14 (70%)
Pain with PVP-I dressing (n)	
• Yes	2 (10%)
• No	18 (90%)
Adherence to the wound (n)	
• Yes	0 (0.0%)
• No	20 (100%)
PVP-I dressing cost (n)	
• Less	18 (90%)
• No difference	2 (10%)
• More	0 (0.0%)
Patient preference (n)	
• PVP-I dressing	17 (85%)
• No opinion	1 (5.0%)
• Other product	2 (10%)

*Two patients withdrew from the evaluation

dressing preference and reason for preference (lack of pain or cost).

A cost-efficiency ratio (CER) of the dressings used was also calculated. Products used to treat the patients in the evaluation were selected to calculate the CER. The product size selected for comparison was either 10×10cm for sheet products, a 10g tube or one paste. The CER is calculated by ranking products from lowest to highest cost, and dividing the lowest cost into the cost of the comparator products. The iodine products compared were Inadine

Table 3. Cost-efficiency ratio of relevant topical antimicrobial products*

Product	Non-adherent product	Cost (CA\$)	Ranking	CER
Inadine	Yes	\$1.95	1	1
Tegaderm Ag Mesh	No	\$8.75	2	4.5
Acticoat	No	\$17.25	3	8.9
Iodosorb (tube)	No	\$21.50	4	11.0
Iodosorb (paste)	No	\$30.23	5	15.5

* Costs from Canadian Diabetes Association store, June 2009; CER=cost-efficiency ratio

and Iodosorb; silver products were Tegaderm Ag Mesh (3M) and Acticoat (Smith & Nephew). As patients purchase their own dressing materials, costs used in the comparison were provided by the Canadian Diabetes Association store and were current as of June 2009. Costs to agencies are generally lower than in some retail settings.

Results

The wounds had a variety of aetiologies (Table 1). Most participants had underlying disease and had previously been treated with both silver and cadexomer iodine dressings. All had experienced dressing pain with a previous dressing. Two patients discontinued the evaluation.

Outcomes

Two patients (10%) withdrew from the evaluation, one due to a history of pain associated with multiple products and the other due to lymphoedema-related skin breakdown. Four wounds (20%) failed to heal during the study period and 14 wounds (70%) closed (Table 2). No wounds deteriorated with the PVP-I dressing.

Dressing experience and preference

The dressing did not adhere to the wound and the majority of patients (n=18; 90%) experienced no pain with the PVP-I dressing and found it comfortable (Table 2). Seventeen patients (85%) preferred the PVP-I dressing to the previous dressing (Table 2). The cost of the PVP-I dressing was less than the previous dressing for 90% of the patients (n=18) and similar for 10% of the patients.

Cost-efficiency ratio

Inadine had the lowest unit cost of the dressings assessed (Table 3). In addition, the non-adherent surface eliminated the need to apply wound bed protection products, which range in price from

CA\$2 to CA\$10 (Canadian Diabetes Association store). Therefore, the cost efficiency of the non-adherent, PVP-I dressing could be underestimated, as wound bed protection products were not included in the calculation and Inadine was the only non-adherent dressing evaluated. The CER ranged from 4.5 to 15.5 (Table 2).

Discussion

The results of this evaluation are consistent with published clinical trials of the non-adherent, PVP-I dressing. In a prospective, randomised controlled trial of 213 consecutive patients with partial-thickness burns over less than 10% of their body surface area, a dressing with 0.5% chlorhexidine (Bactigras; Smith & Nephew, n=102), and non-adherent, PVP-I dressing (Inadine, n=111) were compared.²⁵ Patients treated with the PVP-I dressing required significantly less analgesia (p=0.02) and had reduced treatment duration (p=0.001), number of hospital visits (p=0.01), and time off work (p=0.01). The PVP-I dressing was also anecdotally noted to cause less bleeding than the chlorhexidine, but this did not reach statistical significance.

When forming recommendations, it is important to consider all patients' experience with the product, especially those who, due to the product, may not be concordant or reject the product. In this evaluation, two patients refused to use the product. One of these patients had a history of pain associated with multiple products and the other had lymphoedema-related skin breakdown. Both patients also refused other types of dressing.

The product evaluation found that the non-adherent PVP-I dressing reduced dressing pain. It was also the most cost-effective antimicrobial, compared with cadexomer iodine and the silver dressings evaluated, and was preferred to the previous dressing by most patients. These findings, taken in conjunction with the broad antimicrobial spectrum of iodine and lack of resistance to this agent, suggest that the PVP-I dressing would be a suitable first choice for clinical management where a topical antimicrobial is indicated.

The question that a product review process must answer is whether to include the product in inventory or reject it. Participants were selected for this evaluation because the wound pain they experienced with cadexomer iodine or silver meant they would be unable to have an antimicrobial dressing. Absence of pain would therefore dominate the patient preference decision, and evaluating a single alternative product would bias selection to that product if it did not cause pain. To prevent selection based on that single criterion, the criteria for inclusion in inventory were broadened. In this evaluation, although lack of pain determined patient preference, the decision to include the PVP-I dressing in inventory was based on favour-

able wound outcomes, reduced pain experience, demonstrated cost-efficiency and patient preference.

Limitations

The frequency and intensity of topical antimicrobial-associated pain appears to be unrecognized or under-reported in the literature. The study by Moberg et al.,² involving decubitus ulcers treated with cadexomer iodine, reported three of 16 patients experienced transient pain on treatment. Two studies treating venous ulcers with cadexomer iodine reported pain with application.^{3,26} Holloway³ commented on mild local burning, while Skog²⁶ stated that four of 93 patients experienced pain. In contrast, our clinic treated 596 patients in the month that we identified 20 patients with sufficient pain to refuse treatment. However, we did not quantify the degree of pain or the overall percentage of patients

experiencing pain. Further research should report the incidence and intensity of pain experienced by patients to reduce suffering.

Conclusion

Wound clinicians committed to improvement of clinical outcomes are challenged by the need to select products that are new to the authors not the general wound care community. Having a rational process to consider introduction of a new product ensures the product meets the needs of the patient population served and demonstrates accountability for inventory and introduction costs. The use of a rational product selection process incorporates clinical problem-solving, evidence-based decision making, and accountability for resource management, which can be applied to specific clinical settings. ■

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