To evaluate the safety and efficacy of Retro-Tec® dressings in 50 patients with chronic wounds

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Objective: To evaluate the safety and efficacy of Retro-Tec Dressings (RTD) in 50 patients with chronic wounds. **Methodology:** 50 patients with wounds who were ambulatory and met the inclusion criteria were selected. The study was comprised of a screening and baseline stage during which the wounds were assessed. Medical history, as well as previous wound treatments were assessed and follow-up visits arranged three times per week. The baseline visit included the assessment of wound size and infection. The rate of wound closure was measured in terms of % reduction in area, per treatment day. **Results:** Plantar foot ulcers had an had a complete close rate of 41%, dorsal foot ulcers 56%, toe ulcers 80%, venous leg ulcers 50% and pressure injury 67% within 6 months. **Conclusion:** It appears that the components gentian violet, methylene blue and silver form an efficient antimicrobial dressing. The applied RTD wound dressings were effective in managing challenging wounds that showed signs of infections.

Wound healing begins immediately after any injury to the skin. When the acute open wound does not heal timely within 4 weeks or more from the date of an injury and when complications disrupt the normal healing process, it can transform into a chronic wound (Leaper and Durani, 2008). The World Union of Wound Healing Societies 2016 positioning document 'Triangle of Wound Assessment' (Dowsett et al, 2015) prompts clinicians to assess the status of a wound bed by observing and recording the tissue type, levels of exudate and the presence or absence of local and/or systemic wound infection, i.e. in a similar fashion to the earlier TIME (T = tissue, I = inflammation/infection, M = moisture imbalance, E = edge/epidermal margin) concept (Schultz et al, 2003).

To improve wound healing, non-viable tissue needs to be reduced by debridement (Pai and Madan, 2013) along with reducing infection, exudate and biofilm. Major complications that interfere with wound healing include an increased bioburden introduced into an open wound, which can also lead to infection (Vanwijck, 2001). Up to 60% of chronic wounds reveal the existence of bacterial biofilm, another deterrent factor in wound healing (James et al, 2008; Phillips et al, 2010). Oral antibiotic treatment is only used in confirmed cases of clinical infection, with treatments focused and limited to the shortest effective duration in order to prevent microbial resistance (Lipsky et al, 2016).

Post debridement and cleansing, the choice of dressings varies depending on the healing phase, wound depth, level of exudate, degree of infection and presence of biofilm in a wound (Wiegand et al, 2015). Therefore, an appropriate dressing will be needed to manage the wound. Retro-Tech Dressing (RTD) is a novel dressing that incorporates gentian violet, methylene blue, silver phosphate and surfactant, impregnated into polyurethane foam. The antibacterial action of silver (Ag)-based dressings has long been established in many studies (Demling and De Santi, 2001; Expert Working Group, 2012).

Innovative products are required to address infections by reducing the bioburden in chronic wounds. Novel dressings

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incorporated with compounds that pose no threat in the promotion of organism resistance are preferred. Multiple ingredients that combine to offer synergistic bacterial control with non-selective modes of action may provide an advantage in an antimicrobial dressing. Since the late 18th century, gentian violet (Connell et al,1933; Bakker et al, 1992; Maley and Arbiser, 2013) and methylene blue (Schirmera et al, 2011; Planas et al, 2015; Xiong et al, 2017) have been well-established antifungal and antibacterial compounds and have proven their efficacy in more recent applications. With the addition of silver, the three-component ingredients in RTD wound dressing foam are purported to efficiently manage bioburden and exudate.

The purpose of the study was to evaluate the safety and efficacy of RTD wound dressings in the treatment of difficult-to-heal, infected wounds.

Primary efficacy objective

- To assess the overall percentage of complete (100%) wound closure at the follow-up visit. Wound closure is assessed by consecutive measurements of wound dimensions and epithelialization.

Secondary efficacy objective

- Bacterial bioburden (assessment of the wound bed, according to TIME concept)
- Healing rates of the wounds (assessed by percent change in wound size over preset time units).

Methodology

A total of 50 patients were enrolled in the study. The selected target population recruited for the treatment were patients of either gender, any ethnic group, aged 18 years and above. Investigators screened patients based on the inclusion/exclusion criteria described after a written informed consent and the general medical and dermatological histories are obtained. Patients received an explanation of the study's objectives; their consent was taken for being part of the study and permission to use their wound photographs for publication/research. The baseline visit included the assessment of wound size and wound infection. Treatment with RTD dressings only commenced after all baseline data was collected.

Wound dimensions were assessed before the treatment and during each follow-up visit to evaluate the response to the RTD dressing. Each study subject received treatment with the RTD dressing as the primary wound dressing, in addition to standard treatment for similar wounds. Efficacy was assessed by evaluating the percentage of wound closure (area during follow-up visit, divided by area at baseline). The rate of wound closure was measured in terms of % reduction in area, per treatment day.

Inclusion criteria:

- Male or female patients, above 18 years of age
- Patient with index wounds that must be ≥1 cm^2 and ≤20 cm^2
- Patient with wounds with current clinical signs or symptoms of infection
- Patients able and willing to comply with three-weekly visits to clinic
- Women of childbearing age with a negative pregnancy test, or lactating females. Injectable methylene blue can cause toxicity in pregnant females. However, local applications did not show any adverse events, nevertheless, precautions should be taken to avoid any complications as this is an evaluation study on safety and efficacy
- Patient capable and willing to provide informed consent.

Exclusion criteria:

- Patients with known allergies or side effects to the used product dressing or its ingredients
- Patients with ischemic foot, i.e. ankle brachial systolic index (ABSI) <0.8.

Assessment for wound infection was done after the cleaning and/or debridement of the wound at each visit. Infections were assessed clinically by symptoms and signs. At least two of these signs had to be present:

- Local swelling or induration
- Erythema >0.5 cm around the wound
- Local tenderness or pain
- Local increased warmth
- Purulent discharge.

The various types of wounds were managed using the standard of care whereby:

- Diabetic foot ulcers were off-loaded
- Venous leg ulcers were managed using compression bandaging
- Pressure injuries were managed with standard guidelines, for example, 2-hourly turning with appropriate support surfaces.

Table 1. **Wounds by aetiology**

Wound aetiology	n	%
Diabetic foot ulcer: plantar ulcer	17	34
Diabetic foot ulcer: dorsal ulcer	16	32
Diabetic foot ulcer: toe ulcer	10	20
Venous leg ulcer	4	8
Pressure injury	3	6
Total	**50**	**100**

Table 2. **Percentage of complete wound closure in 6 months (%) – all wounds**

		Patients (n=50)		
		Number healed	% Complete closure	Average time to closure
Complete Closure	n	28	56%	88.39 days
	[Range]			25–184 days

Results

The results of this evaluation are summarized in *Tables 1–8*. Pictures of the wounds of ten patients before and after treatment with RTD dressings are shown in *Case studies 1–10*.

Discussion

The RTD wound dressing was used on diabetic foot ulcers situated in the plantar aspect, toe and dorsal aspects as well as venous ulcers and pressure injuries which had become infected. Plantar diabetic foot ulcers take a longer time in healing compared with dorsal ulcers, which can be attributed to the pressure from walking or standing and requires good off-loading. However, patient compliance and loss of earnings can be a problem. Toe ulcers are the fastest to close and achieved 80% in terms of percentage of complete closure within the stipulated 6 months. This may be because these ulcers are usually not located in weight-bearing areas.

Table 3. **Closure results of chronic wounds, by aetiology**

Wound aetiology (# of patients)	Weighted average of healing (%) at 6 months	Complete closure (%)
Diabetic foot ulcer: plantar ulcer (n=17)	72.06	41
Diabetic foot ulcer: dorsal ulcer (n=16)	70.94	56
Diabetic foot ulcer: toe ulcer (n=10)	94.00	80
Venous leg ulcer (n=4)	75.00	50
Pressure Injury (n=3)	96.67	67

Table 6. **Percentage of complete wound closure in 6 months: toe ulcers**

	Patients (n=10)		
	Number healed	% Complete closure	Average time to closure
Complete closure	8	80%	
Weighted % average complete closure [SD]		94% [4.1]	76.88 days [41.25]
Median (more than 50% of wounds are at this level or above) [Range]		100% [50–100]	66.5 days [35–175]

Table 7. **Percentage of complete wound closure in 6 months: venous leg ulcers**

	Patients (n=10)		
	Number healed	% Complete closure	Average time to closure
Complete closure	2	50%	
Weighted % average complete closure [SD]		75%	83.5 days [0.5]
Median (more than 50% of wounds are at this level or above) [Range]	[1.41]	87.5 days [25–100]	83.5 days [83–84]

Table 8. **Percentage of complete wound closure in 6 months: pressure injuries**

	Patients (n=10)		
	Number healed	% Complete closure	Average time to closure
Complete closure	2	67%	
Weighted % average complete closure [SD]		96.67% [1.08]	102 days [39]
Median (more than 50% of wounds are at this level or above) [Range]	[1.08]	100% [90–100]	102 days [63–141]

Case study 1

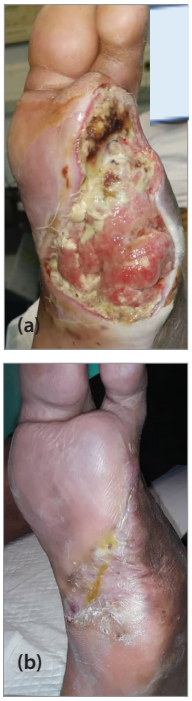

Figure 1. (a) Before (b) after 5 months

Case study 2

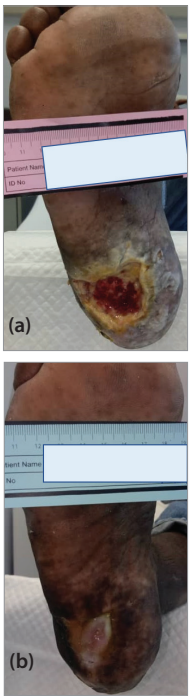

Figure 2. (a) Before (b) after 3.5 months

Case study 3

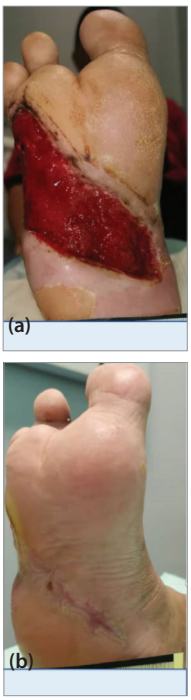

Figure 3. (a) Before (b) after 3.5 months

Case study 4

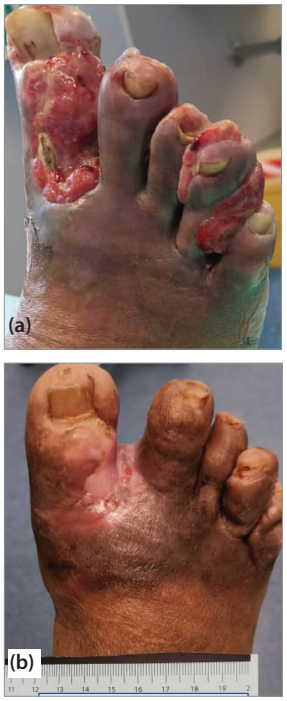

Figure 4. (a) Before (b) after 2.5 months

Case study 5

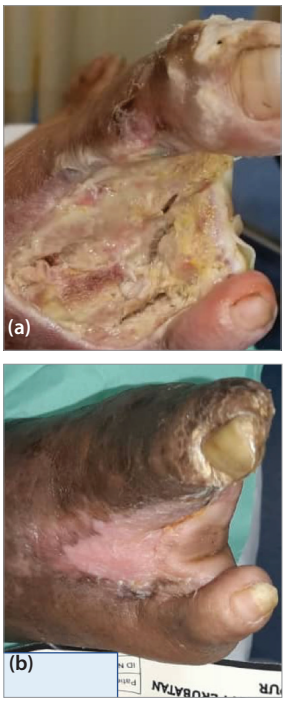

Figure 5. (a) Before (b) after 5.5 months

Case study 6

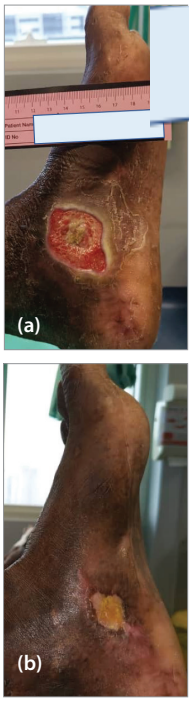

Figure 1. (a) Before (b) after 2.5 months

Case study 7

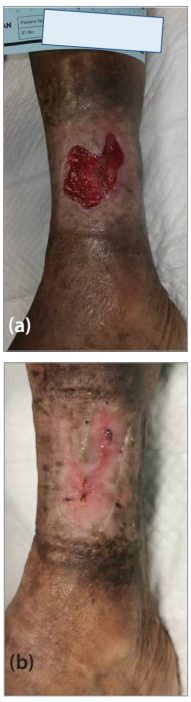

Figure 2. (a) Before (b) after 3 months

Case study 8

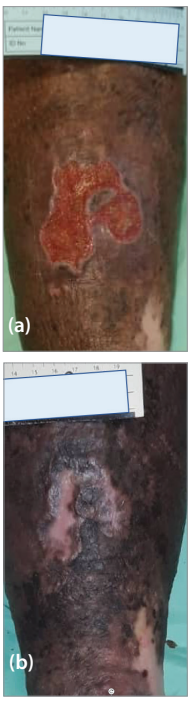

Figure 3. (a) Before (b) after 3.5 months

Case study 9

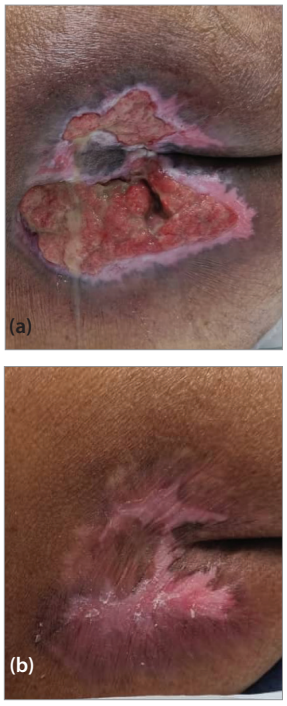

Figure 4. (a) Before (b) after 2 months

Case study 10

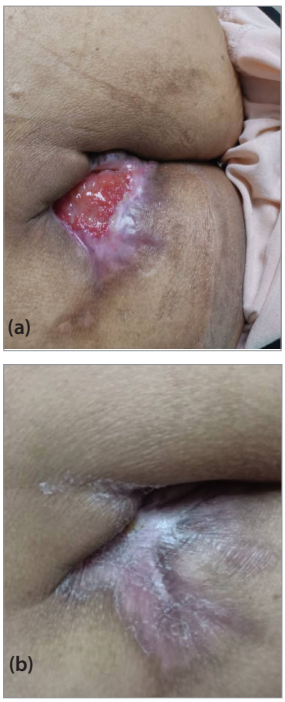

Figure 5. (a) Before (b) after 5 months

Venous leg ulcers had a 50% complete closure rate. As these ulcers have to be managed appropriately, either by compression bandaging or other treatment options, they take a longer time to close. Patient compliance can be challenging especially in Malaysia where the weather is hot and humid. Therefore, a two-layer compression system was used which gives a pressure of 20–25 mmHg which is much lower than the gold standard four-layer bandaging system.

Pressure injuries had a 67% complete closure rate. These can be more difficult to manage due to most patients being non-ambulatory. Two-hourly turning of the patients, ideally on support surfaces to relieve pressure are important standards of care. In addition, incontinence whether it is faecal or urinary incontinence can delay the healing time of the wound. All these factors have to manage comprehensively. In addition, this particular RTD wound dressing appears to be effective in managing bacterial bioburden and wound exudate.

Conclusion

In this evaluation, the applied RTD wound dressings were effective in managing challenging wounds that showed signs of infections. It appears that combining gentian violet, methylene blue and silver provides an effective antimicrobial dressing. The surfactant reduces surface tension and works well on venous ulcers. The polyurethane foam is helpful in managing moisture. This 5 in 1 dressing can be used to manage a variety of wound types effectively. The limitation of this study is due to the small sample size and that there was no comparison with conventional therapy. However, a randomized control trial would be able to prove the dressing's significance in terms of efficacy. WAS

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