Prontosan® solution and Prontosan® Debridement Pad in the treatment of different types of cutaneous wounds: expert-based statements, cases series and review of the literature

Angela Peghetti,[1] Diletta Olivari,[2] Silvia Tedesco,[3] Andrea Bellingeri,[4] Marino Ciliberti,[5] Antonio Di Lonardo,[6] Corrado M. Durante,[7] Antonino Grasso,[8] Elia Ricci,[9] Alessandro Scalise,[10] Giovanni Pomponio[11]

[1]S. Orsola Hospital, Bologna; [2]Internal Medicine, Università Politecnica delle Marche, Ancona; [3]Cystic Fibrosis Center, Ospedali Riuniti di Ancona, Ancona; [4]IRCCS Fondazione S. Matteo Hospital, Pavia; [5]ASL Napoli 3 Sud, Tissue Repair Network; [6]Burns Center, Cisanello Hospital, Pisa; [7]Contra Vulnera Onlus, Rome; [8]UOC Vascular Surgery, AOU Policlinic, Catania; [9]UOA Vulnology, S. Luca Healthcare Center, Turin; [10]UOC Plastic Surgery, Ospedali Riuniti di Ancona, Ancona; [11]Internal Medicine, Ospedali Riuniti di Ancona, Ancona, Italy

ABSTRACT

Prontosan® Debridement Pad (PDP; B. Braun) is a new device designed for mechanical debridement. This paper summarizes the results of a complex initiative aimed to develop consensus among a panel of wound care experts about the optimal use of this new technology. An extensive review of the literature found 27 pertinent papers, which underwent a formal process of critical appraisal and evidence extraction by two independent methodologists. Results are displayed in an evidence report. 12 practical recommendations, concerning management of acute and chronic wounds, have been developed and approved. Main point of strength of this project is the use of a systematic approach to literature review, evidence synthesis and presentation, development and measurement of expert consensus. Moreover, expert panel provided further clinical data, through the reporting of 13 clinical cases managed according to above-mentioned recommendations, with a particular focus on burns and chronic ulcers treatment, both in adult and pediatric patients. Overall, results from literature review and from clinical experience confirm that the combined system Prontosan® Solution and PDP is a promising tool useful in the critical phase of debridement in acute and chronic wounds treatment. Efficacy in debris removal and pain reduction are the main points of strength. Our project may contribute to optimize clinical use of this innovative device.

INTRODUCTION

Concept of Wound Bed Preparation (WBP) is growing stronger, together with the awareness of its key role in the treatment of skin lesions. With the aim to implement the WBP paradigm in clinical practice, the International Wound Bed Preparation Advisory Board introduced the acronym TIME (Tissue, Infection or Inflammation, Moisture imbalance, Epidermal margin), that clearly and systematically establishes 4 fundamental steps to consider in order to identify and properly manage different pathophysiological situations able to block tissue repair process.

Key principles of skin wounds treatment set out by the TIME, mainly concern infections control, necrotic tissue debridement, perilesional edge preservation and exudate management, along with a global assessment of the patient.

Wound Debridement is the initial step in the approach to skin lesions presenting with devitalized tissue, slough or biofilm. Necrotic tissue, indeed, hinders wound healing process and facilitates infections, so increasing mortality rate, hospital stay, pain and costs.

Technological progress aids professionals to correctly implement TIME principles, making available devices whose proper areas of use are supported by evidence that, in addition, provide a good balance in terms of costs/efficacy.[1]

In this context the combined system Prontosan® Solution and Prontosan® Debridement Pad (PDP; B. Braun) is inserted.

Prontosan® Solution is a sterile device based on 0.1% polyhexanide with antimicrobial action and 0.1% undecylen-amidopropyl betaine with a surfactant effect.

PDP is a new, sterile and disposable device designed

Correspondence: Giovanni Pomponio, Internal Medicine, Ospedali Riuniti di Ancona, Ancona, Italy.
E-mail: pomponio@univpm.it

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for mechanical debridement, consisting of two layers, a front layer of microfibre for effective removal of debris and infected exudate and a back layer of absorbent polypropylene.

The microfiber layer, once soaked with Prontosan® Solution, support debris, bacteria and biofilm removal from the wound bed, whereas the excess exudate, absorbed during this phase, accumulates in the external absorbent layer. In practice, the unprinted side of the pad should be soaked with 15-20 mL of Prontosan® Cleansing Solution for wounds. Then, by using circular movements and applying a light pressure, it is possible to clean the surface of the wound with the moistened side. After this cleaning procedure, it is suggested to clean further with Prontosan® Solution, in order to remove detached residues.

In this way, the concept of deep cleansing, introduced by the use of the Prontosan® Solution,[2] is enhanced by the mechanical action of the Pad which allows, among other things, for example in the case of undermining injuries, a deep cleansing and a more accurate and complete mechanical debridement.

Areas of use, supported by the literature, are all chronic skin wounds presenting with a biofilm, critical colonization or signs of infection. Its use is also indicated in acute wounds, mainly in case of burns and traumatic wounds.

Aims

Our work is intended to: i) review current evidence and expert opinions in order to establish expert-based recommendations on best clinical use of the combined system Prontosan® Solution and PDP in current practice; ii) provide further clinical data, basing on exemplificative clinical cases managed according to above-mentioned recommendations, with a particular focus on burns and chronic ulcers treatment, both in adult and pediatric patients.

METHODS OF RESEARCH

Literature review and analysis

An extensive search of the literature has been conducted on MEDLINE, using the following string: '(*prontosan OR polihexanide*) *AND wound**' (limits: human, English), and on B. Braun data files. A manual search was also performed. Retrieved articles has been selected according to following criteria: i) studies reporting data on clinical outcomes from more than one patient affected by acute or chronic wounds treated with polihexanide/polihexanide gel 0.1% or biocellulose-based technology plus polihexanide/polihexanide gel 0.1% AND published on peer-reviewed journals; ii) systematic reviews conducted on the topic of interest.

Selected papers underwent a systematic process of critical appraisal and data extraction by two trained, blinded and independent methodologists (Diletta Olivari, Silvia Tedesco), who warranted a neutral point of view. Characteristics of study design, target population, interventions, outcomes, as well as main results and methodological comments have been summarized in a structured format, producing an evidence report. Figure 1 shows the search flow chart.

Experts identification and selection

A multidisciplinary panel of experts was defined. The panel includes 10 clinicians, doctors and nurses, each of them with more than 20 years of experience in wound care. Specialists in clinical methodology warranted specific support. The differences in areas of competence (decubitus ulcers, burns, venous leg ulcers, diabetic foot ulcers, *etc.*), roles, settings of care and functions among the experts allowed a wide and critical angle of view about procedures, expected results and outcomes.

Evidence presentation and discussion

During a plenary meeting (Milan, March 1st 2019), available evidence have been presented and thoroughly discussed in a structured format, in order to highlight main points of strength and weakness of current research on this topic and to identify priorities for further clinical studies. Meanwhile, experts discussed characteristics of patients and skin lesions prone to the combined system Prontosan® Solution and PDP favorable effects, how to administer this intervention properly, ideal setting of usage, which outcomes should be pursued and how to measure them.

Statements and recommendations building, selecting and grading

Based on plenary discussion, a list of statements and recommendations have been built up. Each statement/recommendation has been sent by mail to the experts, together with collected comments, in order to obtain formal approval. GRADE (www.gradeworkinggroup.org) suggestions were followed to manage voting results and attribute grade of strength. In particular, a scale ranging from 0 (absolutely not recommended/approved) to 9 (strongly recommended/approved) was used. Interquartile ranges (IQR) and medians (M) were calculated to assess the level of agreement. A recommendation or statement was defined as being:

- *Strongly recommended/approved* if M≥8 and the lower level of the IQR>5;
- *Weakly recommended/approved* if M= 6 or 7 and the lower boundary of the IQR≥5;
- *Not recommended/approved* if M<5 and the upper boundary of IQR≤5;

– *Uncertain* in the remaining situations (M=5; M>5 but lower quartile<5; M<5 but upper quartile>5)

The percentage of *Strong Agreement* was also calculated and reported in Results session.

Case series

According to the indications discussed in the plenary session and based on its own background and experiences, a group of experts conducted, in an autonomous way, clinical observations on patients who underwent a debridement procedure with the combined system Prontosan® Solution and PDP. Each expert has selected cases of patients suffering from chronic wounds or burns. Patients have been

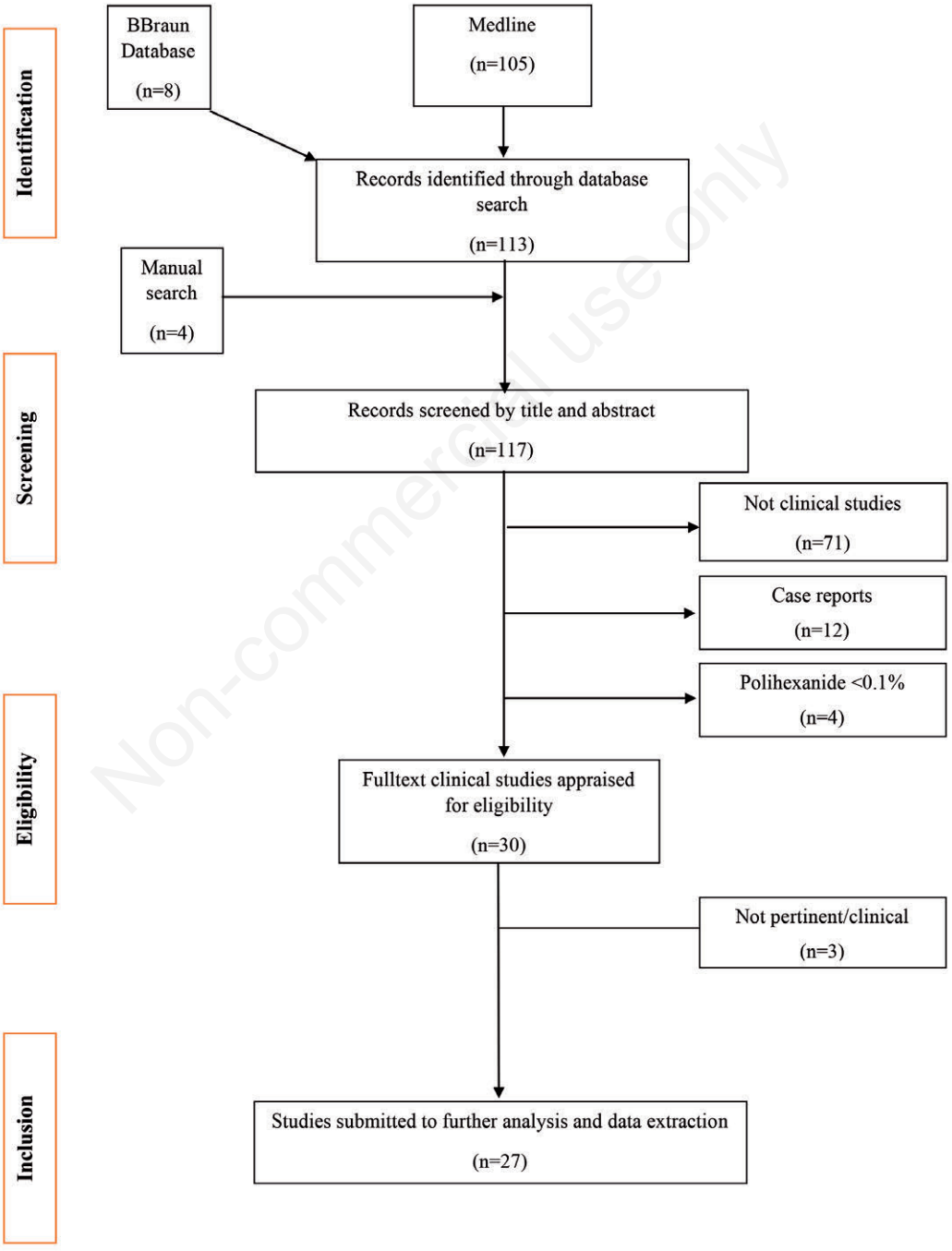

Figure 1. Search procedure flow chart.

followed as in routinely clinical practice. CARE checklist[3] guided writing process.

RESULTS

Evidence report

27 papers have been selected and analyzed. In particular 4 randomized controlled trials (RCTs), 12 non-randomized clinical studies including one systematic review concerning Prontosan®, 7 RCTs and 4 non-randomized studies concerning biocellulose-based technology have been enclosed in final evidence report (Supplementary Tables 1-4). All randomized trials have been evaluated for bias risk, according to Cochrane assessment tool.[4] Major methodological flaws detected in many trials are: i) not concealed or under described randomization process; ii) performance bias; iii) detection bias (Figures 2 and 3).

Overall, studies on Prontosan® showed fair efficacy in enhancing WPB,[1] cleansing[5] (particularly in burns),[6] pain control,[7] but also, although with a lower level of evidence, in promoting wound healing.[6,8,9] Prontosan® appeared to be well tolerated across all the studies with rare and mild adverse events reported (*e.g.*, one case of graft failure and two cases of mild to moderate itch).

Studies on biocellulose-based technology consistently reported efficacy on pain reduction.[10-12] Moreover, favorable effect has been found on wound bed evolution,[11] peri-wound skin condition,[10] likelihood to obtain eradication of biofilm.[13] A note of caution comes from the observation that all cited trials have been conducted using a biocellulose pad not totally comparable to PDP, whose microfibers structure seems to be even more effective in debris removal at least in laboratory proofs.

Recommendations and statements

The panel built up 12 recommendations detailed in Supplementary Table 5. A strong level of agreement has been achieved for all statements. In particular, our experts agree on a wide range of indications for the use of the combined system Prontosan® Solution and PDP. Only undermined pressure ulcers, cancer-related wounds and patients affected by severe cardiopathies or bullous diseases should be excluded from this treatment.

Moreover, precise instructions about effective application of the combined system Prontosan® Solution and PDP have been established (Supplementary Table 5). According to our experts, PDP should be applied by medical and nurse health care professionals with expertise in wound care.

Figure 2. Critical appraisal of 4 randomized controlled trials on Prontosan®.

For clinical or research monitoring, WBP score could be assessed every week for a minimum follow-up of four weeks.

Clinical series

Between March and May 2019, a group of experts have been involved in the project and conducted independent clinical observations on patients who underwent a debridement procedure with the combined system Prontosan® Solution and PDP. Patients have been followed prospectively according to the current clinical practice. The observations have been focused on patients who met the following requirements and criteria: i) need for treatment with PDP for debridement; ii) informed consent to publication of personal data; iii) treatment administered according to good clinical practice as established in above-mentioned statements.

Characteristics of patients, type of lesions, modality and timing of the combined system Prontosan® Solution and PDP application, concomitant treatments, results, modality and timing of outcomes detection and follow-up are displayed in Supplementary Table 6.

Two patients, affected by surgical wound dehiscence, were treated with the combined system Prontosan® Solution and PDP for a median of 19 days [10-28] showing improvement in pain, wound size, presence of biofilm and signs of infection, inflammation and bacterial contamination at the end of the follow-up (Figures 4-7).

Two patients, presenting with intermediate-deep degree burns, underwent the combined system Prontosan® Solution and PDP applications for a median of 23.5 [12-35] days, achieving a fast and effective wound debridement (Figure 7).

Intermediate-deep degree burns are characterized by presence of necrotic dermal tissue. Removal of damaged tis-

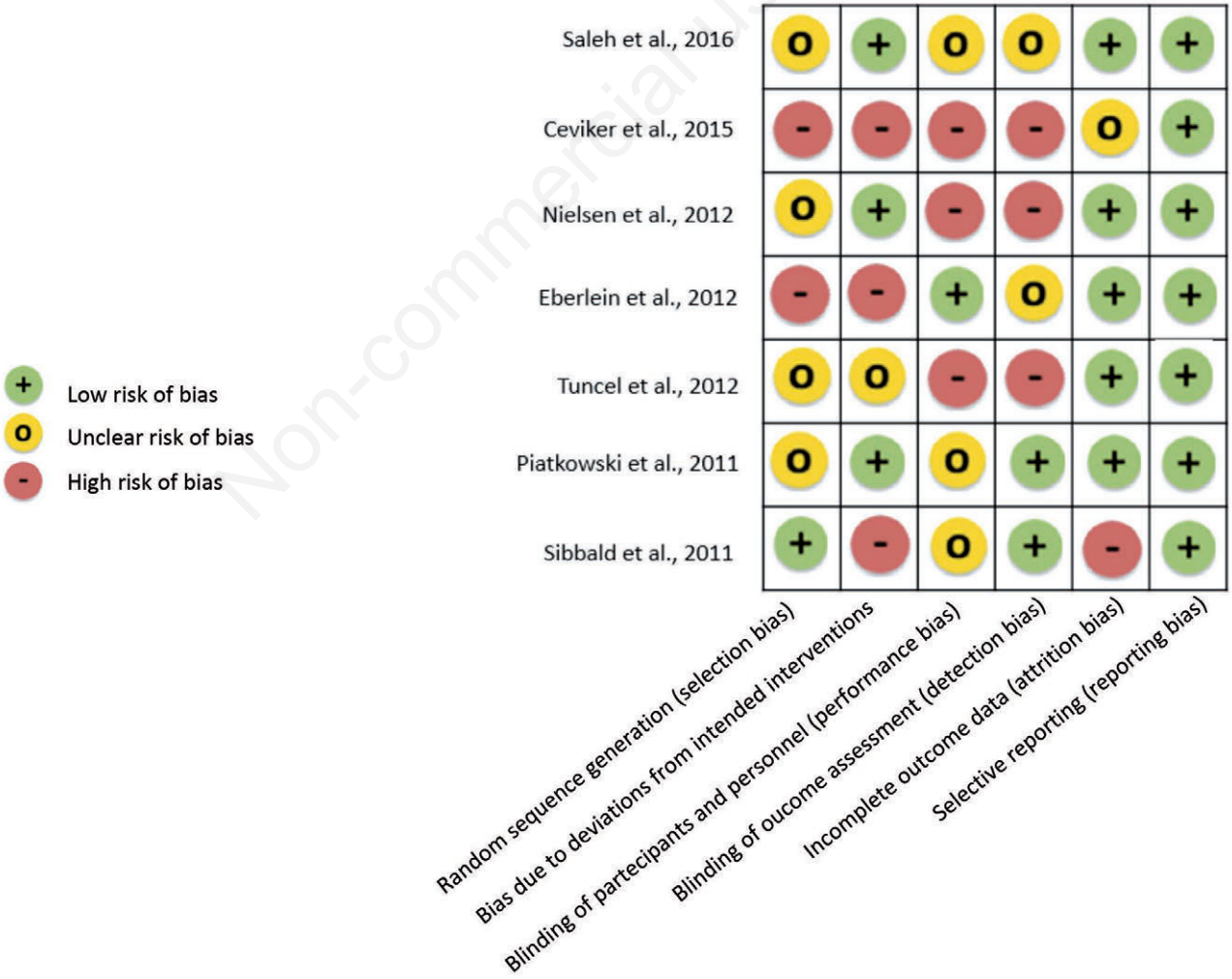

Figure 3. Critical appraisal of 7 randomized controlled trials on Prontosan® plus biocellulose-based pad.

sue is a cornerstone for an effective treatment. Actual standard approach is based on collagenase, after mechanical debridement with cotton gauze. This strategy is affected by limits, as need of prolonged time and high infectious risk. Adding the combined system Prontosan® Solution and PDP to collagenase could speed and improve clinical course.

The capability of the combined system Prontosan® Solution and PDP in cleansing softly enhanced rapid regression of clinical signs of local inflammation and bacterial contamination with exudation, together with wound size reduction (-97%). Whereas in patient 4 pain improved after treatment (-50% Verbal Rating Scale, VRS), in patient 5 the combined system Prontosan® Solution and PDP increased pain, because its action, although softer and more effective than cotton gauze, can evoke pain itself, mainly during re-epithelization phase.

Three patients (cases number 6-8-10, Figures 5 and 6) affected by chronic vasculitic ulcers of lower limbs, were treated for a median of 28 days [21-28] obtaining wound size reduction (-75%) and pain improvement (-50% VRS in patient 6 and -80% VRS in patients 8 and 10) in all patients. Biofilm disappeared as well as signs of infection, inflammation or bacterial contamination at the end of the follow-up.

Prontosan® solution wrap for 5 minutes followed by debridement with the combined system Prontosan® Solution and PDP was effective in three chronic phlebostatic ulcers (cases number 7, 9 and 12) followed for a median of 4 weeks. Disappearance of biofilm, pain reduction (-80% VRS) and wound size reduction (-75%), in absence of signs of Infection, inflammation or bacterial contamination were observed.

The combined system Prontosan® Solution and PDP showed efficacy also in other complex ulcers as gangrenous pyoderma (case number 13), necrotic and infected post-traumatic ulcers (case number 11) and in mixed vascular lesions in patient with chronic osteomyelitis (case number 2). For further details, see Supplementary Table 6.

DISCUSSION

This paper summarizes the results of a complex initiative aimed to develop consensus among a panel of wound care experts about the optimal use of a new technology (PDP) and a new *modus operandi* (based on the combined system Prontosan® Solution and PDP), designed to support the critical phase of WBP. Main point of strength of this project was the use of a systematic approach to literature review, evidence synthesis and presentation, development and measurement of expert consensus.

Literature provides lots of evidence-based recommendations concerning the necessity of using a debridement as first line approach to skin lesions presenting with devitalized tissue, slough or biofilm.[14,15] Wound debridement represents, indeed, the first step of the WBP as necrotic tissue hinders wound healing and offers a microenvironment to bacterial growth, facilitating infections that are correlated with increased mortality rate, hospital stays, pain and costs.[16-18]

Many technologies are nowadays available for cleansing as well as debridement in wound care. Their use aims to prevent infections and support a rapid growth of healthy tissue in order to achieve wound healing, although is not always supported by strong evidence arising from well conducted studies.

The new technology combines the use of Prontosan® Solution and Prontosan® Debridement Pad, allowing to associate the mechanical activity of the Pad to the deep cleansing action of the solution. The combination of these two products corresponds to a mechanical Debridement Combined System that allows the removal of adherent, non-vital or contaminated tissues, while the cleansing product promotes the soiling removal (foreign material or metabolic non-adherent detritus) and reduction of bacterial load. Wound revision, functional tissue resection or any other action requiring sharp instruments are not in-

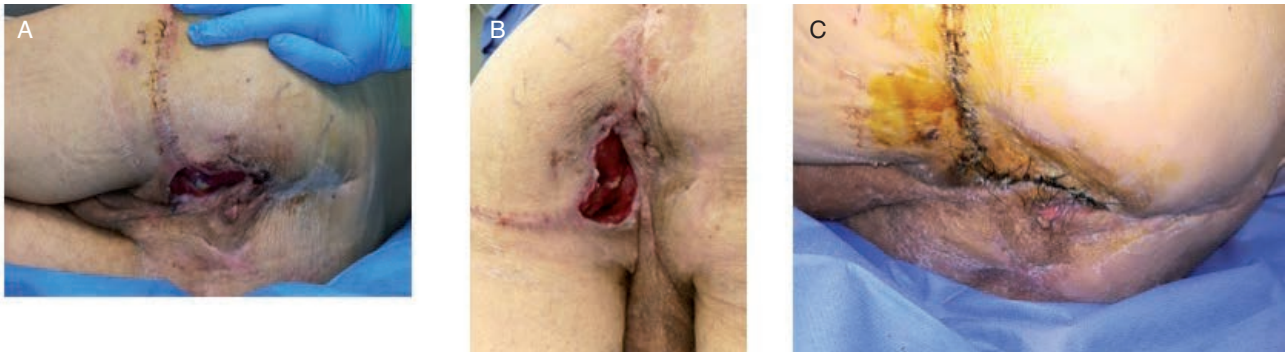

Figure 4. Patient affected by surgical wound dehiscence. A) Taking care of the patient: visit no. 1. B) After Combined Debridement System. C) Follow-up: 20 days.

cluded in the Debridement Combine System synergic action, that aims to remove necrotic material, devitalized, serous-crustose or infected tissues, slough, pus, foreign bodies, detritus, bone fragments or any other type or bioburden and biofilm in order to promote healing (as recommended in the EWMA consensus document).

On the basis of the established efficacy proofs of Prontosan® Solution, experts involved in the project, conducted indipendend observations on patients treated with a debridement procedure by the combined system Prontosan® Solution and PDP, in different clinical scenarios, empirically evaluating the appropriate use of this system.

This new approach of care, namely Debridement Combined System, showed efficacy in pain reduction in any clinical scenario, result achieved also in vasculitic lesions (three patients) characterized by refractory treatment-related pain.[19] To date, pain has represented the main obstacle to the use of a mechanical debridement[20,21] due to the common use of a wet to dry technique, which is ill countenanced by patients and histolesive as frequently involves granulation tissue.

The mode of action of the Debridement Combined System has been observed in different settings, showing efficacy in WBP clinical practice and by promoting and accelerating healing times. Furthermore, Debridement Combined System could be associated with the use of collagenases in burn wounds.

CONCLUSIONS

The combined system Prontosan® Solution and PDP is a new promising tool useful in the critical phase of debridement in acute and chronic wounds treatment. Efficacy in debris removal and pain reduction are the main points of strength. Our project, based on a systematic approach integrating evidence, clinical experiences and experts' opinions, may contribute to achieve the best cost/effectiveness ratio from this innovative device.

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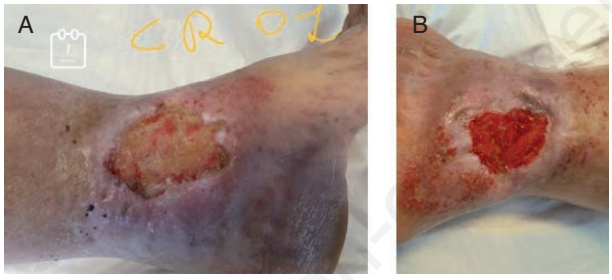

Figure 5. Chronic vasculitic ulcer (patient 8). A) Taking care of the patient: visit no. 1. B) After Combined Debridement System.

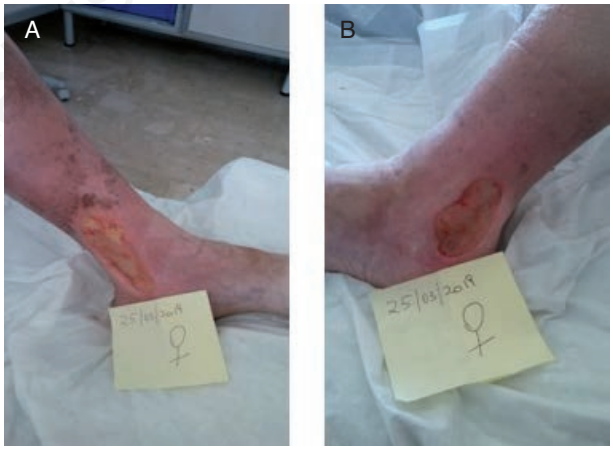

Figure 6. Chronic Vasculitic Ulcer (Patient 10). A) Taking care of the patient: visit no. 1. B) After Combined Debridement System.

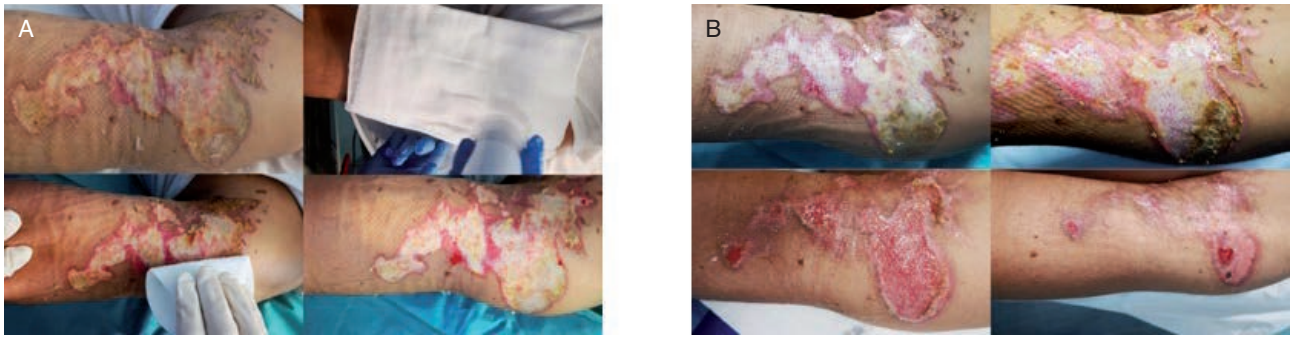

Figure 7. Patient with intermediate-deep degree burn. A) Taking care of the patient: visit no. 1. B) After Combined Debridement System.

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