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# Use of acellular dermal regeneration template combined with NPWT to treat complicated extremity wounds in children

An experience with paediatric burn wounds treated with plant-derived therapeutic

Negative pressure wound therapy: improving the patient experience: Part 3 of 3

SGAP flap: a reliable method for sacral pressure ulcer reconstruction

Development of an algorithm for a wound management formulary

# An experience with paediatric burn wounds treated with a plant-derived wound therapeutic


• **Objective:** To observe the efficacy of a plant-derived wound dressing (1 Primary Wound Dressing®), a mixture of hypericum and neem oil, in different types of paediatric burns.

• **Method:** A retrospective review was conducted over the complete healing course of 9 paediatric patients with a mean age of 8.17±3.35 (1–11 years), presenting mixed, partial or full-thickness burns. The treatment applied by the wound care specialist consisted of daily cleansing of the wound with a saline solution and application of 1 Primary Wound Dressing on the whole wound surface. There was no application of a secondary dressing. The time to heal, wound size, ease of handling, pain and complications were recorded. Procedural and background pain were observed in six of the patients older than 5 years (mean age 9.6±2.39, range 8–11 years). Due to the small number of patients examined during the period studied, it was not possible to perform statistical analyses.

• **Results:** The mean wound size was 50.76±48.32cm$^2$ (4.63–132.0cm$^2$). A rapid induction of granulation tissue and re-epithelialisation was observed. Time to complete healing was 16.6±4.69 days (10–22 days). No complications related to wound infection was observed. The 6 patients older than five years reported a strong relief of pain, from an initial value of 7–8 out of 10 to 0 out of 10 within the first week of treatment. This remained at the 0 out of 10 level during the second and third weeks of treatment.

• **Conclusion:** This retrospective, non-controlled examination suggests that 1 Primary Wound Dressing could be an effective therapy for the treatment of burn wounds, with benefits including pain reduction and simplicity of use. Further evaluations with a larger population are required to document the effectiveness of this plant-derived wound dressing in a controlled fashion.

• **Declaration of interest:** There were no external sources of funding for this study. F. Carnevali is a researcher and co-inventor of 1 Primary Wound Dressing®.


paediatric burns; secondary intention healing; wound spray; neem oil; hypericum oil

In Bolivia, burns are the second most common cause of accidents in children. Statistically, most burns are the result of hot water scalding, especially in small children under five. This situation is very common in Bolivia and also other parts of the world,[1-3] where families live in a single space that constitutes as a kitchen, bedroom, bathroom and living room, thus increasing the accessibility of many dangerous objects which can burn a child (i.e. hot water, free flames, gasoline, electricity). Burns, if not properly treated, can lead to various complications[2,4] including death (lethal infections), severe functional limitations and disfiguration, especially in children in poor living conditions.

In the Paediatric Burn Department at Viedma Hospital, Bolivia, the degree of burn is clinically assessed initially by an experienced burn surgeon and it is monitored and re-examined during the following weeks to reassess the burn depth and identify the best treatment for each patient. This is consistent with many studies,[2,4,5] especially where dedicated instruments such as Laser Doppler Imaging (LDI)[6–8] are not available.[2,8]

The treatment of first degree and partial thickness burns lasts from one week to 10 days, as recommended by many studies.[4,6,9,10] The typical burns protocol at the hospital involves the application of hydrogel (Biopiel; containing chitosan and polyaminopropyl biguanide) daily as a primary wound dressing and to leave it on the wound as long as possible without any secondary wound dressing. In the case of partial/full-thickness and third degree burns, which heal in three weeks to 30 days or more, when there are complications, escharotomy is performed under sedation in the operating theatre.[4,6,9,10] The wound surface is then cleansed daily with a saline solution and a local silver sulfadiazine cream (SSD) mixed with lidocaine (Quemacuran-L, INTI, Lima, Perù) is applied twice a day, or chitosan and polyaminopropyl biguanide once a day as the primary wound dressing. Two weeks after the trauma, based on a reassessment of the residual wound surface area, the burn surgeon decides whether to continue the dressing therapy for secondary intention healing or to perform a homologous skin graft. In this context, one should bear in mind the widely reported risk of developing a keloid reaction and/or hypertrophic burn scars, which is closely related to the

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**Table 1. Case reports of patients treated with 1 Primary Wound Dressing: Burns**

| Patient # | Sex | Age (years) | Burn degree | Healing | Wound size ($cm^2$) | Time to healing (days) | Latency (days) | TBSA (%) |
|---|---|---|---|---|---|---|---|---|
| 1 | F | 11 | Mixed II° | S.I.H. | 57.19 | 13 | 1 | 4 |
| 2 | M | 3 | Mixed II° | P.F.G. | 36.91 | 21 | 4 | 5 |
| 3 | F | 8 | Mixed II° | S.I.H. | 69.18* | 14 | 10 | 8 |
| 4 | M | 1 | Mixed II° | I° G | 14.93 | 21 | 7 | 6 |
| 5 | M | 2 | Mixed II° | S.I.H. | 132.04 | 18 | 1 | 8 |
| 6 | M | 11 | MIxed II° | P.F.G. | 11.64* | 20 | 17 | <3 |
| 7 | M | 11 | Partial II° | S.I.H. | 4.63 | 10 | 1 | <1 |

**M= male, F= female**
**S.I.H.= secondary intention healing**
**P.F.G.= (secondary intention after) partial failure of graft**
**I° G= graft at 13 days**
***= data is intended as the sum of the areas of wounds in different body locations**
**TBSA: Total Body Surface Area**

length of the healing time (i.e. if more than three weeks)[11] and higher among Afro-descendants, Asians, Hispanics and other races with dark skin pigmentation (as in Bolivia), and also among populations with a particular genetic susceptibility.[12–14]

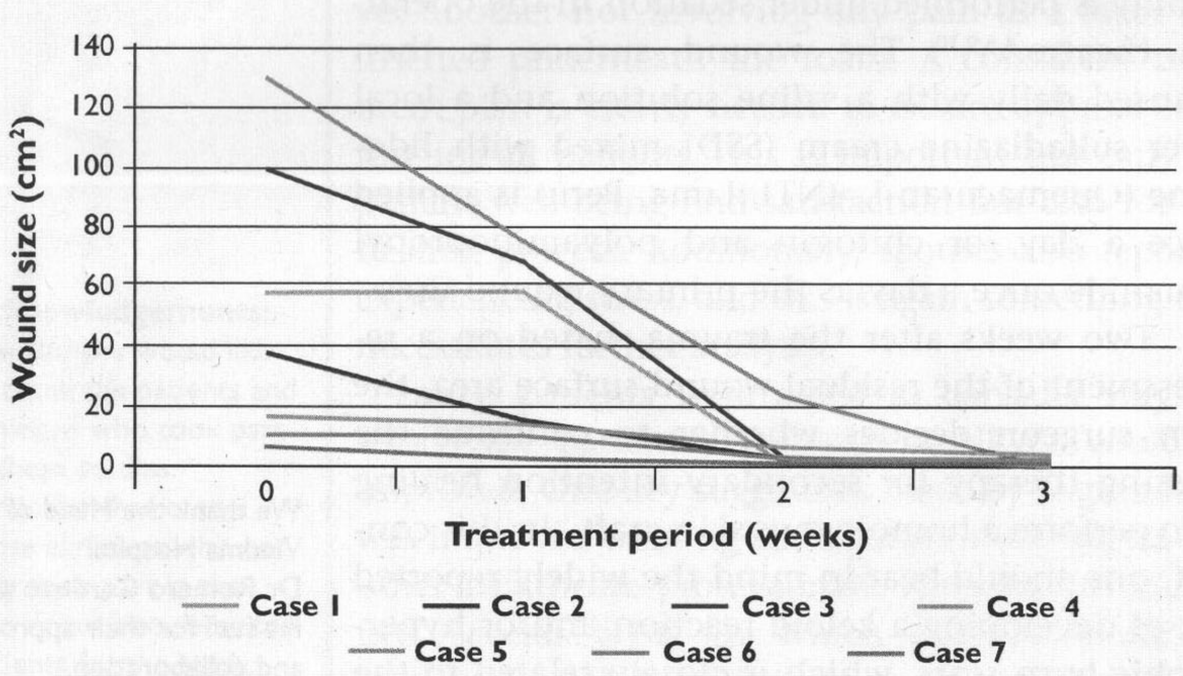
Systemic antibiotics are routinely administered to the patients for about five to seven days or longer if there are infective complications. The patients with full-thickness and third degree burns are admitted to the hospital as inpatients and a skin graft performed. Such patients have to follow a long-term rehabilitation and physiotherapy course during which those developing a keloid reaction have to wear a special secondary compression dressing.[11] Very often, the patients do not comply with the scheduled course of treatment and come back to the hospital only when there are disfiguring keloids that are undergoing ulcerations, which need to be treated to achieve secondary intention healing or removed by surgery.[13]

**Table 2. Case reports of patients treated with 1 Primary Wound Dressing: ulcerations of old keloid**

| Patient # | Sex | Age (years) | Type of wounds | Healing | Wound size ($cm^2$) | Time to healing (days) | Latency (days) |
|---|---|---|---|---|---|---|---|
| 8 | M | 10 | keloid | S.I.H. | 1.79 | 22 | 3 |
| 9 | M | 6 | keloid | S.I.H. | ND | 11 | 3 |

**S.I.H.= secondary intention healing**

**Fig 1. Reduction in wound surface area**




An ideal burn wound dressing should prevent contamination and desiccation, remove exudate, prevent infection and promote wound healing while being both comfortable to apply and remove, easy to use, economical and have a long shelf life.[10] Research suggests that certain antimicrobials (povidone iodine, silver sulphadiazina, chlorhexidine, etc.), besides provoking pain, have cytotoxic effects which impair or delay the healing process.[15] The ideal dressing should not provoke procedural pain (the pain experienced as a direct result of the wound care procedure) and should contribute to the relief of background pain (the burn pain experienced by patients when at rest).[16–18] The literature confirms that such dressings do not yet exist[2,10] and painful cytotoxic antimicrobials are commonly used in conventional management of burns, including with paediatric patients.[2,6,9,19] However, a new plant-derived wound spray has recently been introduced to the Swiss market (1 Primary Wound Dressing; Phytoceuticals AG, Zurich, Switzerland). It consists of a mixture of hypericum oil (*Hypericum perforatum*) and neem oil (*Azadirachta indica*), designed to create a moist wound healing environment, with the oil layer preventing the secondary dressing from adhering to the wound. Results from extensive case studies in different types of acute and chronic wounds suggest that 1 Primary Wound Dressing can be used as an effective primary wound dressing, promoting wound healing and protecting the peri-wound skin.[20] The literature reports that 1 Primary Wound Dressing leads to an impressive induction of granulation tissue, even in very deep wounds.[21] It

has proved to be simple to use and contributes to enhanced patient comfort.[21] Furthermore, it is thought to have an antimicrobial effect without provoking pain, and promotes the regeneration of the epidermis.[21,22] Because the composition of this plant-derived wound dressing is similar to that of the normal constituents of tissue (free saturated and unsaturated fatty acids), it is not expected to irritate the skin, which is a potential problem with topically applied exogenous materials.[23,24] Thanks to the simple mode of application (spray) and its wide range of actions, it could prove to be suitable for the treatment of burns and an effective alternative to the existing treatment options which rely on the use of local antibiotic ointment and painful cytotoxic disinfectants/antimicrobials.

In this retrospective, non-controlled study, we observed the effects of this product on (a) mixed partial and full-thickness burns healing under secondary intention, (b) failed skin grafts of burns treated as described above and (c) ulcerations of previously healed burns which had developed a keloid reaction. An assessment of pain relief was carried out only on patients older than five years as they were able to answer questions about pain medication and pain relief. When patients were treated at home, the parents were instead asked to report on pain and pain relief.

## Method

The patients in this study were recruited from Viedma Hospital, Cochabamba, Bolivia from June to August 2012. The patients that stopped attending check-ups before complete wound healing were not included in the study. A retrospective review was performed on 9 patients with a total of 18 wounds: 9 mixed partial and full-thickness burns, 1 partial thickness burn, 2 keloid ulcerations, and 6 partial failures of skin grafts, all but one left to heal by secondary intention. One case underwent a skin graft 13 days after the trauma. The standard treatment applied by the wound care specialist consisted of daily cleansing of the wound with a saline solution and application of 1 Primary Wound Dressing on the whole wound surface without applying any secondary dressing. Granulation tissue formation, epithelialisation, wound area (using scaled digital photographs processed with CAD software), pain relief

**Fig 2a Patient #1: mixed second degree burn. First examination**

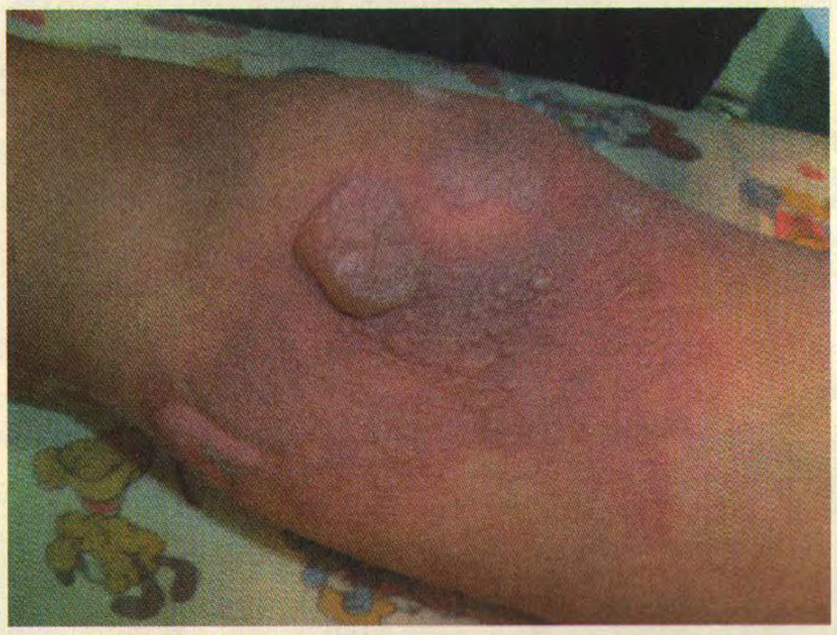


**Fig 2b After 3 days treatment with 1 Primary Wound Dressing**

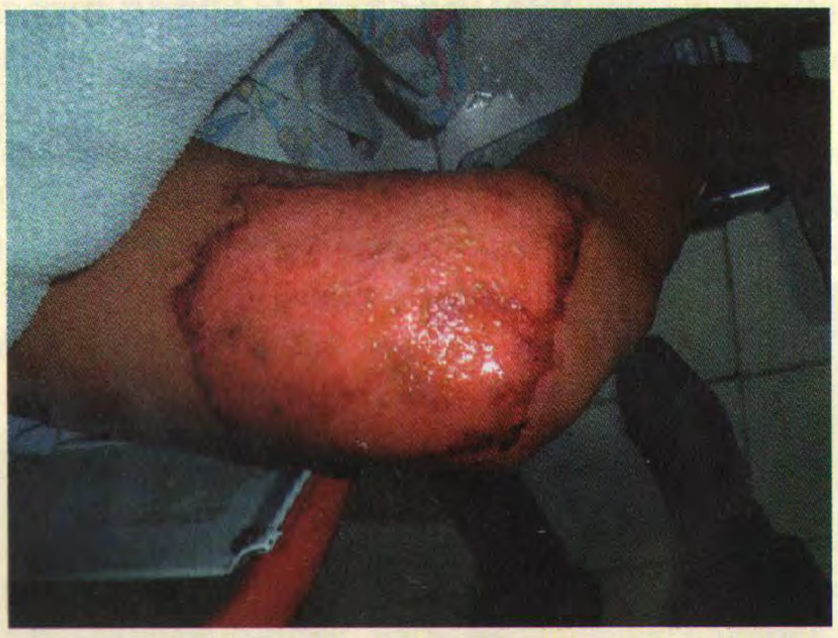


**Fig 2c After one week treatment with 1 Primary Wound Dressing; re-epithelialisation of 25% of the wound surface.**

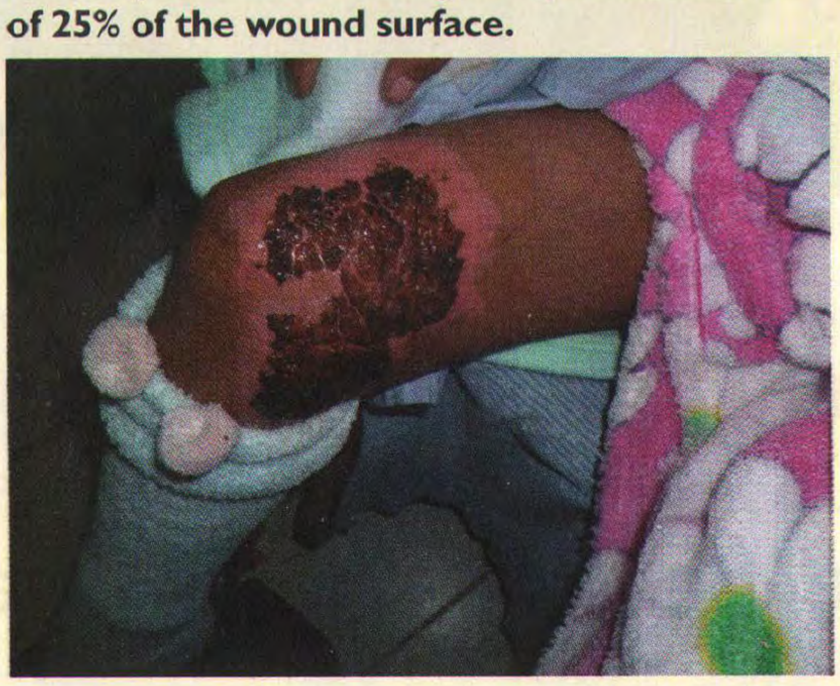


**Fig 2d After two weeks treatment with 1 Primary Wound Dressing; re-epithelialisation of 100% of the wound surface.**

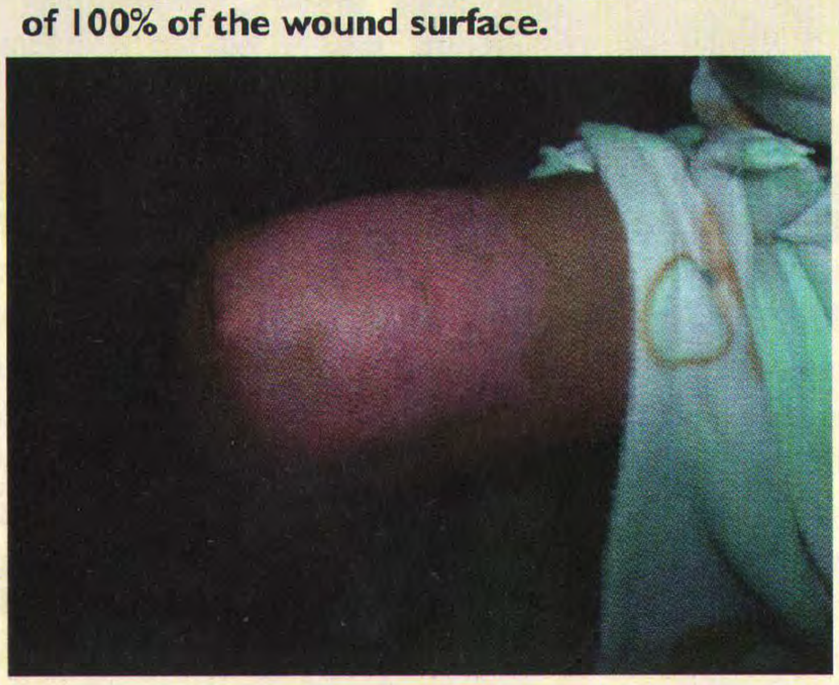


**Fig 3a Patient #1: second wound, mixed second degree burn (first visit).**

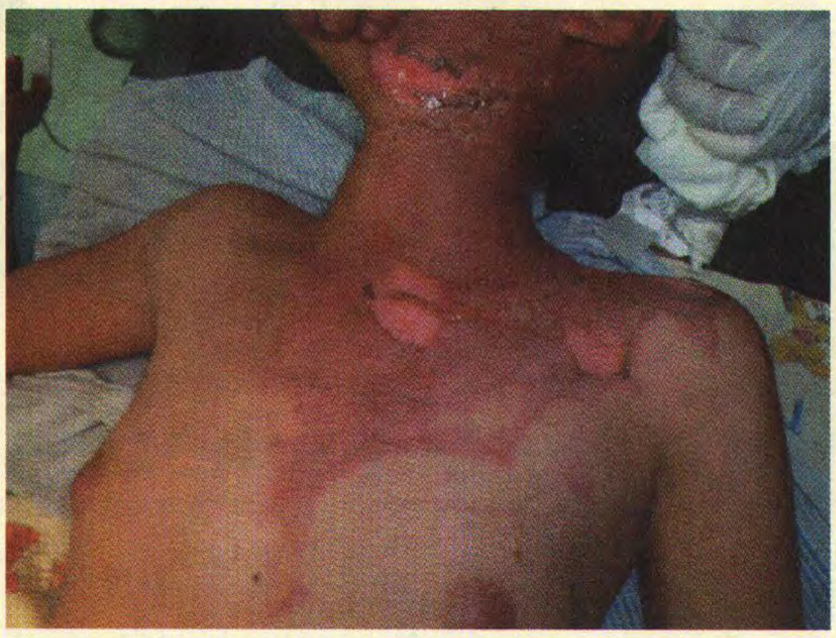


**Fig 3b After 3 days treatment with Biopiel**

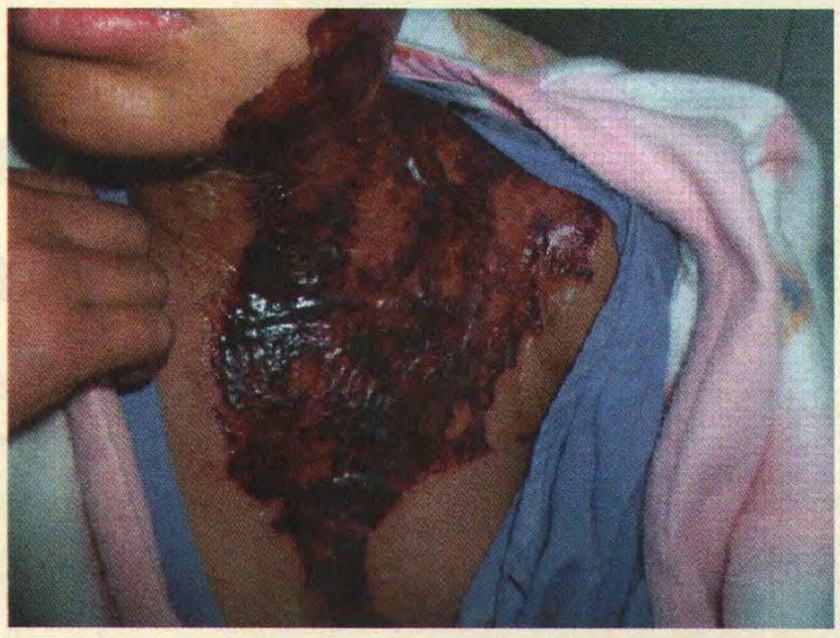


**Fig 3c After 10 days of treatment with Biopiel; re-epithelialisation of 25% of the wound surface**

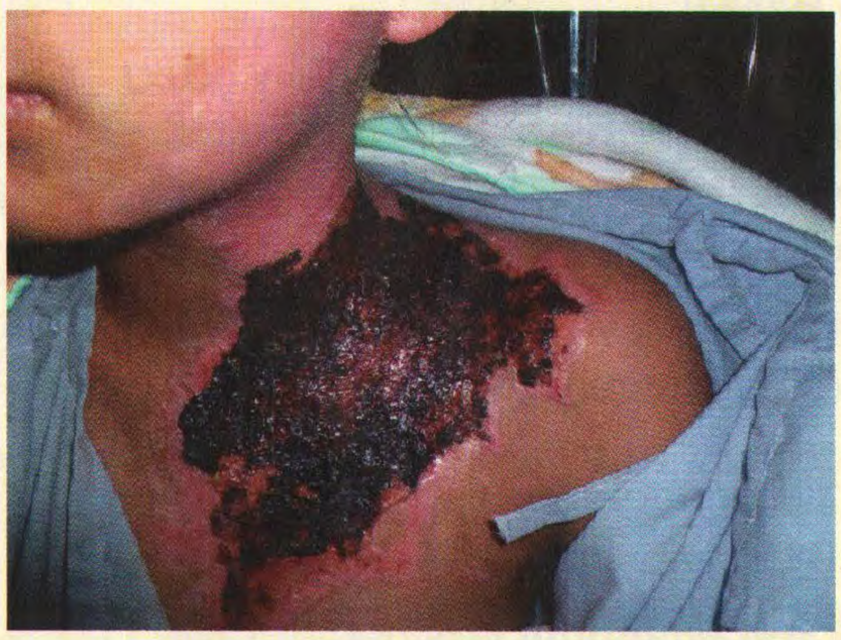
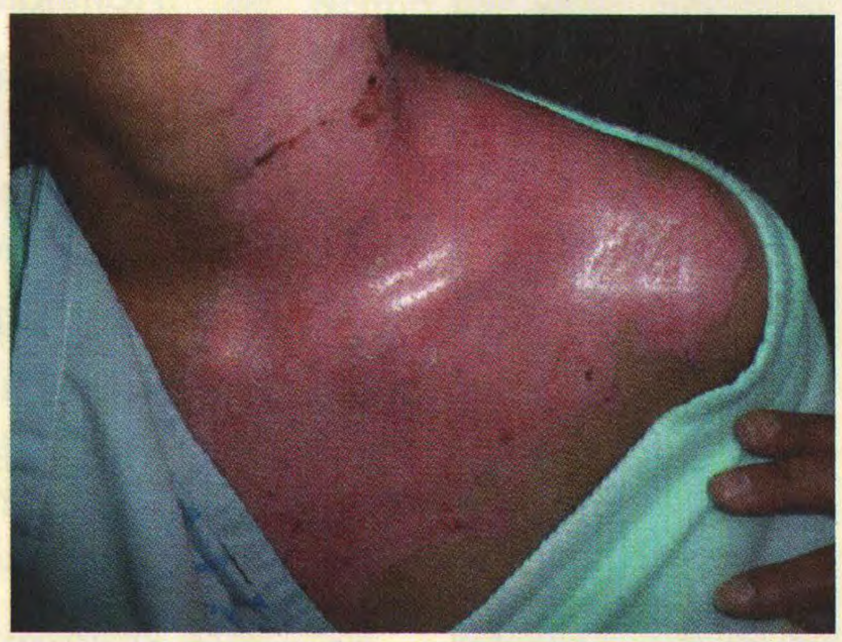


**Fig 3d After 2 weeks of treatment with Biopiel; re-epithelialisation of 100% of the wound surface**



(using a Visual Analogic Scale (VAS) system ranging from 0 to 10) and time to healing were recorded weekly by the same wound care specialist. An external specialist processed the digital data (scaled photographs). Pain relief was documented during the initial week after trauma for several patients older than five, however due to the high drop-out rate, the pain relief in the next two weeks was recorded for only 6 patients. Because the previously mentioned Biopiel protocol does not include the use of bandaging, which is very painful if the secondary dressing sticks to the wound surface, the evaluation of the procedural pain was limited to the daily cleansing of the wound surface using saline solution and renewal of medication.

Patient #1 (Fig 2 and 3) had two wounds located in different parts of the body. The wound located on the chest was treated using the Biopiel protocol while the wound located on the knee was treated with 1 Primary Wound Dressing in order to potentially demonstrate the differences between the protocols. Owing to the consistent pain relief reported by the patient in the wound site treated with 1 Primary Wound Dressing, it was decided to discontinue this comparative case, including when other patients bearing more than one wound were recruited, given the strong pain provoked by the Biopiel protocol.

Treatment was continued until complete epithelialisation, and in the cases that underwent grafting the treatment was continued until the skin graft was assessed to have been successful. The treatment period was defined as the time between the first application of the wound dressing and complete wound closure by secondary intention healing or graft attachment. Due to the small number of patients examined during the period studied, it was not possible to perform statistical analyses. This observational study obtained the ethical approval of the hospital and the informed consent of patients' relatives.

## Results

Nine patients of the initial group recruited completed the study period. Data and cases are summarised in Table 1 for burns and Table 2 for ulcerations of old keloids. The mean age of the 9 patients was 8.17+3.35 (1–11 years) and they had a total of 18 wounds. The mean size of the mixed partial and full-thickness burns was 50.76±48.32cm² (4.63–


**References**

**1** Burd, A. and C. Yuen, A global study of hospitalized paediatric burn patients. Burns 2005; 31: 4, 432–438.

**2** Kim, L.K.P., H.C.O. Martin, and A.J.A. Holland, Medical management of paediatric burn injuries: Best practice. J Pediatr 2012; 48: 4, 290–295.

**3** Tse, T., C.H.Y. Poon, K.H. Tse, et al., Paediatric burn prevention: An epidemiological approach. Burns 2006; 32: 2, 229–234.

**4** Palmieri, T. and D. Greenhalgh, Topical treatment of paedatric patients with burns: a practical guide. Am J Clin Dermatol 2002; 3: 8, 529–534.

**5** National Burn Care Review Committee, UK, 2006. Available from www.britishburnassociation.org [Accessed November 2013].

**6** Jefferey, S.L.A., Current burn wound management. Trauma 2009; 11: 241–248.

**7** Monstrey, S., H. Hoeksema, J. Verbelen, et al., Assessment of burn depth and burn wound healing potential. Burns 2008; 34: 6, 761–769.

**8** Pape, S.A., C.A. Skouras, and P.O. Byrne, An audit of the use of laser Doppler imaging (LDI) in the assessment of burns of intermediate depth. Burns 2001; 27: 3, 233–239.

**9** Papini, R., ABC of burns - Management of burn injuries of various depths. British Medical Journal 2004; 329: 7458, 158–160.

**10** Singer, A.J. and A.B. Dagum, Current management of acute cutaneous wounds. New England Journal of Medicine 2008; 359: 10, 1037–1046.

**11** Deitch, E.A., T.M. Wheelahan, M.P. Rose, et al., Hypertrophic burn scars - analysis of variables. J Trauma 1983; 23: 10, 895–898.

**12** Al-Attar, A., S. Mess, J.M. Thomassen, et al., Keloid pathogenesis and treatment. Plast Reconstr Surg 2006; 117: 1, 286–300.

**13** Butler, P.D., M.T. Longaker, and G.P. Yang, Current progress in keloid research and treatment. J Am Coll Surg 2008; 206: 4, 731–741.

**14** Wu, Y., B. Wang, Y.H. Li, et al., Meta-analysis demonstrates association between Arg72Pro polymorphism in the P53 gene and susceptibility to keloids in the Chinese population. Genet Mol Res 2012; 11: 2, 1701–1711.

**15** Fraser, J.F., L. Cuttle, M. Kempf, et al., Cytotoxicity of topical antimicrobial agents used in burn wounds in Australasia. ANZ J Surg 2004; 74: 3, 139–142.

**16** Abdi, S. and Y. Zhou, Management of pain after burn inury. Curr Opin Anaesthesiol 2002; 15: 5, 563–567.

**17** Burns Management Guidelines 2012, Victorian Adult Burns Service, The Royal Children's Hospital, Melbourne. Available from www.vicburns.org.au [Accessed November 2013].

**18** Chan, E.A., J.W.Y. Chung, T.K.S. Wong, et al., Application of a virtual reality prototype for pain relief of pediatric burn in Taiwan. J Clin Nurs 2007; 16: 4, 786–793.

**19** Rosanova, M.T., D. Stamboulian, and R. Lede, Systematic review: which topical agent is more efficacious in the prevention of infections in burn patients? Arch Argent Pediatr 2012; 110: 4, 298–303.

**20** Hunziker, T., M. Hafner, S. Streit, et al., Plant wound spray for acute and chronic skin wounds. Wound Manage 2012; 6: 270–274.

**21** Lauchli, S., J. Hafner, C. Wehrmann, et al., Post-surgical scalp wounds with exposed bone treated with a plant-derived wound therapeutic. J Wound Care 2012; 21: 5, 228–233.

**22** Desbois, A.P. and V.J. Smith, Antibacterial free fatty acids: activities, mechanisms of action and biotechnological potential. Appl Microbiol Biotechno 2010; 85: 6, 1629–1642.

**23** Drake, D.R., K.A. Brogden, D.V. Dawson, et al., Thematic review series: Skin lipids – Antimicrobial lipids at the skin surface. J Lipid Res 2008; 49: 1, 4–11.

**Fig 4a Patient #8: partial failure of skin graft, day of surgical debridement under sedation and start of 1 Primary Wound Dressing treatment**

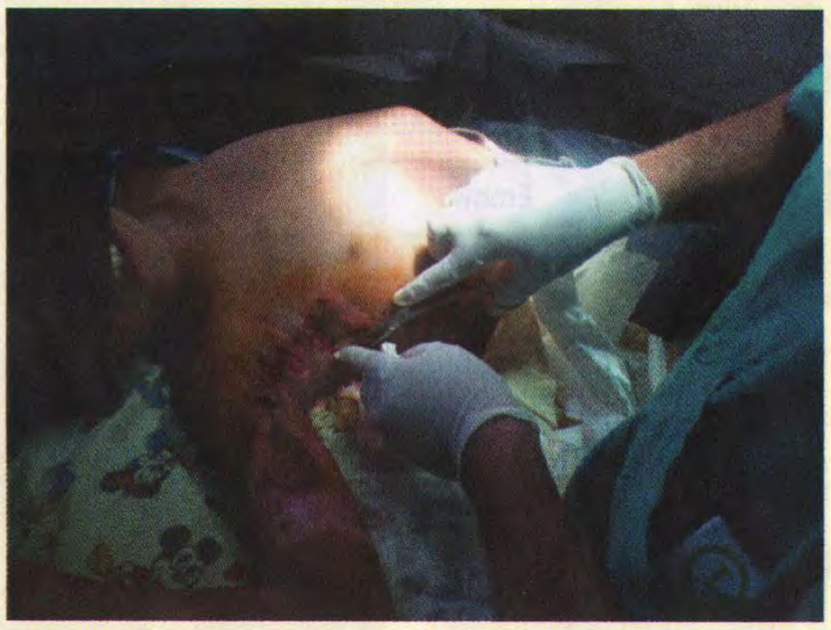


**Fig 4b Partial failure of skin graft, appearance of the wounds after surgical debridement under sedation**

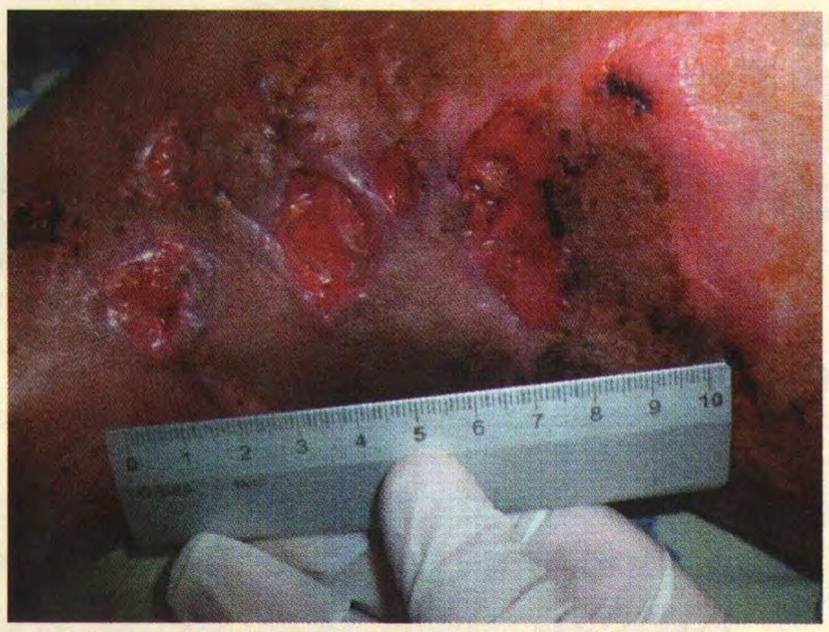


**Fig 4c Following one week of 1 Primary Wound Dressing treatment**

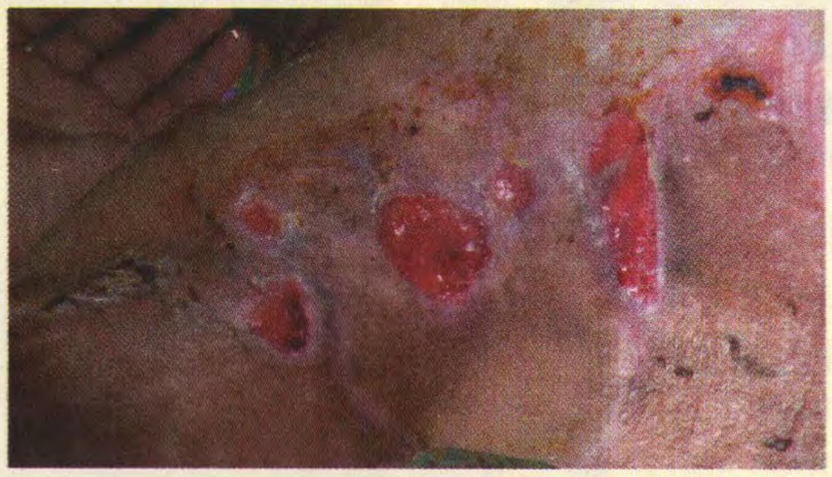
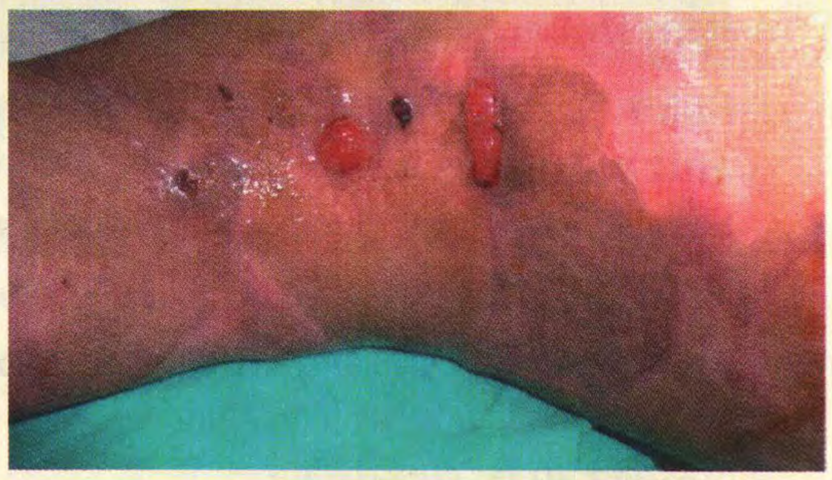


**Fig 4d Following two weeks of 1 Primary Wound Dressing treatment**



132.0cm²). In all burn cases, the Total Body Surface Area (TBSA) was less than 10%. The size of the keloid ulcerations was 1.79 cm² in one case and similar but not measured in the other case (Table 2).

Six of the patients recruited that completed the study were older than five (mean age 9.6±2.39 years: 8–11 years) and could be questioned about pain sensation and pain relief during and after treatment application. All of them reported that the initial pain rating of 7–8 out of 10 decreased to 0 out of 10 on the VAS, adopted after 3–5 days of treatment with 1 Primary Wound Dressing, and continued to report no pain during the second and third weeks of treatment. Fourteen out of 15 wounds (8 cases) healed by secondary intention without any further interventions. Patient #2 (Fig 4) and patient #6 exhibited partial failures of skin graft, (Table 1), while patient #4 underwent a successful skin graft at 13 days after trauma . The mean time to healing for all the wounds considered was 16.6±4.69 days (10–22 days) (See Tables 1 and 2). Figure 1 shows treatment period (weeks) and reduction of wound surface area for mixed partial/full-thickness burns (7 cases).

Patient #1 (comparative case; Fig 2 and 3) displayed the same healing time for both wounds. The patient complained about a continuous and strong pain in the site treated with Biopiel during the first and second weeks, but not in the site treated with 1 Primary Wound Dressing.

No wound exhibited clinical evidence of superficial or deep infection. None of the patients showed signs of allergic reaction and no other side effects were observed. A review of the clinical photographs of the healed wounds showed a cosmetically satisfactory outcome for all patients.

## Discussion

One of the most important aims when treating paediatric burn patients is to alleviate their pain as much as possible. The burn pain and wound care procedures often increase burn patients' anxieties, which exacerbates their perception of pain.[25] This is especially true for children, who, owing to their fear of pain, typically experience a high level of anxiety before and during burn wound care treatment.

At Viedma Hospital, it is commonly known that the local protocols for the treatment of burn wounds do provoke both procedural and background pain. We observed that the application of 1 Primary Wound Dressing never provoked procedural pain

and the children did not become stressed during wound care, but instead became confident in the spray procedure and demanded to be sprayed due to the strong background pain relief obtained after it. The pain relief experienced by the paediatric patients was also reported by the parents of the outpatients after scheduled dressing treatment at home. The requests to be sprayed were more frequent during the first week after trauma (inflammatory phase) than in the following period where no other applications other than the daily wound care procedure were scheduled. The inflammatory phase involves high levels of background pain due to the strong presence of metabolic activity at the injury site, and the high level of oxygen free radicals, different types of catabolites deriving from the injured tissue, chemical mediators and inflammatory cells, which act to repair damaged tissue.[26,27]

Burn pain is also derived from exposed sensitive fibres of damaged nerves left uncovered by the trauma, which get stimulated by the air. Some folk remedies, in which different sources of oil or grease are included, are typically applied to impede contact between the air and the damaged surface, especially in the case of painful deep burns (full-thickness burns).[28] Modern burn treatments include several occlusive dressings in order to obtain pain relief and protect the damaged area. Due to the high volumes of exudate during the inflammatory phase, however, and the risk of infection under occlusive dressings, it is not always possible to completely isolate the burn surface from contact with the air to obtain complete pain relief.[6,26,29] Indeed, secondary intention healing is commonly considered painful with a high infection rate, and therefore requires extensive care, and possibly results in inferior cosmetic outcomes.

In this case series, we observed that secondary intention healing was not associated with infection or pain. 1 Primary Wound Dressing acts by forming an oily protective layer (mechanical isolation) on the damaged surface, which is likely responsible for the pain relief reported during the most painful period (1–2 weeks after trauma). The high volume of exudate from the wound surface during this first phase of healing caused the superficial oily layers created by the dressing to break up more rapidly, so that it needs to be re-applied more than once a day in order to re-establish a protective and pain-relieving mechanical barrier. The healing period observed for the 7 burn cases followed until complete epithelialisation (see Table 1) was similar to the expected period for full-thickness burns in which painful antimicrobials/disinfectant are used (from 15–21 days).[2,4] We obtained this result without using antimicrobials/disinfectant; there was a progressive filling up of the wound surface and re-epithelialisation, without any infective complications. This effect may be explained by the antimicrobial activity of the fatty acids contained in 1 Primary Wound Dressing[22] and by the balanced moist environment obtained due to the semi-occlusive layer the oil creates.[30] The early pain relief obtained also points to this plant-derived oil having an anti-inflammatory effect. It leads the healing process towards healthy granulation tissue formation and epithelialisation, although these particular properties need to be confirmed by an appropriate clinical study. The most remarkable clinical implications of this study finding are related to the possibility to reduce the use of topical antimicrobials/disinfectants without exposing the patients at risk of infective complications, while at the same time obtaining pain relief and a high quality cosmetic outcome.

## Limitations

There are a number of limitations to this study. There was only a small sample of patients recruited from a single centre and treated by only one specialist, with data analysed retrospectively. This makes interpretation of the results challenging; indirect comparison with published data on the management of such wounds has to be undertaken carefully, even if the characteristics of the wounds included in this study, and their prognostic indicators, are similar to those reported in other published trials. Even though these results appear to compare favourably with those from the literature, a larger, more robust clinical trial needs to be designed for verifying the repeatability of the results obtained.

## Conclusion

The results of this retrospective, non-controlled analysis suggest that the plant-derived wound spray 1 Primary Wound Dressing is clinically effective in treating burnt soft tissue, even though the mechanism underlying how the plant-derived oil worked to treat the burn is still yet to be determined. Further studies, with a larger population, are required to document the effectiveness of this wound spray in a controlled setting. ■


**24** Lauchli, S., Primary Wound Dressing: clinical experience. A novel wound dressing, formulated from natural oils, promotes effective healing, protects periwound skin and leads to an impressive induction of granulation tissue, even in deep wounds. Hospital Healthcare 2012; 1–3.

**25** Chapman, C., Psychological factors in postoperative pain and their treatment. In: Smith, G., Covino, B.G. (eds). Acute Pain. Butterworths, 1985.

**26** Latha, B. and M. Babu, The involvement of free radicals in burn injury: a review. Burns 2001; 27: 4, 309-317.

**27** Pedersen, J.L. and H. Kehlet, Hyperalgesia in a human model of acute inflammatory pain: a methodological study. Pain 1998; 74: 2-3, 139-151.

**28** Cuttle, L., J. Pearn, J.R. McMillan, et al., A review of first aid treatments for burn injuries. Burns 2009; 35: 6, 768-775.

**29** Cleland, H., Thermal burns Assessment and acute management in the general practice setting. Aust Fam Physician 2012; 41: 6, 372-375.

**30** Sharman, D., Moist wound healing: a review of evidence, application and outcomes. Diab Foot 2003; 6: 112–120.