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Procutase® versus 1% silver sulphadiazine in the treatment of minor burns

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ABSTRACT

The purpose of this randomised comparative study was to evaluate the use of silver sulphadiazine (SSD) 1% cream (Group A) with the use of Procutase® (Group B) in treating burns with a TBSA <10% and a depth not greater than 2nd degree burns and thus suitable for outpatient management. The two groups were similar in age, gender, race, and extent of burn. Procutase® is an ionic hydrogel composed of natural hydrophilic polymers in an active ionic solution with an inhibitor of matrix metalloproteinases MMP-1, -3 and -9 (collagenase/gelatinase). Subjects were seen in follow-up biweekly, and wounds of patients in SSD group were compared with those of Procutase® group for healing time, pain score at dressing change, compliance with therapy and complication rate. The result of this study showed that Procutase® treated patients had statistically significantly less pain and shorter wound healing time. Procutase® can be used successfully in patients with burns that do not require hospital admission.

1. Introduction

S. Andrea University Hospital in Rome serves 500,000 people, and is located in a mixed urban area where crowded apartment buildings and small factories and workplaces coexist. The inhabitants include many non-EU citizens whose comprehension of the Italian language is often poor. The hospital does not have a Burn Unit, thus ambulances transporting severe burns go directly to the Regional Burn Unit for treatment. Burns admitted to the Emergency Department (ED) occur because of work incidents (36%), domestic incidents (43%), and trauma (21%). At admission the plastic surgeon on call is consulted and the burns are treated according to international protocols [1]. Eighty percent of the burns treated between March 2005 and March 2008 presented with <10% TBSA burns and a depth up to the 2nd degree. Patients were otherwise healthy and were treated in the outpatient regime at the plastic surgery clinic.

Many dressings are in use in the treatment of partial thickness burns in outpatient burn management [1], with SSD 1% cream being the most commonly used material [2]. All claim to promote healing and prevent infection and to present no discomfort for the patients. There are differences in costs, properties, frequency of application and pain during treatment [3–5].

Procutase® is an ionic hydrogel, commercially available in a tube or in spray form. The hydrogel in the tube is thicker than the spray form: both require a secondary treatment (gauze). It is composed of natural hydrophilic polymers in an active ionic solution with trace metals and with an inhibitor of matrix metalloproteinase MMP-1, -3 and -9 (collagenase/gelatinase). Matrix metalloproteinases (MMPs) play a role in the regulation of cellular migration in wound repair and exhibit proteolytic activity. The tissue inhibitor of metalloproteinases (TIMPs) counteracts the proteolytic activity [6] and this interaction may

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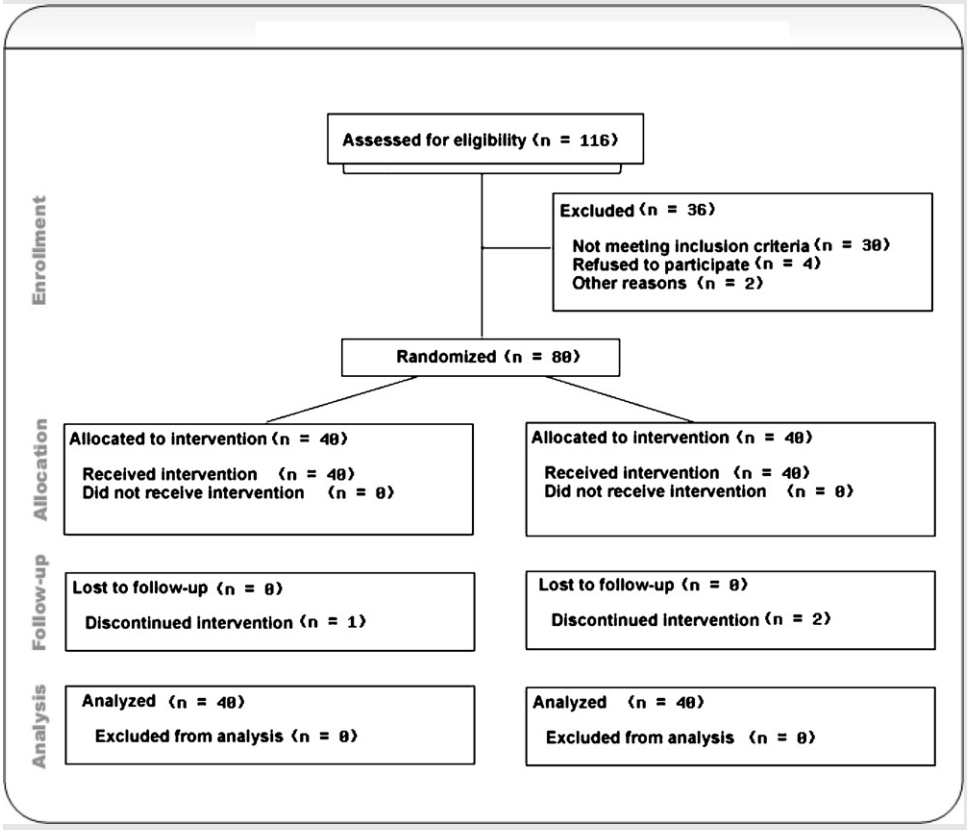
Table 1 – SSD vs Procutase® in ambulatory burns care.



be critical for better healing [7,8]. Dasu et al. reported on the changes in MMPs and TIMPs-1 serum levels occurring in burns patients [9]. Procutase® acts creating a moist environment that promote fibroblastic proliferation as well as the healing process. The TIMPs in the formula act on MMP-1 and -9 blocking the lysis process of the extra-cellular matrix and helping the collagen neosynthesis and the re-epithelization. The product has shown good biocompatibility with the skin and the mucosa and an absence of irritating effects as evaluated in laboratory tests using the MTT assay developed by Mossman [10]. It also promotes the absorption of the exudates and maintains the hydration of the wound bed. In laboratory tests it has been shown to have a good level of antimicrobial activity.

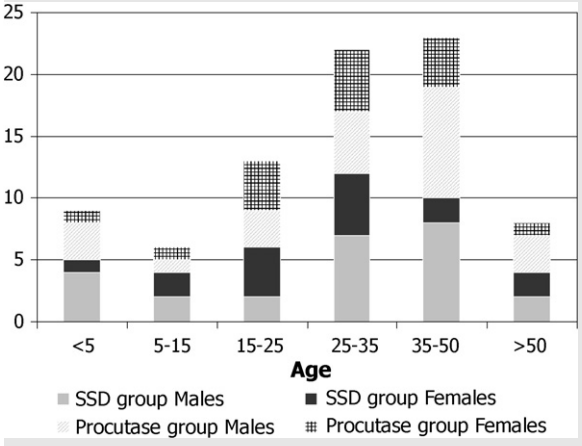
After Procutase® proved to be an effective, inexpensive and easily employed dressing in the care of skin ulcers [11], its use was extended to the care of minor burns.

The aim of this randomised comparative trial with Procutase® dressing versus silver sulphadiazine (SSD) 1% cream in the treatment of partial thickness burns, was to evaluate the results in terms of healing time, pain score at dressing change, and patient compliance with therapy.

2. Materials and methods

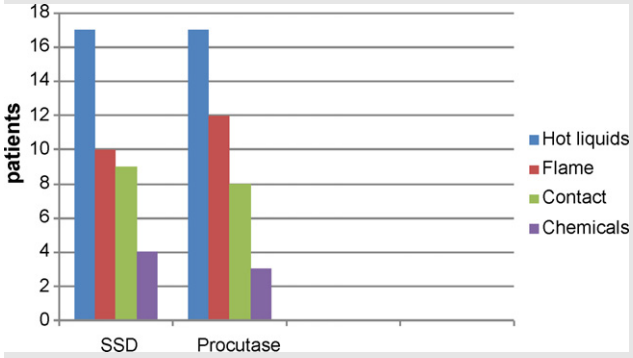
A total of 116 patients presenting with burns from January 2006 to January 2008 were assessed for eligibility in the study (Table 1). Each burn was evaluated by the plastic surgeon to assess the TBSA and the depth assessed by clinical evaluation of wound appearance, capillary refill, and burn sensibility to touch and pin prick. Of these, 80 patients (31♀ and 49 ♂), aged 2–65 years, seeking treatment for 2nd degree burns with TBSA <10%, were enrolled in the study after obtaining informed consent from the patient or his/her legal representative (Table 2). Four patients refused to participate, two agreed to

Table 2 – Demographic characteristics of sample.



Age and gender of the 80 patients included in the study: 49 males and 31 females. Males show a predominance among infants because of domestic accidents, and from age 25 to 50 because of accidents at work.

Table 3 – Aetiology of burns of the sample.



Aetiology of the burns of the 80 patients included in the study: contact with hot liquids (water, milk, coffee, tea, cooking oils, etc.) was the most frequent cause of burns. Flame was the second most frequent cause, followed by burns due to contact with hot metal (pans, iron, etc.). Chemicals burns were rarely reported.

participate but were excluded because they were travelling away from Rome in a short time. The burn aetiology was diverse; the most frequent cause was hot liquids, then flame, contact, and finally chemicals (Table 3).

At admission to the ED the burn area was cleaned with clorexidine and normal saline, and at random SSD or Procutase® was applied directly onto the burns. Then paraffin gauze was applied followed by a sterile gauze bandage. To randomise the study population a computer random number generator was used while planning the study. Once the patient was found to meet enrollment criteria (ambulatory burn not >10% TBSA, not deeper than 2nd degree, not comorbidities) he or she was assigned to one arm or the other of the treatment tree.

At PBD (post burn day) 2, in Group A SSD was applied again at burn site, in Group B only the outer gauze bandage was removed, and Procutase® was nebulized onto the paraffin gauzes and a new sterile gauze bandage was applied. From this point on subjects in Group A were instructed to apply SSD cream once a day at dressing change, while subjects in Group B were instructed not to remove the bandage until PBD 6, when a full change of dressing was scheduled for both groups at the plastic surgery outpatient clinic. At PBD 6 the wound was inspected and treated as in ED. Group A subjects continued to apply SSD cream, Group B subjects were instructed to nebulize Procutase® onto the paraffin gauzes every day. Biweekly assessments at the outpatient clinic were scheduled until healing was complete. During each visit the burn area was inspected to assess the wound bed and wound margin healing. Swabs were taken when suspicious secretions occurred. The patient's compliance with the therapy was investigated along with the ease of dressing application and removal. Complete healing was defined as complete re-epithelization of the wound at the point that no more dressings were required, as assessed by a blinded outcome assessor represented by the plastic surgeon in charge of the outpatient clinic, that differs according with the week schedule. The surgeon was unaware which treatment arm was assigned to the subject, and evaluated the wound after the removal of dressing and its cleaning with saline by the nurse.

Pain was assessed after the initial debridement of the burns, starting with the first dressing change: the analgesic requirements were recorded and the pain due to the dressing change was scored on a visual analogue score for pain (VAS) [12]. The VAS was administered at the end of the dressing change by the nurse. Children from the age of 5 used the Wong–Baker faces pain rating scale [13].

All patients completed PBD 2 and PBD 6 VAS for pain, from this day onwards some of the patients were healed.

2.1. *Statistical analysis*

Statistical analysis was carried out with a Mann–Whitney test to check differences in VAS for pain between the two groups at PBD 2 and PBD 6 values, with exclusion of nine children under 5 years of age. Student's *t*-test (independent sample *t*-test) was used to check differences in healing time between the two groups, including all 80 subjects. Significance was assumed at a p level of <0.05. All statistical calculations were performed by the SAS for Windows (version 8) statistical package.

3. Results

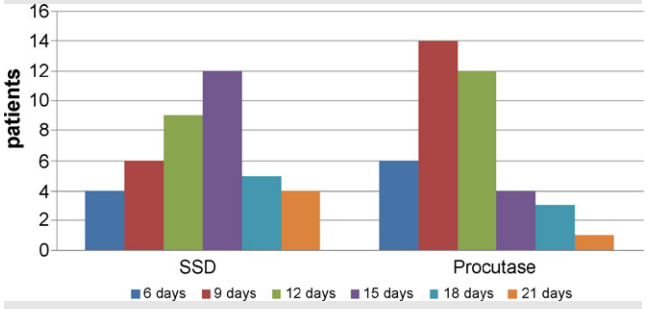
There were no differences in burn groups regarding age, gender or burn characteristics.

The mean time to healing of SSD treated burn areas (mean 13.5 days) was statistically longer ($p < 0.007$) than that of Procutase® (mean 11 days) (Table 4).

The differences in the degree of pain at the time of medication were statistically significant ($p < 0.002$), with patients in SSD group showing more severe pain, often requiring painkillers drugs prior medication, than patient in Procutase® group, when the change of dressing caused only some discomfort never requiring any drug for control (Table 5).

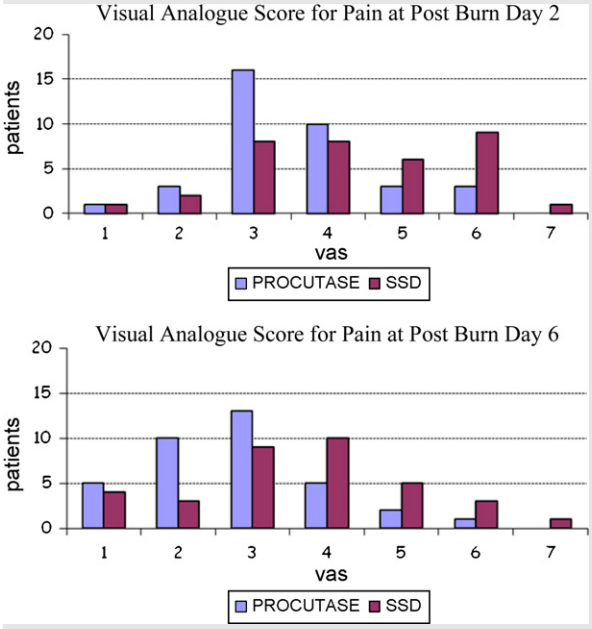
There were no differences in wound infection between both groups: no local or systemic adverse effects were observed in Procutase® group, one patient in SSD group had an infection by *Pseudomonas aeruginosa* requiring antibiotic therapy after susceptibility testing on isolated bacteria from swabs on culture media.

Table 4 – Healing time of sample.



Time to heal in 80 patients. Most of the patients in Procutase® group were healed in 12 days, while patients in SSD group required a little longer time to heal.

Table 5 – Assessment of pain.



VAS for pain as recorded at PBD 2 and PBD 6 in 71 patients. Children under 5 years of age were excluded from this test. The overall pain rating is higher in SSD group.

Three subjects (1 in SSD group and 2 in Procutase® group) from outside the European Union had their dressings changed three times a week exclusively at the outpatient clinic because the of a problem with language comprehension.

4. Discussion

Clinical evaluation of the burn wound is a widely used method of assessing burn wound depth, although its accuracy is not as reliable as methods investigating the cutaneous circulation and/or tissue perfusion [14], in particular when assessing burns in the intermediate depth. Unfortunately this equipment is not available at S. Andrea University Hospital. For the purposes of this study the European working party guidelines for the management of partial thickness burn were followed [15]: all the burns healed within three weeks confirming their initial classification as minor burns.

Although there is no unanimous consensus, a wide range of satisfactory options exist in the outpatient management of minor burns [2].

While silver sulphadiazine (SSD) cream is used and offers a high level of antibacterial activity it has also shown adverse effects in terms of high cost, healing time, frequency of dressing changes and pain at the time of medication [3,16,17].

In this trial Procutase® has been shown to have the same properties in preventing the onset of infections in minor burns as silver sulphadiazine, but with fewer and more comfortable dressing changes, without the unfavourable effects on fibroblast effects of the silver [17].

The majority of subjects found medications easy to proceed correctly with the home dressing change as prescribed, and compliance with therapy was good in both groups.

Frequent applications of Procutase® onto the paraffin gauze maintain a moist wound environment to promote a rapid epithelialization, with healing time similar to that associated with other dressings [4,5,18]. In this study treatment of 2nd degree burn wounds with Procutase® led to faster healing compared with treatment with SSD cream. Hydrocolloid dressings have been shown to replace skin function while healing is taking place, providing a moist environment that allows rapid epithelialization, but they are expensive and therefore are not included in the dressings chosen by the Health Manager to be acquired by the hospital. The cost of 50 ml of Procutase® hydrogel is 13.50 euro and the cost of 100 ml of Procutase® hydrogel spray is 11.00 euro. The vast majority of patients in Procutase® group required one tube of hydrogel and one hydrogel spray for the whole treatment until healing, with four subjects requiring four tubes of hydrogel and two or three hydrogel spray until healing. The cost of 30 g of SSD 1% cream is 8.95 euro, the cost of 50 g of SSD 1% cream is 10.50 euro and the cost of 180 g of SSD 1% cream is 14.53 euro. The vast majority of subjects in SSD group required one tube of 180 g and three tubes of 50 g of SSD 1% cream until healing, with six subjects required two tubes of 180 g and six tubes of 50 g of SSD 1% cream. Three subjects required two tubes of 180 g and nine tubes of 50 g of SSD 1% cream until healing. In Italy the 180 g of SSD 1% cream is for hospital use only and cannot be bought at pharmacy.

Dressing change in the Procutase® group caused discomfort only in the paediatric patients, showing a VAS for pain similar to the nonbiologic dressings [19,20], otherwise medication was not comfortable in SSD group.

In this trial Procutase® ionic hydrogel has proved to be of great benefit in the promotion of healing in minor burns and in preventing infection at the burn site.

The majority of patients in both groups found easy to proceed correctly with the home dressing change as prescribed, and referred a good compliance with both therapies.

The use of Procutase® resulted in decreased pain at dressing change, due to the modality of application of the hydrogel, with an easiness of care of the burn area for the patient leading to a good compliance with the treatment.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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