A silver sulphadiazine-impregnated lipidocolloid wound dressing to treat second-degree burns

- **Objective:** To evaluate the efficacy and tolerance of Urgotul SSD dressing (Laboratoires Urgo) in the treatment of second-degree burns.
- **Method:** This was a national multicentre phase III non-comparative open-label prospective study involving 10 burns units. The 41 subjects were non-immunosuppressed adults with second-degree thermal burn(s), which were clinically non-infected, less than 24 hours old, had a surface area less than 500cm^2 and warranted the local use of silver sulphadiazine. For four weeks, subjects were followed up weekly with a clinical assessment, bacteriological swabs and photographic recording.
- **Results:** Of the 41 patients, 24 healed within a mean of 10.8 days and 13 had a skin graft on the study burn within a mean of 11.5 days. There were four premature study withdrawals. The total number of cumulative treatment days was 445, and 298 treatments were performed (including 257 dressing changes). Mean dressing wear time was 1.73 days. None of the subjects acquired a secondary infection. Researchers took 121 bacteriological samples, and wound colonisation with *Staphylococcus aureus* was found in only one patient. At follow-up nursing staff reported that dressing acceptability was good.
- **Conclusion:** Use of Urgotul SSD led to a good wound outcome — wounds healed or were grafted.
- **Declaration of interest:** This study was sponsored by Laboratoires Urgo, Dijon, France.

silver sulphadiazine-impregnated dressing; second-degree burns; infection

Infection is the main cause of morbidity and death in patients with second and third-degree burns.[1] However, since the start of the 1970s the use of topical antibacterial agents such as silver sulphadiazine (suphonamide and silver combination) has reduced the risk of infection.[2]

Silver sulphadiazine is a broad-spectrum topical antibacterial agent which is active against Gram-positive cocci, *Staphylococcus aureus* and Gram-negative bacilli, particularly *Pseudomonas aeruginosa*.[3,4]

Its widespread use is justified by its bacteriological profile, its efficacy in the prevention of colonisation of lesions by pathogenic microorganisms and its good local and systemic safety.[5-8]

Available as a cream, silver sulphadiazine is applied to the burn and covered with greasy sterile gauze (which is similar to paraffin gauze), a secondary dressing and a bandage.

Following the efficacy of silver sulphadiazine and Urgotul, a non-bactericidal dressing used to treat acute and chronic wounds,[9,10] particularly superficial second-degree burns,[11] Laboratoires Urgo developed a silver sulphadiazine-impregnated wound dressing, Urgotul SSD. This aims to:

- Prevent secondary infection
- Ensure a known dose of silver sulphadiazine is delivered. (Urgotul is impregnated with 3.75% silver sulphadiazine. The amount delivered to the wound has not been measured)
- Reduce dressing change frequency.

This prospective clinical study aimed to evaluate the efficacy, tolerance and acceptability of Urgotul SSD in the local treatment of second-degree burns at risk of secondary infection.

Materials and method

This was a phase III multicentre non-comparative open-label trial conducted in 10 burn units in France. Approval of the Versailles Hospital (78) ethics review committee was obtained. Under French law, this covered all of the centres involved in the study.

Forty-one hospitalised patients with second-degree burns were included. Staff at the burn units did the medical and nursing follow-up. Each patient was treated with Urgotul SSD dressing for a maximum of four weeks.

To be included, the burns had to be:

- Of less than 24 hours' duration
- Of thermal origin
- Have a surface area less than 500cm^2
- Be clinically non-infected.

They also had to warrant the local use of silver sulphadiazine in accordance with the investigating department's treatment procedures.

Only parts of the total burn surface area that best matched the selection criteria were treated with the Urgotul SSD dressing. Remaining burn areas were treated at the investigators' discretion, in accordance with the usual treatment procedures.

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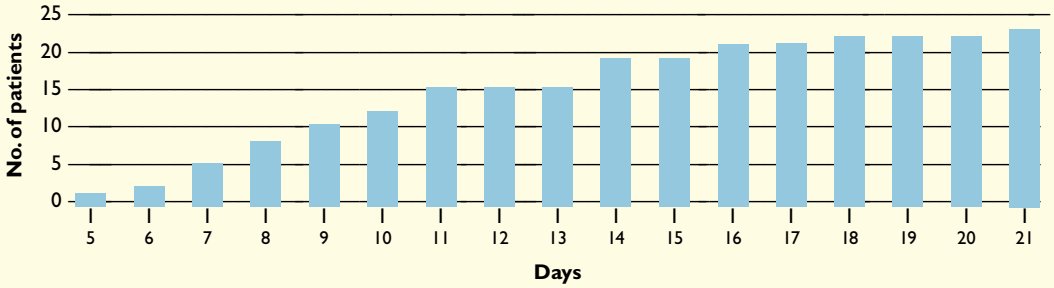
Fig 1. Healing time (cumulative histogram)



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The study dressing

Urgotul SSD dressing comprises a polyester mesh impregnated with carboxymethylcellulose, Vaseline and silver sulphadiazine (3.75%). In this study, the non-occlusive dressing used had a surface area of 100cm^2 (10 x 10cm).

Silver sulphadiazine is composed of suphonamide, which is bacteriostatic, and silver, which is bactericidal. Its mechanism of action results from the synergetic activity of the suphonamide and silver components, which inhibit the replication of bacterial DNA.

Earlier studies

Before this clinical trial, the test dressing's performance was assessed in animals (guinea pigs), on which a dermoepidermal wound measuring 9cm^2 was created.

With a dressing change frequency of every two days, wound healing (which was measured by image analysis) was documented for each of the three dressings tested:

- Urgotul
- Urgotul SSD
- Gauze plus silver sulphadiazine cream.

No delay in healing with Urgotul SSD was observed compared with Urgotul. Wounds dressed with gauze plus silver sulphadiazine cream took longer to heal than those dressed with Urgotul SSD, and bleeding occurred on removal due to adherence to the wound.

Unpublished *in vitro* studies into the antimicrobial properties of Urgotul SSD, also undertaken by Laboratoires Urgo, show that the dressing becomes active whenever it comes into contact with *Staphylococcus aureus* and *Pseudomonas aeruginosa*, and is antibacterial for 72 hours.

In the clinical study described here, saline solution was recommended for dressing removal, which was performed every day during the first week, and then every two days. The study sponsor recommended the researchers use this protocol alongside the department's usual treatment procedures for silver sulphadiazine.

Evaluation and assessment criteria

In the present study, weekly follow-up, undertaken for a maximum of four weeks, comprised:

- Clinical assessment
- Bacteriological swabs
- Photographic records.

Healing progression was assessed in terms of time to healing and/or the need for skin grafting. This was the primary outcome measure.

The bacteriological samples were taken at inclusion and then on a weekly basis. If the presence of a local infection was suspected, the investigators took additional samples for confirmation.

The investigators also looked out for signs of colonisation by pathogenic bacteria, *Staphylococcus aureus* and *Pseudomonas aeruginosa* in particular, in the treated wounds. At the burns units in this study, colonisation without local or general signs of infection is not considered to need treatment.

The investigating physician evaluated tolerance (lack of adverse events). Nursing staff evaluated acceptability at each dressing change — judged by ease of removal, adherence or bleeding on removal and conformability to the wound. These constituted the secondary outcome measures.

Statistical analysis

Descriptive statistical analysis was conducted by a biometrics department independent of the sponsor. It was performed on an intent-to-treat basis, and concerned both the main and secondary assessment criteria. Data relate to all patients in this trial.

Results

Patients/study condition

Table 1 outlines the patient demographic data and Table 2 characteristics of the burn injuries. The study population did not present any significant medical histories that could affect healing outcomes.

Before inclusion, 35% of the study burns had been treated with silver sulphadiazine cream, 21% had received no treatment, 32% had been given greasy sterile gauze and 12% had received other

treatments.

The thickness of the burns was not uniform, and there were often several degrees of thickness in the same lesion. All burns, which had a mean surface area of 192cm^2 and had been present for an approximate mean time of 14 hours before inclusion, were treated with the study dressing.

Clinical outcomes of study burns

None of the 41 patients presented any clinical signs of local secondary infection in the study burn.

Analysis of efficacy showed the following:

- Twenty-four patients (58.5%) healed within a mean of 10.8 ±4.3 days (range: 5–21 days) (Fig 1).
- Thirteen patients (31.7%) had a skin graft within a mean time of 11.5 days (range: 4–24 days).

Four patients discontinued treatment prematurely:

- The wound obstructed healing on day 10. This patient developed an eschar on the burn. His burn centre surgically excises all burns that do not show signs of healing after 10 days
- The patient was discharged on day 6 and follow-up was not possible
- Treatment was deemed unsuitable on day 12 as the burn depth necessitated a skin graft
- The patient withdrew consent on day 3.

Bacteriological swabs

The researchers took 121 bacteriological swabs during the trial, at least two from each patient.

In eight of the 41 patients (19.5%), a pathogenic microorganism, *Staphylococcus aureus*, but no clinical secondary infection was identified. Seven patients healed. The eighth was withdrawn due to the development of eschar on the treated wound.

Tolerance

The investigating physicians only documented one adverse event: one patient developed pain on the third day of treatment, although this did not warrant discontinuation of treatment.

Acceptability

In all, 298 treatments — including 257 Urgotul SSD dressing applications — were conducted and documented by the hospital nursing staff. The total number of treatment days was 445, and the mean duration of application was 1.73 days, with a minimum of one day and a maximum of five days between two dressing changes. Results for each of the parameters evaluated are outlined in Table 3.

Non-adherence of the test dressing (absent or slight for 82.4% of dressing changes) made dressing removal 'very easy or easy' (92.3%) with no bleeding on removal (absent or slight in 95.3% of cases).

Discussion

Like most burn-treatment studies, this was non-comparative. Therefore, only parallel analysis with data published in the literature can be undertaken.

Generally, mapping of bacterial flora on burned zones is performed on admission to burn units, although this depends on local policy. After that, routine bacteriological swabbing is not undertaken unless clinical signs of local secondary infection are present or wound healing is not progressing.

Microorganism count is very rarely conducted, simple swabbing being preferred to identify bacteria. Consequently, only bacteriological swabs as a qualitative evaluation of bacterial flora were required in this study.

Table 1. Patient demographic data at inclusion into the study (n=41)

Female	9 (22%)
Male	32 (78%)
Age (years) (range)	39.2 ±15.2 (20–82)
Weight (kg) (range)	71.6 ±12.5 (43–94)
Height (cm) (range)	171.5 ±9.9 (150–197)
Total burn surface area (%) (range)	14.1 ±9.6 (1.5–43)

Table 2. Burn characteristics

Duration of burn (hours) (range)	
14.1 ±11.3 (1–48)	
Initial burn surface (cm^2) (range)	
192.7 ±151.1 (30–629)	
Location of burn	
Lower limb	36.6%
Upper limb	31.7%
Hand	19.5%
Other	12.2%
Estimated thickness*	
Superficial/intermediate second degree	36.6%
Deep second degree	75.6%
Third degree	4.9%
Causal agent of the burn	
Flame	56.1%
Hot liquid (water, oil, etc)	36.6%
Other	7.3%
Nature of previous treatment	
Silver sulphadiazine cream	34.1%
Greasy dressing	31.7%
Other	12.2%
No treatment	22.0%

*Total does not add up to 100% as the thicknesses of these burns were sometimes combined

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19 Stern, H.S. Silver ▶

Table 3. Acceptability of the dressing

Ease of dressing removal	
Very easy/easy	92.3%
Difficult/very difficult	7.7%
Adherence to wound bed	
Absent/slight	82.4%
Moderate/important	17.6%
Conformability to wound	
Very good/good	72.9%
Average/poor	27.1%
Bleeding on removal	
Absent/slight	95.3%
Moderate/important	4.7%

Testing for colonisation with *Staphylococcus aureus* and *Pseudomonas aeruginosa* was undertaken as these cause secondary infection of burns.[4] *Staphylococcus aureus* was detected in eight of the 41 patients (19%), but *Pseudomonas aeruginosa* was notably absent.

This is a lower colonisation rate than that presented in Inman or Snelling et al.'s studies (64% and 54% respectively),[12,13] but greater than that in Pegge's comparative study[14] (9.2%) and Heinrich et al.'s retrospective study (2%).[15]

Mean healing times in burns treated with Urgotul SSD have been reported as: 11.3 ±6 days[16]; 16.1 ±0.6 days[17]; 15 ±1.2 days[18] and 19.2 days.[19] These patients were treated with silver sulphadiazine on an outpatient basis until complete healing occurred.

Moreover in the present study, of the 17 burns that did not heal with Urgotul SSD, 13 received a skin graft in a mean time of 11.5 days.

Only one adverse event — pain — was reported, at a tolerance level reported elsewhere.[12,20]

No systemic effects that could be related to treatment with silver sulphadiazine were reported, again reflecting the literature, where only a few rare cases of sulphadiazine sensitivity, reversible leucopenia or argyria have been reported.[21-23]

Conclusion

The results observed for the parameters 'ease of removal' and 'conformability of dressing' can be compared with those reported in previous research into Urgotul.[9-11] Our study demonstrated that the dressing had 82.4% non-adherence and caused no bleeding or trauma of the newly formed tissue.

The results of this clinical study demonstrate the good clinical outcome of burns covered with Urgotul SSD, and the good tolerance and acceptability of the dressing in the local treatment of second-degree burns at risk of secondary infection. ■

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