Treatment of Thermally Injured Patients with Betadine® Solution and Cream

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Topical antiseptic agents have important roles in the up-to-date treatment of burn wound surfaces. Superficial burns heal virtually spontaneously in response to any type of care in uncomplicated cases. In deep second degree burns, the dermis (the epithelial elements of which are absolutely necessary for the healing process) is destroyed in different thicknesses. The necrotized area is a culture medium for pathogens. In case of the infection spreading, even the uninjured epithelial elements will be destroyed and there is no more possibility for healing. The prevention of infection makes the avoidance of the development of a threatening complication and obtaining epithelization possible. According to the current conception surgical intervention is the preferred method: the earliest possible removal of the necrotized area and covering the wound to prevent infection. For performing an operation certain conditions are required. The use of antiseptic agents allows to postpone the intervention until the optimal moment. In case of third-degree burns, when the skin is destroyed to its total, surgical intervention is absolutely necessary. The prevention of infection is prerequisite of a successful operation. Local pre-operative treatment has to be applied by all means to burn patients arriving late with already infected wounds.

In the treatment of burns topical agents have to meet the following requirements:

1. Lack of toxicity and metabolism-influencing action,
2. broad bactericidal spectrum,
3. penetration through the eschar,
4. lack of live tissue injuring action,
5. lack of antigenic activity,
6. the pathogens should not develop resistance,
7. should possess desiccating (or crusting) action,
8. applicability made possible also without dressing.

Betadine®, marketed by EGIS Pharmaceuticals, under licence of Mundipharma AG of Switzerland, was made available for a clinical trial at our department in early 1991. The drug contains a polyvinylpyrrolidone-iodine complex.

Iodine was first describing as a local antiseptic (in 1839) [6]. It is still used as a skin disinfectant but its use has raised several problems. These were the following: firstly anaphylactogenic action, then problems of absorption, and poor water solubility. Since that time investigations have been performed with the aim to decrease the deleterious properties of the drug. The complex of iodine with polyvinylpyrrolidone met these requirements.

Polyvinylpyrrolidone (PVP) is a polymer with high molecular weight which was used as a plasma expander in World War II [14]. PVP forms a watersoluble complex with iodine. Shelanski [15] and Bogash [4] were the first to report on the topical use of the product in 1956. having an untight bond, iodine immediately exerts a microbicidal action when getting in contact with the skin or mucosa. For instance, it kills the majority of bacteria within 15-30 minutes.

The properties of Betadine® are the following:

1. It exerts a bactericidal action against Gram-positive as well as a Gram-negative bacteria, a fungicidal action against most fungi, sporocidal action against several spores, and has tuberculocidal action.
action as well as a virucidal action against a number of viruses (such as for instance polio or herpes viruses).

2. Even in a low concentration its action develops within a very short time, resistance to the drug does not develop.

3. In contrast to the well-known anaphylactogenic action of iodine, Betadine® is very well tolerated as proved by target specific examinations. Bogash [4] observed dermatitis in two of the 5900 treated patients, while Shelanski [15] did not find hypersensitivity to Betadine® in patients hypersensitive to iodine.

4. It has a dark brown colour and a characteristic odour. Due to its water solubility the new spots may easily be removed from the textile materials.

5. It remains stable for 3 years if stored unopened, protected from light, in a cool place. At higher temperatures or in response to sunlight it starts to decompose, its colour becomes less intensive. For this reason the solution has to be prepared shortly before use.

6. The action of the drug in humans and animals has been examined by several authors. These observations proved that the absorption of iodine causes the increase of serum iodine level. As a result, T3 (tri-iodothyronine) and T4 (thyroxine) values decrease besides the moderate increase of TSH (thyroide-stimulating hormone). According to the congruent opinion of the authors thyroid function is not injured [3, 8, 21, 22, 23]. Lavelle [10] and Pietsch [12] reported on metabolic acidosis, renal failure, and do not recommend the use of Betadine® in cases of renal functional problems or in cases of burn surfaces larger than 20%. Other investigators did not find renal functional disorders [7, 8, 16, 23]. In spite of these observations de Wet [19] and Hunt [8] also mentioned renal functional disorders as contraindications for the use of Betadine®.

7. It is readily absorbed through the normal skin, mucosa, and it penetrates through the necrosis caused by burns as well. Its desiccant action is very marked [9, 16, 17, 19, 23].

**Material and Methods**

Betadine® has been tried out in forms of solution and 10% cream. The actions of the products were examined in the treatment of superficial and deep second-degree burns as well as third-degree burns and in the preoperative treatment of skin donor areas. One to ten dilution of Betadine® solution was applied to the wounds or to the pretreated skin areas. For bathing the patients 1:100 dilution was used. Gauze sheets soaked Betadine® solution of 1:100 dilution prepared shortly before were applied to impregnate sheets prepared at our department (occasionally to Jelonet® sheets). In other cases the gauze sheets were applied directly to the burnt surfaces. According to our observations the use of Betadine®-soaked gauze sheets without impregnated sheets is much more favourable but its removal is more painful than the change of a bandage, therefore it may be rarely used. In general, the bandages were changed once daily. When pretreating the skin donor areas, the Betadine® soaked sheets were applied after bathing the patients and after shaving the area, if necessary, in the morning of the operation day. Among the routinely performed laboratory examinations the changes in blood counts and urinalysis findings as well as the serum creatinine values reflecting the excretion of iodine through the kidneys were considered. T3, T4, and TSH were examined for controlling the absorption of iodine or the changes caused eventually by iodine absorption.

In the first half of 1991 the treatment of a total of 23 patients was documented. It has to be noted, however, that the post-treatment of burns with small surfaces less than 1% of body surface and wounds of lentil to coin sizes, remaining after earlier operations but not surpassing 1-1.5% of body surface, was not documented. Exact data referring to the number of patients in whom the skin donor areas had been pretreated with Betadine® were not recorded either. The number of these treated non-documented outpatients and inpatients may be approximately 200.

Among the 23 documented patients 18 were men and 5 women. The age of the patients varied between 22 and 76 years (average 49.9 years). The causes of the burns were flame in 10 cases, boiling water or food in 8 cases, flaming arc in 2 patients, bitumen or burning hot oil in 1 patient each, and 1 patient suffered from contact burn. The shortest period elapsing between the burn injury and the onset of Betadine® treatment was some hours, the longest three weeks (average: 6.08 days). The duration of the application of the agent varied between 3 and 22 days (average: 10.3 days). Betadine®-soaked bandage was applied as a pretreatment of the donor areas in the morning on the day of operation- once only in all patients. To patients who had only superficial burn the agent was not applied. The agent was not applied to superficial burn. All patients also suffered from deep second degree burns of at least transitional depth, 12 of them had also (for solely) third-degree burns. The extent of burns varied between 1 and 75%, average it was 12.9% (Table I). Eight patients spontaneously healed, operation was performed in 12 patients, in 6 of them within 6 days, in the other six after 10-12 days. Four

| Age: 22-76 years (average: 49.9 years) |
| Extent of burn: 1-75% (average: 12.9%) |
| Deepness of burn: deep second-degree 11 patients third degree 12 patients |
patients died: one patient suffering from 55% TBSA (total burned surface area) died of sepsis and ARDS (adult respiratory distress syndrome) on day 14 following injury. One of the operated patients also died of sepsis and ARDS with almost healed wounds on day 29 following the burn injury of 18% of body surface. A patient with 75% TBSA died on day 5. An elderly patient, suffering from diabetes, hypertension, cardiopathy and from 14% deep burn of body surface, died because of the interaction of the severe primary diseases and the burn injury on day 5 as well (Table II).

Table II
Outcome of the Disease

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<th>Spontaneous healing:</th>
<th>Postoperative healing:</th>
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<tr>
<td></td>
<td>8 (average: 13.75 days)</td>
<td>1 (average: 56.36 days)</td>
<td>4 (average: 13.33 days)</td>
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Results

Considering the laboratory findings the changes observed in the blood counts corresponded only to the expectable changes due to burns. Moderate increase in serum creatinine values was registered only in the deceased patients 1–2 days prior to death. According to our opinion, however, this could rather be attributed to sepsis developing in each case than to the deleterious effect of iodine absorption. For supporting our opinion it has to be mentioned that Betadine® was applied only for a short period to all four patients. (Two patients died on day 5 following injury, one patient was operated on after a 4-day Betadine® treatment whereafter iodine was not applied anymore, and the patient died only on the 25th postoperative day). The fourth deceased patient was the only one among our patients treated until now in whom massive green-coloured Pseudomonas wound infection was observed along with the application of Betadine®. The treatment was discontinued for this reason after 4 days. Death occurred on day 14 due to Pseudomonas sepsis and ARDS.

The examination of T3, T4, and TSH values one week before and one month after applying Betadine® could not be performed in each case, partly because of death, partly because of the fact that some discharged patients did not return for control. It may be said that the values virtually did not surpass the normal ranges. In the majority of cases, T3 and T4 values moderately decreased as expected, whereas they increased again, while both the increase and decrease of TSH values could be registered (Table III). As an explanation for the values remaining within the normal ranges, the extent of wound surfaces of the patients may be considered, that is, these were not so extended as to have the iodine absorption overload the organism. Nevertheless, according to data of references, significant change was not observed in these values after Betadine®-treatment in a great number of patients with burns of 50–60–70% body surface either [3, 16, 22, 23].

When examining the results of wound discharge cultures in the course of therapy Staphylococcus aureus was identified in one patient, Proteus mirabilis in three patients, and Pseudomonas aeruginosa in three patients. Wound biopsy and quantitative bacteriological examination of the biopsy material cannot be performed at our department due to technical reasons. Considering the results of cultivations it has to be mentioned that one Pseudomonas-positive patient was a foreigner sent to our department from his country for treatment only on the 12th post-burn day. He had arrived with inflamed wounds in a septic condition and became operable only after another 16 days. Before this date he remained positive for Pseudomonas besides an increasing resistance for antibiotics. The other remark is that, eventually only by chance, almost 50% of the positive cultures were positive for Proteus. Considering the total microbiological findings at our department the rate of Proteus strain was significantly higher in these cases when compared to the other cases.
Discussion

The effectivity of wound treatment was evaluated on the basis of objective as well as subjective observations. In the course of the pretreatment of skin donor areas—although numerical data were not recorded either in earlier or in the current examination, because such study was never performed by our team—wet donor areas were observed less frequently when examined following the use of Betadine® than after pretreatment with the earlier used Neomagnol®.

The results obtained in 8 spontaneously healed patients have to be emphasized. Though the burns were deep second degree in each patient (in three of them an eventual operation could not have been excluded on the day of injury) in general rapid (in certain cases especially quick) epithelization was observed in response to Betadine® treatment. In the course of Betadine® pre-operative treatment the wounds of the third-degree burn patients remained free of inflammation due to the tanning effect of Betadine®. In one patient transferred to our department with dry necroses on the 3rd post-burn day—since the early operation was contra-indicated by the internist because of cardiac problems—Betadine® treatment was started. After controlling the cardiac symptoms the patient was operated on day 18. The operated wounds were not inflamed. After escharectomy on a 6% surface Betadine® treatment was continued for one day whereafter autotransplantation of split thickness skin was performed. The transplants adhered except for an area of 2 cm². According to earlier observations in similar cases chemical escharectomy should have been performed. In such patients the clearing of the remaning suppurating wound surface and the adherence of transplant would have created significantly less advantageous conditions for the healing process and an expectably longer recovery period. This case proved that Betadine® penetrated through necrosis [9, 16, 17, 19, 23].

Some authors recommend the change of bandage several times daily [5, 7, 13, 16, 19]. This method would probably improve the results. We planned the comparison of Betadine® with the PVP-J containing magistery Jodosept solution and Dermazine® cream containing silver sulphadiazine on the same patient. In the course of the examination only two patients were suitable for this purpose. Among them one was the mentioned deceased patient, the only one who did not respond to Betadine®. Because of the low number of observations we cannot draw final conclusions but it has to be mentioned that during Betadine® treatment the wounds remained dry (except for the mentioned one case) against the “soaked” wounds observed during the use Dermazine®. The patients often complained of disagreeable, stinging sensation in the course of the use of the Jodosept solution. Such complaint, referring to discomfort, developed in an insignificant number of cases during Betadine® treatment. According to our observations the desiccant effect of Betadine® is also more marked. During Dermazine® treatment Gram-positive bacteria may be more often indentified by wound discharge cultivation. As mentioned previously, during Betadine® treatment this occurred in one case only. Although the subject of our present report is Betadine® treatment of burn patient, it has to be mentioned that Betadine® ointment was tried out in one chronic crural ulcer patient previously having been treated for months—at the department of dermatology of the hospital—and unsuccessfully operated on at our department. The previously unresponsive ulcer almost healed. This observation supports the favourable results obtained by several authors in this condition [11, 18, 20] and makes it possible for us to extend the application fields of Betadine®.

Although the number of our observations over 6 months in documented 23 patients and the non-documented cases is low, these support the data of references dealing with burns which prove that Betadine® meets almost all requirements raised to topical agents.

Finally, it has to be mentioned that we reported on our first observations at the Burn Congress held on May 31, 1991. The colleagues fully agreed considering the introduction of the agent in Hungary. Several physicians reported on the very good responses obtained with Betadine® (made available from abroad) in a low number of cases. They also supported the importance of completing our present arsenal used in the treatment of burns with Betadine®.
Summary

The effect of Betadine® solution and cream was examined in the treatment of burn patients (23 documented and about 200 non-documented) during the first six months of 1991. The laboratory examinations did not reveal changes in T₃, T₄, TSH values. Renal failure due to iodine absorption was not observed. Hypersensitivity to the agent was not recorded. Healing of superficial and deep second-degree burns was especially rapid in some cases. In cases of third-degree burns the wounds remained "dry" until the operation. Favourable effect was also observed in the pretreatment of the donor skin areas. The authors found Betadine® to be definitely advantageous in the treatment of burn patients.

References