Experiences with the Use of Povidone-Iodine-Containing Local Therapeutics in Dermatological Surgery and in the Treatment of Burns: Testing for Allergic Sensitization in Postsurgery Patients

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**Key Words**
Povidone-iodine · Dermatologic surgery · Burns · Multilayer bandage · Epicutaneous testing

**Abstract**
In dermatological surgery where the lesions to be removed are very often contaminated with bacteria, local use of antiseptics that are effective against a wide range of germs is often indicated. Polyvinylpyrrolidone (povidone = PVP)-bound iodine (in Hungary marketed as Betadine®) is used successfully in our department. After excision and suture in per primam healing wounds as well as after tissue destruction in per secundam healing wounds, a thin layer of Betadine ointment on the dressing right after surgery and at dressing changes may reduce the risk of wound infection. When the defect requires split-thickness skin grafting, a combination of tulle gras and a layer of gauze soaked with 1:10 dilution of Betadine solution is suggested. In the treatment of leg ulcers, Betadine is used for cleansing and for impregnating the gauze on top of the tulle gras layer both in the debridement and in the epithelization phases. PVP-I is beneficial on burn wounds due to its effect reducing bacterial colony counts. Its use is advised for superficial (grades 1 and 2a) burns as well as surgical debridement of deep burns or temporary xenograft or definitive autograft coverage of these wounds. After treating a large number of patients with Betadine, a statement can be made: despite its theoretical risk, no cytostatic effect is seen in the clinical setting. No allergy towards Betadine was observed among the author’s patients over several years of its use. Fifty patients previously treated with PVP-I were challenged with epicutaneous patch testing, and no sensitization was found. An account is made on the adverse effects attributed to Betadine found in the scientific literature, and its use with regard to the proper indications is suggested.

Iodine has been used as an antiseptic for a long time; the concept of its bactericidal effect was established at the end of the nineteenth century [1]. It is effective against gram-negative, gram-positive and mycobacteria as well as treponema, fungi, viruses and protozoa. Its unique biological effect is characterized by the lack of resistance against iodine. Polyvinylpyrrolidone (= polyvidone = povidone = PVP)-bound iodine was developed by the NASA for the Apollo program, and it was first used during the Apollo 11 space travel in 1969. Very soon it was adapted to medicine, to dominate the arsenal of surgical disinfection ever since. External preparations containing PVP-I are available in many formulations and under several patent

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In traumatology and general surgery, it is used for scrubbing both as an aqueous and alcoholic solution. In abdominal and thoracic surgery, lavage is done with the 1:10 dilution of PVP-I. By in vivo testing the substance was found to be faster acting and more effective against a larger number of pathogens than locally administered combined antibiotics [2]. In the PVP-I molecule, organic iodine forms a loose complex with the surfactant component, thus enhancing its solubility and providing continuous release of the effective substance [3]. The formulation is suitable to exert its effect also in the presence of blood, serum, proteins and necrotic tissue debris [4].

In Hungary, PVP-I is used mostly as an ointment and as an aqueous solution. Indications for its use in dermatological surgery and in the conservative and surgical therapy for burns are discussed as follows (table 1).

**The Use of Betadine® in Dermatological Surgery**

*Disinfecting the Operative Field – Scrubbing*
Cleansing of normal healthy skin as an excision site or donor area can be done with full-strength undiluted aqueous solution. For genital mucosa or skin and for open wounded surfaces, like those after removal of temporary dressings between surgical sessions, we use a 10-fold dilution of Betadine®.

*Surgical Excision*
Despite meticulous cleansing, the operating field may not be germ free in the daily dermatosurgical praxis. We often have to remove lesions that are infected or contaminated. Skin lesions with uneven warty surfaces, benign tumors that have been wounded, cysts or exulcerated tumors may harbor bacteria even after scrubbing. In our practice PVP-I-containing external preparations are widely used to impregnate the dressing material freshly after excisions. Following excision and suture, a thin layer of Betadine ointment on the gauze reduces the risk of infection (fig. 1a–c). Should the surgical coverage of the defect require split-thickness skin grafting, we apply a layer of gauze impregnated with a 1:10 dilution of Betadine solution over the contact nonadherent dressing (fig. 2).

*Wound Dressing after Destruction of Lesions (Curettage, Kryotherapy, Electrodesiccation)*
It is fairly common in the dermatosurgical praxis that wounds, as a result of the destruction of a lesion by various means, are let to heal by second intention. It is mandatory for the wound healing during the inflammatory phase, under the forming crust and later during the proliferation phase in the granulation tissue, that the degradative processes attributed to pathogens should not overcome the reparative processes of the healing tissue. In our practice, the dressing changes of these – usually minor — wounds are done by the patient in his/her home, and we advise the wound toilette to be done with a 1:10 dilution of Betadine solution and the impregnation of the overlaid gauze with a thin layer of Betadine ointment. These dressing changes are tolerated very well and are said to be less painful than the previously used method utilizing a wound powder.

**Table 1.** The most common contaminated skin lesions or skin conditions prone to infections in the author's praxis where preparations with PVP-iodine are recommended

<table>
<thead>
<tr>
<th>Benign lesions or malignant tumors</th>
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<tbody>
<tr>
<td>Lesions often presenting with broken surfaces or signs of inflammation</td>
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<tr>
<td>Angiosarcoma Kaposi</td>
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<tr>
<td>Carcinoma spinocellulare</td>
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<tr>
<td>Carcinoma basocellulare (nodular ulcerative type)</td>
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<tr>
<td>Granuloma pyogenes</td>
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<tr>
<td>Hemangiomata</td>
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<tr>
<td>Neuroacanthoma</td>
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<tr>
<td>Melanoma malignum</td>
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<tr>
<td>Nevus dermalis</td>
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<tr>
<td>Unguis incarnatus</td>
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<tr>
<td>Lesions often contaminated with intact surfaces</td>
</tr>
<tr>
<td>Carcinoma basocellulare (cysticum, superficiale)</td>
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<tr>
<td>Cysta epidermalis</td>
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<tr>
<td>Dermal nevi with warty surfaces</td>
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<tr>
<td>Epidermal nevi</td>
</tr>
<tr>
<td>Keratosis solaris, keratoma senile, cornu cutaneum</td>
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<tr>
<td>Seborrhoic keratosis</td>
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<tr>
<td>Verruca vulgaris, condyloma acuminatum, molluscum contagiosum</td>
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<table>
<thead>
<tr>
<th>Defectus cutis</th>
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<tbody>
<tr>
<td>Arterial, venous or mixed leg ulcers</td>
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<tr>
<td>Metabolic ulcers (urate diathesis, diabetes mellitus)</td>
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<tr>
<td>Tumorous ulcers (ulcus rodens, ulcus terebrans)</td>
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<tr>
<td>Postoperative defects (granulating wounds, nail resection, Mohs surgery etc.)</td>
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<tr>
<td>Burns</td>
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<tr>
<td>Superficial burns (1st grade, 2a grade)</td>
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<tr>
<td>Spontaneous epithelization</td>
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<td>Deep burns (2b and 3rd grades)</td>
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<tr>
<td>Desloughing</td>
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<tr>
<td>Temporary wound coverage (porcine skin, cadaver allograft, synthetic skin substitutes)</td>
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<tr>
<td>Definitive wound coverage (over meshed autologous skin graft)</td>
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PVP-I in Dermatologic Surgery

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**Leg Ulcer Treatment**

Betadine is used effectively both in the desloughing and in the epithelization phases of treatment. Washing off with a PVP-I-containing liquid soap is often used. Cleansing is done with a 10-fold dilution of Betadine solution. For impregnating the gauze layer, we use Betadine in the form of either an ointment or a diluted solution mostly over tulle gras.

**The Possibilities of Using Betadine in Burn Surgery**

**Conservative Treatment of Partial-Thickness Burns**

Betadine has a favorable effect in the treatment of burns by the reduction of bacterial colonization. In partial-thickness burns (grades 1 and 2a), a sufficient number of basal keratinocytes remains on the wound bed for the epithelization of the burn wound through migration. Deep burns may epithelize spontaneously only from the keratinocytes of skin appendages (grade 2b) or from wound edges (3rd grade), resulting in prolonged wound healing and the formation of disfiguring scars, so these wounds require a surgical approach. According to our experience PVP-I-containing external preparations are effective in the treatment of burns, wound healing is optimal with their use. We use the ointment for burn wounds of minor extent and the diluted solution for larger wounds. These preparations help to maintain the wound free from germs; thus, bacterial colonization does not hinder wound healing.

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![Fig. 1. a Skin biopsy site on the face, day 0 (patient 52 years old, male; diagnosis: sebaceous adenoma). b Traditional gauze dressing with a thin layer of Betadine ointment to be applied on the suture site from start until removal of stitches. c Per primam wound healing, reaction-free excision site on day 14 (7 days after removal of stitches).](image-url)

![Fig. 2. Composition of the multilayer bandage used over split-thickness skin grafts applied on contaminated skin defects.](image-url)

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Fig. 3. Phases of operative treatment of a third-degree burn wound (total BSA 45%) on the right thigh of a 15-year-old male patient using multilayer bandages soaked with 1:10 diluted Betadine solution. 

a Day 0, necrotomy.

b Day 2, necrectomy.

c Day 2, temporary coverage with frozen porcine skin xenograft.

d Day 7, final wound coverage with autologous split-thickness skin mesh graft.

e Day 21, excellent take of the graft, healing almost complete.

f Acceptable scar upon control at 6 weeks after the trauma.
Operative Burn Care

Deeply burned, necrotic tissues provide excellent ‘culture media’ for microorganisms. It is very important to keep the bacterial count of exposed tissue before and after surgical interventions low. Betadine can be used for pre-operative disinfection as a scrubbing agent, irrigation of the wound during surgery and as an impregnating material for the wound dressing. We use the solution routinely for impregnating the gauze layer over temporary xenografts, allografts or over meshed autografts applied as definitive wound coverage (fig. 3). This method provides a moist environment, which is a prerequisite for fast wound healing.

Because of the possible side effects of iodine getting absorbed from open wounds, and the opportunity to develop allergy towards PVP-I, in the following we review some aspects regarding the safe use of the substance and analyze the results of our testing for hypersensitivity in a group of patients.

Epicutaneous Testing for Hypersensitivity towards Betadine in Dermatosurgical Patients

Materials and Methods

We did epicutaneous testing at the Department of Dermatology, University of Debrecen, Medical and Health Science Center, among our operated patients who used Betadine solution or ointment or both, 0.5–5 years after therapy, to determine the rate of hypersensitivity. Fifty patients (25 male and 25 female) were enrolled into the survey, the youngest patient being 4, the eldest 90 years old (mean 55.4 years). Their dermatological diagnoses were as follows: 24 patients with malignant skin tumor (20 basal cell cancer, 3 melanoma, 1 classical Kaposis sarcoma), 16 patients with benign lesions (5 nevi, 7 solar keratoses, 1 leg ulcer, 2 keratosis seborrhoeica, 1 adenoma sebaceum), 10 patients with burns [5 cases of 10–20% body surface area (BSA), 2 cases of 20–30% BSA, 1 case of 30–40% BSA, 2 cases of 60–70% BSA burns]. During wound management, 8 patients had contact with Betadine solution only, 32 patients with the ointment form and 10 patients with both. All tested individuals had at least 4 contacts with the substance, patients with larger BSA burns used it several times more during their long course of therapy. Twenty patients who had not been exposed to Betadine treatment were enrolled and tested as controls. Hypoallergenic adhesive tape with 3 chambers (Leukotest®, Beiersdorf AG, Hamburg, Germany) was applied to the hairless skin of the tested individuals (to the flexor surface of the forearm, medial surface of the arm or onto the back). One chamber carried Betadine ointment, another chamber was soaked with Betadine solution and the third chamber was soaked with physiological saline as control. The tapes were removed 24 h later, evaluations of the test sites were done at this point and on the next day (24 and 48 h after initiation of exposure, respectively). In our protocol there was a third reading scheduled at 72 h only for those cases suspicious for allergy at any reading, but no such cases were identified.

Results

The skin under the test chambers after 24 h of incubation with physiological saline, Betadine ointment or solution was unchanged at the evaluations in all 70 tested individuals. Neither the tested patients nor the controls had allergic or irritative reactions. This finding supports our favorable clinical experiences, gained during the decade-long, widespread use of Betadine, regarding the safety of these products.

Discussion

Side Effects Attributed to External Preparations Containing PVP-I. It is well known that sensitization may occur at a rather high rate following the local administration of antibiotics on the skin surface. That is why well-tolerable local disinfectants are valuable in the clinical praxis. The natural resin component of Peruvian balsam (balsam of Peru), formerly widely used by surgeons and plastic surgeons, causes allergic sensitization in 15–65% of cases [5]. There are publications about the side effects of other extensively used disinfectants regarded as safe [6, 7].

In the medical literature there are case reports about mediastinal lavage with PVP-I followed by reversible kidney failure [8] or convulsions with central nervous system involvement [9]. Cases of peritonitis were reported to follow peritoneal irrigation and dialysis [10]. In the USA, a series of peritonitis cases were traced back to a batch of a PVP-I preparation contaminated with Pseudomonas cepacia, used for peritoneal dialysis [11, 12]. While the causative role of PVP-I in the convulsions is questionable [13], the risk of other complications experienced during its intracavitval application can be reduced significantly by dilution and reduction of the length of exposure. The industry has introduced stricter controls into the technology of production to prevent any similar contamination in the future.

Iodine is a cytotoxic agent; there are objections against its use in wound healing [14]. In fact, a cytotoxic effect of PVP-I was shown only under in vitro circumstances [15] and even in these instances the differences were not striking. It is not easy to adapt toxicological data obtained in cell cultures to in vivo circumstances, because isolated cells without their matrix or monolayer cultures may not be able to compensate those mild cytotoxic effects that are effectively fought by the complex network of live cells within a tissue. The literature review of Niedner [16] collected data from a number of research groups that show no detrimental effect of PVP-I on either normal wound healing (suction blister) or wound healing under patholog-
ical circumstances (burns, Mohs surgery). Our own experiences obtained during the undisturbed healing of several hundreds of patients who had skin transplantation due to burns or other skin defects confirm that the theoretical inhibitory effect on the migration of fibroblasts and keratinocytes does not appear in the clinical setting! There were reports on the disturbances of thyroid function tests with no clinical signs in premature infants after extensive use of PVP-I-containing compounds [17], but there was no correlation between their use and neonatal thyroid dysfunctions in controlled trials [18]. Certainly caution is advised when PVP-I is used in neonates due to the increased permeability of their skin and in individuals with known thyroid dysfunction [19].

The most serious complication ever reported was metabolic acidosis and fatal kidney failure in an extensively burnt patient, attributed to the prolonged use of PVP-I over a large BSA. In this case, the causative role of the compound could be effectively challenged, because of the simultaneous sepsis and deteriorating general condition of the patient [20].

A locally administered substance must have a minimal irritative and contact sensitizing effect. There are literature reports on irritative contact dermatitis caused by PVP-I [21, 22]; interestingly the symptoms appeared on the back of patients lying on sheets soaked with PVP-I during surgery lasting several hours in both cases. Acute allergic reactions were also reported [23–25] against the iodine and povidone components as well. It is difficult to determine the extent of allergic sensitization in the treated patient population. Epicutaneous testing revealed hypersensitivity against PVP-I in less than 1% of 6,000 tested patients [26], whereas another research group found allergy against any form of PVP-I in 35 out of 104 patients [27]. In our clientele we have not noted allergy towards Betadine during many years of its use. Our patients tested and found negative for hypersensitivity had previously been exposed repeatedly to Betadine, some of them over a prolonged time on rather large surfaces. In a number of cases, Betadine was used inadvertently on individuals whose positive allergic history to iodine was unrevealed at the operation because of incomplete anamnesis. This observation supports the dichotomy of hypersensitivity to tinctures of iodine and PVP-I, observed by others [23] and indicates the mistaken or euphemistic judging of irritative dermatitis frequently seen in the past after cleansing with ethanolic tincture of iodine. As iodine gets released from its binding to PVP during its action, in case of real allergy to iodine there may be undesirable reactions; therefore even a suspicion of allergy to iodine means a strict contraindication to the use of PVP-I. To avoid complications, similarly to other drugs, the use of PVP-I must also be limited subject to indications. This safe and effective local therapy agent, like other antiseptics or antibiotics, would not absolve the surgeon from acting under the obligatory rules of asepsis and using atraumatic operative techniques.

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References


