

In search of a better patch test concentration for povidone-iodine

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Povidone-iodine (PVP-I) is widely used as a skin disinfectant in wound care and preparation for surgery, most frequently as a solution containing 10% PVP-I. Adverse reactions in terms of allergic or irritant contact dermatitis have been reported, the latter mainly occurring after prolonged occlusive skin contact under pressure (1, 2). For diagnostic purposes, that is, patch testing, PVP-I 10% aq. is commercially available (SmartPractice Europe, Reinbek, Germany) and routinely used. The results of patch tests with lower concentrations or dilution series, although most of them have been performed in a limited number of patients, suggest that a non-negligible proportion of positive patch test reactions to PVP-I 10% aq. are false-positive (3, 4). Lachapelle performed repeated open application tests (ROATs) in 14 patients with positive patch test reactions to PVP-I 1% aq., and found only 2 of them to be positive in the ROAT with PVP-I 10% aq., both of them with a history of dermatitis after application of PVP-I-containing skin antiseptics (4).

In order to improve the diagnosis of true sensitization (allergic reactions) to PVP-I, a test series consisting of a PVP-I dilution series and iodine 0.5% pet. was established in 2011 in the department of dermatology at the University of Göttingen.

Materials and Methods

Seventy-nine patients were patch tested in our clinic between 2011 and 2015 with PVP-I 10%, 1%, 0.1% and 0.01% aq., and with iodine 0.5% pet. in parallel. Regarding their history, 32 of 79 individuals (40.5%) were tested because of suspected allergic contact dermatitis (ACD) caused by antiseptics. The remaining 47 patients had

Table 1. Patch test results on day 3 in 79 patients tested with the povidone-iodine (PVP-I) dilution series and iodine

	PVP-I 10% aq.	PVP-I 1% aq.	PVP-I 0.1% aq.	PVP-I 0.01% aq.	Iodine 0.5% pet.
Negative	45	76	79	78	65
?	13	3	0	1	6
+	6	0	0	0	2
++	3	0	0	0	2
+++	2	0	0	0	0
Irritant	10	0	0	0	4

experienced anaphylaxis, mostly with exanthema, during the administration of iodine-containing contrast media and/or general anaesthesia, with drug-induced allergy rather than PVP-I or iodine being the suspected cause of the incident. In these cases, patch tests with the PVP-I series were performed as part of a complete allergological work-up. Patch test allergens were exposed for 48 h by the use of Finn Chambers® on Scanpor® tape (SmartPractice), and read on day (D) 2, D3, and D4, according to the guidelines of the German Contact Dermatitis Research Group (5). Both the various aqueous PVP-I solutions and iodine 0.5% pet. were prepared by our in-house pharmacy. PVP-I solutions did not contain nonoxynol-9.

Results

Patch test results on D3 are shown in Table 1. With PVP-I 10% aq., positive reactions were elicited in 11 patients (13.9%). In addition, 13 patients had doubtful (erythematous) reactions, and irritant reactions were seen in another 10 patients. Lower concentrations of PVP-I did not elicit positive reactions, but only a few doubtful reactions. With iodine 0.5% pet., positive reactions were seen in 4 patients (5.1%). In addition, six doubtful and four irritant reactions occurred.

Concomitant reactivity to PVP-I 10% aq. and iodine 0.5% pet. is shown in Table 2. Of the 6 patients with weak positive reactions (+) to PVP-I, 4 showed negative reactions and 2 showed doubtful reactions to iodine 0.5% pet.

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Table 2. Concomitant reactivity to povidone-iodine (PVP-I) 10% aq. and iodine 0.5% pet.

PVP-I 10% aq.	Iodine 0.5% pet.					Total
	Negative	?	+	++	Irritant	
Negative	44	0	0	0	1	45
?	11	2	0	0	0	13
+	4	2	0	0	0	6
++	0	1*	1	1	0	3
+++	0	0	1	1†	0	2
Irritant	6	1	0	0	3	10
Total	65	6	2	2	4	79

*Possible allergic contact dermatitis caused by Betaisodona®-gauze.

†Strongly suspected allergic contact dermatitis caused by Braunol® solution.

Four of the 5 patients with strong positive reactions (++, +++) to PVP-I 10 aq. also reacted to iodine 0.5% pet. Of these 4 patients, 2 were nurses with frequent exposure to skin disinfectants who suffered from chronic hand dermatitis. The third patient had repetitively applied different disinfectant agents during thrombophlebitis of the arm, and had developed severe dermatitis. The fourth patient suffered from a severe skin reaction upon application of the antiseptic Braunol® solution (B. Braun Melsungen, Melsungen, Germany) during intracardiac catheter examination. Braunol® solution contains 7.5% PVP-I, which has 10% releasable iodine. In contrast, none of the 6 patients with weak positive reactions to PVP-I 10% aq. was suspected of having ACD caused by PVP-I or iodine. The patient showing a strong positive reaction (++) to PVP-I 10 aq. (but a doubtful reaction to iodine 0.5% pet. only) had a history of burn injury that was treated with different antiseptics, including Betaisodona®-gauze (Mundipharma, Limburg, Germany), for several weeks.

Discussion

In our group of patients, only strong positive reactions to PVP-I 10% aq. had probable or proven clinical relevance in terms of ACD caused by PVP-I solution; weak positive

reactions to this patch test preparation rather seemed to be false-positive. In addition, there was a remarkable concordance of strong positive reactions to PVP-I 10% aq. and positive reactions to iodine 0.5% pet.

Our results indicate that 10% aq. is too high a test concentration for PVP-I, yielding more doubtful and irritant than positive reactions, and obviously eliciting weak false-positive reactions. This is confirmed by data from the Information Network of Departments of Dermatology, which showed that, when PVP-I 10% aq. was patch tested in 37 466 patients from 1996 to 2015, 3040 (8.1%) had positive reactions. The reaction index was -0.15 and the positivity ratio was 81%, also showing that this patch test preparation is not very reliable with regard to differentiating between allergic and irritant reactions (6). However, we have to admit that our search for a better, that is, lower, test concentration has not been successful so far, as we did not see any positive reactions with PVP-I 1% aq., 0.1% aq., or 0.01% aq. Some authors have suggested that PVP-I 1% aq. should be used for patch testing (4, 7). Nishioka et al. found PVP-I 2% aq. to be the highest non-irritating patch test concentration (in 10 patients) (3). According to our results, the optimal patch test concentration is in the range between 1% and 10% PVP-I. We therefore recommend patch testing with PVP-I 2% aq. and 5% aq. in the future. Additional patch testing with iodine seems to be useful. In our study, we found a promising correlation between positive patch test reactions to iodine 0.5% pet. and patients' history of adverse reactions to antiseptics, in particular to PVP-I-containing preparations. In addition, our results indicate that the irritant potential of iodine 0.5% pet. is lower than that of 10% PVP-I.

In conclusion, the clinical relevance of a positive patch test reaction to PVP-I 10% aq. may be verified by a use test or a ROAT. However, as these procedures take several days, it might be helpful to patch test with iodine 0.5% pet. in parallel in order to interpret positive test reactions to PVP-I 10% aq. correctly.

References

- Borrego L, Hernandez N, Hernandez Z, Penate Y. Povidone-iodine induced post-surgical irritant contact dermatitis localized outside of the surgical incision area. Report of 27 cases and a literature review. *Int J Dermatol* 2016; **55**: 540–545.
- Vandergriff T W, Wasko C A, Schwartz M R, Hsu S. Irritant contact dermatitis from exposure to povidone-iodine may resemble toxic epidermal necrolysis. *Dermatol Online J* 2006; **12**: 12.
- Nishioka K, Seguchi T, Yasuno H et al. The results of ingredient patch testing in contact dermatitis elicited by povidone-iodine preparations. *Contact Dermatitis* 2000; **42**: 90–94.
- Lachapelle J M. Allergic contact dermatitis from povidone-iodine: a re-evaluation study. *Contact Dermatitis* 2005; **52**: 9–10.
- Schnuch A, Aberer W, Agathos M et al. Performing patch testing with contact allergens. *J Dtsch Dermatol Ges* 2008; **6**: 770–775.
- Geier J, Weissshaar E, Lessmann H et al. Bewertung von Epikutantestreaktionen auf 'Problemallergene' mit vermehrt fraglichen oder schwach positiven Reaktionen. *Dermatol Beruf Umwelt* 2010; **58**: 34–38.
- Velazquez D, Zamberk P, Suarez R, Lazaro P. Allergic contact dermatitis to povidone-iodine. *Contact Dermatitis* 2009; **60**: 348–349.