Prospective observational case series of povidone iodine-induced contact dermatitis

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Background
Povidone iodine (PVI) is a broad-spectrum bactericidal agent and is also effective against viruses, protozoans, and fungi. With this advantage comes the disadvantage of irritation at the site of application. The sensitization rate of PVI was found to be 0.7%.
Aim
The aim of this study was to identify the cases of contact dermatitis (CD) due to PVI and to study the various clinical patterns, severities, and causalities of the cases.
Settings and design
This study is a prospective observational case series report.
Method
Thirty patients diagnosed with CD due to PVI were included in the study and evaluated on the basis of causality, severity, and preventability with standardized questionnaires like Naranjo's algorithm and WHO causality scale, Hartwig–Shigel severity scale, and modified Schumock and Thorton scale for preventability, and they were followed up at days 5 and 10.
Results and conclusion
Male patients dominated the study population (M : F, 3 : 2), and the most frequently encountered age group was 20–50 years. The most common locations of CD were the lower limb (50%), trunk (31.81%), and upper limb (18.19%). The concentration of PVI used for all of the cases was 10%, and similar brands of PVI were used on all patients. Eighteen cases were mild and 12 were moderately severe on the Hartwig scale. Causality assessment was performed using Naranjo's algorithm and the WHO causality scales. It was found that all cases were probable on Naranjo's algorithm and possible on the WHO causality scale. The cases were found to be preventable on the modified Schumock and Thornton scale. All cases were avoidable according to the P-method. PVI is the most common antiseptic used in the surgical field, and sensitization to PVI is not uncommon, as mentioned in the literature. A PVI concentration of 10% has a higher propensity for causing side effects, but it also has a higher efficacy in reducing the bacterial load.

Keywords:
contact dermatitis, pharmacovigilance, povidone iodine

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Introduction

Contact dermatitis (CD) forms a very small part of cutaneous adverse drug reactions. CD is an inflammatory response of the skin to an exogenous substance [1]. There are more than 3700 agents that are responsible for causing CD, one of the most common being topical drugs [2]. Epidemics of allergy to topical medicaments are not new phenomena, and this was first observed with the topical use of penicillin because of which it is not permitted for topical use [3].

A wide range of drugs have the capacity of causing drug-induced CD, including antiseptics [4]. One of the most common antiseptics used is iodophor. Iodophors are complexes of elemental iodine (tri-iodine) linked to a carrier and have several advantages, such as (i) greater solubility in aqueous solution than elemental iodine, (ii) a sustained-release reservoir for iodine, and (iii) reduced equilibrium concentrations of free elemental iodine. The most common iodophor used is povidone iodine (PVI) [5].

CD due to PVI is not very common, considering its widespread use. There are reports of allergic CD as well as irritation CD, but it is often difficult to distinguish between the two types of because of the lack of uniformity in the concentration of iodinated compounds used and the vehicles used when performing diagnostic patch tests [6]. The sensitization rate for PVI is found to be around 0.73% [7].

Methods

This was a prospective observational case series that included cases presenting between 1 January 2014 and 31 December 2014. These cases were documented at Smt. Kashibai Navale Medical College and General Hospital, Pune, Maharashtra (http://www.sknmcgh.org).The aim of this study was to note the demography and clinical patterns of CD, and to assess the severity, causality, and preventability of the reactions. Patients who directly (outpatients) presented to the Dermatology Department with a reaction and other patients (inpatients) under ongoing treatment who were referred to the Dermatology Department from other departments (Surgery, Orthopedics, etc.) with CD from PVI were enrolled in this study. All patients were diagnosed by specialist dermatologists. Inclusion criteria were patients of both sexes of any age having history of drug application and symptoms of CD around the contact area. Patients having any other dermatological disorder were excluded from the study. This study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all of the patients. General case history and detailed drug history (time of application of the drug, number of applications, chronology of symptoms) of each patient were obtained on the day of enrolment, and the patients were followed up on days 5 and 10. Itching was also measured on the basis of the visual analog scale score [8]. The latency period for each patient was noted, which is defined as the time between exposure to a disease-causing agent and development of symptoms. Causality, severity, and preventability were also assessed using the WHO scale [9] and Naranjo's algorithm [10], modified Schumock and Thornton scale [10], and Hartwig scale [10], respectively [11]. These data were input into Excel (Microsoft, Redmond, USA) and quantified and prepared for descriptive analysis.

Results

A total of 22 patients were enrolled between 1 January 2014 and 31 December 2014. Of the 22 patients, 13 were male and nine were female (M : F, 13 : 9), and the mean age of the patients was 30.64±2.74 years, with 19 patients in 20–50-year age range. Indications for surgeries were trauma, hernia, and soft-tissue infections. Sixteen patients were recruited from the Surgery Department and the remaining 6 from the Orthopedics Department (Table 1). They all were referred to the Dermatology clinic. The lower limb is the most commonly affected area (11 cases), followed by the abdomen (seven cases) and upper limb (four cases; Table 2).

Table 1 Demography of the enrolled patients

Total patients (*n*)	22
Male/female	13/9
Mean age (in years)	30.64±2.74
Department	
Surgery	16
Orthopaedics	6
Indications for surgery [*n* (%)]	
Trauma	8 (36.36)
Hernia	7 (31.81)
Soft tissue infection	7 (31.81)

Table 2 Common sites affected

Lower limb	11 (50%)
Abdomen	7 (31.81%)
Upper limb	4 (18.18%)

Table 3 Common symptoms at patient enrolment and follow-up

Symptoms	0 day	5th day	10th day
Rash	22	10	0
Itching (VAS)	19 (5.2)	9 (2.7)	0 (0)
Burning	8	1	0
Edema	8	3	0

VAS, visual analog scale.

The most commonly occurring symptoms were rash, itching, burning sensation, and edema. The most common symptom was rash, which was present in all patients at enrolment, followed by itching (19 cases), with a visual analog scale score of 5.2, burning, and edema (eight cases each). The symptoms decreased on subsequent follow-up (day 5), and all patients were cured by day 10 (Table 3). Seven patients required symptomatic treatment during their follow-up visits and were treated with antihistamines and emollients. Only two patients had diabetes and were receiving treatment for same, and their blood glucose levels were well-controlled. No patient had a prior history of drug 'allergy'.

The latency period was found to be 30–32 h. The concentration of PVI used in all patients was uniform (10%), and all cases were caused by the same brand (RAMADINE, Raman & Weil, Mumbai, Maharashtra) of PVI, which is used in our institution, and the manufacturer of PVI was the same in all cases. Causality was assessed by the WHO scale and Naranjo's algorithm, and all cases were found to be either probable or possible. On the severity scale, 15 cases were found to be mild and seven, moderately severe. All seven patients required treatment for their

symptoms and were treated symptomatically (antihistamines and emollients). The cases were found to be 'not preventable' on the Schumock and Thornton preventability scale. All cases were avoidable according to the P-method [12].

Discussion

PVI (10%) is an iodine compound (0.001% releasable iodine and 1% available iodine), and povidone with additives like disodium phosphate, glycerin, nonoxynol-9, polyoxyethylene, nonylphenyl ether, alcohol, and citric acid. The additive that is used in our brand of PVI is 9-propanol, which also has the potential to cause CD [13]. PVI is routinely used as an antibacterial agent as well as an antiseptic and has low irritant and allergic potentials [14].

PVI-induced CD is a much more common adverse event than that previously believed and remains underdiagnosed or misdiagnosed [6]. Barbaud *et al.* [15] studied contact allergy to antiseptics. They performed a multicenter 2-year retrospective study in which they included 75 sensitized patients with a mean age of 42 years, which fits our age range. They reported 14 cases as being due to PVI, and the concentration that they used for patch testing was 10%, the same concentration as that used in our study.

Nishioka *et al.* [16] presented a case series with 10 patients (M : F, 8 : 2), with an age range of 39–80 years. Patch testing was done with two preparations (10 and 5%) of PVI and its ingredients. The reactions were scored at 30 min after removal and 3 or 5 days after application. Results showed that all cases showed positivity for 10% PVI and five cases, for 5% of PVI. No reactions and stronger reactions were observed for 10% glycerin and 1–10% polyvinyl pyrrolidone, respectively. Li *et al.* [17] also showed that the bacterial load-reducing capacity of 10% PVI was superior to that of 5 or 1% PVI; hence, a 10% PVI was preferred.

de la Cuadra-Oyanguren *et al.* [6] presented a case series with seven patients and found that 10% PVI (in petrolatum as well as water) had irritancy potential, which is similar to the findings of our study, but in our case, the vehicle used was only water and not petrolatum. The irritancy potential of PVI decreases at 5 and 1% concentrations. The latent period was 48 h, as compared with 32 h in our study, and the intensity of the reaction increased over the next 48 h. Reyazulla *et al.* [18] and Velazquez [14] also presented case reports with similar results.

There is ambiguity with regard to which agent actually causes CD, but previous reports [6,16] have shown that PVI is the main cause of CD. We recommend switching the brand of PVI to those containing additives that do not cause CD and conducting a new study in which both agents and additives are tested separately.

Conclusion

PVI caused CD more commonly than previously believed. Although 10% PVI has a higher propensity for causing side effects, it also has a higher efficacy in reducing the bacterial load; therefore, it is the optimum concentration to be used. Early detection of CD, at first appearance of symptoms, will help in mitigating the intensity of the reaction. A drug alert card needs to be given to all these patients.

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Conflicts of interest

There are no conflicts of interest.

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