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Contact sensitizations to disinfectants containing alcohols or quaternary ammonium compounds are rarely of clinical relevance

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Abstract (max 200)

Introduction: The use of disinfectants is part of the everyday life of people, especially in the medical profession. During the COVID-19 pandemic, the use of disinfectants continues to increase and is of fundamental importance in infection control.

Objective: To determine the frequency of sensitization and the value of patch testing to didecyldimethylammonium chloride (DDAC) and the alcohols: ethanol, 1-propanol and isopropanol.

Methods: Clinical patch test data of 145 patients with suspected contact allergy to disinfectants were retrospective analyzed.

Results: Among the 145 patients patch tested with the different alcohols, only one nurse was detected with a possible allergy to 1-propanol. Additional patch testing in 84 patients with DDAC 0.05% resulted in five patients with weakly positive reactions only, without clinical relevance. Patch testing with DDAC 0.03% showed no positive reactions at all on day 3 readings.

Conclusion: DDAC and alcohols are rarely responsible for allergic contact dermatitis. The accused products of the patients should be checked for other allergens and further additives with skin irritating properties. Individual susceptibility and mishandling of the disinfectants should be considered.

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Introduction

Disinfectants are widely used in hospitals and nursing homes for cleaning of surfaces, instruments and skin disinfection. In the current COVID-19 pandemic, they gained high importance also in the everyday use in private households. Rare cases of allergic contact dermatitis to didecyldimethylammonium chloride (DDAC) have been published earlier [1-4]. DDAC (CAS no. 7173-51-5) is a quaternary ammonium compound widely used for disinfection of surfaces and instruments mainly in hospitals and nursing homes, but also on industrial sites and in agricultural processes. We previously reported on patch testing with DDAC and suggested novel patch test concentrations [5]. Here, we present (i) patch test experiences with these new patch test preparations, and (ii) patch test results with three alcohols widely used for disinfection. Ethanol (CAS no. 64-17-5), 1-propanol (CAS no. 71-23-8) and isopropanol (synonyms: 2-propanol, isopropyl alcohol; CAS no. 67-63-0) are monohydric alcohols with various applications. In medicine and beyond, they are used for disinfection of the skin and mucosae, as well as surfaces and instruments due to their bactericidal, fungicidal, and limited virucidal properties. With regards to efficiency and possibility of local production, the World Health Organization (WHO) recommends alcohol-based handrub formulations based on 80% ethanol or 75% isopropanol especially during the COVID-19 pandemic [6].

Patients and methods

We retrospectively analyzed data of 145 patients with suspected contact sensitization to ingredients of occupationally used disinfectants, who underwent patch tests with ethanol 70% in water (aq.), isopropanol 10% aq., and 1-propanol 10% aq. from 2014 to 2019. Eighty-five of these patients received an additional patch test with DDAC pet. at the concentrations of 0.03% in petrolatum (pet.) and 0.05% pet. between 2017 and 2019. As no clinically validated DDAC patch test preparation is commercially available, this compound is not being tested routinely, and the best patch test concentration and vehicle have not yet been established. In our opinion, a pet.-based patch test preparation is preferable, as it is easier to handle and may be less irritating than DDAC in water. Patch test preparations were made by our in-house pharmacy. DDAC was purchased from Merck (Darmstadt, Germany), ethanol from Dr. Hetterich (Köln, Germany), isopropanol from Caelo (Hilden, Germany), 1-propanol from Chemsolute (Reningen, Germany). Patch tests were exposed for 48h by use of Finn Chambers® (inner diameter 8 mm) on Scanpor tape. Reading of results was performed on D2 and D3 according to the current

guidelines of the German Contact Dermatitis Research Group [7, 8]. Patients with positive results underwent an additional D7 reading. As a standard operating procedure in our clinic for patch tests, patients were reminded to re-visit our clinic in case of any novel reaction on day 7. In case of uncertainty, patients were asked to send in a photo in advance, if they refrained from taking the trip to our hospital. No such re-visit was necessary on or around day 7 in our study cohort.

Results

Patch test results are presented in tables 1 and 2. Altogether, eight patients reacted positively to at least one of the allergen preparations tested. No strong positive reactions such as ++ or +++ occurred. All patch test reactions had subsided or even cleared at D7.

Five patients reacted to DDAC 0.05% pet. at D3, and only 1 of these (pat. no. 7 in table 2) had a positive reaction at D2 to the lower test concentration, with a decrescendo pattern (D2: +; D3: ?). No positive reactions to DDAC 0.03% pet. were observed at D3. None of the positive DDAC patch tests was regarded clinically relevant. There were no concomitant positive reactions to benzalkonium chloride (CAS no. 8001-54-5) 0.1% pet. in the DDAC-positive patients.

Regarding the alcohols, we found three positive tests with 1-propanol, one with ethanol, and one with isopropanol. No positive reaction occurred on D2 or D7 (Tab. 2). Clinical relevance of positive patch test results to alcohol-based disinfection was controlled by repetitive open application tests (ROATs) twice daily over seven days with the individual hand and skin disinfectant, containing the component in question. Only one nurse with positive 1-propanol-testing demonstrated a positive ROAT. Although this patient did not show positive patch test reactions in other regular patch test series, she was lost to a second ROAT with the suspected 1-propanol alone.

Discussion

In our previous study, we assumed that a DDAC test concentration of 0.01% pet. was too low, resulting in negative reactions only [5]. Furthermore, the concentration of DDAC 0.1% appeared to be too high, resulting in a high proportion of non-relevant, presumably false-positive reactions [5]. In this current study, we faced the dilemma that no patient had a clinically relevant allergy to DDAC. Since DDAC 0.05% pet. resulted in weak positive reactions in five

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individuals, none of whom reacted to DDAC 0.03% pet., patch testing with DDAC at 0.05% pet. might be the best option. Still, we cannot rule out the possibility of false-positive reactions. Clinically relevant sensitization to DDAC therefore seems to remain very rare [1, 2, 5]. However, the significance of this conclusion is limited due to the small sample size of our study group (n=84).

Very few more or less convincing cases of contact sensitization to ethanol, 1-propanol and isopropanol have been reported [9-13]. In a larger series, 1 450 patients underwent patch testing with isopropanol ('as is'), and 44 patients demonstrated a positive patch test result [10]. Thirty-seven of them were considered clinically relevant. However, these results did not remain unchallenged [14]. It was argued that isopropanol was patch tested "as is", and thus irritant reactions seemed possible. Furthermore, it was discussed whether patients with positive patch test reactions to isopropanol at higher concentrations might have a malfunction of the enzyme alcohol dehydrogenase (ADH), resulting in an accumulation of toxic metabolites, such as acetone [14]. Remarkably, this exact mechanism was recently observed in a nurse with a "positive" patch test to isopropanol [15]. She had a heterozygous mutation of the ADH1B gene, causing an increased ADH activity, which leads to an accumulation of (toxic) acetone, causing a false-positive patch test reaction. In our study group, we found one nurse only with a possibly relevant allergic contact dermatitis to 1-propanol. In the literature, two cases with contact allergy to 1-propanol have been described [9, 12]. However, in none of these cases, enzyme activity was measured or genetic analyses were performed. In another small study, ten volunteers were tested with 1-propanol 10%, 25% and 50% with negative results and thus ruled out an irritant reaction [9]. We may conclude that contact sensitization to alcohols in disinfectants seems to be very rare. The skin-irritating character of the disinfectants can be mitigated by the addition of moisturizers [16]. Our results indicate that patch tests alone cannot establish contact allergy to disinfectants due to their irritant properties. For a reliable relevance assessment, a ROAT should be performed. However, even ROATs may display irritant skin reactions, thus interpretation of ROATs with disinfectants remains a clinical challenge [17, 18]. Thus, testing all other ingredients of the disinfectants such as fragrances, emollients etc. may be another suitable diagnostic approach, as well as semi-open tests. This should be considered in the allergological workup. This topic might be even of higher importance in the present COVID-19 pandemic, where the use of disinfectants is ubiquitously enforced.

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Tables

Table 1. Patch test results on D3 of patients tested with didecyldimethylammonium chloride (DDAC) 0.03%, DDAC 0.05%, isopropanol 10%, 1-propanol 10% and ethanol 70%. [n] = number of tested patients, neg = negative, ir = irritant, pos = positive.

Substance	**[n]**	**neg**	**?**	**+**	**++**	**+++**	**ir**	**% pos**
DDAC 0.03% pet.	85	83	2	0	0	0	0	0.0
DDAC 0.05% pet.	84	75	4	5	0	0	0	6.0
Ethanol 70% aq.	144	141	2	1	0	0	0	0.7
Isopropanol 10% aq.	144	142	1	1	0	0	0	0.7
1-Propanol 10% aq.	145	139	3	3	0	0	0	2.1

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Table 2. Detailed presentation of positive patch test results to the different disinfectants. ROATs were performed twice daily over seven days with the individual hand and skin disinfectant, containing the component in question.

Patient no.	**Substance**	**D2**	**D3**	**D7**	**ROAT with accused product**
1	1-Propanol 10% aq.	?	+	?	positive
2	1- Propanol 10% aq.	-	+	-	negative
3	1- Propanol 10% aq.	?	+	-	negative
	Ethanol 70% aq.	?	+	-	negative
	Isopropanol 10% aq.	?	+	-	negative
4	DDAC 0.05% pet.	-	+	-	-
5	DDAC 0.05% pet.	?	+	?	negative
6	DDAC 0.05% pet.	?	+	-	-
7	DDAC 0.05% pet.	+	+	?	-
	DDAC 0.03% pet.	+	?	?	
8	DDAC 0.05% pet.	-	+	-	-