

Occupational allergic contact dermatitis from 2-N-octyl-4-isothiazolin-3-one

KRISTINA AALTO-KORTE¹, KRISTINA ALANKO¹, MAJ-LEN HENRIKS-ECKERMAN²,
OUTI KUULIALA¹ AND RIITTA JOLANKI¹

¹Control of Hypersensitivity Diseases Team, Finnish Institute of Occupational Health (FIOH), Helsinki FI-00250, Finland ²Chemical Agents Team, Finnish Institute of Occupational Health (FIOH), Turku FI-20500, Finland

2-N-octyl-4-isothiazolin-3-one (OIT) is an antimicrobial agent that is mainly used in industrial settings. The objective of the study was to find the significance of OIT contact allergy at our clinic of occupational dermatology. We looked through our patient material from 1991 for allergic reactions to OIT and analysed the clinical records. We found 8 patients with ordinary allergic reactions to OIT and 1 late reaction. 2 workers in the manufacture of paints had occupational allergic contact dermatitis from OIT in biocides. 2 patients were machinists and 3 were female farmers: in these cases, however, we could not find any exposure. A sewing machine operator had patch test reactions to 2 of her mattress textiles, and chemical analysis of them showed 40–50 parts per million OIT. In conclusion, OIT is a rare sensitizer, and its contact allergies occur mainly in paint manufacturing. It is infrequently used in metal-working fluids and possibly sensitizes machinists. Although it is also used in some biocides recommended for use in the textile industry, there are no previous reports of contact allergy in this field. Our sewing machine operator with OIT contact allergy had probably been sensitized from mattress textiles.

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2-N-octyl-4-isothiazolin-3-one (OIT; Kathon 893[®], Skane M-8[®], Ochtilinone, CAS 26530-20-1) is a preservative belonging to the isothiazolinone group (1). It was developed specially for latex paints and oil-based paints (2). It is marketed for use in fabrics, adhesives, wood preservatives and metal-working fluids (MWFs) (3), and it occurs in stains (4), cleaning agents and polishes (1). It is also used in the leather industry (4) and in the manufacture of plastic (5, 6).

Occupational allergic contact dermatitis (OACD) from OIT has been reported in a total of 8 patients: 3 workers had used Skane M-8[®] biocide (contains 45% OIT) in the manufacture of paints (2, 3), 2 were painters (4, 7), a laboratory worker had handled the chemical (5) and a shoe factory worker had used a preparation containing OIT (8). A case of non-OACD from leather shoes was also reported (4). In Germany, 2 patients reacted to OIT in a MWF patch test series, but the relevance of the allergic reactions was not reported (9). To our knowledge, there are no previous reports of OIT allergy from textiles.

We looked through our patient material from January 1991 to September 2005 to find all patients with allergic reactions to OIT to study the significance of OIT contact allergy at our clinic of occupational dermatology.

Materials and Methods

OIT has been patch tested at the concentration of 0.1% in petrolatum (pet.). In the beginning, the test substance was made at Finnish Institute of Occupational Health (FIOH) from Skane M-8[®] biocide, but since August 1992, a commercial preparation (Chemotechnique Diagnostics[®], Malmö, Sweden) has been used in our antimicrobial series. We analysed our skin test files for reactions to OIT and checked the clinical records of the patients with an allergic reaction (+/+ + /+++) to OIT for symptoms, exposure, skin test reactions to other isothiazolinones and diagnosis.

Results

Between January 1991 and September 2005, a total of 2222 patients were patch tested with OIT (137

with the in-house preparation and 2085 with the commercial one). 8 (0.004%) of the patients had allergic reactions, all of which were to the commercial preparation. Irritant or doubtful reactions were seen in 52 patients (2.3%). The clinical details of the patients with allergic reactions are presented in Table 1, and 1 of the patients (no. 7) is described in detail below. We also found one late reaction to OIT, which has been described previously (10).

Case Report

The patient was a 41-year-old, female, sewing machine operator in a company that manufactured mattresses. She had a history of palmoplantar and axillary dermatitis in the early 90s but no history of atopy. In 1994, on patch testing in a local hospital, she had allergic reactions to the mixture of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one (CMI/MI; Kathon CG[®]; ++), fragrance mix (+), chlorhexidine gluconate (++) and lichen mix (++) . She started to use fragrance-free cosmetic products, and the dermatitis on her feet and axillae healed, but she still had intermittent vesicular dermatitis on the palmar sides of her fingers, predominantly

on the left side. In October 2003, there was a vesicular exacerbation of the dermatitis on the fingers and palm of her left hand. She suspected mechanical irritation from the mattress textiles that she handled with her left hand. On sick leave, the symptoms always improved. Then she was able to continue her work by using a cotton glove on her left hand.

At FIOH, in March 2004, she presented dry, relatively mild dermatitis on the palmar side of her left II–IV fingers and distal palm. Patch tests (with the standard and fragrance series, antimicrobials, coco fatty acid derivatives, plastics and glues series, dilution series of formaldehyde and cobalt chloride) showed reactions to fragrance mix (+++), formaldehyde (+), chlorhexidine gluconate (+), triethyleneglycoldiacrylate (+++), the mixture of chloromethyl isothiazolinone (CMI) and methyl isothiazolinone (MI) (++), atranorin (+), evernic acid (+), 2-bromo-2-nitropropane-1,3-diol (Bronopol; +), benzylhemiformal (+), Biopan CS 1135 (+), Bioban CS 1243 (+) and OIT (0.1%; +). The test substances also included 11 mattress textile samples, and she had weak reactions to 4 of them (Table 2). Patch tests with mattress textile A and B and the respective ultrasound extracts were negative in 9 control patients.

Table 1. Patients with allergic reactions to OIT, their occupation, patch test results, exposure and diagnosis

Patient no.	Sex	Occupation	Patch test results			Exposure	Diagnosis
			OIT	MCI/MI	BIT		
1	Female	Machinist	++	–	–	No present exposure to OIT (<0.005% in the mineral oil ^a). Possible past exposure to OIT in MWFs or their biocides	OACD from a mineral oil
2	Female	Dairy farmer	++	–	–	No known exposure to OIT	OICD from wet work
3	Female	Dairy farmer	+	–	–	No known exposure to OIT	OACD from Compositae plants
4	Female	Dairy farmer	++	–	–	No known exposure to OIT	Occupational contact urticaria and protein contact dermatitis from cow dander
5	Male	Paint manufacturer	++	–	–	OIT (45% to 48%) in a biocide ^b	OACD from OIT in a biocide
6	Male	Machinist	++	–	–	No present exposure to OIT ^c . Probable past exposure to OIT in MWFs or their biocides	OICD from MWFs
7	Female	Sewing machine operator (Case Report)	+	++	–	OIT in textiles (2–50 p.p.m. ^a)	OACD from OIT in textiles, OICD from mechanical friction
8	Male	Operator in the manufacture of paints	+	++	–	OIT (7% to 10%) and MI (7% to 10%) in biocides ^b	OACD from MIT and OIT in biocides

BIT, benzisothiazolinone; MCI, 5-chloro-2-methyl-4-isothiazolin-3-one; MI, 2-methyl-4-isothiazolin-3-one; MWF, metal-working fluids; OACD, occupational allergic contact dermatitis; OICD, occupational irritant contact dermatitis; OIT, 2-N-octyl-4-isothiazolin-3-one; p.p.m., parts per million.

^aChemical analysis at the Finnish Institute of Occupational Health.

^bInformation in the material safety data sheet, label or product description.

^cInquiries from the manufacturers.

Table 2. Patch test reactions to 4 mattress textile samples of patient no. 7, and the concentrations of BIT and formaldehyde in the same samples

Mattress textile	Patch test reaction		BIT concentration (p.p.m.)	Formaldehyde concentration (p.p.m.)
	As is, moistened with water	Ultrasound extract to ethanol		
A	+	+	40	19
B	+	+	50	<10
C	–	?+	2	21
D	–	?+	10	19

BIT, benzisothiazolinone; p.p.m., parts per million.

We suspected that the mattress textiles could contain some of the chemicals to which she had allergic reactions. Therefore, we analysed mattress samples A, B, C and D for their formaldehyde, acrylate and OIT content. For OIT and acrylate analysis, the mattress sample was dissolved in acetone, and the identification and quantification of the dissolved compounds was performed on a gas chromatograph (Agilent 6890) equipped with auto-sampler and a mass-selective detector (Agilent 5973N) in the splitless mode. OIT and acrylates were identified by comparing their mass spectra with the mass spectra in the Wiley library and quantified against triethyleneglycoldiacrylate. The detection limit was 10 parts per million (p.p.m.). For formaldehyde analysis, the textile sampled was leached for 1 hr at 40°C and then filtered. The formaldehyde concentration of the leachate was determined by the acetylacetone method. This method is based on the reaction between formaldehyde, acetylacetone and ammonium ion. The reaction forms yellow lutidine derivate, which was measured spectrophotometrically at 415 nm.

Results of the OIT and formaldehyde analysis are given in Table 2. Analysis of the same samples did not show any acrylates.

Mattress samples A and B, which gave the allergic reactions on patch testing, also contained the largest amounts of OIT, 40 and 50 p.p.m. We concluded that the patient had OACD from OIT in the mattress textiles.

Discussion

The previous reports of contact allergy to OIT are sparse and mainly individual case reports, and the number of OIT allergic patients in our clinic was also low. We only had 2 patients (no. 5 and 8, Table 1) whose allergic reactions had clear relevance: they had used biocides with high OIT concentrations. They were both involved in the manufacture of paints, as 3 of the 8 cases in the previous literature.

2 of our patients (no. 1 and 6) were machinists, but we could not find OIT in their own products. In a recent unpublished survey of 18 MWFs from the Finnish market, only 1 MWF concentrate contained 360 p.p.m. OIT, which corresponds to 18 p.p.m. in the diluted emulsion. However, 1 of our 2 machinists (no. 1) had allergic patch test reactions to another MWF concentrate of the same manufacturer. Impurities disturbed the chemical analysis of this MWF, so that the detection limit for OIT was 50 p.p.m., and the manufacturer denied the use of any isothiazolinones. Thus, although OIT is not used so frequently in the MWFs, it possibly causes contact allergy in some machinists.

Antimicrobial agents are added to textiles to prevent odour, rotting and mildew. Reports of contact dermatitis are sparse. Tributyltin oxide has caused epidemic irritant contact dermatitis when used in excess to disinfect soldiers' socks (11), cresol has caused allergy in the silk industry and organic mercury salts has caused allergy in tent canvas industry (12). Triclosan in 'odour eater' socks has also caused contact allergy (13). We have not found any previous reports of skin problems from OIT in textiles.

The question arises whether the small quantities of OIT in the textiles of patient no. 7 can sensitize or elicit contact allergy. OIT is chemically related to the extremely strong allergen CMI/MI, and while the concentrations of OIT in the mattress textiles were low, they were a little higher than the ordinary concentrations of CMI/MI in the cosmetic products (3–15 p.p.m.) (14). Mattress samples A and B elicited stronger patch test reactions and also contained higher amounts of OIT than samples C and D. We originally performed the chemical analyses because we suspected formaldehyde or acrylates. However, there were no acrylates, and the formaldehyde content of the samples did not match the patch test reactions and were lower than the OIT concentrations (Table 2). Besides OACD from OIT, mechanical friction from the mattress textiles probably contributed to the dermatitis, and the patient also had other contact allergies, although we could not find any present occupational relevance to them. Defective skin barrier due to previous hand dermatitis might have enhanced sensitization to OIT.

3 of our 8 patients were female dairy farmers. We did not find OIT in any of their products, but all of them had used different brands of household-type polyvinyl chloride (PVC) gloves from the same manufacturer. OIT is one of the antimicrobial agents that are used in plastic products to reduce microbe populations both within the material and at the surface (6, 15). We have recently

reported that small amounts of benzisothiazolinone (BIT) in disposable PVC gloves (20–31 p.p.m.) may sensitize patients who already have hand dermatitis (16). As the manufacturer of the household-type gloves in Malaysia refused to reveal the antimicrobial agent, in 2006, we analysed new gloves of the same 2 brands for OIT and BIT with negative results. Thus, we could not show any relevance in these cases.

The patch test concentration of OIT has varied in previous reports. In a cumulative insult human patch test study from the USA, a concentration of 250 p.p.m. Skane M-8 in pet. (corresponds to 0.011% OIT) was recommended (17). We have used the most commonly used concentration, 0.1% in pet. (4, 5, 7, 8). In a French study, this commercially available concentration gave an irritant reaction in 1 of 20 control persons (8). Similarly, there were some irritant reactions at our clinic. On the other hand, a concentration of 1% in pet. is definitely too high because it gave irritant reactions in 50% of control persons in the French study (8).

Despite the similarities in their chemical structures, OIT is not considered to cross-react with CMI/MI or BIT (17–19). The ranking in frequency of sensitization in the literature is MCI/MI > BIT > OIT (19). The same order in the extent of use partly explains the differences. 2 of our 8 OIT allergic patients also reacted to CMI/MI and none to BIT. The other patient (no. 8) was exposed to a biocide that contained 7% to 10% MI, thus our series also supports the idea of separate sensitization to these chemicals.

In summary, OIT is a rare sensitizer and its contact allergies mainly occur in paint manufacturing. OIT is used in some MWFs and may sensitize machinists. OIT occurs in biocides that are recommended for use in the textile industry, but there are no previous reports of contact allergy from this field. We reported here a sewing machine operator with OIT contact allergy and suggest that she was probably sensitized to OIT in mattress textiles, as in chemical analysis, the textile samples contained small amounts of OIT.

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Address:

Kristiina Aalto-Korte
Control of Hypersensitivity Diseases
Finnish Institute of Occupational Health (FIOH)
Topeliuksenkatu 41 a A
FI-00250 Helsinki
Finland
Tel: +358 30 4741
Fax: +358 9 5875 449
e-mail: kristiina.aalto-korte@ttl.fi