

Occupational allergic contact dermatitis from *N,N*-methylene-bis-5-methyl-oxazolidine in coolant oils

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Contact with metal working fluids (MWF) is an important factor in the development of occupational hand dermatitis in patients working in the metal processing industry. Biocides are added to MWF as preservatives and are known sensitizers. We analysed 318 patch test reactions to *N,N*-methylene-bis-5-methyl-oxazolidine 1% in petrolatum (5-methyloxazolidine, Grotan OX[®], CAS no. 66204-44-2, a formaldehyde releasing biocide) present in coolant oils in patients exposed to MWF and with suspected occupational dermatitis (OD). Positive allergic reactions were noted in 15 (4.7%) cases. In 7 (47%) cases, we were able to confirm relevance by examining the material safety data sheets and these showed that *N,N*-methylene-bis-5-methyl-oxazolidine was present in the oils used by the patients. No certain relevance could be proved in 8 cases, but in these instances, further information on the biocides used in the oils could not be obtained. Positive reactions to formaldehyde were seen in 11 (73%) patients. Sensitization either to this biocide and/or formaldehyde allergy was considered to have been likely to have made a contribution to the workers' dermatitis.

Key words: allergic contact dermatitis; biocides; CAS no. 66204-44-2; Grotan OX[®]; *N,N*-methylene-bis-5-methyl-oxazolidine; occupational. © 2006 The Authors. Journal compilation © 2006 Blackwell Munksgaard.

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Contact with synthetic and semi-synthetic coolants is common in workers employed in metal working plants. Metal working fluids (MWF) are used for cooling, lubricating, corrosion inhibition and flushing away of the metal chips in drilling, cutting, turning and grinding of metal parts. A wide range of additives including emulsifiers, stabilisers, buffers, antifog compounds, foam inhibitors, tensides, solubility enhancers, lubricants, corrosion inhibitors and extreme-pressure-additives are added to MWF (1).

Contact with MWF is an important factor in the development of occupational hand dermatitis in patients working in metal processing industry. MWF are a major cause of occupational dermatoses in these workers (2). A 20%–25% prevalence of hand eczema has been noted in metal workers exposed to MWF with irritant contact dermatitis being more common than allergic contact dermatitis (3).

Biocides (bactericides and fungicides) are added to MWF as preservatives and are known sensitizers. Biocides may be contained in the

original MWF or be added later. The low molecular weight of these biocides allows penetration into the skin and permits reaction with endogenous proteins (4). Sensitization is therefore not uncommon, making biocides one of the commonest groups of oil constituents inducing occupational allergic contact dermatitis of the hands (5).

Patients and Methods

This study was conducted in the Contact Dermatitis Investigation unit of the University of Manchester from October 1998 to April 2005. 318 patients with suspected occupational dermatitis (OD) and a history of exposure to MWF were patch tested to *N,N*-methylene-bis-5-methyl-oxazolidine (1% pet), a formaldehyde-releasing biocide present in the coolant oils. *N,N*-methylene-bis-5-methyl-oxazolidine is included in our oil and coolant series. Patch tests were read on days 2 and 4 and positive patch test reactions were analysed with an aim to establish their relevance.

Results

Allergic positive reactions were noted in 15 (4.7%) cases. Of these, relevance was established in 7 (47%) cases. In 8 cases, relevance was not proven as in these instances, further information on the biocides used in the oils could not be obtained in full. Concomitant allergic positive reactions to formaldehyde were noted in 11 (73%) patients. There were 5/7 cases in the relevant group and 6/8 in the unproven relevance group. 6 patients (40%) showed positive patch test reactions to cobalt. Positive patch test reactions to nickel were seen in 3 patients.

There were also 3 cases of concomitant allergy to monoethanolamine and 2 to triethanolamine.

Discussion

N,N-methylene-bis-5-methyl-oxazolidine (5-methyl-oxazolidine, Grotan OX[®]) is a formaldehyde-releasing biocide added to coolant oils. Allergic contact dermatitis to *N,N*-methylene-bis-5-methyl-oxazolidine from nylon spin finish has been reported (6). It was also found to be a strong sensitizer on guinea pig maximization testing (5).

2 recent German studies have retrospectively analysed metalworkers attending for patch testing. *N,N*-methylene-bis-5-methyl-oxazolidine when tested at 1% pet induced positive reactions in 4.5% and 2.3% of those tested (1, 7). A further German study showed 14.8% positive reactions to *N,N*-methylene-bis-5-methyl-oxazolidine when associated with positive reactions to the coolant and 4.7% when reaction to the oil was negative (8). None of these studies, however, state whether *N,N*-methylene-bis-5-methyl-oxazolidine was demonstrated to be present in the oil and therefore if the patch tests were relevant.

In our study, we were able to confirm relevance in 7 cases by examining the material safety data sheets and these showed that *N,N*-methylene-bis-5-methyl-oxazolidine was present in the oils used by the patients. In the remaining cases, we were unable to confirm whether or not the biocide was present in the working environment. Nevertheless, sensitization either to this biocide or formaldehyde was considered to have been likely to have made a contribution to the workers' dermatitis.

It is difficult to know in those cases where there is associated sensitization between *N,N*-methylene-bis-5-methyl-oxazolidine and formaldehyde whether the allergy is primarily from formaldehyde or whether the biocide is concomitantly

acting as a sensitizer. Sensitization independent of formaldehyde allergy has nevertheless occurred in 4 cases.

It has been suggested that caution needs to be taken in testing some formaldehyde-releasing biocides particularly Biobans as positive reactions are often weak, non-reproducible and without relevance (9). We agree that this is correct with regard to Biobans. We have patch tested 318 patients to *N,N*-methylene-bis-5-methyl-oxazolidine, and all the positive reaction have been + or ++ and the remainder were negative. No +/- were seen and this suggests to us that false positive reactions results are not as common.

Cobalt and nickel allergy is reported to be at increased levels in metalworkers and is therefore probably relevant in our patients.

We have previously demonstrated that monoethanolamine is a relevant allergen in coolants (10) and the subsequent German studies have found high levels of allergy to both monoethanolamine and to a lesser extent triethanolamine in metalworkers (1, 8, 9). These materials, which are used for rust prevention would seem to be important potential allergens in MWFs. They stress that monoethanolamine is present in only small amounts in the coolants but reaction products are also frequently present.

In view of the above findings, we believe it is important to screen metalworkers with *N,N*-methylene-bis-5-methyl-oxazolidine as well as monoethanolamine and triethanolamine.

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