Contact Allergy to Acrylates

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Anthony Goon defended his thesis on 11 November 2010 in Malmö, Sweden. The thesis was supervised by Associate Professor Marléne Isaksson from the Department of Occupational and Environmental Dermatology, Skåne University Hospital Malmö, Lund University, Sweden. The co-supervisors were Professor Magnus Bruze and Associate Professor Erik Zimerson from the Department of Occupational and Environmental Dermatology, Skåne University Hospital Malmö, Lund University, Sweden, Professor Chee Leok Goh from National Skin Centre and Professor David Koh from the Department of Epidemiology and Public Health, National University of Singapore. The opponent was Associate Professor Kristiina Alanko from Helsinki University Central Hospital, Skin and Allergy Hospital, Helsinki, Finland. Professor Emeritus Torkel Fischer, Stockholm, Associate Professor Liselott Lindh, Malmö, and Associate Professor Jörn Nielsen, Lund were members of the assessment committee.

The term "acrylates" is used for a group of transparent plastics made from polymers of acrylic acid or methacrylic acid and their derivatives. Those made from methacrylic acid and their derivatives are more accurately termed "methacrylates". Polymers are made from numerous repeating subunits called monomers. We investigated skin allergies caused by the monomers of acrylates.

Early uses of these plastics included coatings and dental applications. More well-known products in this family of transparent plastics are made in the form of fibres (e.g. Acrilan) and sheets (e.g. Perspex). More recently, by modifying the monomers in different ways, acrylates have been used in various other applications, such as ultraviolet-curable inks, photopolymers, adhesives, artificial nails, dental composite resins and super-absorbent polymers (e.g. in nappies).

Acrylics were first used in dentistry in 1935, and by the 1940s they were being used extensively for removable dental prostheses, individual impression trays, orthodontic devices, occlusal splints, fixed crowns and bridges. Hypersensitivity to methyl methacrylate (MMA) was first reported in 1941.

Although experimental data has shown that acrylate monomers have weak to moderate potential to cause allergies, allergies to acrylate monomers have been reported with increasing frequency due to increasingly widespread use of their finished products. Acrylate skin allergy is frequently seen in the occupational as well as non-occupational setting. These allergies are almost completely due to sensitization to the acrylate monomers, as the finished polymers are very unlikely to cause allergy.

Skin allergies to acrylates are confirmed by patch testing, where multiple suspected allergens (including various acrylate allergens) are specially prepared and applied to the backs of patients with suspected acrylate allergy for 48 h. The result of the patch test is determined by a dermatologist, who will look for redness and elevation of the skin at the individual test site for each allergen. A positive reaction would mean that a patient has developed an allergy to the tested substance and may be the explanation for the patient's skin condition (dermatitis).

Fig. 1. Anthony Goon defended his PhD thesis in Lund University. Marléne Isaksson (*left*) has acted as supervisor and Kristiina Alanko (*right*) from Helsinki University was the opponent.

Most patch test centres apply a baseline series to every patch-tested patient. This baseline series contains the most common

allergens causing skin allergies for the individual centre's patient population. However, acrylate allergens are not present in the baseline series of most patch test centres around the world. Current practice in most centres is such that acrylate patch test preparations are applied on a patient only when the dermatologist specifically suspects a skin allergy to acrylates in that particular patient. This would result in a proportion of acrylate-allergic patients with missed diagnosis if acrylate allergens were not applied by their dermatologist during their patch tests. We aimed to make it easier to test for acrylate allergy by formulating a shortened acrylate series or an acrylate mix that could be added to the baseline series. However, our attempt was not a success, as described later in this summary.

Altogether, we have published five articles on this topic. The first two were studies of past acrylate-allergic patients performed at the Department of Occupational and Environmental Dermatology at Malmö University Hospital, Malmö, Sweden.

The first was on 1,632 dental staff and dental patients who had been patch-tested for allergy to dental acrylates. Forty-eight of them had positive results to one or more acrylates. From this data, the most common patch test positive allergen for dental patients and dental personnel was 2-hydroxyethyl-metacrylate (2-HEMA), followed by ethyleneglycol dimethacrylate (EGDMA), triethyleneglycol dimethacrylate (TREGDMA), and MMA. Screening for acrylate contact allergy with 2-HEMA alone would have detected 96.7% (29/30) of our acrylate-allergic dental patients and 100% (18/18) of our acrylate-allergic dental personnel. The addition of bisphenol-A-glycidyldimethacrylate (bis-GMA) in dental patients would increase the pick-up rate to 100%.

The second study was on 90 patients with dermatitis, suspected to be caused by acrylates, who had been patch tested with industrial acrylates and/or nail acrylics. There were 10 patients with acrylate allergies caused by their employment. The most common allergens in these subjects were triethyleneglycol diacrylate (TREGDA), diethyleneglycol diacrylate (DEGDA), and 1,4-butanediol diacrylate (BUDA). All 10 of these patients would have been detected by a short screening series combining TREGDA, 2-hydroxypropyl methacrylate (2-HPMA), and BUDA or 1,6-hexanediol diacrylate (HDDA). Among the 14 acrylate-allergic nail patients, the most common allergens were EGDMA, 2-HEMA, and triethyleneglycol dimethacrylate. Screening for 3 allergens, i.e. 2-HEMA plus EGDMA plus TREGDA, would have detected all 14 nail patients.

Combining the results of the first two studies, we concluded that a short screening series combining 2-HEMA, EGDMA, TREGDA, 2-HPMA, bis-GMA, and BUDA or HDDA would have detected all our past study patients (dental, industrial, and nail).

In our third study for approximately 2 years we had tested all patients sent for patch testing in Malmö and Singapore to a short series of five specially-selected acrylate allergens. Altogether, 38 patients had positive patch tests to acrylates during the study period in both populations. In Malmö, there were 26 patients (1.4%), while in Singapore, there were 12 patients (1.0%) with positive patch tests to acrylate allergens. If we had not added these allergens to the baseline series, we would not have patch-tested 13/26 (50%) of the positive reactors in Malmö and 11/12 (92%) of the positive reactors in Singapore. Hence, we would have missed 24/38 (63%) positive reactors in the combined population.

Thus, our goal to make it easier to test for acrylate allergy by formulating a shortened acrylate series or an acrylate mix that could be added to the baseline series became even more important. We had formulated two mixes: one containing 2-HEMA, TREGDA, and EGDMA and another with 2-HEMA and TREGDA. However, our mixes were found to induce frequent false positive reactions in our patients even though patch tests to the individual components in the same patients were negative. After double-checking the mixes to ensure that the concentrations were correct, and repeating the entire formulation and testing process, the same outcome of frequent false positives was found, and we decided to abandon the attempt to introduce acrylate mixes to the baseline series.

In the fourth study, we tested acrylate patch test preparations that had been currently used for routine patch testing in 9 different patch test departments around the world to determine whether the measured allergen concentrations were as stated on the syringe labels. We found that, for the more volatile acrylate allergens, MMA and 2-HPA, the measured concentrations in the samples were below the acceptable range of 80% or more of the stated concentration, while most of the other less volatile allergens (2-HEMA, EGDMA and TREGDA) were within the acceptable range.

In our final study, we investigated whether acrylate patch test preparations decreased in concentration over time when stored at different temperatures. We found that the concentration of allergens in IQ chambers decreased much more rapidly than in the syringes. In general, the decrease in allergen concentration was most rapid at room temperature (+23˚C), followed by refrigerator (+4˚C) and freezer (–18˚C), i.e. the higher the temperature, the faster the allergen loss.

These results have practical implications for the clinical practice of patch testing. For optimal stability, acrylate/methacrylate patch test preparations are best stored in the freezer, or at least in the refrigerator, rather than at room temperature. This is even more important in tropical climates, where the average room temperature is higher. Furthermore, patch test preparations of volatile allergens should be applied only to chambers immediately before application of the patches to the test site on the skin, and not pre-loaded one day or more before, as has been the practice in some patch test centres.