

Editorial

Asthma and methacrylates – gluing together the evidence

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Acrylates are a group of reactive compounds frequently handled in many different occupations. They cure rapidly without separate addition of hardener; polymerization is catalyzed by light, heat, or oxygen. There are two important groups of acrylates, methacrylates, and cyanoacrylates; both are used as glues. Exposure to cyanoacrylates has been linked to asthma in several case reports and one epidemiological study (1–4).

Methacrylates are also used as plastic filling material leading to exposure among dental and surgical personnel and workers in different biotechnical and pharmaceutical industries. In Scandinavia, work with methacrylates has been common among dental personnel for some decades now. The use of composite resin materials for dental restoration has increased because of the replacement of mercury based materials, such as amalgam. Although these newer plastic fillings (composite resins) are made from different varieties of less volatile methacrylates, the bondings consist of more volatile acrylates, such as 2-hydroxyethyl-methacrylate (HEMA) and triethylene glycol dimethacrylate (TEGDMA). Studies conducted in Finland and Sweden to measure exposure to HEMA among dental nurses have shown rather low median levels, around $3 \mu\text{g}/\text{m}^3$ (5, 6). However, higher levels were found when working around the patient's mouth, during mixing of the components and when removing old fillings. The highest short-term concentrations of HEMA were $68 \mu\text{g}/\text{m}^3$ in the Finnish study (5) and $20 \mu\text{g}/\text{m}^3$ in the Swedish study (6). The only European Union country which has an occupational exposure limit for HEMA is the Netherlands, where the limit is $270 \mu\text{g}/\text{m}^3$, for 8 h work.

It has not previously been clear whether exposure to methacrylates increases the risk for asthma. One early publication describes a dental assistant who developed asthma after manufacturing prosthetic dental trays, probably because of exposure to methyl methacrylates (1). There is also one early case report from Poland about a dental technician who developed asthma after working with methyl methacrylate (7) and more recent case reports among Finnish dental personnel (8, 9). Methacrylates are already well known as inducers of contact dermatitis.

In the current issue of *Allergy*, Jaakkola et al. (10) from UK and Finland present an important study showing that exposure to methacrylates is associated with adult-onset asthma. Within a cohort of dental assistants/nurses they observed that the use of methacrylates increased the risk for asthma; and in a dose-dependent manner, the risk for rhinitis. Both exposure and outcome were based on self-reporting. Exposure was based on reporting of job-specific tasks, a method that has rather high validity (11). The main outcome, physician-diagnosed asthma, is considered to have a high validity, albeit with a bias towards severe disease, as subjects with mild disease tend to under-report their asthma (12). However, as the authors also point out, the most problematic bias occurs if the dental assistants using methacrylates falsely over-report a diagnosis of asthma, a phenomenon known to epidemiologists as dependent misclassification. This is always a problem in studies where both the outcome (disease) and exposure are based on self-reporting. The authors argue against this possibility by pointing out that there was no increased risk associated with the use of latex gloves. If

dental assistants were prone to over reporting, then subjects exposed to latex, a well-known sensitizer, would have falsely over reported the presence of asthma. Like the authors, I believe that dependent misclassification is probably of minor importance in this study.

An important limitation of the study design is that it is not possible to definitely conclude whether the observations were as a result of true onset of asthma in relation to exposure or to exacerbation of adult-onset asthma (with onset before exposure) because of methacrylates, as the authors only investigated subjects with current exposure (in the past 3 months) to methacrylates. An improved design would be to compare the incidence of asthma in relation to the timing of the exposure, making it possible to analyze whether methacrylates really induced new-onset asthma among the exposed.

Atopy is an important host risk factor for sensitization to high-molecular weight agents, although its predictive value is low (13). Regarding low-molecular weight allergens, such as methacrylates, our knowledge is limited (14). There is a tendency for atopics to have an increased production of specific IgE against conjugates of different

small chemical compounds, such as platinum salts, or acid anhydrides (15–17). Atopy may also play a role in the occurrence of red cedar asthma. In the current study, exposure to methacrylates was associated with a higher risk for asthma among atopics compared with nonatopics. This finding is interesting, and there is a need for further epidemiological studies, which stratify subjects according to atopy.

This study is an important contribution to the field of occupational asthma, as it indicates that exposure to methacrylates increases the risk for asthma.

Three messages can be extracted from the results:

To physicians – when investigating patients with asthma, ask the patient about their occupation, and find out if they handle any kind of glue or any products containing methacrylates.

To employers – the results underline, that despite low exposure levels, safer and improved handling of methacrylates is needed in dentistry.

To policy makers – there is a need for threshold limit values for methacrylates, which reflect the risks for asthma, contact dermatitis and sensitization.

References

- Lozewicz S, Davison AG, Hopkirk A, Burge PS, Boldy D, Riordan JF et al. Occupational asthma due to methyl methacrylate and cyanoacrylates. *Thorax* 1985;**40**:836–839.
- Kopp SK, McKay RT, Moller DR, Cassidy K, Brooks SM. Asthma and rhinitis due to ethylcyanoacrylate instant glue. *Ann Int Med* 1985;**102**:613–615.
- Savonius B, Kekinen H, Tuppurainen M, Kanerva L. Occupational respiratory disease caused by acrylates. *Clin Exp Allergy* 1993;**23**:416–424.
- Torén K, Balder B, Brisman J, Lindholm N, Löwhagen O, Palmqvist M et al. The risk of asthma in relation to occupational exposures: a case-control study from a Swedish city. *Eur Respir J* 1999;**13**:496–501.
- Henriks-Eckerman M-L, Alanko K, Jolanki R, Kerosuo H, Kanerva L. Exposure to airborne methacrylates and natural rubber latex allergens in dental clinics. *J Environ Monit* 2001;**3**:302–305.
- Hagberg S, Ljungqvist G, Andreasson H, Karlsson S, Barregård L. Exposure to volatile methacrylates in dental personnel. *J Occup Environ Hyg* 2005;**2**:302–306.
- Wittzak T, Palczynski C, Szule B, Gorski P. Bronchial asthma with inflammation of the mucous membrane induced by occupational exposure to methyl methacrylate in a dental technician. *Med Pr* 1996;**47**:259–266 (in Polish).
- Piirilä P, Kanerva L, Keskinen H, Estlander T, Hytönen M, Tuppurainen M et al. Occupational respiratory hypersensitivity caused by preparations containing acrylates in dental personnel. *Clin Exp Allergy* 1998;**28**:1404–1411.
- Lindström M, Alanko K, Keskinen H, Kanerva L. Dentist's occupational asthma, rhinconjunctivitis and allergic contact dermatitis from methacrylates. *Allergy* 2002;**57**:543–545.
- Jaakkola MS, Leino T, Tammilehto L, Ylöstalo P, Kuosma E, Alanko K. Respiratory effects of exposure to acrylates among dental assistants. *Allergy* 2007;**62**:648–654.
- Tielemans E, Heederik D, Burdorf A, Vermeulen R, Veulmans H, Kromhout H et al. Assessment of occupational exposures in a general population: comparison of different methods. *Occup Environ Med* 1999;**56**:145–151.
- Torén K, Palmqvist M, Löwhagen O, Balder B, Tunsäter A. Accuracy of self-reported year of asthma-onset. *J Clin Epidemiol* 2006;**59**:90–93.
- Gautrin D, Newman-Taylor AJ, Nordman H, Malo J-L. Controversies in epidemiology of occupational asthma. *Eur Respir J* 2003;**22**:551–559.
- Lemiere C, Charpin D, Vervloet D. Is atopy a risk factor for occupational asthma. *Rev Mal respire* 1995;**12**:231–239 (in French).
- Venables KM, Topping MD, Howe W, Luczynska CM, Hawkins R, Newman Taylor AJ. Interaction of smoking and atopy in producing specific IgE antibody against a hapten protein conjugate. *Br Med J* 1985;**290**:201–204.
- Venables KM, Dally MB, Nunn AJ, Stevens JF, Newman Taylor AJ. Smoking and occupational allergy in workers in a platinum refinery. *Br Med J* 1989;**285**:939–942.
- Nielsen J, Welinder H, Hortmann V, Skerfving S. Allergy to methyltetrahydrophthalic anhydride in epoxy resin workers. *Br J Ind Med* 1992;**49**:769–775.