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Role of dermal exposure in systemic intake of methylenediphenyl diisocyanate (MDI) among construction and boat building workers

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HIGHLIGHTS

- Workers may be exposed to methylenedianiline (MDA) when handling one-component MDI-containing raw materials.
- It is important to minimize skin exposure to MDI in order to reduce the risk of allergic contact dermatitis and possibly also asthma.
- The use of chemical protective gloves lowered the skin exposure of the hands to MDI.
- Indication of dermal uptake of MDI can be detected in next morning urine samples.

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ABSTRACT

The causal relationship between inhalation exposure to methylenediphenyl diisocyanate (MDI) and the risk of occupational asthma is well known, but the role of dermal exposure and dermal uptake of MDI in this process is still unclear. The aims of this study were to measure dermal exposure to and the dermal uptake of MDI among workers (n = 24) who regularly handle MDI-urethanes. Dermal exposure was measured by the tape-strip technique from four sites on the dominant hand and arm. The workers with the highest exposure (n = 5) were biomonitored immediately after their work shift, in the evening and the next morning, using urinary 4,4′methylenedianiline (MDA) as a marker. Dermal uptake was evaluated by comparing workers' MDA excretions both when they were equipped with respiratory protective devices (RPDs) and when they did not use them. The measured amounts of MDI on their hands varied from below 0.1 to 17 μg/10 cm^2 during the test. MDI concentrations were in the range of 0.08 to 27 μg m^{-3} in the breathing zone outside the RPDs. MDA concentrations varied from 0.1 to 0.2 μmol mol^{-1} creatinine during the test period. The decreasing effect of RPDs on inhalation exposure was absent in the next morning urine samples; this excretion pattern might be an indication of dermal uptake of MDI.

1. Introduction

Isocyanates, a diverse group of reactive chemicals with the functional group NCO, are well-known causes of occupational asthma worldwide. Due to its low volatility, methylenediphenyl diisocyanate (MDI) has become the most commonly produced and technically used isocyanate. Commercial MDI or polymeric MDI (PMDI) is chemically a mixture of monomeric and oligomeric MDI. MDI or pure MDI is a mixture of primarily 4,4′-MDI with small amounts of 2,4 and 2,2′ isomers. PMDI typically contains 25–65% MDI monomers with the balance consisting of oligomeric polyisocyanate homologues of MDI. MDI monomers are classified as respiratory and skin sensitizing, and cases of allergic contact dermatitis to MDI have also been reported (Aalto-Korte et al., 2012; Engfeldt et al., 2013). Several cases of occupational asthma related to low levels of airborne MDI have been reported. A case report of two nurses' asthma due to MDI-containing orthopedic plaster casts has been published (Suojalehto et al., 2011). These nurses were exposed to airborne MDI concentrations of 0.11 μg NCO m^{-3} during the casting, which is less than 3% of the Finnish 15-min

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occupational exposure limit (OEL), 35 μg NCO m^{-3}. These and other similar cases have raised the question: can respiratory sensitization and the development of asthma be accelerated by skin contact with MDI (Bello et al., 2007; Redlich, 2010)?

A poor correlation was observed between airborne MDI levels and 4,4′-methylenedianiline (MDA) concentrations in urine during a moulding process (Kääriä et al., 2001), indicating possible dermal uptake of MDI, found as MDA in urine. Later, tape-strip methods were developed to determine dermal exposure to isocyanates (Fent et al., 2006; Liljelind et al., 2010). A study of total exposure to 1,6-hexamethylene diisocyanate (HDI) during spray painting indicated that both dermal and inhalation exposure to HDI contributed to the urine levels of its metabolite 1,6-hexamethylene diamine (HDA) (Gaines et al., 2010). Liljelind et al. (2010) studied dermal and inhalation exposure to MDI in iron foundry workers but did not carry out biological monitoring. Thus, there is a need to investigate dermal exposure to MDI and its relationship with the systemic dose, including the role of protective gloves. The target of such a study should be manual handling of MDI that results in a high risk of skin exposure.

The aims of this study were to evaluate the dermal exposure and dermal uptake of MDI. Dermal exposure was measured among workers mostly handling MDI manually in different processes in construction work and the boat building industry, using the tape-strip method. Workers showing the highest dermal exposure were selected for monitoring of urine MDA levels.

2. Materials and methods

2.1. Participating enterprises, participants and study design

We contacted approximately 15 enterprises, in which manual handling of MDI was common. Twelve of these participated in the study: they were small to medium sized enterprises, representing the boat building industry (5), construction work (6) and production of prefabricated units (1). In each enterprise, 2–4 workers regularly handled MDI formulations without respiratory protection. The processes included foaming, moulding, gluing, laminating, and coating with polyurethane, which is mixture of polyols and MDI hardener. The size of the mixed polyurethane batches varied from 200 g to 5 kg. Each batch process was repeated 2–20 times per shift, on 3–5 days of the working week.

Twenty-four workers were interviewed and observed in 27 different working situations in which MDI formulations were handled. Many workers wore T-shirts, exposing bare skin on the arms. Fourteen workers (58%) did not use gloves at all, or used gloves that were not intended for chemical protection. We used the tape-strip technique to determine the dermal exposure of these 24 workers to MDI during our first visit. On the basis of field observations and results from other studies (Liljelind et al., 2010), the dominant hand and arm of each worker were chosen as sampling sites for studying dermal exposure and to find workers with high dermal exposure.

The samples were taken once from each worker after the exposing job (15–60 min for the batch process) was finished. The tape-stripping is described in Section 2.3. The workers showing the highest dermal exposure in the tape-strip measurement were asked to participate in a biological monitoring study in order to determine if dermal exposure to MDI could be seen in their urine MDI metabolite level (urine MDA).

During our second visit to the workplaces, we carried out urine sampling, took tape-strip samples and collected air samples. The collection of urine samples started on the third working day (usually Wednesday) and the first sample was given after the exposing work was finished for the day. It continued during the fourth and fifth working day and over the weekend or days off. The last urine sample was given on the morning before the next working week started. The urine sampling procedure is described in detail in Section 2.7. Air samples were also collected at the same time during the exposing job on day 4 and day 5, and tape-strip samples were taken immediately after the job was finished. Respiratory protective devices (RPD) were used when handling MDI on day 4 and day 5.

Of the 24 workers who gave their consent, only five were able to participate in the second part of the study, due to practical reasons. Four of these workers were provided with powered filtering RPDs with a hood (class TH3A2B2E2K2P), which should be efficient enough to minimize inhalation exposure when performing MDI work. The fifth worker used the RPD (TH2A2P) provided by his employer. Inhalation exposure to MDI was measured by sampling in the breathing zone and inside the hood during the exposing work. The condition of the RPDs was checked before and after the air measurements. In the spraying process, the RPD filters were changed daily and before the air measurements; in the gluing or laminating processes the filters were used for two days.

The field measurements were performed from December 2010 to May 2012. The Ethics Committee of the Hospital District of Helsinki and Uusimaa approved the study (reference number 298/13/03/00/2010). All participants gave their written informed consent.

2.2. Chemicals

The chemicals used in this study were acetonitrile (HPLC grade S, Rathburn), acetic anhydride, formic acid, sulphuric acid, toluene, potassium dihydrogenphoshate, sodium hydroxide and ethyl-acetate (all of analytical reagent grade or purer, Merck). Hepta-fluorobutyric anhydride (HFBA) was from Pierce Chemical. Solid derivatives of 2,4′-MDI and 4,4′-MDI with 1-(2-methoxyphenyl) piperazine (2MP, Aldrich) were used to quantify MDI monomers. They were prepared as described in the ISO 16702 standard (2007). The deuterated 4,4′-d_2-MDA (used as an internal standard in the biological monitoring analysis) and d_3-2MP (used to prepare an internal standard for MDI) were from Ramidus Ab (Lund, Sweden). The MDA was from Sigma and its internal standard ethylenedianiline (EDA, purity 95%) was from Acros Organics. PMDI (Merck Schuchardt) was used to determine recovery from the tapes. Citric acid (Fisher Scientific, general purpose grade) was used to stabilize the urine samples.

2.3. Determination of dermal exposure – field sampling and work-up procedure

MDI monomers on the skin of 24 workers were measured using the tape-strip technique described by Liljelind et al. (2010). The tape-strips (2.5 × 4 cm^2, Fixomull®, BSN medical GmbH & Co., Hamburg, Germany) were applied to four different skin sites on the dominant hand and arm: forefinger, middle finger (palmar side of the fingertip), palm (middle) and wrist (palmar side on which bare skin was visible) or arm (where bare skin was visible). Whether wrist or arm was chosen depended on where bare skin was visible. Otherwise the sample was taken from the point at which the glove ended. Three consecutive tape-strip samples were collected from each skin site. The sum of these three collections was reported as the result. After collection, each tape was immediately placed in a clean glass vial containing 2MP (1 mg ml^{-1}) in dry acetonitrile (5 ml). Two blank tapes representing field blanks were also placed in 2MP containing vials during the collection. Samples were stored at room temperature for one day to allow complete derivatization. After this, the internal standard was added and with the use of 50 μl of acetic anhydride, the amines in the sample were acetylated for at least 4 h before analysis.