Cleaning Agents and Asthma

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Abstract

Although cleaners represent a significant part of the working population worldwide, they remain a relatively understudied occupational group. Epidemiological studies have shown an association between cleaning work and asthma, but the risk factors are uncertain. Cleaning workers are exposed to a large variety of cleaning products containing both irritants and sensitizers, as well as to common indoor allergens and pollutants. Thus, the onset or aggravation of asthma in this group could be related to an irritant-induced mechanism or to specific sensitization. The main sensitizers contained in cleaning products are disinfectants, quaternary ammonium compounds (such as benzalkonium chloride), amine compounds, and fragrances. The strongest airway irritants in cleaning products are bleach (sodium hypochlorite), hydrochloric acid, and alkaline agents (ammonia and sodium hydroxide), which are commonly mixed together.

Exposure to the ingredients of cleaning products may give rise to both new-onset asthma, with or without a latency period, and work-exacerbated asthma. High-level exposure to irritants may induce reactive airways dysfunction syndrome. Cleaning workers may also have a greater relative risk of developing asthma due to prolonged low-to-moderate exposure to respiratory irritants. In addition, asthma-like symptoms without confirmed asthma are also common after exposure to cleaning agents.

In many cleaners, airway symptoms induced by chemicals and odors cannot be explained by allergic or asthmatic reactions. These patients may have increased sensitivity to inhaled capsaicin, which is known to reflect sensory reactivity, and this condition is termed airway sensory hyperreactivity.

Key words: Asthma. Cleaning agents. Cleaners. Bronchial hyperresponsiveness. Irritant-induced asthma.

Resumen

Aunque los trabajadores de limpieza representan una parte significativa de la población laboral en todo el mundo, constituyen un grupo ocupacional escasamente estudiado. Los estudios epidemiológicos han mostrado una asociación entre el trabajo en limpieza y el asma, pero los factores de riesgo son desconocidos. Los empleados en limpieza están expuestos a una gran variedad de productos que contienen tanto sustancias irritantes como sensibilizantes, así como a diversos aeroalérgenos comunes y contaminantes. La aparición o agravamiento del asma en trabajadores de limpieza puede estar relacionado con un mecanismo inducido por irritantes o una sensibilización específica. Los principales agentes sensibilizantes en los productos de limpieza son los desinfectantes, los compuestos de amonio cuaternario (como el cloruro de benzalconio), las aminas y las fragancias. Los irritantes más potentes en estos productos son la lejía (hipoclorito sódico), el ácido hidroclórico y las sustancias alcalinas (amoníaco e hidróxido sódico), que a menudo se mezclan entre si.

La exposición a estos ingredientes de los productos de limpieza puede dar lugar a la aparición de asma de novo, con o sin periodo de latencia, o a un asma exacerbada en el trabajo. La exposición a concentraciones altas de irritantes puede inducir un síndrome de disfunción reactiva de las vías respiratorias (RADS). Los trabajadores de limpieza también tienen un mayor riesgo de desarrollar asma por la exposición continua a concentraciones bajas o moderadas de irritantes. Además, también son relativamente frecuentes los síntomas similares al asma, sin asma confirmada, tras la exposición a productos de limpieza. En muchos empleados en limpieza, lo síntomas respiratorios causados por sustancias químicas y olores fuertes no se explican por reacciones alérgicas o asmáticas. Estos pacientes pueden mostrar un aumento de sensibilidad a la capsaicina inhalada, lo que refleja reactividad sensorial, trastorno que se conoce como "síndrome de hiperreactividad sensorial de la vía aérea".

Palabras clave: Asma. Productos de limpieza. Trabajadores en limpieza. Hiperreactividad bronquial. Asma por irritantes.

Introduction

Exposure to substances in the workplace causes more than 10% of all cases of adult-onset asthma [1,2]. Cleaning has been described as an occupational risk due to an increased incidence of asthma and asthma-like symptoms among cleaning workers [3-6]. It was first identified as a high-risk occupation in a cross-sectional analysis of the European Community Respiratory Health Survey (ECRHS), an international population-based study carried out in 1990-95 [7]. The excess risk was consistent in several countries, with Spain among those with the highest risk.

A follow-up ECRHS study carried out a few years later revealed that the occupations with the highest risk of developing new-onset asthma included cleaning and nursing [2]. Two systematic reviews on this topic strengthened the evidence for an association between exposure to cleaning products and a higher risk of asthma among domestic and nondomestic cleaners [8,9].

In some studies, however, although asthma symptoms among cleaners were associated with exposure to cleaning products, most patients did not have bronchial hyperresponsiveness (BHR) [4], indicating that exposure to cleaning agents may give rise to asthma-like symptoms without asthma. Indeed, work-related respiratory symptoms in individuals without asthma could represent a large proportion of individuals assessed for possible work-related asthma [10].

The pattern of exposure to cleaning agents and the resulting health hazards is a complex issue, and the contribution of sensitization to specific agents or exposure to irritants in the pathogenesis of respiratory symptoms associated with cleaning remains to be clarified.

This review focuses on epidemiological evidence of an association between asthma and cleaning and deals with the main cleaning products and their irritating and sensitizing potential. It also examines the possible underlying mechanisms involved in the pathogenesis of asthma-like symptoms caused by cleaning agents.

Epidemiological Studies

Although cleaners represent a significant proportion of the working population worldwide, they remain a relatively understudied occupational group. Cleaners undertake diverse tasks, ranging from domestic cleaning to cleaning in offices, hospitals, kitchens, public buildings, and industrial plants. It has been reported that 3% of the female workforce in Finland [3] and 4% in the United States [8] have a job in this field, and in Spain, approximately 10% of women over 16 years old worked as cleaners in the year 2000 [11].

Both population-based epidemiological studies and analyses of occupational disease registry-based data have shown that cleaners have an increased risk of asthma. Kogevinas et al [2] estimated the relative and attributable risks of new-onset asthma in relation to occupations, work-related exposures, and inhalation accidents among 6837 participants from 13 countries who previously took part in the ECRHS (1990-95) and did not report respiratory symptoms or a history of asthma at the time of the first study. Asthma was assessed by methacholine challenge test and by questionnaire data on asthma symptoms. A significant excess risk of asthma was seen after exposure to substances known to cause occupational asthma (relative risk [RR], 1.6; 95% confidence interval [CI], 1.1-2.3) and also to cleaning agents (RR, 1.8; 95% CI, 1.01-3.18). A higher risk of new-onset asthma was found in 358 individuals who had been employed in cleaning or caretaking during the 9-year follow-up period as compared with 4143 employed in professional, clerical, or administrative jobs during the same period (RR, 1.7; 95% CI, 0.9-3.2). The authors used an asthma-specific job exposure matrix, which revealed that the incidence of new-onset asthma for individuals exposed to cleaning products across all occupations in the study was significantly higher than for those unexposed to any agent (RR, 1.8; 95% CI, 1.0-3.2). Asthma risk was also increased in participants who reported an acute symptomatic inhalation event such as fire, mixing cleaning products, or chemical spills (RR, 3.3; 95% CI, 1.0-11.1). An increased risk of incident asthma was also observed for the group of 291 nurses (RR, 2.2; 95% CI, 1.3-4.0). A study carried out using data from job-specific questionnaires that had been obtained for nurses in the ECRHS II interviews showed that the highest risks of incident asthma were among nurses who used ammonia, bleach, and/or cleaning products in spray form at work [12].

Zock et al [13] carried out the first epidemiologic study that evaluated the risk of adult new-onset asthma related to nonoccupational use of common household cleaning products among 3503 participants of the ECRHS II who did the cleaning in their own homes and did not have asthma at baseline. The use of cleaning sprays at least weekly (42% of participants) was associated with the incidence of asthma symptoms or medication (RR, 1.49; 95% CI, 1.12-1.99) and wheeze (RR, 1.39; 95% CI, 1.06-1.80). The incidence of physician-diagnosed asthma was higher among those participants who used sprays at least 4 days per week (RR, 2.11; 95% CI, 1.15-3.89). Risks were found predominantly for commonly used glass-cleaning, furniture, and air freshener sprays. Cleaning products not applied in spray form were not associated with asthma. In summary, this study showed a significant 30%-50% increased risk of incident asthma related to the use of products in spray form at least once a week, and the risk increased when the frequency of use or number of different sprays increased. Among products not contained in spray applications, weekly use of hypochlorite bleach was not significantly associated with new-onset asthma (RR, 1.1-1.3). It can be speculated that asthma could have been at least partly irritant-induced.

Another cross-sectional analysis of the ECRHS II participants who did the cleaning in their homes showed that frequent use of bleach was associated with the prevalence of lower respiratory tract symptoms and with BHR [14]. The study also showed an inverse association between bleach use and the prevalence of atopic sensitization to common environmental allergens and allergic symptoms. This association was apparent for specific IgE to both indoor allergens (cat) and outdoor allergens (grass pollen), and was consistent in various subgroups, including those without any history of respiratory problems. Dose-response relationships

were apparent for the frequency of bleach use and sensitization rates. Lower respiratory tract symptoms, but not allergic symptoms, were more prevalent among those using bleach 4 or more days per week. The use of bleach was not associated with indoor allergen concentrations. The authors hypothesized that this could be explained either by direct exposure to volatile chlorinated agents released during or shortly after bleach use, or indirectly due to a cleaner home environment [14].

Risk factors for asthma were studied among indoor cleaners participating in the Spanish part of the ECRHS in 1992 [15]. More than half of those surveyed reported work-related respiratory symptoms, and domestic cleaners were the most likely to report such symptoms. The asthma risk of domestic cleaners was mainly associated with kitchen cleaning and furniture polishing, and with the use of oven sprays and polishes [15]. Medina-Ramón et al [11] conducted a cross-sectional study in 4521 Spanish women aged 30-65 years and found that 25% of asthma cases were attributable to domestic cleaning. These authors [4] reported that, among female domestic cleaners, lower respiratory tract symptoms were more common on working days and were predominantly associated with exposure to bleach (both diluted and undiluted), undiluted ammonia, degreasing and glass cleaning sprays/atomizers, and air fresheners.

In the USA, the states of California, Massachusetts, Michigan, and New Jersey conduct work-related asthma surveillance as part of the Sentinel Event Notification System for Occupational Risks (SENSOR) [16]. The Californian surveillance system showed that janitors and cleaners had the highest incidence of work-related asthma [17]. Rosenman et al [5] reviewed reports on work-related asthma associated with cleaning products and found that a cleaning product was 1 (or more) of the 3 suspected agents identified in 236 (12%) of the 1915 confirmed cases. Of the products identified, bleach was the most frequent.

Cleaning Agents

A cleaning product is defined as any material used for cleaning or disinfecting surfaces in general work environments [5]. These products have become an indispensable part of modern life, as they are used on daily basis in nearly all workplaces and homes. A wide array of cleaning agents has been developed to facilitate dust and dirt removal, and for disinfection and surface maintenance.

Most cleaning agents have an irritating effect on mucous membranes and the skin, and occasionally a sensitizing potential (Table 1). Thus, these products have been implicated in different cutaneous and respiratory conditions, including work-related asthma [18]. They contain chemicals that may elicit new-onset asthma, exacerbation of asthma symptoms among individuals with pre-existing asthma, asthma-like symptoms without asthma, or other respiratory conditions (Table 2). Most of the cleaning agents associated with asthma-like symptoms have harmful irritative and/or sensitizing properties and may be involved in the development of chronic respiratory symptoms [19].

Both professional and domestic cleaners are exposed to a large number of particulate and gaseous compounds. Arif et al [20] carried out a qualitative study among domestic and industrial cleaning workers in the United States. Domestic cleaners demonstrated a significant skills deficit for job training, chemical exposure, and competence as compared with industrial cleaners; they were also more frequently exposed to respiratory irritants and sensitizers. Domestic cleaners reported more adverse respiratory symptoms than industrial cleaners. These data show that domestic cleaners are at risk of exposure to respiratory irritants and/or sensitizers.

The cleaning products used for common janitorial tasks are mixtures of many chemicals, which are usually classified in product categories according to their application. The main

Table 1. Chemicals in cleaning products commonly involved in work-related respiratory symptoms

Sensitizers
• Amine compounds (eg, monoethanolamine) • Disinfectants (eg, aldehydes) • Quaternary ammonium compounds (eg, benzalkonium chloride) • Scents containing terpenes (eg, pinene, d-limonene), eugenol • Isothiazolinones, formaldehyde (preservatives) • Others: natural rubber latex
Irritants
• Chlorine (bleach) • Ammonia • Hydrochloric acid • Monochloramine • Mixing bleach and acid or ammonia • Sodium hydroxide (caustic soda) • Quaternary ammonium compounds • Monoethanolamine

Table 2. Different asthma and asthma-like disorders that may develop as a consequence of exposure to cleaning products

New-onset asthma
• Sensitization (IgE-mediated or non IgE-mediated) • High exposure to irritants (RADS or irritant-induced asthma)
Work-exacerbated asthma
• Worsening of asthma symptoms associated with changes in lung function
Work-related respiratory symptoms without asthma
• Large proportion of subjects • May be related to airway sensory hyperreactivity syndrome

Abbreviation: Ig, immunoglobulin; RADS, reactive airway dysfunction syndrome.

chemical components of cleaning products include disinfectants, detergents, alkaline agents (eg, sodium hydroxide, ammonia), acids, complexing agents (water softeners), solvents, corrosion inhibitors (eg, monoethanolamine), film formers and polishes (eg, acryl polymers, polyethylene), preservatives (eg, benzalkonium chloride, isothiazolinones, formaldehyde), and perfumes or scents [19].

Common sources of toxicology information on these products are labels, material safety data sheets, manufacturer's websites, chemical suppliers, the National Library of Medicine, and several webpages (http://toxnet.nlm.nih.gov/; http://chem.sis.nlm.nih.gov/chemidplus/; http://www.acgih.org/; www.cdc.gov/niosh/npg/).

In Spain, useful information is available at http://informtoxic.varro.es/ (tab: domestic cleaning agents), http://www.fichasdeseguridad.com/toxicologia.htm, and http://www.guialimpieza.net/atl/intoxicacionytratamiento1.htm

Disinfectants

Disinfectants destroy bacteria and other microorganisms. It is important to differentiate between disinfectants and antiseptics. Whereas both are applied to surfaces, disinfectants are used on inanimate objects and antiseptics are used on living organisms. The health problems caused by antiseptics (eg, chlorhexidine) are beyond the scope of this review.

The main chemical classes of disinfectants are alcohols (eg, ethanol, isopropanol), aldehydes (glutaraldehyde, ortho-phthalaldehyde), oxidizers (eg, sodium hypochlorite, H_2O_2), phenolics (phenol, thymol, o-phenylphenol), and quaternary ammonium compounds. Disinfectants have been identified as the most hazardous group of cleaning agents [21].

Bleach

Bleach, whose active compound is sodium hypochlorite, and ammonia are among the most common chemicals used in cleaning products. The main component of household bleach is sodium hypochlorite in amounts that are equivalent to 3%-10% available chlorine; it usually also contains 1% sodium hydroxide as a stabilizer. Chlorine is a very toxic gas and exposure to levels as low as 1 ppm for a few minutes can irritate the eyes, nose, and throat. Chlorine also has a strong irritant effect on the airways and may increase BHR [22,23]. The occupational exposure standard for chlorine is 0.5 ppm time-weighted average over 8 hours, or 1 ppm over 10 minutes. Chlorine can be detected by smell at around 1 ppm.

Mixing hypochlorite from bleach with ammonium salts from dishwashing liquids or organic matter may lead to the release of chloramines. Symptoms of irritation of the eye, nose, and throat, but not permanent BHR, have been associated with exposure to chloramines among cleaning and disinfecting workers in the food industry [24]. Occupational asthma caused by exposure to chloramines has been reported among swimming pool workers [25].

Quaternary Ammonium Compounds

Quaternary ammonium compounds, which are also known as quats, are widely used in cleaning products as antiseptics, disinfectants, detergents, and preservatives. They have been reported to promote respiratory allergy, although the underlying mechanism remains unclear [26]. Quats can cause occupational asthma, which has seldom been reported to date, despite widespread use of these products. Bernstein et al [27] described a case of occupational asthma caused by prolonged workplace exposure to a cleaning solution containing benzalkonium chloride. Purohit et al [28] reported 3 female nurses who manifested asthma symptoms upon handling disinfectant solutions containing benzalkonium chloride. The diagnosis was confirmed by challenge tests in a closed chamber where the patients were exposed to the suspected disinfectant on a tray.

One case report described a pharmacist who developed severe occupational asthma after entering his office, which had been cleaned with a product containing lauryl dimethyl benzyl ammonium chloride [29].

Exposure to quats can occur either by inhalation of aerosolized liquid particles generated during application or by inhaling these liquid particles absorbed into the dust particles that are resuspended in the air [30].

Aldehydes

Glutaraldehyde and ortho-phthalaldehyde are extensively used in medical facilities for disinfecting heat sensitive equipment such as fiberoptic endoscopes. They can cause mucous irritation, respiratory symptoms, and immunoglobulin (Ig) E–mediated hypersensitivity reactions, and are well-known causative agents of occupational asthma [18,31,32].

Chloramine T

N-chloro tosylamide sodium salt, marketed as chloramine-T, is an N-chlorinated and N-deprotonated sulfonamide used as a biocide and a mild disinfectant. It is generally supplied in a 5% solution, but is also available in powder form. Chloramine-T is used in hospitals as a disinfectant and for sterilization of endoscopy instruments, but also in cleaning butcheries, kitchens, and operating theaters. Occupational asthma due to this agent, which is thought to be IgE-mediated, has been reported mostly among nurses and instrument maintenance personnel [33-35].

Detergents

Detergents, such as fatty acid salts (soap) and organic sulphonates, reduce the surface tension of water. More aggressive and effective detergents are increasingly used and may cause irritation of the skin and mucous membranes. The surfactants from detergents could interfere with IgE-mediated sensitization to ubiquitous environmental allergens. Only sparse data exist in relation to surfactants and allergic sensitization. It has been hypothesized that the strong surfactant properties of some ingredients of modern detergents may interfere with various intricate cellular interactions taking place along immunological pathways, including formation of type 2 helper T cytokines [36].

Alkaline Agents

Agents such as ammonia, sodium hydroxide, silicates, and

carbonates dissolve fatty acid substances, act as disinfectants, and inhibit corrosion of metal surfaces. They are very irritating to the eyes, skin, and mucous membranes. Household ammonia is commercially available in a 4%-10% solution and is very volatile. Heavy exposure to ammonia may result in chronic obstructive bronchitis and BHR [37].

The active component of oven and degreasing sprays is caustic soda (sodium hydroxide [up to 5%]), which can cause irritation of the skin and mucous membranes. Irritating effects can be expected after inhalation of aerosols containing caustic soda, and these are similar to those caused by ammonia [37], which has also been reported to cause cutaneous burns [38].

Acids

The acids used in cleaning products (to dissolve calcium) are phosphoric acid, acetic acid, citric acid, sulphamic acid, and hydrochloric acid. Hydrochloric (chlorhydric) acid 20%, widely used as a cleaning product in Spain and known as aguafuerte or salfumán, is a strong irritant of the mucosa.

Complexing Agents

Also known as water softeners, complexing agents regulate the pH and dissolve and bind cations such as calcium. Tripolyphosphates and EDTA belong to this group and can irritate the skin, eyes, and mucous membranes [19].

Solvents

Solvents, such as alcohols and glycol ethers, dissolve fatty substances. They are irritants and can be neurotoxic. 2-Butoxyethanol is a glycol ether commonly used in cleaning products, including window, carpet, and other surface cleaners. Exposure to vapors at high concentrations (above 2 ppm or 10 mg/m^3) can cause sensory irritation [39], and skin exposure may be relevant in the work environment.

Corrosion Inhibitors

Monoethanolamines, which are used as surfactants and to protect metal surfaces, are the most representative chemicals in this group. Exposure to these agents may provoke irritation of the mucous membranes and airways, causing cough, dyspnea, and wheezing. Exposure to ethanolamine from cleaning agents has been reported to induce occupational asthma [40]. The permissible exposure limit for monoethanolamine is 3 ppm and the short-term exposure limit is 6 ppm.

Film Formers and Polishes

Film formers and polishes are used in cleaning products to provide surface care. Acryl polymers and polyethylene contained in waxes may cause irritation of the mucosa and sensitization [41,42].

Perfumes and Scents

Perfumes and scents are common components of many cleaning products. Pine scent containing terpenes can act as a sensitizer [43], as can limonene [44], eugenol [45], and other fragrances. Terpenes can cause secondary emissions due to reactions of the primary exposures with oxidizers present in indoor air [46]. These reactions can release secondary ultrafine particles that may be responsible for respiratory irritation symptoms [47].

Challenge Studies

No population-based studies have been carried out to assess occupational exposure among cleaners. Some studies have investigated the short-term effect of challenge with cleaning compounds on respiratory symptoms and BHR.

Medina-Ramón et al [48] analyzed 43 female domestic cleaners with asthma, chronic bronchitis, or both who performed peak expiratory flow (PEF) measurements for 2 weeks. Lower respiratory tract symptoms were more common on working days and were predominantly associated with exposure to diluted bleach, degreasing sprays/atomizers, and air fresheners. However, associations with upper respiratory tract symptoms and PEF measurements were less apparent. Only 11 women (30%) scored positive for work-related asthma.

Bernstein et al [49] carried out a 12-week prospective study to assess the effects of cleaning on PEF rates and upper and lower respiratory tract symptoms in 25 women with asthma and 19 without asthma. No effect was observed on PEF rates after cleaning between the groups. After adjustment for the chemical severity exposure index and duration of cleaning, upper respiratory tract symptoms increased after cleaning for both groups. However, the change in the number of lower respiratory tract symptoms (after cleaning minus before cleaning) was statistically significant for asthmatic patients compared with nonasthmatic patients. The results suggest that cleaning activities are associated with increased lower respiratory tract symptoms in asthmatic patients, independently of the chemical severity exposure index and duration of cleaning.

D'Alessandro et al [50] exposed individuals with BHR and controls to 0.4 and 1 ppm of chlorine. After inhalation of 0.4 ppm of chlorine, there was no significant change in lung function. However, at 1 ppm, the BHR group experienced greater specific airway resistance than the controls, and the same difference was found in the proportional change in forced expiratory volume in 1 second (FEV_1) after 1 ppm of chlorine as compared to baseline reactivity. These data indicate that persons with hyperreactive airways manifest an exaggerated airway response to chlorine at 1.0 ppm and suggest that, when large numbers of persons are exposed to chlorine, a susceptible subpopulation may respond acutely with a greater decrement in lung function. Another study [51] showed that BHR to methacholine in asthmatics was significantly increased after a 12-minute immersion in a chlorinated whirlpool bath (chlorine in the air was not measured).

Sastre et al [52] investigated the effects of bleach inhalation on pulmonary function and inflammatory parameters among cleaning employees with and without BHR. Cleaners with work-related asthma-like symptoms, asthmatic controls, and atopic individuals without BHR not exposed to cleaning products were challenged with placebo or bleach (at 0.4 ppm of chlorine). Mean maximum fall in

FEV_1 during the bleach challenge was significantly higher than during the placebo challenge. The bleach challenge elicited 2 isolated late asthmatic reactions and 1 dual asthmatic reaction. Of all the patients challenged with bleach, only 1 had a significant decrease in the PC_{20} of methacholine 24 hours after the challenge. There were no clinically significant changes in sputum cell counts or fraction of exhaled nitric oxide (FE_{NO}) after bleach challenges. These results suggest that inhalation of bleach (chlorine gas) at a concentration of 0.4 ppm causes a substantial decrease in FEV_1 in individuals with and without BHR.

Taking into account that the no-effect level for chlorine is estimated at 0.5 ppm, these findings suggest that some individuals may experience respiratory symptoms and changes in lung function after exposure to chlorine levels below the recommended 8-hour limit.

Medina-Ramón et al [4] reported that airborne exposure levels of chlorine and ammonia during domestic cleaning work were detectable (>0.1 ppm) in all 10 measurement sessions. Chlorine was detected during all sessions, with median levels of 0 ppm to 0.4 ppm and peaks up to 1.3 ppm. Airborne ammonia was also detectable during all sessions, with median levels of 0.6 to 6.4 ppm and peaks of more than 50 ppm. Sastre et al [52] reported that peak chlorine airborne concentrations during a 5-minute bathroom-cleaning simulation were 1.41 ppm and 1.22 ppm.

Cleaning agents contain both volatile and nonvolatile substances. The application of common cleaning products results in excessive exposure to potentially harmful volatile pollutants. The major toxicologically significant constituents of the evaporative substances are volatile organic compounds (VOC), defined as substances with boiling points in the range of 0ºC to about 400ºC [21]. Both field studies and emission testing indicate that the use of cleaning agents results in a temporary increase in the overall VOC level. This increase usually occurs during cleaning, although airborne levels of these chemical agents may remain elevated for many hours after cleaning. These agents can act as airway irritants.

The airborne concentrations of glycol ethers (regulated toxic air contaminants) and terpenoids (including d-limonene) were measured during and after the application of 5 different cleaning products and air fresheners in a 50-m^3 room ventilated at 0.5 m^3/h [46]. The results indicated that some cleaning agents can yield high levels of VOC, including glycol ethers and terpenes, which can react with ozone to form a variety of secondary pollutants including formaldehyde and ultrafine particles.

Eleven patients sensitized to isoeugenol and 10 patients sensitized to hydroxyisohexyl-3-carboxaldehyde were exposed for 60 minutes to 1000 $\mu g/m^3$ of these compounds in an exposure chamber at rest [53]. There were no significant changes in lung function, although a tendency towards increased BHR was observed after exposure (up to 72 h) to any of the compounds. The respiratory symptoms reported by some patients were unrelated to objective measures, while the skin symptoms observed corresponded to the patients' specific sensitization. Thus, inhalation of high concentrations of fragrance allergens apparently poses a risk of developing manifest contact dermatitis in some patients, while changes in the respiratory tract are limited to symptoms with no objective changes in lung function.

Possible Pathogenic Mechanisms

Cleaning workers are exposed to a large variety of cleaning products containing both irritants and sensitizers, as well as to common indoor allergens and pollutants (eg, house dust mites, animal dander, cockroaches, endotoxins, chemical agents). Thus, the onset or aggravation of asthma in cleaners could be related to an irritant-induced mechanism or to specific sensitization. Exposure to cleaning products may give rise to both new-onset asthma, with or without a latency period, and work-exacerbated asthma (Table 2). In addition, asthma-like symptoms without confirmed asthma are also common after exposure to cleaning agents. In a cross-sectional study conducted in our department of 39 female cleaners who reported asthma symptoms, asthma was confirmed by objective means in only 25% (unpublished data). Exposure to different cleaning compounds, including fragrances, has been reported to cause asthma-like symptoms with no significant changes in lung function [53].

Cleaning products contain chemicals that could contribute to the development of asthma or to exacerbation of symptoms among asthmatics through sensitization or irritative mechanisms. Several pathogenic mechanisms have been suggested [54].

High-level respiratory irritant exposures can induce new onset of asthma with no latency period, namely, reactive airways dysfunction syndrome [55,56]. Cases of this syndrome have been reported with different respiratory irritants, mainly chlorine, but also with other agents such as ammonia, alkaline agents, and hydrochloric acid [57,58]. The respiratory accidents reported among cleaners are predominantly related to inadequate mixtures of bleach with either hydrochloric acid or ammonia, leading to a rapid release of important amounts of free chlorine or chloramines, respectively [54].

Recent population studies suggest that cleaning workers may also have a greater relative risk of developing asthma, as a result of low-to-moderate exposure to respiratory irritants. However, it is not possible to exclude coincidental asthma in such patients [59]. Chronic low-level exposure to irritants in cleaning compounds may cause inflammatory changes [60]. Airway inflammation is a characteristic feature of asthma and occupational asthma, and an increase in airway eosinophilia is usually observed after positive bronchial inhalation challenges [61,62]. The airway inflammatory pattern is usually eosinophilic, although it can be neutrophilic, both eosinophilic and neutrophilic, or neither (paucigranulocytic). In patients with work-exacerbated asthma, exposure to irritants usually elicits either no changes in airway inflammatory markers [63] or a neutrophilic type of airway inflammation [64,65].

Sastre et al [52] have reported that, after challenge to chlorine, neutrophil counts in induced sputum remained unchanged. However, individuals with BHR showed a trend towards a higher percentage of neutrophils 24 hours after the challenge than those without BHR. In individuals with an asthmatic reaction due to bleach inhalation, an increase in neutrophils 24 hours after challenge was observed in one patient, while another experienced an increase in eosinophils.

In many cleaners, airway symptoms induced by chemicals and odors cannot be explained by allergic or asthmatic reactions. Previous studies have shown that these patients often have increased sensitivity to inhaled capsaicin, which is known to reflect sensory reactivity. The term airway sensory hyperreactivity has been proposed for this condition [66]. Johansson et al [67] examined the relationship between asthma and airway sensory hyperreactivity, and investigated whether patients with this condition show signs of increased psychiatric morbidity. Patients completed a quantitative questionnaire on self-reported affective reactions and behavioral disruptions caused by odorous/pungent substances. In addition, a standardized capsaicin inhalation test was performed and a questionnaire to assess psychiatric morbidity was administered in patients with pronounced chemical sensitivity to identify those with airway sensory hyperreactivity. No strong relationship was found between sensory hyperreactivity and either asthma or psychiatric morbidity, indicating that this disorder may have different and as yet unknown pathways. Dysfunction of the upper airway, particularly work-associated irritable larynx syndrome, has recently been identified as an important cause of work-associated respiratory symptoms [68].

Summary and Conclusions

Cleaning agents are used in large quantities throughout the world. Epidemiological studies have shown an association between cleaning work and asthma, but risk factors are uncertain. Cleaning workers are at risk of acute and chronic exposure to volatile compounds and aerosols generated from cleaning products. Use of cleaning products in various occupations has been related to new-onset asthma, although it is unclear to what extent such exposures also contribute to work-exacerbated asthma. Cleaning products are mixtures of many chemical ingredients that may affect workers' health through air and cutaneous exposure. Cleaning agents are known to contain sensitizers, such as amine compounds, benzalkonium chloride, disinfectants, and fragrances, as well as strong airway irritants. Exposure to bleach (chlorine) and other irritants has been associated with lower respiratory tract and asthma symptoms both in the workplace and at home.

Exposure to cleaning products is a function of both product formulations and product application. Factors inherent to the environment where cleaning is done or the type of cleaning agents used may explain the differences observed between the different types of exposure. For instance, the use of cleaning products in spray form facilitates inhalation, and sprays may contribute to the burden of asthma in adults who do the cleaning in their homes. The ingredients of cleaning products should be systematically evaluated, and exposure in the workplace and at home should be assessed. A combination of product evaluation and exposure data is necessary to develop strategies for protecting exposed individuals from cleaning hazards.

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