

Reduction of exposure in the management of occupational asthma

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Purpose of review

The management of immunologically mediated occupational asthma may be difficult in clinical practice since complete avoidance of exposure to the sensitizing agent is associated with a substantial adverse socio-economic impact. The purpose of this review was to critically analyze the available information on the effectiveness of reducing exposure as an alternative to complete avoidance.

Recent findings

Short-term exposure studies showed that respiratory protective devices can reduce bronchial responses to sensitizing agents in patients with occupational asthma, but do not provide complete protection. Recent systematic reviews of long-term follow-up studies of workers with occupational asthma indicated that reduction of exposure to the causal agent is associated with a lower likelihood of improvement in asthma symptoms and a higher risk of worsening of symptoms and nonspecific bronchial hyper-responsiveness. There are insufficient data to compare the socio-economic consequences related to both of these management options.

Summary

Available data indicate that a reduction of exposure to the agents causing occupational asthma cannot be routinely recommended as an alternative to complete avoidance. However, due to the methodological weaknesses of the published studies, further investigations are required to determine the evidence-based cost-effectiveness of the occupational asthma management strategies.

Keywords

asthma, management, occupational diseases

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Introduction

There is growing evidence that work-related asthma contributes significantly to the global burden of asthma due to its high prevalence, approximately 15% of adult asthma being attributable to the workplace environment [1]. For workers affected with immunologically mediated occupational asthma (i.e. ‘allergic occupational asthma’ or ‘sensitizer-induced occupational asthma’ or ‘occupational asthma with a latency period’), complete and definitive removal from exposure to the sensitizing agent has usually been recommended as the most efficient therapeutic approach [2^{••},3^{••}]. Thus, workers with occupational asthma who remain exposed to the causal agent experience long-term worsening of their asthma symptoms, airway obstruction, and nonspecific bronchial hyper-responsiveness [4^{••}]. Moreover, there is currently insufficient evidence that antiasthma medications are able to prevent the long-term deterioration of asthma in patients who remain exposed to the causal agent [5,6]. However, the management of occupational asthma remains a difficult issue in clinical practice because

cessation of exposure, either by relocation of the worker to an unexposed job or elimination of the sensitizing agent from the workplace, is often not feasible or is associated with substantial adverse economic consequences for the worker, the employer, and society as a whole [7]. Available data indicate that about one-third of workers with occupational asthma remain exposed to the causal agent [7].

Various interventions can be implemented to reduce the workers’ exposure, including the introduction of materials with lower asthmagenic potential, use of personal protective equipment, engineering changes to the workplace (e.g. improved ventilation and enclosure of industrial process), or relocation of the worker to a less exposed area or job. Recent clinical practice guidelines have acknowledged that the reduction of exposure could be considered as an alternative to complete avoidance in order to minimize the socio-economic impact of occupational asthma when avoidance of exposure is not feasible [2^{••},3^{••}]. The purpose of this review is to provide a critical analysis of the available information on the effectiveness and

socio-economic impact of reducing exposure in workers with occupational asthma. Given that there is a lack of published original studies on this topic over the past 5 years, all available relevant articles identified through a PubMed search studies had to be taken into consideration to meet the objective of this review.

Short-term health effects

One challenge study confirmed *in vivo* that exposure to materials with a reduced content in allergen can reduce the risk of asthmatic reactions in workers with occupational asthma [8]. In this study, the bronchial response to various brands of latex gloves with a lower content in protein, either powdered or nonpowdered, was assessed through laboratory inhalation challenges in eight health-care workers, who had developed an asthmatic reaction when challenged with the powdered gloves used in their workplace. Each worker completed inhalation challenges with at least two of the three types of 'hypoallergenic' latex gloves in a random order. Exposure to low-protein latex gloves resulted in the absence (in six workers) or a significant reduction (in two workers) of the bronchial response. The protective effect of other 'substitutive' materials or compounds with a lower 'asthmagenic' potential, such as oligomers of isocyanates or encapsulated formulations of enzymes, has not been prospectively assessed in humans.

The effectiveness of respiratory protective equipment (RPE) in patients with occupational asthma has been investigated in five studies. Various types of RPE were assessed through inhalation challenges in the laboratory with organic farm allergens [9] and latex [10] or during workplace exposure to laboratory animals [11], aluminium potroom atmosphere [12], or farming activities [13]. The protective effect of RPE was assessed by comparing symptoms and lung function parameters in the same individuals with and without RPE; one study [11] did not include a control period without RPE. The individuals were exposed for 1 h in laboratory challenge studies or for periods ranging from a few weeks (i.e. 2 weeks [12] and 6 weeks [11]) to 10 months [13]) in workplace exposure studies. Only two studies applied a randomized controlled design [10,12]. The level of exposure during the periods with and without RPE was quantified in only one study [10].

Challenge studies in the laboratory demonstrated that the use of RPE can significantly reduce the respiratory symptoms and changes in functional parameters during short-term exposure to latex gloves [10] and farm dusts [9], although the respiratory responses were not completely abolished. Workplace exposure studies documented a significant improvement in peak expiratory flow rates while wearing RPEs [12,13]. By contrast, RPE had either

no effect on respiratory symptoms [12] or only a slight reduction in respiratory symptoms, with the exception of sputum production and rhinitis [13]. One study [13] found that there was no protective effect in workers with a more severe disease (i.e. airway obstruction) and in those who used RPE irregularly. None of these studies provided information on practical issues (e.g. compliance) that could result from the long-term use of RPE.

In addition, one retrospective study [14] assessed 48 of 68 workers with occupational asthma induced by Western red cedar dust who remained exposed to the causal agent for an average of 6.5 (range 1–13) years. The authors compared the workers who remained stable ($n = 30$) with those who deteriorated ($n = 18$) three out of the following parameters: methacholine PC20 value, forced expiratory volume in one second (FEV₁), asthma symptom score, and medication requirement. They found that the proportion of workers who used a twin-cartridge respirator was higher among the group with stable asthma (30%) than among the group with a deterioration of asthma (0%), whereas the use of paper masks or air-purifying respirators did not differ between the two groups.

Long-term health effects

The Agency for Healthcare Research and Quality (AHRQ) issued a systematic review of studies [4^{••}] pertaining to the management of workers suffering from occupational asthma that were published up to 2004. The authors analyzed the outcome of asthma symptoms [15–23], medications [15–18,24], FEV₁ [15–17], and nonspecific bronchial hyper-responsiveness (NSBHR) [15–17] after the reduction of exposure in patients with occupational asthma due to various agents. This review found some improvement in asthma symptoms; no clear pattern of changes in medication use; an improvement in FEV₁ over time in less than half of the studies; and there were insufficient data on the changes in NSBHR. The authors concluded that there were insufficient data to draw evidence-based conclusions about the effectiveness of reducing exposure.

More recently, a systematic review [25] focusing on the effectiveness of reduction of exposure has been conducted by a European Respiratory Society Task Force as part of a broader review on the management of occupational asthma. By contrast with the AHRQ document [4^{••}], this review was restricted to studies that presented a direct comparison between the outcome of workers with immunologically mediated occupational asthma who reduced their exposure and those who completely avoided exposure to the causal agent. Given the substantial heterogeneity of clinical and functional outcomes reported in follow-up studies of occupational asthma

Table 1 Characteristics of the selected studies

Causal agent	Country	No. of patients		Available outcomes		
		Reduction of exposure	Cessation of exposure	Symptoms	NSBHR	Reference
Colophony	UK	8	20	+	+	Burge, 1982 [15]
Isocyanates	France	7	20	+	+	Rosenberg <i>et al.</i> , 1987 [17]
Red cedar	Canada	42	136	+	–	Chan-Yeung <i>et al.</i> , 1987 [27]
Various (90% LMW agents)	Italy	7	18	+	–	Moscato <i>et al.</i> , 1993 [28]
Isocyanates	Italy	7	9	–	+	Paggiaro <i>et al.</i> , 1993 [29]
Isocyanates	Italy	17	43	+ ^a	–	Pisati <i>et al.</i> , 1993 [30]
Platinum salts	Germany	19	55	+	–	Merget <i>et al.</i> , 1999 [21]
Latex	Belgium	20	16	+	+	Vandenplas <i>et al.</i> , 2002 [16]
Latex	USA	20	4	+	–	Bernstein <i>et al.</i> , 2003 [31]
Persulfate salts	Spain	3	7	+	+	Munoz <i>et al.</i> , 2008 [32]

LMW, low molecular weight; NSBHR, nonspecific bronchial hyperresponsiveness.

^a Changes in asthma status were defined by a combination of parameters: (1) recovery = no symptoms, no medication for the past 12 months, normal FEV₁ and absence of NSBHR; (2) improvement or deterioration = significant change in symptom score (>1 grade on a 0–4 scale) or medication score (>1 grade on a 0–4 scale) together with a significant change in FEV₁ (>10% from initial value) or NSBHR (change in PD15 >1 doubling dose).

[4^{••}], the analysis was restricted to the outcome of asthma symptoms and NSBHR as proposed by Rachiotis *et al.* [26]. These outcomes were categorized in a qualitative manner as ‘recovered’, ‘improved’, or ‘worsened’ according to the criteria used in each study. A meta-analysis of these predetermined outcomes (i.e. recovery, improvement, or worsening of asthma symptoms and NSBHR) was conducted.

Ten studies fulfilled the inclusion criteria (Table 1) [15–17,21,27–32]. The studies included 478 patients with occupational asthma including 186 patients who had reduced exposure and 292 who had avoided exposure to the causal agent. The most commonly identified causal agents (seven of ten publications) were low-molecular-weight agents, including isocyanates [17,29,30], colophony [15], red cedar dust [27], platinum salts [21], and persulphate salts [32]. Two studies [16,31] involved a high-molecular-weight agent (i.e. natural rubber latex) and one study [28] evaluated patients with occupational asthma caused by various agents, of which 90% were low-molecular-weight agents. The median or mean follow-up periods ranged from 14 to 63 months.

Nine publications described the outcome of asthma symptoms after reduction (179 patients) or cessation (283 patients) of exposure (Table 2). Six of these studies relied on a qualitative assessment of the changes in asthma symptoms, whereas only three studies used a

quantified symptom score [16,30,32]. Asthma medications during the follow-up period were described in three of these nine studies [16,30,32]. The effects of the changes in medications on the outcome of asthma symptoms were not analyzed, whereas one study [30] reported a ‘clinical score’ that combined changes in symptoms, spirometry, and NSBHR (Table 2). Among the patients who reduced their exposure, the pooled rates were 60% [95% confidence interval (CI) 24–88%] for symptom improvement, 18% (95% CI 6–42%) for symptom recovery, and 21% (95% CI 4–64%) for symptom worsening, as compared with 81% (95% CI 55–94%), 38% (95% CI 29–48%), and 9% (95% CI 4–17%), respectively, for those who avoided exposure. Only five studies reported on the changes in NSBHR after reduction (44 patients) or cessation (66 patients) of exposure (Table 2) [15–17,29,32]. For the changes in NSBHR, the pooled rates were 39% (95% CI 15–70%) for improvement, 16% (95% CI 6–36%) for recovery, and 21% (95% CI 8–44%) for worsening after reduction of exposure, as compared with 52% (95% CI 39–64%), 29% (95% CI 10–59%), and 5% (95% CI 2–16%), respectively, after cessation of exposure. The meta-analysis of these pooled data showed that a reduction of exposure was associated with a lower likelihood of improvement [odds ratio (OR) (95% CI) 0.16 (0.03–0.91), random effect model] and recovery [OR 0.30 (0.11–0.84), random effect model] of asthma symptoms and a higher risk of worsening of symptoms [OR 10.23 (2.97–35.28), fixed effect model] and NSBHR

Table 2 Outcome of symptoms and nonspecific bronchial hyper-responsiveness

Intervention	Asthma symptoms			Nonspecific bronchial hyper-responsiveness		
	Recovery	Improvement ^a	Worsening	Recovery	Improvement ^a	Worsening
Reduction of exposure	50/179 18% (6–42%)	34/59 60% (24–88%)	15/54 21% (4–64%)	5/44 16% (6–36%)	21/44 39% (15–70%)	4/24 21% (8–44%)
Cessation of exposure	109/283 38% (29–48%)	78/105 81% (55–94%)	5/92 9% (4–17%)	17/66 29% (10–59%)	35/66 52% (39–64%)	1/50 5% (2–16%)

The denominators are the number of patients for whom the specified outcome was available. The pooled prevalence estimates (and 95% confidence intervals within parentheses) of each outcome after reduction or cessation of exposure have been computed using a random-effect model.

^a Patients with improved asthma symptoms and nonspecific bronchial hyper-responsiveness including those who recovered.

[OR 5.65 (1.11–28.82), fixed effect model] as compared with complete avoidance of exposure.

These findings further support the statements that reduction of exposure ‘is not always effective’ in the guidelines issued by the British Occupational Health Research Foundation [2**] and that ‘there is little evidence for using this approach’ in the guidelines of the American College of Chest Physicians [3**]. In addition, these systematic reviews clearly show that available data are potentially affected by a number of biases and confounding factors. Published data are observational, nonrandomized, follow-up studies, and the rationale behind the intervention decision (i.e. reduction or cessation of exposure) is unknown. Most studies (i.e. 8 out of 10 cohorts) assessed workers with occupational asthma caused by low-molecular-weight agents, whereas the few studies pertaining to high-molecular-weight agents involved only natural rubber latex. Available studies are very heterogeneous in their sample size, methods of assessment, and outcome reporting. In addition, the information on the interventions that were undertaken to reduce exposure and the effectiveness of such interventions is very limited, and none of the studies relied on quantitative exposure assessments to document the magnitude of the reduction of exposure.

Socio-economic outcomes

Two studies compared the socio-economic outcomes after reduction or avoidance of exposure in workers with occupational asthma caused by colophony [15] and natural rubber latex gloves [16]. These studies revealed that the rate of employment at the follow-up visit was significantly higher among workers who reduced exposure (8/8 in colophony-induced occupational asthma and 20/20 in latex-induced occupational asthma) as compared with those who avoided exposure (7/20 in colophony-induced occupational asthma, $P=0.004$ and 9/16 in latex-induced occupational asthma, $P=0.003$). The study by Vandenplas *et al.* [16] reported that a major loss of income was more frequent in workers with latex-induced occupational asthma who ceased exposure to latex (9 out of 16) than in those who remained exposed to reduced levels of latex (3 out of 20, $P=0.023$). The median actual reduction in earnings was 20% from the initial value (25th–75th percentiles: 0–51%) after avoidance of exposure and 0% (25th–75th percentiles: 0–16%, $P=0.038$) after the reduction of exposure. Asthma-related quality of life at the follow-up visit did not significantly differ between both of these management options.

Conclusion

Very few studies have assessed the protective effects of RPEs and materials with a reduced ‘asthmagenic potential’. Overall, the result from short-term studies indicated

that such interventions can reduce the severity of respiratory symptoms and airway obstruction in workers with occupational asthma who are exposed to sensitizing agents, but they are unable to provide a complete protection. In addition, information on the long-term effectiveness and practical issues raised by RPEs is lacking. Accordingly, RPEs should not be regarded as a long-term therapeutic option, especially in patients with severe asthma.

Available data indicate that the reduction of exposure to the causal agent may lead to an improvement or a resolution of symptoms and NSHR in some workers with occupational asthma. Nevertheless, studies comparing the long-term effects of reducing as compared to avoiding exposure provide some evidence that a reduction of exposure is associated with a lower likelihood of improvement and recovery of asthma symptoms and a higher risk of worsening of symptoms and NSBHR. These findings indicate that the reduction of exposure cannot be routinely recommended as a safe treatment strategy. However, the methodological weaknesses of the available studies prevent us from drawing a definitive conclusion on the effectiveness and safety of reducing exposure to occupational asthmagens. Further investigations are required to determine for which causal agents and for which workers this management option – under close medical surveillance – could be considered a reasonably safe alternative to complete avoidance.

Very few studies provided analyzable information on the socio-economic outcomes. Two studies found that the reduction of exposure resulted in a lower rate of unemployment than the avoidance of exposure. Accordingly, it remains uncertain whether reduction of exposure results in a lower socio-economic impact than complete avoidance.

In conclusion, there is a clear need for further assessment of the cost-effectiveness of the different management options of occupational asthma in order to provide evidence-based recommendations to affected workers, employers, and policy makers. This would require prospective, large-scale studies evaluating occupational asthma due to various causal agents through the outcomes that have been validated for the evaluation of asthma in general and quantitative evaluation of interventions aimed at reducing exposure.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 150).

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