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SHORT COMMUNICATION

# Change in airway responsiveness over a workweek in organic waste loaders

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**Abstract**
*Objective* Organic waste workers are exposed to high endotoxin levels that may result in respiratory health effects. This study describes changes in lung function and methacholine airway responsiveness over a workweek in household organic waste loaders.
*Methods* Assessment of lung function and methacholine airway responsiveness before and after a workweek in six organic waste loaders with and ten loaders without regular respiratory symptoms. Methacholine responsiveness was expressed as dose–response slope, i.e. % fall in $FEV_1$ per mg methacholine compared to either the post-saline value ($DRS_{sal}$), or the highest $FEV_1$ ($DRS_{max}$).
*Results* Monday morning, $FEV_1$ was similar in cases and controls. Over the workweek, $FEV_1$ and MMEF decreased slightly in both cases and controls ($P > 0.10$). In contrast, DRS increased in cases and decreased in control subjects ($P < 0.10$). The difference in % change of DRS was statistically significant after adjustment for smoking and age.
*Conclusion* Our results suggest exaggeration of pre-existent airway inflammation during the workweek in organic waste loaders with regular respiratory symptoms. This needs confirmation in larger studies.

**Keywords** Organic waste · Methacholine challenge · Lung function · Pre/post workweek change

## Introduction

Many countries have introduced separate collection of household organic waste as part of an environmental protection policy. Workers handling organic waste are highly exposed to bio-aerosols (Gladding et al. 2003; Heldal et al. 2003; Sisgaard et al. 1994). A number of studies have shown adverse health effects in these workers, mainly due to respiratory, gastro-intestinal and systemic flu-like symptoms (Bunger et al. 2000; Ivens et al. 1997). Previously, we reported a higher prevalence rate of respiratory symptoms in waste workers compared to office workers (Wouters et al. 2002). To evaluate the nature of these symptoms more in detail, we performed a case–control study among waste loaders with and without symptoms and evaluated changes in lung function and airway responsiveness to methacholine over a workweek.

## Materials and methods

The study comprised of an extension of a cross-sectional survey among 47 municipal waste loaders, all males (Wouters et al. 2002). Subjects were classified as cases and controls by questionnaire data of the initial survey. A case was defined by the presence of a weekly report of symptoms at work of cough, phlegm, shortness of breath, or chest tightness in the past 12 months. Controls did not have a weekly report of respiratory symptoms in the past 12 months. Cases and controls

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were invited for methacholine airway challenge on Monday and Friday morning prior to the work shift of organic waste collecting. Aiming at minimization of diurnal variation, airway challenge tests were performed at the same time of the day. Furthermore, blood was collected for IgE assessment. All measurements occurred during the same month of the year, i.e. February. The Ethical Board of the Wageningen University, the Netherlands, approved the protocol.

Serum IgE was determined using an enzyme immuno-assay as previously described (Doekes et al. 1996). Atopy was defined by a total IgE > 100 kU/L or a positive test result for any of the tested allergens, i.e. grass pollen mix, birch pollen, cat dander.

Lung function was assessed according to ERS guidelines using a pneumotachometer (Jaeger, Germany). Subjects were asked to withhold smoking for 1 h, and beta-agonists for 6 h. Methacholine (Sigma, USA) was inhaled in quadrupling doses from 0.01–2.53 mg, using a breath-actuated dosimeter (Jaeger GmbH, Germany) driven by compressed air at 20 psi. The test was stopped after inhalation of the last dose step or if $FEV_1$ fell 20% or more compared to the post-saline $FEV_1$. Salbutamol was administered to relieve airway obstruction. Test results were expressed by the dose–response slope (DRS) which was calculated as the % fall in $FEV_1$ per mG inhaled methacholine, compared to the post-saline $FEV_1$ (=$DRS_{sal}$), and the highest $FEV_1$ during the challenge (=$DRS_{max}$) (O' Connor et al. 1987; Seppala 1991).

Statistical analyses were performed using the SAS 8.02 software package (SAS Institute, Cary, NC). Differences in atopy, asthma and smoking between cases and controls were evaluated using $\chi^2$ test. Differences in age and Monday morning lung function parameters were tested using student's *t* test. For each worker, the change in lung function parameters ($FEV_1$ and MMEF) and airway responsiveness ($DRS_{sal}$ and $DRS_{max}$) were expressed as the percentage change over the workweek:

$$\frac{100\% \times [\text{value(Friday)} - \text{value(Monday)}]}{\text{value(Monday)}}$$

Differences between cases and controls in % change of lung function parameters and airway responsiveness were assessed using linear regression analysis.

## Results

Of the initial 47 workers, all males, 16 were lost to follow-up due to temporary employment, 4 had incomplete questionnaire data, 3 were not willing to participate, and 6 were excluded because of daily use of asthma medication. Additionally, two subjects did not complete the study protocol. The final population comprised 16 male waste loaders of whom were 6 cases and 10 control subjects. All cases reported weekly respiratory symptoms in the past 12 months, and 4 control subjects reported respiratory symptoms in each month. Participants did not differ from the initial 47 workers with respect to age, smoking, atopy, wheeze or asthma ($P > 0.10$). Compared to controls, cases were slightly younger (median age 32 vs. 38 years), more frequently smokers (83 vs. 50%), but differences did not reach statistical significance ($P > 0.10$). Data on atopy were available for six cases and eight of the ten controls, and prevalence rates were 33 and 12%, respectively ($P > 0.10$). Cases and controls did not differ in mean values for Monday morning $FEV_1$ (4.249 and 4.358 L) and $FEV_1$ % predicted (110 and 111%).

Table 1 shows the fall in $FEV_1$ and DRS values during methacholine challenge for each participant. DRS increased in 4 (67%) cases and 3 (30%) controls for $DRS_{sal}$, and in 5 (83%) cases and 6 (60%) controls for $DRS_{max}$. Table 2 summarizes results of the change over the workweek in lung function parameters ($FEV_1$, MMEF), and DRS ($DRS_{sal}$, $DRS_{max}$). The mean decrease in $FEV_1$ and MMEF over the workweek was similar for cases and controls, i.e. 1.7% (0.09 l) and 1.5% (0.06L) for $FEV_1$ and 1.3% (0.14 L) and 1.4% (0.08L) for MMEF ($P > 0.10$). For DRS, the change over the workweek was more pronounced in cases compared to controls. In cases, $DRS_{sal}$ increased with 72.6% compared to a decrease with 32.8% in controls ($P = 0.09$). For $DRS_{max}$, changes were 71.6% in cases and –7% in controls, respectively ($P = 0.07$). Differences in change of DRS became statistically significant after adjustment for age, and smoking. Additional adjustment for Monday–Friday difference in baseline $FEV_1$ did not change the results.

Exclusion of case-6 who showed an extreme increase in DRS over the workweek did not essentially change the results. The change of DRS decreased, but the difference compared to controls remained statistically significant after adjustment for age and smoking ($P < 0.05$). Exclusion of the three atopic subjects neither changed the results essentially.

## Discussion

In municipal organic waste loaders, methacholine airway responsiveness increased over the workweek, though only in workers with regular respiratory

**Table 1** Percentage fall in $FEV_1$ and dose-response slope (DRS) using the post-saline $FEV_1$ ($DRS_{sal}$) or the highest $FEV_1$ ($DRS_{max}$) during methacholine challenge testing

| | Post-saline $FEV_1$ | | | | | Highest $FEV_1$ | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Monday | | Friday | | %change DRS | Monday | | Friday | | %change DRS |
| | %Fall $FEV_1$ | DRS | %Fall $FEV_1$ | DRS | | %Fall $FEV_1$ | DRS | %Fall $FEV_1$ | DRS | |
| Case-1 | 21 | 8.30 | 19 | 7.51 | –9.5 | 21 | 8.30 | 19 | 7.51 | -9.5 |
| Case-2 | 10 | 3.95 | 12 | 4.74 | +20.0 | 11 | 4.35 | 13 | 5.14 | +18.2 |
| Case-3 | 4 | 1.58 | 2 | 0.79 | –50.0 | 4 | 1.58 | 5 | 1.98 | +25.3 |
| Case-4 | 4 | 1.54 | 7 | 2.77 | +79.9 | 4 | 1.54 | 7 | 2.77 | +79.9 |
| Case-5 | 6 | 2.37 | 7 | 2.77 | +16.9 | 6 | 2.37 | 7 | 2.77 | +16.9 |
| Case-6 | 10 | 3.95 | 24 | 18.90 | +378.5 | 12 | 4.74 | 24 | 18.90 | +298.7 |
| Control-1 | 12 | 4.74 | 1 | 0.40 | –91.6 | 12 | 4.74 | 5 | 1.98 | –58.2 |
| Control-2 | 1 | 0.40 | 0 | 0.00 | –100.0 | 3 | 1.19 | 4 | 1.58 | +32.8 |
| Control-3 | 5 | 1.98 | 10 | 3.95 | +99.5 | 7 | 2.77 | 12 | 4.74 | +71.1 |
| Control-4 | 15 | 5.93 | 12 | 4.74 | -20.1 | 15 | 5.93 | 12 | 4.74 | –20.1 |
| Control-5 | 10 | 3.95 | 7 | 2.77 | –29.9 | 11 | 4.35 | 10 | 3.95 | –9.2 |
| Control-6 | 10 | 3.95 | 5 | 1.98 | –49.9 | 13 | 5.14 | 7 | 2.77 | –46.1 |
| Control-7 | 11 | 4.35 | 15 | 5.93 | +36.3 | 11 | 4.35 | 15 | 5.93 | +36.3 |
| Control-8 | 7 | 2.77 | 11 | 4.35 | +57.0 | 8 | 3.16 | 11 | 4.35 | +37.7 |
| Control-9 | 4 | 1.58 | –3 | –1.19 | –175.3 | 4 | 1.58 | 1 | 0.40 | –74.7 |
| Control-10 | 13 | 5.14 | 6 | 2.37 | –53.9 | 13 | 5.14 | 7 | 2.77 | –46.1 |

**Table 2** Change in $FEV_1$, MMEF, and dose response slope (DRS) over the workweek for cases and controls

| | % change over the workweek (standard error) | | *P* value | |
|---|---|---|---|---|
| | Cases | Controls | Unadjusted | Adjusted for age and smoking |
| $FEV_1$ | –1.67 (2.19) | –1.53 (1.36) | 0.95 | 0.62 |
| MMEF | –1.34 (6.10) | –1.45 (5.20) | 0.99 | 0.42 |
| $DRS_{sal}$ | +72.6 (382.0) | –32.8 (148.5) | 0.09 | 0.02 |
| $DRS_{max}$ | +71.6 (282.3) | –7.7 (90.2) | 0.07 | 0.02 |

symptoms. There was no change in $FEV_1$ and MMEF over the workweek.

To our knowledge this is one of the first studies that evaluated change in airway responsiveness over the workweek in waste loaders. Our results are consistent with in vivo experiments that have shown an increase in airway responsiveness after endotoxin exposure, particularly in asthmatic subjects (Malmberg and Larsson 1993; Michel et al. 1989; Sundblad et al. 2002). In a follow-up study among pig farmers, an occupational group highly exposed to endotoxin, increase in histamine airway responsiveness was most pronounced in symptomatic farmers with the highest levels of organic dust exposure (Vogelzang et al. 2000). A similar trend was observed for the relationship of airway responsiveness with endotoxin exposure, though not statistically significant ($P = 0.06$). However, airway responsiveness was assessed by $PC_{10}$, which may have affected the results due to a lower sensitivity compared to the DRS.

In this study, we used the DRS to express the results of the airway challenge test, which provides a measure of airway responsiveness for each individual. A disadvantage of the DRS however may be the occurrence of negative values due to a rise in $FEV_1$ during challenge. This can be avoided using the highest achieved $FEV_1$. during challenge testing as the reference value. In our study, the results were essentially the same regardless whether the highest $FEV_1$ or the post-saline $FEV_1$ was used as the reference value, suggesting that both methods yield robust and stable estimates for changes in airway responsiveness.

Despite consistency with previous studies, our results cannot be considered conclusive due to a number of limitations. First, the number of subjects is small which limited statistical analysis. One might argue that cases in our study population were less healthy than controls since smoking and atopy occurred more frequently in cases compared to control subjects. However, differences were not statistically significant and results did not change after including these variables in the regression models. Moreover, our control subjects were not free of symptoms and cases may be considered 'mild' since those using asthma medication were excluded ($N = 6$). Therefore, our results may well be an underestimation of the effect. Nonetheless, the small sample size does not completely rule out selection bias.

Second, actual data on allergen and endotoxin exposure at the time of lung function measurements were not available. Previously, we have reported exposure levels in this population (Wouters et al. 2002). Shortly, waste loaders were exposed to higher levels of endotoxin than drivers (53.4 vs. 25.4 EU/$m^3$, $P < 0.05$), and collecting organic waste yielded higher levels than residual waste (41.4 vs. 35.0 EU/$m^3$). Levels were considerably higher compared to those found in office workers according to Reynolds et al. (2001) (0.5–3.0 EU/$m^3$). In this study we have only included waste loaders. Our results thus apply to higher endotoxin exposure. All subjects were studied in the same month of the year to minimize exposure variance due to meteorological factors.

Third, statistical power of our data analysis was limited due to the small population size. This limited multivariate analysis, and sensitivity analysis for atopy. The limitations of this study need emphasis that our results should be considered explorative and not conclusive. Nevertheless, the topic of this study is relevant for a considerable group of workers and our results suggest relevant health effects in otherwise healthy individuals. Larger studies are needed to evaluate health effects of endotoxin exposure in organic dust-exposed workers more in detail.

In summary, in this small study, organic waste workers with weekly respiratory symptoms experience an increase in airway responsiveness during the workweek. This may suggest exaggeration of pre-existent airway inflammation in symptomatic workers during a workweek of organic waste loading. However, our results need to be confirmed in larger studies before final conclusions can be drawn.

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