Daily changes of peak expiratory flow and respiratory symptom occurrence around a soy processing factory

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Abstract

Objectives. To evaluate sensitization and acute respiratory health effects in inhabitants living in the vicinity of a factory producing soy oil.

Methods. Two panels of potential responders were created on the basis of a response to a short screening questionnaire sent to random samples of 1,000 exposed and 1,000 non-exposed individuals living around the factory and a control area. Individuals responding to the questionnaire were invited for a medical evaluation, including a respiratory symptom questionnaire and skin prick testing, for a panel of common allergens and a soy allergen extract. This resulted in 53 atopic and/or asthmatic inhabitants from the area surrounding the factory and 30 comparable control subjects. In these subjects, morning and evening Peak Expiratory Flow (PEF), respiratory symptoms and medication use were recorded daily during a 10-week period in the autumn. At the same time, soy allergen and endotoxin concentrations were determined in airborne dust in the exposed and the control area. The wind direction relative to the location of a subjects’ house and the factory was used to determine whether an individual was exposed on a particular day.

Results. Only few of the atopic subjects were sensitized to soy. PEF showed a decrease, respiratory symptoms and bronchodilator use, an increase among soy sensitized subjects after having been downwind from the factory. Airborne soy allergen was found more frequently in the area surrounding the factory and levels were higher than in the control area. Highest levels were found on the factory premises. Only a weak association was found with wind direction. Airborne endotoxin concentrations did not show a consistent pattern with distance, but levels were clearly higher on the factory premises.

Conclusion. Sensitization to soy allergen was not increased among the population sample living in the vicinity of the factory. Soy sensitized individuals living in the surroundings of the factory reported more respiratory symptoms, used bronchodilators more often and had a lower PEF after having been downwind of the factory.

Key words

Soy allergen, endotoxin, soy sensitization, environmental exposure, soy beans, respiratory symptoms, peak flow, PEF

INTRODUCTION

The influence of exposure to organic matter, emitted by different sources into the ambient air of relatively densely populated areas has been studied in a number of situations. Early studies conducted in the USA [1], South Africa [2] and Brazil [3] around castor bean processing factories showed that dust exposure is positively associated with the occurrence of positive skin prick tests to castor beans and with the development of asthma attacks, either naturally or experimentally. These observations are supported by findings from occupational settings where soy sensitization is highly prevalent among soy allergen exposed workers [4–8].

Outbreaks of asthma exacerbations in the Spanish city of Barcelona have been found to be positively associated with the unloading of soy beans using a large harbour silo without bag filters on top. In total, 26 outbreaks of asthma have been described between 1981 – 1988 causing an excess of 1,155 emergency room admissions among 687 persons [9]. After replacing the defect filters on top of the silo it was shown that airborne soy bean allergen concentrations during unloading were reduced 10-fold. Installation of the filters also prevented subsequent outbreaks of asthma [10]. Reports followed of comparable situations in other Spanish coastal cities involving soy bean unloading. In Valencia [11] and Cartagena [12] also associations between unloading of soy beans and asthma epidemics were found.

In the presented study, the possible emission of soy bean dust was caused by the presence of a soy bean oil factory situated in a residential area. The soy bean dust exposure related with acute changes in respiratory symptoms, bronchodilator use and Peak Expiratory Flow (PEF) were studied in a panel of atopic subjects selected from the area surrounding the factory, and in a panel obtained from a control group from the other side of the town.

METHODS

Situation. The oil-producing factory has been situated in Utrecht since 1908, a city in the centre of The Netherlands. Before 1974, production consisted mainly of linseed oil. Since the 1990s, and up to the time of this study, only soybean oil...
was being produced. Soybeans were delivered to the factory by ship via the Amsterdam-Rijn canal. The produced soybean oil was also transported by ship. Soy scrap, which remained after extraction, was removed by trucks. The production process made use of cyclo-hexane extraction, and as a result, the remaining soy scrap was very dry and dusty. Unloading of soybeans from ships on the canal adjacent to the factory was carried out without dust reducing technology and caused visible dust emissions. Loading ships with soybean oil did not cause any problems of this nature. Loading trucks with soy scrap also caused dust clouds around the factory area. The factory operated continuously throughout the day and night. Once a week, the unloading of soybeans was stopped, to load the oil. Loading of oil took place at exactly the same location on the canal. The transport route of the trucks ran through the surrounding neighbourhood. Soy scrap regularly fell off the trucks, and this may have contributed to residential soybean dust exposure. The factory was surrounded by two residential areas, 'Oog in Al' on the west side, and 'Lombok' on the east side. Complaints of residents in the area mostly dealt with the odour emitted by the factory and the trucks running straight through their neighbourhood.

Selection of subjects and measurement of health parameters. Short questionnaires on allergies and respiratory symptoms were sent to a random samples of 1,000 subjects in the two quarters surrounding the factory (exposed area) and to 1,000 subjects in two quarters located on the other side of the same town, 4 – 5 km from the factory (control area). These random samples were obtained through the municipal registries. Subjects who reported a doctor-diagnosed allergy to house dust, pets and/or pollen or doctor diagnosed asthma were selected for subsequent evaluation. Invited subjects filled out a detailed questionnaire on respiratory symptoms, smoking habits, work-related exposure and home characteristics. Skin prick tests (SPT) to house dust mite, trees, grasses, moulds, cat, dog (ALK-Benelux, The Netherlands) and soy (ALK-Benelux, The Netherlands, Product No. SQ57.06; Lot No. 94K24–0200) were performed in selected individuals.

PEF was measured 3 times in the morning and 3 times in the evening, using a Mini-Wright Peak Flow Meter. The highest of 3 measurements at the same moment was used in further analyses. Respiratory symptoms used in the analyses were 'lower respiratory symptoms' (question on wheezing and/or question on shortness of breath and/or question on attacks of shortness of breath with wheezing positive), 'upper respiratory symptoms' (question on runny or stuffed nose and/or question on sore throat positive) an 'cough' (question on cough and/or question on cough with phlegm positive). Bronchodilator use (in this study only Ventolin, Brycanyl and Foradil) was also recorded.

Dust sampling and analysis. In the same period, air samples were taken using a High Volume sampler (GROMOZ) at a flow rate of approximately 50 m³/hr. Dust was sampled on 150 mm glass fibre filters (Whatman GF/A). Sampling time was usually 10n hours (11:00 – 21:00). Dust sampling was carried out at 2 locations in the surrounding quarters, one location in the control area and the other on the factory premises. Because of the noise produced by the equipment its use was restricted to daytime; unfortunately it was not possible to carry out nighttime measurements. Also, rainy days were excluded, because the glass fibre filters became clogged by water and the pressure drop was too large for the GROMOZ pumps. The filters were conditioned for at least 48 hours before weighing at 20°C and 50% relative humidity. Weighing was undertaken using a Mettler analytical balance. After sampling, the filters were again conditioned for at least 48 hours at 20°C and 50% relative humidity. The filters were cut into pieces with a clean pair of scissors and extracted by shaking for one hour in pyrogen-free glassware with 40 ml of pyrogen free water with 0.05% tween-20 added. After centrifugation for 10 minutes, about 15 ml of the supernatant was removed and stored at -20°C ('endotoxin extract'). The removed supernatant was replaced by the same volume of PBS (Phosphate Buffered Saline). The samples were again extracted by shaking for one hour and centrifugation for 10 minutes. After centrifugation again, about 15 ml of the supernatant was removed and stored at -20°C ('allergen extract'). In the 'endotoxin extract' endotoxins were determined, using a quanitative kinetic chromogenic Limulus Amebocyte Lysate method (Kinetic-QCL No. 50–650U; Bio-Whittaker; Lot No. LAL 4L1850A; Lot No. Standard 4L2350). Details are described elsewhere [13, 14]. In the 'allergen extract' soy allergens were determined, using an inhibition ELA. A soy extract (10 µg extract/in 1 ml PBS) was used to coat the micro-titer plates. The extract was obtained by dializing and freeze drying an extract of soybeans. Dilution of the dust extracts and standards were carried out using PBS (pH=7.4).

Definition of exposure and statistical methods. For day-to-day analyses of the association between health outcomes and exposure to products from the factory we used hourly wind direction data obtained from the Royal Dutch Meteorological Institute located less than 10 km from the factory (Bilthoven, The Netherlands). When the wind direction had been more than 90° different from the direction of the factory to each subject's home for 24 hours, it was assumed that no exposure had occurred. When the difference was smaller than 90° for 10 or more hours it was assumed that exposure had occurred. When the difference was smaller than 90° for more than zero hours and less than 10 hours the observation was considered non-exposed. Analyses were carried out for the PEF and respiratory symptoms directly after exposure, and 1, 2 and 3 days after exposure (time lags of 0, 1, 2 and 3 days). Days with reports of fever were excluded from all analyses to account for days with respiratory infections.

Differences in PEF were analyzed using linear auto-regression analysis accounting for first order auto-correlation, adjusting for day of the week (weekend days opposed to weekdays), linear trend and the minimum temperature 2 days before measurement of the PEF. This was done because the minimum temperature 2 days before measurement of the PEF had the strongest influence in the expected direction, i.e. colder days showed a lower PEF. Individual results were combined using linear regression analysis, with the individual difference (L/min) in PEF between exposed days and unexposed days as dependent variable and skin prick test positivity to soy, age, gender, and smoking as independent
variables. Unfortunately, some subjects had been exposed for only a small number of days, resulting in poor estimation of the difference in PEF between days with and days without exposure; therefore, only subjects with more than 3 days exposure were included in further analyses. All subjects with a positive skin prick test to soy had been exposed for more than 3 days. For analysis of the day-to-day changes in reported respiratory symptoms (i.e. 'Lower respiratory symptoms', 'Upper respiratory symptoms' and 'Cough') and bronchodilator use, the individual difference (%) between the prevalence of a symptom on exposed days and the prevalence of a symptom on unexposed days was calculated. Again linear regression analysis was used with the same independent variables as used in the PEF analyses.

Measurements of dust, soybean allergens and endotoxin were also compared to the wind direction with regard to the factory. The samples were allocated into 3 groups, depending on the length of the period the sampling location had been 'exposed'. In these analyses, also an angle of 90° was used as cut-off point in determining exposure of the measuring location. When a sample had not been exposed during sampling time it was placed in the category 'not exposed', when it had been exposed for less than half of the time it was placed in the category 'partly exposed', and when it had been exposed for half of the time or more (usually 5 hours or more) it was placed in the category 'exposed'.

RESULTS

Among the 2,000 individuals asked to fill-in a screening questionnaire, the response rate was 18.9% and a total 108 persons were asked to participate. These individuals had responded to the questionnaire that they had an allergy or were ever diagnosed with asthma. Of these, 53 subjects from the exposed area and 30 subjects from the control area participated. A total of 46 subjects in the exposed area participated in skin prick testing (of those who refused, 2 had recently undergone skin prick testing in a clinic). Skin prick testing was performed in 26 of the subjects in the control area. Histamine was used as positive control tests and the negative control test did not show a reaction in any of the tested subjects. Wheal size diameters of 3 mm after 15 minutes were regarded as positive. For soy, all visible (which in this study means larger than 1.8 mm) wheals were regarded as positive. Daily records of respiratory symptoms and PEF were between the area surrounding the factory and the control area for about 10 weeks from October – December. Data were to be entered in a diary once daily.

Table 1 shows that age and smoking habits of the participants of the presented study did not differ significantly between the area surrounding the factory and the control area. Table 1 also shows the number of subjects from both areas with a positive skin prick test to one or more of the common allergens tested (house dust mite, trees, grasses, moulds, cat and dog). In the control area, as well as in the area surrounding the factory, 81% of the subjects who were initially selected by questionnaire also had a positive skin prick test to one of the 'common allergens'. This indicates that a selective potential responder population was selected with the screening questionnaire with a high proportion of atopics. In both areas, about 11% of the subjects had a positive skin prick test to the soy extract.

Table 2 shows the results of the multiple regression analyses with the difference in morning and evening PEF as dependent variables. In this Table, the differences are shown for individuals with a negative skin prick test and a positive skin prick test to soy separately. The differences are shown for the area surrounding the factory and the control area separately, and for a possibly delayed reaction to exposure by applying different time lags. For the morning PEF, as well as for the evening PEF, no statistically significant differences in the expected direction were found for individuals living in the control area. Individuals living in the area surrounding the factory with a positive skin prick test to soy had a statistically significantly lower PEF on days when the home was downwind from the factory, as opposed to days when the home was upwind. For the morning PEF, lower values were found, especially 1 – 2 days after a downwind day. For the evening PEF, this difference was most pronounced directly after exposure, decreasing gradually. A 25 L/min difference between days corresponds to a decrease in PEF of about 5% in this small sample of soy positive subjects. No significant changes occurred in the results when analyses were adjusted for age, gender and smoking, or average daily temperature.

Table 3 shows the difference in prevalence of reports of respiratory symptoms and of the use of bronchodilators between days when the home was downwind and upwind from the factory. In the area surrounding the factory the...
prevalence of lower and upper respiratory symptoms tended to be higher on or after downwind days among soy positive individuals only. The use of bronchodilators was statistically significantly higher, especially 2 – 3 days after the home was downwind from the factory. In the control area, the prevalence of lower and upper respiratory symptoms among soy negative subjects was lower after days of exposure from the direction of the factory. No difference was found for soy negative subjects was lower after days of exposure from the factory. In the control area, the prevalence of lower and upper respiratory symptoms tended to be different on days with exposure compared to days without exposure. Adjustment for age, gender, smoking and exposure. The prevalence of cough did not appear to be higher on or after downwind days among soy positive subjects. The prevalence of cough did not appear to be different on days with and days without exposure. The prevalence of cough did not appear to be different on days with and days without exposure. The prevalence of cough did not appear to be different on days with and days without exposure. The prevalence of cough did not appear to be different on days with and days without exposure.

| Lag (days) | Soy SPT- n=27 | Soy SPT+ n=4 | Soy SPT- n=23 | Soy SPT+ n=3 |
|-----------|---------------|--------------|---------------|--------------|
| 0         | -0.3 (-2.6;2.0) | 4.6 (-1.1;10.3) | 0.1 (-1.8;2.0) | -0.1 (-5.5; 5.3) |
| 1         | -0.3 (-2.6;2.0) | 4.2 (-1.3; 9.7) | -2.8 (-9.0;3.4) | 2.8 (-15.7;21.3) |
| 2         | -0.7 (-3.4;2.0) | 7.7 (1.2;14.2) | -0.9 (-5.8;4.0) | 0.9 (-13.5;15.3) |
| 3         | -0.5 (-3.0;2.0) | 10.0 (4.1;15.9) | -0.5 (-3.8;2.8) | 0.5 (-9.0;10.0) |

Table 3. Mean difference (%)(95% confidence interval) in bronchodilator use (A), lower respiratory symptoms (B), upper respiratory symptoms (C) and cough (D), in subjects with negative (soy SPT-) and subjects with positive (soy SPT+) skin prick test to soy, between days with and days without exposure.
DISCUSSION

The results of this panel study of susceptible individuals living in the vicinity of a soy processing factory show that acute changes in daily recorded PEF and reports of respiratory symptoms and the use of bronchodilators by soy sensitized individuals are possibly associated with exposure to dust from this factory. Individuals chosen for the presented study were selected by questionnaire. Only about 11% of the selected individuals had a positive skin prick test to soy, which is comparable to 6.5% soy bean positive skin prick tests among atopic French agricultural workers [6], and less than the percentages positive reactors [19 – 39 among asthmatic bakery workers [7, 8]. No data are available for more comparable groups of subjects. No difference was seen for soy-sensitization between the area surrounding the factory and the control area. Although comparison of the 2 areas was not the main aim of the study, and could be hampered by selection bias, it seems that sensitization to soy does not seem to occur very often among susceptible individuals living around the factory. All individuals with a positive skin prick test to soy also showed a positive skin prick test to one or more of the common allergens.

In this study, the exposure of each individual had to be considered separately, day-by-day, because of the nature of the source and the study subjects living randomly around the factory. It was not possible to take dust samples each day for each individual. Therefore, the prevailing wind direction with regard to the position of the factory was used to construct a daily exposure variable for each person. Although samples taken downwind contained soy allergen significantly more often than samples not taken downwind, the measurements of soy allergen also showed that in the quarters through which the soy scrap is transported, some samples also contained soy allergen. The study subjects sensitized to soy.

Interestingly, parallel to this environmental study, a survey among the workers in the factory was also completed. This survey among 47 out of 70 workers from the factory showed that of the 35 tested by skin prick test for soy sensitization were positive and 31% were atopic. The average exposure of the factory and upwind samples. Sometimes, however, high endotoxin concentrations were encountered in the area surrounding the factory, and these exceeded the provisional threshold level of 90 EU/m3 which has been proposed for the working environment [18]. Especially, the 4 dust samples taken from the factory premises all contained relatively high concentrations of endotoxin.

CONCLUSION

The presented study shows that that exposure to dust from the factory containing soy allergen was associated with a decreased PEF and increased respiratory symptoms in subjects sensitized to soy.

The results of this survey have been reported to the city council. It was later decided by the city to buy out the company and the factory has been relocated to an industrial area. The office buildings have been transformed into a high school.
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