Variation in airway obstruction in the general population

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Summary

Chapter 1 gives an introduction on the variation in airway obstruction in the general population. Airway caliber, which determines the extent of airway obstruction, varies at an endogenous, circadian rhythm. The magnitude of the diurnal and circadian changes in airway caliber are frequently enhanced in individuals with obstructive airway disease, especially so after inhaling allergic and non-allergic stimuli.
There are different ways to investigate (variation in) airway obstruction in the general population. An individual's *variation in airway obstruction* or *airway lability* can be determined by measurement of peak expiratory flow (PEF) variability, measurement of bronchial hyperresponsiveness (BHR) to methacholine, or measurement of reversibility of airway obstruction. Data on the relation between PEF variability, BHR and reversibility in the general population are very sparse. A lot is still unknown about the variation in airway obstruction in the general population. The aim of this thesis is to increase our knowledge on the variation in airway obstruction in general populations, and factors that potentially affect this variation.

In *Chapter 2* the distribution of PEF variability in a random population sample of 511 adults aged 20-70 yrs, and its relationship to age, gender and smoking habits have been described. Participants performed PEF measurements in the morning after waking up and again in the afternoon, between 5:00 and 6:00 P.M.. In the 511 subjects who were studied we found a training effect in PEF measurement. The absolute PEF values on the first measurement day were significantly lower than on the following 6 days. Mean morning PEFs were lower than mean afternoon PEFs. Females had lower absolute PEF values than males, and their PEF variability was greater than in males. In the older age groups, the absolute PEF values were lower and the amplitudes % mean were significantly higher than in the younger age groups. Smoking was significantly associated with lower mean PEFs and greater amplitude % mean PEF. We observed lower mean values of the amplitude % mean than other investigators, possibly related to lower frequency of PEF recording (twice daily) in our study. The conclusions of the analyses were that absolute PEF values have a normal distribution and PEF variability has a log normal distribution. Because PEF variability is dependent on age, gender and smoking habits, these factors should be taken into account when studying PEF variability in random populations.

In *Chapter 3* we aimed at defining simple criteria to identify subjects with (increased risk of) lung function impairment. We investigated whether subjects with respiratory symptoms were more likely to have lung function impairment or increased airway lability, and whether this association is stronger in older subjects was studied in 468 subjects (20-70 yrs). The symptoms studied were: wheeze, dyspnea $\geq$ grade 3, nocturnal dyspnea, cough, phlegm, and history of allergy. Lung function level was measured by PEF and FEV_1, and PEF variability was used as an index for airway lability. The results showed that FEV_1 and PEF were lower with increasing numbers of symptoms. Older people reported more symptoms and had greater PEF variability than younger ones. Subjects with 1 symptom had a fourfold increased risk to have an FEV_1 of <70% of predicted, and this risk increased with an increasing number of symptoms. Subjects with 3 or more symptoms had an increased risk to have a PEF <70% of predicted and airway lability. Airway lability intensified with increasing age and with higher numbers of reported symptoms and appeared to be significantly greater in subjects with nocturnal dyspnea and cough. In conclusion, the analyses showed that symptoms can be considered to be important indicators for the presence of lung function impairment.

In *Chapter 4* the coherence of BHR and PEF variability in their relation to allergy markers and respiratory symptoms was described. BHR, PEF variability, asthma-like and COPD-like symptoms, and markers of allergy (serum total IgE (RAST), number of peripheral blood eosinophils, skin tests and serum specific IgE for housedust mite, cat, and pollen) were determined in 399 randomly selected subjects. Subjects who reported asthma-like symptoms were more likely to have BHR and a higher PEF variability than those who did not. Subjects with COPD-like symptoms had increased diurnal PEF variation compared to those without these symptoms. Increased PEF variability was associated with the presence of BHR. Yet, subjects with any positive skin test or specific IgE and higher serum total IgE had a higher risk for having BHR to methacholine, but not for a higher PEF variability. The conclusion of these analyses was that BHR and PEF variability are differently associated with markers of allergy, and thus, in epidemiological settings, they cannot be used interchangeably.

In *Chapter 5* the distribution of breathlessness in an elderly population, and its occurrence in combination with respiratory disease, cardiac disease and overweight, has been described. We analyzed whether breathlessness was an independent predictor of lung function impairment, reversibility of airway obstruction (reversibility) and PEF variability. Data on breathlessness, lung function, reversibility, PEF variability, respiratory symptoms, cardiac disease, and overweight were collected in a random sample of 210 out of 462 elderly (>55 yr) who participated in a physical fitness test. Breathlessness was rated using the Borg-scale. Individuals with a Borg score >0 (n=50, 24%) were regarded to have breathlessness. Subjects with breathlessness were 3 to 5 times more likely to have a low lung function and large reversibility than subjects without breathlessness. These increased risks were independent of the presence of respiratory symptoms, cardiac disease or overweight, although these 3 factors were all associated with low lung function and a large reversibility and PEF variability. Reversibility was not associated with PEF variability, neither in subjects with a Borg score >0, respiratory symptoms, cardiac disease or overweight, nor in the total population. The conclusion drawn from this study was that in elderly breathlessness, as assessed with a Borg-scale, is frequently present. It is an important predictor of low lung function and large reversibility of airway obstruction, whether respiratory symptoms, cardiac disease and overweight are present or not.

Chapter 6 presents a study on the question whether children with both BHR and above median values of serum total IgE (i.e. >60 kU/L) are a susceptible group for air pollution. Data were collected in a panel study that was performed during 3 winters in both rural and urban areas. In a total of 459 selected children (7-11 yrs) the acute effects of particulate matter with a diameter <10 μm (PM10), black smoke (BS), sulphur dioxide (SO_2) and nitrogen dioxide (NO_2) with lag0, 1 and 2 and 5-day mean on the prevalence of lower respiratory symptoms (LRS), upper respiratory symptoms (URS) and decreases in lung function (PEF) were studied. The study showed that children with BHR and relatively high levels of serum total IgE (BHR/IgE positive group; n=121, 26%) are especially susceptible to air pollution. This susceptibility is expressed as an acute effect of increased levels of air pollution on the prevalence of URS, as well as in a sub-acute effect of 5-day mean increased levels of air pollution on the prevalence of LRS. We found no significant positive associations between increased levels of air pollution and the prevalence of URS or LRS in the control group of children (no BHR, and serum total IgE <60 kU/L; n=169). The hypothesis that the children in our BHR/IgE positive group might genetically be the more susceptible ones, compared to those with only BHR or high levels of total IgE, was confirmed by lack of consistent associations between air pollution and the prevalences of LRS, URS, or PEF decreases in those children with merely BHR and those with merely above median values of total IgE.

Whether BHR and PEF variability, both expressions of airway lability, can be used (interchangeably) to identify adults who are susceptible to ambient air pollution was investigated in *Chapter 7*. Data on BHR, PEF variability (defined as amplitude % mean PEF >5%, for at least 1 day) and lower respiratory symptoms (LRS), upper respiratory symptoms (URS), cough and phlegm were collected in 189 adults (48-73 yr). The acute effects of particulate matter with a diameter <10 μm (PM10), black smoke (BS), sulphur dioxide (SO_2) and nitrogen dioxide (NO_2) (lag0) on the prevalence of LRS, URS, cough and phlegm were studied during 3 months in the winter of 1993/94. The study showed that adults with airway lability, both when expressed as PEF variability (69%) and BHR (28%), had significantly increased prevalences of respiratory symptoms with an increase in levels of ambient air pollution. Specifically subjects with PEF variability >5% for a substantial number of days (>33%) during a 8-day period with low levels of air pollution had increased prevalences of URS, cough and phlegm with an increase in levels of ambient air pollution. We found no consistent positive associations between increases in levels of air pollution and the prevalences of respiratory symptoms in adults without airway lability. The conclusion of the study was that in adults, PEF variability, and to a smaller extent BHR, can be used to identify subjects who are susceptible to ambient air pollution. PEF variability and BHR cannot be used interchangeably in studies on the acute effects of ambient air pollution.