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Time Series and Case-Crossover Design-Two Methods to Study the Short-Term Effect of Environment on Pneumothorax.

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Abstract

Spontaneous pneumothorax (SP) does not seem to occur at random. The clinical impression of many physicians is that the patient's admissions in hospital for pneumothorax are clustered. It supports the hypothesis that the meteorological conditions, or some factors associated with infectious and chronobiological factors, could play an important role in the mechanism of development SP.

Keywords:

Weather; Atmospheric pressure; Temperature; Humidity; Air pollution.

Introduction

The relationship between health degradation and weather change has already been suggested by Hippocrate at the 5th century B.C [1,2]. For more than forty years, many authors were interested in analyzing the impact of meteorological factors, such as atmospheric pressure, temperature, humidity, precipitation, wind speed and the occurrence of SP. The impact of air pollution on these respiratory diseases has been studied more recently. However the results are contrasted or even contradictory, and it is not possible at present to conclude formally at a significant and causal relationship, whether for the daily value of atmospheric pressure, temperature, humidity, precipitation, wind speed or air pollution [3–8]. A great part of the heterogeneity of these results comes from two points: i) different design are applied (cross-sectional, longitudinal, cohort study or case crossover study…); ii) exposure is assed using different approaches and is differently quantified among the studies: daily mean maximum and minimum value, range, increase or decrease fluctuation, whether on the day of the onset of SP or few days before the occurrence of SP.

Following this context, environmental epidemiology is increasingly applied in the SP literature, but the question of the appropriate study design remains unclear. The aim of this mini methodological review is to present a focus on the points of method and the two main designs used in epidemiological studies focused on the pneumothorax-environment relationship. Conversely to the most of the environment-health studies, especially for cancers or other chronic diseases, pneumothorax-environment relationship is lying on an induction delay (the interval between exposure to the agent and the onset of the disease) of few hours or days, which define short term effect. Two different method could be used: i) the ecological studies where aggregated number or events (collective health indices) are linked to collective exposure assessment, and ii) individual studies where the health status and the exposure are individually considered.

Two study design are particularly suitable for study of short term environmental factors exposure and allow to assess the delay between the exposure and the onset of health events (induction delay): time series and case-crossover study design. The time series studies, based on aggregated and not individual data, were used by several authors for analyzed the relationship between air pollution and respiratory disease [6,9]. The principle consists on summing the number of heath events that occurred on a given population by consecutive time period (days, weeks, months…). The numbers of events are compared among the successive time units and the relationship with exposure time series could be quantified. For example, within a given city, the relationships could be analyzed between the daily ambient air pollution concentrations and the daily number of consultation, admission or mortality. The statistical unit is not the individual but the time (usually the day). It is also necessary to take into account the potential confounding factors. These factors are associated with the variation of the exposure level and are also risk (or preventing) factor for the health event. Environmental exposures often vary over long periods (yearly trend) or medium or short periods (seasonality, weekly trend). Co factors could be correlated to the observed exposure. A confounding effect could occur if these co factors are implied in the occurrence of the studied health event (meteorological factors when considering respiratory events in relation with air pollution). Furthermore, periodic (seasonal) and secular trend effects have to be identified and correctly neutralized. In order to control for these potential bias, a daily data collection of three or four years is the required [10]. Individual factors are considered as constant on average over the study period (age, sex, status of smoking, professional exposure) and are not considered as confounding factors. Stratified analyses may be performed on subgroups of patients (according to age or sex) but modification of effect (especially interaction) could not be easily assessed.

The design of case-crossover studies is well suited to the explore of short-term health effects of air pollution [4,11]. This is a variant of the matched case-control design: each case becomes its own control [12]. This design is attractive because it only involves cases and each case is compared to himself/herself, there by controlling for time-invariant personal factors. The principle is to compare the exposure of the case immediately prior to or during the case-defining event with the exposure of the case at distant period time from the period of occurrence. Various sampling strategies were successively proposed to define the appropriate control periods in order to control for confounding by time-varying factors: time trend and confounding by both season and day of the week [12–14]. To avoid "overlap" biased estimation, the pre-specified reference windows (named time-stratified designs) is now commonly used (Figure 1).

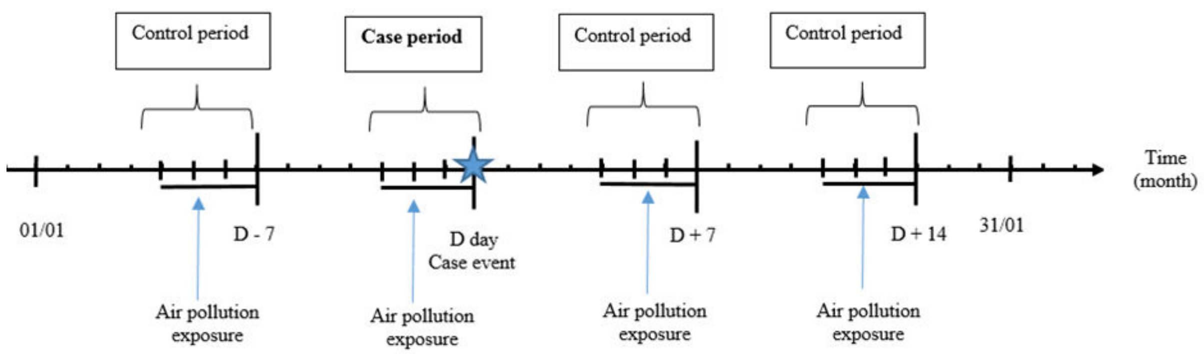

Figure 1: Schemes for time-stratified case-crossover designs

The stratification can be tailored to match on the most important time-dependent confounders. Stratifying on year and month (as well as one or more of the following variables: day of the week, temperature, measurement time, and copollutants) is adequate for some case [15,16]. However, a recent study suggested that time-stratified schema could fail on controlling the weekly time trend, and recommend to do adjustment for weekly time trend of exposures and covariates in the case-crossover application studies [17].

Discussion

Few studies compared time series and case-crossover analyses. Some authors concluded that time-series analysis performed better than time-stratified–case-crossover analysis, as there was far less autocorrelation in the residuals in the time-series analysis. This result could be caused by the case-crossover design assuming a step-like seasonal change, whereas the time series assumed a smoothly changing seasonal pattern [18–20]. Time series design can however present some disadvantages. The recording of the health events should be hardly reproducible among the study period, and only few missing data could occur. This approach is based on the two strong and binding hypotheses. First, the exposure-health relationship is assumed to be homogeneous among the whole study population. This design does not directly consider the potential particularity of a more at-risk subgroup population. Mediation or modification of effect including synergic, antagonistic effect, or interaction could not be directly analyzed. Second, the exposure is assumed to be homogeneous among the whole study population. This former hypothesis could be relaxed when using case-crossover design because exposure could be individually quantified.

Conclusion

Time series and case–crossover analyses mostly conducted to close results when estimating short-term impact of environment on health. The database, the underlying assumptions and the research hypotheses should however, be carefully considered for the interpreting results or when choosing a study design.

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