Use of Quantitative Epidemiologic Data in Regulatory Approaches to Air Pollution

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Ambient air is a complex mixture containing a variety of substances, some of which are known to be carcinogenic. To develop a homogeneous approach for regulating the emission of these compounds, their individual carcinogenic potential needs to be placed on a comparable scale. The unit risk may be considered as an appropriate measure that condenses dose-response analyses of epidemiologic data into a single, easily interpretable estimate. Given the information on the carcinogenic potency of single compounds, more information on the occurrence of the components and the relation of emissions to specific emitters needs to be considered. In Germany, an approach has been developed that combines different assumptions on complex mixtures for the regulation of the overall risk. This paper outlines some of the principal aspects of the underlying concepts. — Environ Health Perspect 102(Suppl 4):183–185 (1994).

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Introduction

Following cardiovascular diseases, cancers represent the second largest group of causes of death in most developed countries. Lung cancer occurs most frequently in males. The causation of lung cancer by tobacco smoke has clearly been demonstrated. There are also some occupational exposures that are associated with lung cancer risk.

Whether air pollution contributes to the occurrence of lung cancer is a matter of wide debate. Ambient air in urban or industrialized areas can be contaminated by chemicals, some of which are definitely known to be carcinogenic. These substances also may affect a limited amount of the ambient air in rural areas.

Many data from descriptive epidemiology demonstrate an increased lung cancer risk in urban and industrialized areas as compared to more rural areas. Frequently those differences have been explained by differences in air pollution; however, such correlations also might have other explanations and cannot represent final conclusive evidence. Therefore, analytic epidemiological studies (cohort studies or case-control studies) are required to clarify whether there is an increased risk of developing lung cancers for individuals with more exposure to air pollution.

Although estimates about the proportion of cancers attributable to air pollution generally are in a very low order of magnitude (1), the quality of ambient air is a matter of immediate public concern. Therefore, regulations to control emissions or imissions are therefore called for frequently. In order to proceed in such debates on reasonably solid scientific grounds, the following levels of information need to be accumulated: a) qualitative assessment determining whether air pollution represents a cancer risk, b) which individual agents present in air pollution contribute to this and to what extent, and c) which reduction in risk could be expected due to the reduction of exposure to certain substances.

Substances that are known to be carcinogenic and occur in ambient air are arsenic, asbestos, benzene, cadmium, particulate diesel exhaust, and polycyclic aromatic hydrocarbons. However, environmental measurements of such substances in large detail available over a longer period of time and for a larger geographical area are available rarely. More frequently, measurements of sulfur dioxide (SO2) and total suspended particles have been used as indicator measurements for immissions. These have been used in some epidemiological studies to quantify individuals’ exposure to air pollution.

In a case-control study in Cracow, Poland, an independent effect of air pollution on lung cancer risk and the effect of smoking and occupational exposures were demonstrated. Cracow has strong air pollution, and SO2 concentrations of above 100 mg/m3 and total suspended particulate concentrations of about 150 mg/m3 are common (2).

In a similar case-control study on lung cancer in China (3), benzo[a]pyrene was used to represent exposure to air pollution. Self-estimated high exposure to air pollution was associated with a 2.5-fold risk. The benzo[a]pyrene concentration in months with high exposure rose to 60 ng/m3. Thus, considering whether air pollution does represent an additional lung cancer risk seems justified. In order to approach the other two questions in relation to the regulation of air pollution, epidemiological studies conducted in environments with higher exposure such as occupational settings need to be explored and quantitative risk estimates need to be derived. These then have to be combined to represent a coherent regulatory approach.

Risk Potential of Single Components

Ambient air is a complex mixture containing a variety of substances, some of which are known to be carcinogenic. In order to develop a homogeneous approach for regulating the emission of these compounds, their carcinogenic potential needs to be placed on a comparable scale. This requires a number of assumptions whose impact on the outcome must be considered.

Epidemiologic data should be used to derive measures of carcinogenic potency that will be applied to human populations. This would help eliminate any uncertain steps of interspecies extrapolation. However, the low availability of appropriate epidemiologic data may be a severe limiting factor.
Dose-response analyses of epidemiologic data can be based on the assumption of various effect measures (absolute risk, relative risk) and statistical models (additive, multiplicative, and others). Quantitative risk assessment can be performed only if a single, easily interpretable estimate results from the exercise. The unit risk, which can be considered for this purpose, is the additional probability (above background) of developing or dying from a disease under a lifelong exposure of 1 µg/m³ of the substance of interest.

Because there are many assumptions going into such an estimation procedure, the sensitivity needs to be explored. Becher and Wahrenrodt (4) showed that unit risk estimates for arsenic and benzene do not vary much with different statistical models and between different epidemiologic data sets.

Regulation of Complex Mixtures

Given that information on the carcinogenic potency of single components of a complex mixture such as ambient air is available, more information on the occurrence of the components and the relation of immisions to specific emitters needs to be considered. Information on occurrence can be derived from a standardized, routine measurement system that continuously monitored immersion. The relation of measured immisions to certain emitters needs to be considered when regulations are established for the population at large. Furthermore, a quantitative limit of an acceptable overall risk that can serve as a yardstick for the quantitative considerations needs to be established.

Rather than using a concrete example, the principal aspects will be developed subsequently in an abstract way. Assume the complex mixture contains components A1, A2, A3, A4, etc. for which estimates of the unit risk r1, r2, r3, r4, etc. are available. From this, a unit dose, defined as that dose of the component at which one excess case of cancer can be expected in a population of 100,000, also can be derived. These may be denoted by d1, d2, d3, d4, etc.

Data from monitoring systems giving average concentrations of the immersion in urban area may be denoted by k1 (a), k2 (a), k3 (a), k4 (a), etc. Then r1 × k1 (a), r2 × k2 (a), etc. represents the risk associated with each component,

\[ R^{(a)} = \sum r_i k_i^{(a)} \]

the total risk,

\[ p_i^{(a)} = r_i k_i^{(a)}/R^{(a)} \]

the proportion contributed by the \( i \)th component. Similar data for immisions found in rural settings may be denoted by \( k_i^{(r)} \), \( R^{(r)} \), \( p_i^{(r)} \) (\( i = 1, 2, \ldots \)).

For general regulations, the proportion of the population living in urban or rural areas has to be incorporated into the approach. There is also the possibility to use more than just two strata of different pollution levels in this approach.

Equivalent Dose Approach

Similar to radiation carcinogenesis, this approach calculates for all individual components of the complex mixture their biologically equivalent dose in relation to a reference compound. A maximum level on this dose scale is derived by dividing the acceptable risk by the unit risk of the reference compound. The relative contribution of the different compounds to the maximal level of biologically equivalent dose is not further considered.

Proportionate Reduction

After establishing a level of acceptable risk, \( z \), this approach would result in a proportionate reduction of the exposure levels of all components. With \( k_i \) (\( i = 1, 2, \ldots \)) being the actual concentrations associated with an overall risk \( R \), new exposure limits would be postulated to be \( k_i z/R \) (\( i = 1, 2, \ldots \)). This approach does not select any component of the complex mixture but proceeds in a uniform fashion. However, it does not reflect any specific feasibility of controlling exposure to single components.

Geometrical Ordering

Different components of the complex mixture may contribute over the overall acceptable risk \( z \) in different ways. A geometrical allocation in which the first component contributes one-half, the second contributes one-quarter, the third contributes one-eighth, incrementing to the acceptable overall risk would allow one to weigh the component according to its importance. Assuming that the components of the mixture that are most important in terms of risk and exposure are identified, implies that these identified compounds are regulated with highest priorities. However, there remains the possibility to regulate newly identified compounds in further rounds with the assumption that their potency is not likely to be large.

Operational Proposal

An approach that attempts to combine aspects of those outlined above has been developed in the Federal Republic of Germany. It represents a combination of proportional reduction and geometrical ordering. Three major classes of compounds are defined: organic compounds, inorganic compounds, and other compounds, especially those that exhibit an effect due to their physical and chemical property. These classes may be denoted by \( C_1 \), \( C_2 \), and \( C_3 \). Considerations about the relative importance of these classes, both in terms of risk and exposure, lead to fixed proportions \( q_1 \), \( q_2 \), and \( q_3 \) which represent the relative contribution of these three classes to the acceptable excess risk \( z \). The proposal developed in Germany allocates 45% to organic compounds, 20% to inorganic compounds, and 35% to other compounds. Within each class, specific compounds are then allocated according to a geometrical ordering. This ordering must not strictly follow the steps 1/2, 1/4, 1/8, etc., as the following examples will illustrate.

In the class of organic compounds, polycyclic aromatic hydrocarbons are given priority and allowed to contribute 1/2 to the proportion \( q_1 \). The second position is left vacant, and benzene ranked third with 1/8 and far down 2,3,7,8-TCDD with 1/8192. This leaves open the regulation of compounds such as vinyl chloride open later when quantitative data become available.

In the class of inorganic compounds, arsenic and cadmium are placed on an equal level with their respective related compounds and allocated to contribute each 1/4 to the first half. The remaining 50% of \( q_2 \) is left open for compounds such as nickel and chromium.

In the third class of other compounds, diesel exhaust particles play a major role. They may occupy as much as 1/2 and 1/4 combined, which is 3/4, of the risk proportion \( q_3 \). Asbestos is considered next with 1/8. Then only 12.5% of this class are left open for future compounds to be regulated.

Conclusions

Epidemiologic data are important mostly for establishing carcinogenic risks to humans (4). Beyond the qualitative risk assessment, frequently there is a need for quantitative risk estimation. This entails a variety of assumptions and pragmatic simplifications. In order to shed light on the uncertainties involved it is essential that the dependency of the results, ideally simple understandable parameters, from these assumptions and simplifications needs to be explored.
The concept of unit risk has been applied broadly in this field, and that estimates appear to be fairly stable. When the quality of ambient air is to be regulated, an approach that takes the variety of compounds contributing to this complex mixture into account needs to be developed. Data about prevailing exposures derived from monitoring systems are important when deriving the quantitative components of the overall risk. An example of differential regulations developed for the components of a complex mixture (control of emissions in order to limit excess cancer risks from air pollution) illustrates the far-reaching need for solid quantitative epidemiologic data.

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