

Clinical Versus Epidemiological Appreciation of Risk: the Reasons of the Difference

Confronto fra Valutazione Clinica e Valutazione Epidemiologica del Rischio: i Motivi della Differenza

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Riassunto: Le differenze fra la valutazione del rischio in clinica ed in epidemiologia sono dovute all'utilizzazione, fatta dal clinico, del concetto di rischio ai fini della diagnosi e dell'intervento terapeutico. Infatti, soltanto fattori di rischio elevati sul piano individuale sono utili nel processo diagnostico e soltanto rischi suscettibili di essere affrontati sul piano dei comportamenti individuali sono oggetto dell'attività di prevenzione clinica. Queste differenze sono illustrate con esempi riferiti ad alcune malattie dell'apparato respiratorio e ad alcune esposizioni: fumo attivo, fumo passivo ed inquinamento atmosferico. Si fa cenno, infine, utilizzando un esempio tratto dall'esperienza degli autori nel campo delle malattie respiratorie, alla necessità dei clinici di disporre di valutazioni dei rischi conseguenti a molti interventi terapeutici, valutazioni non adeguatamente fornite dagli studi clinici sperimentali, ma ottenibili soltanto con un maggiore impegno negli studi di epidemiologia clinica e di farmaco-epidemiologia.

Keywords: Individual risk, Population risk, Clinical epidemiology

Introduction

The interest of the clinician is usually focused on the peculiar characteristics of any individual affected by a specific disorder, in order to single out the disease that is the most likely cause of that disorder and to choose the intervention with the highest chance of cure for that disease. Both clinical activities (diagnosis and therapy) are associated with the concept of risk.

In the diagnostic process, the probability of the presence of a specific disease in an individual affected by a specific disorder corresponds to the prevalence of that disease in the population of subjects with the same disorder and the same pattern of risk factors. That prevalence, or a-priori probability, is the determinant of the predictive value of a diagnostic test, characterized by its sensitivity and specificity, when applied to that individual. It is clear that only risk factors which may substantially increase or decrease the a-priori probability of a specific disease significantly contribute to the efficiency of the diagnostic process (Sackett 1985).

The advantages of any therapeutic intervention should be compared with the disadvantages associated with that intervention (side effects of drugs, burden of the

intervention on the individual, his family and community, etc). Therefore, the information needed by the clinicians for a sensible decision about a therapeutic intervention is not limited to the Number Needed to Treat (NNT) and its upper limit of confidence, all data that can be easily derived from the randomised controlled trials, but should also include the lower limit of confidence of an acceptable NNT, a measure that takes into account all the possible consequences of a therapeutic intervention. The absence of, or the uncertainty about, the lower limit of confidence of an acceptable NNT characterizes the majority of therapeutic interventions suggested from the guidelines for the clinical management of diseases with a huge impact on the public health (Guyatt, 1995, 2000; Dans 1998) This situation contributes to some uncertainty in defining the usefulness of many therapeutic interventions in the clinical practice.

The epidemiologists certainly help in the improvement of the clinical practice by defining a set of risk factors for many diseases that may be used by the clinicians both in the diagnostic processing and in the preventive counselling of any individual. When facing a multi-factorial disease, as it is the case for the most of chronic disease in the affluent countries, the clinicians select the risk factors that may improve the efficiency of the diagnostic process, as reported above, and also the risk factors that may be the goal of an individual counselling. The selection among many risk factors on the basis of their clinical usefulness is a specific marker of the clinical thinking about a set of risk factors for any multi-factorial disease.

However, the choice of an intervention is too often not supported by a satisfactory knowledge of the set of consequences caused by the alternative therapeutic options. All the results produced by the clinical and pharmaco-epidemiological research to fill this gap of knowledge would be welcomed from the clinicians.

We'll try to illustrate these concepts by using some examples derived from our experience in the respiratory medicine.

Active smoking

Active tobacco smoking is the main risk factor for Lung Cancer and Chronic Obstructive Pulmonary Disease. Moreover, it is a very relevant risk factor for some cardiovascular diseases such as Myocardial Infarction and Stroke. Overall, it is considered as the most important preventable cause of death in the westernized world (Doll 2004). This evidence, coupled with the definition of tobacco smoking as an individual addiction, greatly stress the responsibility of the clinicians in Asking their patients about their smoking habit, Advising about the risk associated with smoking and urge them to quit, Assessing the willingness of patients to make a quick attempt to quit, Assisting them in this attempt, and Arranging for a follow-up visit to help in a sustained quitting. This five "A's" strategy is now a well defined operating clinical procedure based on the knowledge of the dimension of risk for any individual and on the demonstrated efficacy of the clinical approach to this addiction (Istituto Superiore di Sanità 2003). However, also in this ideal situation, the clinical practice is not as compliant with the guidelines as it should be. This situation may be simply due to ignorance but it is interesting to look at the results of some Italian studies that demonstrate how the personal addiction interferes with the perception of risk of tobacco smoking among clinicians. In general we may say that the personal beliefs and habits greatly interfere with the translation of science in the clinical practice, at least as far as the primary prevention is concerned (Nardini 1998).

Passive smoking

Passive smoking is a well defined risk factor for lung cancer and myocardial ischemia in adults as well as a risk factor for the sudden death of infants and for some diseases affecting the upper and lower airways of children (Cook 1999). The debate about the association between passive or involuntary smoking and lung cancer, whether it was due to causation or to confounding, went on for more than twenty years and came to its end in 2004, with the inclusion of involuntary smoking among the certainly carcinogenic exposures to humans from the International Agency for Research on Cancer (IARC 2004). This debate, with its political and legal implications, was quite ignored from the clinicians, mainly because of the relatively small individual dimension of risk and because only some political decisions and not the clinical counselling could decrease the level of exposure. However, the association of involuntary smoking during childhood with some diseases of children raised the attention of clinicians because this exposure is mainly due to the presence of smoking parents at home and may be decreased by the counselling of individuals. Actually, the avoidance of the in-uterus exposure to tobacco smoke, due to the smoking of mother during pregnancy, is one of the most popular targets of the preventive medicine. It is interesting to note that the attention paid by the clinicians to the involuntary smoking during childhood may also decrease the incidence of COPD during the adulthood (Forastiere 1994, Corbo 1996). Sometimes, prevention goes far beyond its initial purposes!

Outdoor pollution

The mixture of chemicals produced from the human activities in the atmosphere is very relevant in deteriorating the human health. The impact of outdoor pollution on public health is generally measured by using mortality as the main outcome, in this way possibly underestimating the impact of morbidity and disability in the same populations. In spite of their limitations, some recently published papers clearly demonstrate the importance and the urgency of the abatement of outdoor pollution (Kunzli 2000). At same time, those papers recognize that air pollution abatement strategies are usually political in nature, targeting at policies, regulation and technology in mobile or stationary sources rather than at individuals. As far as the respiratory medicine is concerned, a substantial fraction of lung cancer and probably COPD may be attributed to outdoor pollution (Pope 2002, Vineis 2007). However, the small dimensions of risk associated with many outdoor pollutants at the individual level and the political nature of the interventions clearly turned off the attention of clinicians from the outdoor pollution.

The consequences of a clinical intervention (the tale of the inhaled corticosteroids therapy in COPD)

The appropriate role of inhaled corticosteroids in COPD is controversial. Many studies have shown that inhaled corticosteroids do not substantially modify airway

inflammation in COPD, and four large, long-term clinical trials comparing inhaled corticosteroids with placebo found that these drugs do not appreciably alter the rate of decline in lung function (Pauwels 1999, Vestbo 1999, Burge 2000, The Lung Health Study Group, 2000). This absence of physiological effects, as well as differences in inflammatory phenotype between COPD and asthma, has led many investigators to conclude that these drugs are ineffective in COPD (Sutherland 2004).

More recently, however, some results from the same trials and a couple of new trials demonstrated that an improvement of the quality of life and a reduction of the number of exacerbations that characterize the clinical course of COPD were significantly higher in patients treated with inhaled corticosteroids than in patients treated with alternative therapies (Calverley 2003, Vestbo 2004). On this basis, the most authoritative guidelines suggest the use of inhaled corticosteroids for the long term therapy of patients affected by a severe COPD.

In the same period, some observational studies suggested that the long term use of inhaled corticosteroids could reduce the mortality of patients affected by COPD but those results could be biased and were strongly criticized (Soriano 2003, Suissa 2004).

To end that debate, a clinical trial using mortality as the primary end point was designed and performed using a four arm parallel design on more than 6000 subjects affected by COPD. Unfortunately, the results of this trial regarding the primary end point were inconclusive and only some secondary end points gave some results in favour of the therapy with inhaled corticosteroids. At same time, the incidence of acute lower respiratory tract infections was higher in patients treated with inhaled corticosteroids (Calverley 2007).

In conclusion, the therapy with inhaled corticosteroids in COPD is performed on the basis of a weak evidence of efficacy and without a satisfactory knowledge of the many possible side effects, mainly in the elderly people, which constitutes the majority of the patients treated. The risks associated with the inhaled corticosteroid therapy is a typical example of the risks perceived as very important from the clinicians and their definition is what the respiratory clinicians ask from the clinical and pharmaco-epidemiological studies.

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