

Measuring exposure to organochlorinated pesticides

Medindo a exposição a pesticidas organoclorados

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Abstract *Environmental epidemiological investigations in cancer remain, with rare exceptions, inconclusive. The difficulties of establishing patterns of measurements of exposure in the human body is one of the limitations of these studies. The findings of six recent epidemiological studies that analyzed the association between organochlorinated compounds and breast cancer are reviewed in considering the problems of measuring environmental exposure through biological markers. The epidemiological evidence based on these studies do not indicate a risk of breast cancer related to organochlorines. Some aspects that may partially explain this absence of risk are discussed regarding the investigation of environmental carcinogenic agents in populations with low but homogeneously sprayed levels of exposure.*

Key words *Breast Neoplasms; Pesticides; Environmental Exposure*

Resumo *As investigações epidemiológicas sobre câncer ambiental permanecem, com raras exceções, inconclusivas. As dificuldades em se estabelecerem padrões de mensuração de exposição no corpo humano são algumas das limitações desses estudos. Os achados dos seis estudos epidemiológicos recentes que analisaram a associação entre compostos organoclorados e câncer de mama foram revistos, considerando os problemas de se medir a exposição ambiental por meio de marcadores biológicos. A evidência epidemiológica com base nesses estudos não indica risco de câncer de mama relacionado a organoclorados. Alguns aspectos que podem, parcialmente, explicar essa ausência de risco são discutidos considerando-se a investigação de agentes carcinogênicos ambientais em populações com níveis de exposição baixos, porém homogeneamente disseminados.*

Palavras-chave *Neoplasias Mamárias; Praguicidas; Exposição Ambiental*

Background

Environmental epidemiological investigations in cancer remain, with rare exceptions, inconclusive. On one side, there is no single agent in the environment that may be harmful; on the other side, the effects have, in general, long periods of induction involving complex interactions between environmental and host factors. Human data linking environmental agents to human cancer are rarely available. Recently, environmental epidemiology has largely focused on chemical and physical agents such as volatile organic compounds, metals, particulate matter, pesticides and radiations.

In contrast to environmental epidemiology in occupational study groups of workers that are exposed to chemical and physical agents, in general, there are higher levels if compared to one community. It is possible to clearly define between exposed and not exposed individuals, as well as divide the exposed group within the categorized levels of individual exposure.

In order to discuss the problems of measuring one environmental exposure through biological markers, the epidemiological studies that analyzed the association between organochlorinated compounds and risk of breast cancer were reviewed as an example.

Organochlorines and breast cancer

Experimental evidence shows that organochlorines with xenoestrogen properties act as carcinogens in animals (Davis et al., 1993). The biological hypothesis relating organochlorines to breast cancer is based mainly on their persistence in the environment as contaminants, that had been already identified in fish, human tissue, blood and milk, and in their estrogenic activity. Human exposure to these compounds happens in general throughout contaminated food, and in special animal products. These compounds accumulate in adipose tissue and persist for decades, being slowly excreted through feces, urine and lactation (Rogan et al., 1986). Through analytic chemistry procedures, residue levels of these compounds can be detected in serum or adipose tissue with high specificity (Kutz et al., 1991). Although the use of DDT [2,2-bis(*p*-chlorophenyl)-1,1,1-trichloroethane] and others organochlorines employed as pesticides in agriculture was banned in industrialized countries, they are still exported and used in others developing countries with inadequate protection (Dich et

al., 1997). In South America, they were largely used until recently in vector control programs.

Measuring serum levels of organochlorine residues

During the last five years six epidemiological studies (three in the United States, one in Europe, one in Mexico and one in Brazil) were conducted in order to analyze the association between residues of organochlorines in serum or adipose tissue and breast cancer (Wolff et al., 1993; Krieger et al., 1994; Van't Veer et al., 1997; López-Carrillo et al., 1997; Hunter et al., 1997; Mendonça, 1997). Only Wolff et al. (1993) found a positive association. In their study, the mean serum concentration of DDE (dichlorodichlorophenyl ethylene) was significantly higher among cases than among controls and the odds ratio of breast cancer, after adjustment for possible confounders, of women at upper quintile compared to the lowest quintile was 3.68 (95% CI 1.01-13.50).

In five studies, the mean levels of DDE measured in serum or adipose tissue from control subjects varied from from 2.5 to 7.7 ng/mL. The study of Krieger et al. (1994), which analyzed organochlorine residues in stored serum samples of a case-control nested to a cohort of 57,040 women, showed a mean DDE level (43.1 ng/mL) five to nine times as high as those in the others studies, nevertheless no association was found. These high serum levels observed can be explained because all samples were collected before the restriction for DDT commercial use, when levels of exposure were consequently higher.

The results of these studies are much more applicable to populations with low levels of exposure. The epidemiologic evidence concerning the relation between organochlorines and breast cancer may seem inconclusive, and some aspects may partially explain this. First, the levels that the organochlorine residues are currently detected at are too weak to lead to any effect (Adami et al., 1995). In experimental research the growth of mammary tumors in male rats was promoted after an intake of 25 mg/kg/day in the diet (Scribner & Mottet, 1981). Second, the exposure is almost homogeneously sprayed among control and case subjects and only a small percent of the studied populations had undetectable levels of DDE in serum or adipose tissue.

As Talbott et al. (1997) has pointed out, a flaw in environmental epidemiologic studies is the investigation of "unexposed" populations.

The absence of an adequate gradient of exposure can underestimate the effect. The epidemiologic evidence based on the referred studies is not sufficient to exclude the possibility that DDE could show a real risk for breast cancer at higher levels of exposure. In exposed populations, such as farmers and pesticide applicators, the risk may be different. When expo-

sure are relatively low, the assessment of them to individuals is difficult and the risks tends to be weak. However, any conclusion toward one environmental carcinogenic agent should be analyzed with caution, because if a small risk exists, then potentially everybody from the base population would be exposed, and a large number of cancer cases would be expected.

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