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Dichlorodiphenyltrichloroethane (DDT) and breast cancer

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Abstract

Several organochlorines identified as "hormone disruptors" have been proposed as possible risk factors for breast cancer. DDT is a chemical (organochlorine) with insecticidal properties. It was used during the Second World War by the military to control malaria-carrying insects, and subsequently in areas where malaria is found. These effective sprays of DDT are likely to have side effects on health. Many previous studies have evaluated whether DDT is associated with the risk of breast cancer. This review presents eleven studies, two of which support the hypothesis that DDT can predict breast cancer in women. The evaluation of these studies showed that the available data are not sufficient to establish a causal relationship between DDT exposure and breast cancer. In order to confirm that DDT is a predictor of breast cancer, it is essential to conduct further experimental studies, taking into account several factors including the use of similar epidemiological methodologies to ensure comparability of results between studies.

Key words: Breast cancer, Pesticide, Exposure, o,p´-DDT, organochlorines, p,p´-DDE, p,p´-DDT.

Introduction

Breast cancer is the most common cancer among women, accounting for the highest estimated death rate among all types of cancer. Signs of breast cancer may include a lump in the breast, a change in the shape of the breast, dimples on the skin, fluid from the nipple, a newly inverted nipple, or a red or scaly ski patch[1].Factors that may influence breast cancer include: obesity, lack of exercise, alcoholism, hormone replacement therapy during menopause, ionizing radiation, being early at first menstruation, being older, having a family history of breast cancer[2].Since breast cancer is a hormone-dependent cancer, and pesticides have hormone-disrupting properties, the question arises as to whether the incidence of breast cancer may be due to these pesticides as a factor, using dichlorodiphenyltrichloroethane DDT as an example.

DDT is a chemical product with insecticidal and miticidal properties; it is a colorless, highly hydrophobic solid with a slight odor. Insoluble in water, it dissolves easily in most organic solvents, fats and oils, DDT is a powerful insecticide; the reason why it was used during the Second World War by the military to control malaria-carrying insects, and then afterwards into where malaria is found as Cameron[3], Keny[4] and Taiwan[5].These effective sprays of DDT are likely to have side effects on either the environment[6].DDT has several compounds; DDE is one of those compounds that will often be found in the studies.

While DDT might be useful in controlling malaria evidence of its adverse effect on human health is needed to balance between risk and benefits of DDT use.

This mini review designed to determine whether exposure to DDT is associated with breast cancer risk in women, basing on many previous studies that clarify how the intensity of this pesticide is considered as one of the factors of increasing breast cancer risk for younger and adult women and explain how the age can have an influence.

Methodology

An extensive search was conducted mainly in PubMed, Google Scholar, Scopus, web science and direct science, the search was based on the combination of keywords (DDT, breast cancer, insecticide, pesticide, cancer), articles were pre-selected based on a pre-screening of titles first and abstracts second.

Discussion

Eleven case-control studies that analyzed exposure to DDT and breast cancer were identified in this mini- review.

Two studies have linked DDT exposure to breast cancer. (OR=3.7; 95% CI:1.5-9.0)[7]. and (OR = 1.95; 95% CI:1.10-3.52) [9].Although the majority of studies (nine remaining studies) do not support the hypothesis that DDT is associated with breast cancer risk. The first study found that the exposure to p,p'-DDE has been associated with a dose-related increased relative risk of having both lymph node involvement and significant tumor involvement;(OR= 2.54; 95 %CI:1.20-5.35)between the highest and lowest tertile, (OR=2.33; 95% CI:0.94-5.77) in the second tertile and (OR=3.51; 95% CI:1.41-8.73) in the third tertile(9).The second study reported a statistically insignificant odds ratio (OR=1.15; 95%CI:0.74–1.79)[10].Another study found no

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substantial elevation in breast cancer risk in relation to the highest quintile levels of DDE,(OR=1.02, 95%CI:0.61-1.72)[11]. Median DDE concentrations were lower in cases than in controls in both periods [11.7% lower in 1974 (P = 0.06) and 8.6% lower in 1989 (P = 0.41)],the risk of developing breast cancer in women with the highest concentrations of DDE was about half that of women with the lowest concentrations, based on 1974 (OR=0.50; 95% CI,0.27-0.89) or 1989 (OR, 0.53; 95% CI, 0.24-1.17)[12].The next study conducted that the median level of DDE was lower among case patients than among controls, therefore the exposure to high levels of DDE has been associated with a non-significant risk of breast cancer (OR= 0.72 ,95%CI:0.37-1.40)[13].The fifth study examined risk factor for breast cancer in women located primarily in the northeastern United States is multivariate OR for associated breast cancer; No statistically significant associations were observed in these analyses (OR=0.99 ,95% CI,0.77-1.27)[14].In the following study Age-adjusted odds ratios for breast cancer for the serum DDE were(OR= 0.69;95% CI,0.38-1.24) and (OR=0.97 95% CI,0.55-1.70) for the contrasts between the first tertile(lowest level) and tertiles 2 and 3, respectively. These results do not support the hypothesis that DDT is linked to breast cancer and do not rule out the possibility that higher levels of exposure may still play a role in the etiology of this tumor[15].The seventh study of African-American women and white women in North Carolina indicates that factors such as parity, breastfeeding, race and body mass index influenced the relationship between organochlorines and breast cancer. ORs for DDE were not elevated among women who lived or worked on farms with pesticide exposures, suggesting the absence of a strong effect for DDE on cancer (OR=1.41; 95%CI:0.87-2.29) (OR=0.98;95%CI:0.67-1.43)[16].The latter showed no dose-response relationship between serum DDE levels and breast cancer (OR=0.96;95%CI:0.67-1.36)[17].These results are summarized in the following table:

Table 1: DDT exposure and estimate of breast cancer risk.

Authors	Year of blood draw,Place	Age at blood draw (years)	Cases , Controls	The DDT compound	Odds Ratio	Risk estimate (95 %IC)	P value	Reference
(Cohn)	1959-1967, Oakland, California	26,9	118, 354	o,p'-DDT	3.7	1.5–9.0	0,04	(7)
(Demers)	1996 ,Quebec	53	315, 219	p,p'-DDE	2,54 2,33 3,51	1,20-5,35 0,94-5,77 1,41-8,73	NR	(9)
(Gammon)	1996, Long Island	24–96	633, 418	DDT	1.15	0.74–1.79	>0.05	(10)
(Gatto)	1997, African-Americans	35-64	335, 327	DDE	1,02	0,61, 1,72	0,74	(11)
(Helzlsouer)	1974 or 1989, Maryland	20% ≤40 2.9 %≤40	346, 346	DDE	0.50 0.53	0.27-0.89 0.24-1.17	0,02 0.08	(12)
(Hunter)	1990, U.S. Nurses	59	372, 372	DDE	0,72	0,37-1,40	0.14	(13)
(Laden)	1989 ,North Carolina	41-85	154, 192	DDE	0,99	0,77-1,27	0.14	(14)
(Lopez)	1995 ,Mexico	50	141, 141	DDT	0,69 0,97	0,38-1,24 0,55-1,70	0.44	(15)
(Millikan)	1995 ,North California	50 50	292, 270 456, 389	DDE	1,41 0,98	0,87-2,29 0,67-1,43	NR	(16)
(Olaya-Contreras)	1995 ,Colombia	≥30	153, 153	DDE	1,95	1.10-3,52	0.09	(18)
(Zheng)	1996, Connecticut	17% ≤45	475, 502	DDE	0.96	0.67–1.3	NR	(17)

Results

The results found are diverse and the studies that support the relationship between DDT exposure and breast cancer risk are limited. This dissimilarity between the results found can be explained by differences in the design of the study including: The diverse biological activity; Different compounds related to DDT do not have the same biological activity. The compound p,p'-DDE acts as an antiandrogen but not as an estrogen; o,p'-DDT acts as an extremely weak estrogen; and p,p'-DDDT has little or no androgenic or estrogenic activity[18,19]. Exposure at critical times; Previous studies have not measured exposure during critical periods of sensitivity[20] for the human breast, the critical periods seem to be during the fetal period, adolescence and early reproductive life, especially before

pregnancy, so the critical periods of breast development are in utero, during puberty or during pregnancy[21] Furthermore, the age of serum exposure to DDT was only associated with breast cancer in women who were potentially exposed at a young age (before 14 years), these women would also mostly have been < 20 years old when the DDT exposure peaked, similar interpretations of results obtained in studies of exposure to atomic bomb radiation, where an excess risk of breast cancer has been observed primarily in women who were at a young age at the time of exposure[22].The year of the blood test may influence the associations between DDT and breast cancer; In almost all previous studies, blood samples were taken around the 1970s and most were taken much later, with the U.S. EPA. estimated that the peak use of DDT occurred in 1959, and that dietary DDT peaked around 1965[23] Hence the age at the time of the blood test. The majority of previous studies were based on blood samples obtained from middle-aged or older women, whereas in the first study, blood samples were obtained at an average age of 26 years[24]Therefore, the lack of increased risk in the remaining studies may be explained by the fact that the breast is only vulnerable to the carcinogenic effects of DDT during the early growth and development of the breast. Breastfeeding after pregnancy may contribute to the elimination of lipophilic DDT-related compounds acquired early in life, breastfeeding is not a risk factor for breast cancer, and the possible elimination of p,p'-DDT due to breastfeeding after pregnancy does not seem to confuse the association of p,p'-DDT with breast cancer(7) However, breastfeeding was infrequent and short-lived among the women in the first study, with only 34% of women breastfeeding, and among those who did, 60% breastfed for less than four months, which would be short compared to the WHO recommended duration for partial breastfeeding (up to 2 years). In another study of postmenopausal breast cancer, results showed a stronger association of body burden of organochlorines in mothers who had never breastfed, suggesting that breastfeeding may contribute to breast protection[25].

It should be noted that serum p,p'-DDT is one of the least persistent compounds linked to DDT and is therefore an indicator of recent exposure[26] Furthermore, these diverse results could be explained by different metabolic pathways and thus variable exposures to metabolic intermediates. Metabolic studies have shown that the rate of metabolism of these compounds differs, (notably o, p'-DDT is eliminated more rapidly).

Other reasons such as the direct toxicity of DDT, the induction of enzymes that produce other genotoxic intermediates and DNA adducts, or covariance with another as yet unknown factor are possible explanations for the relationships we have observe[27] Different exposures can also be added to environmental factors, including chemical compounds, diet and very local (genetically and/or geographically determined) cultural aspects. It can be concluded that this relationship is related to the interdependence of these factors on individual susceptibility to breast cancer and that these interdependent factors have not yet been fully considered and incorporated into previous research.

Conclusion

It is too early to definitively decide whether or not DDT exposure is related to breast cancer risk. However, exposure to p,p'-DDT at an early age can have a significant negative effect on public health. Future studies should take several factors into account by using similar epidemiological and laboratory methodologies to ensure comparability between results from different studies. Experimental studies are also essential for approving results and uncovering the mechanisms.

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