

Narrative Review:

Risk of Leukemia and Brain Tumors in Children Exposed to Pesticide Residual in Households and Approaches to Reduce its Side Effects



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ABSTRACT

Context: Using various pesticides to control pests and vectors of diseases has a long history in households worldwide. However, most pesticides are considered toxic to and harmful to the environment.

Evidence Acquisition: Electronic databases such as Google Scholar, PubMed, and Scopus were searched using the following search terms: "Children", "Pesticide residues", "Risks", "Leukemia", and "Brain neoplasms". This review was designed to identify the relevant electronic studies published from January 2000 to February 2020.

Results: Children are more susceptible to pesticides because of their underdeveloped metabolic processes and disability to detoxify chemicals. Over 30% of the children's diseases are due to environmental factors, including pesticides. The possibility of children's pesticide exposure inside of urban houses is more than outside. In general, children can be exposed to pesticides in two ways: Direct and indirect contact. Direct contact refers to hand-to-mouth behavior in daily plays that absorbs household pesticides. Indirect contact refers to exposure via their parents' work in hazardous environments and during pregnancy. There is a significant association between pesticide exposure via households and some cancers in children, such as leukemia and brain tumors.

Conclusions: Due to the positive association between pesticide residues in households and the risk of cancers in children, public health policies must be adopted to minimize children's exposure to pesticides in the urban household.

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1. Context

Using various pesticides to control pests and vectors of diseases has a long history (1) as the Chinese, and ancient Romans used different chemicals to control pests. The usage of a substance as a pesticide was recorded by Homer (a Greek poet for thousand years BC), who referred to the burning of sulfur for housekeeping and pests control (2). The history of pest control has been recorded in the first human civilizations. Ancient societies used religious, magical, and natural materials to keep away from the damages and troubles of pests (3).

In general, the need for pest control in human habitations in cities indicates unhealthy conditions that, if not controlled, can hurt humans. It is also the truth that pests can be a vector of diseases to humans. Based on the definition, a pest is any animal or plant detrimental to humans or human concerns, including crops, livestock, and forestry. In general, "any creature that conflicts with the interests of man" is called a pest. There are different pests based on various damages to human beings, for example, agricultural pests, household pests, and vectors of diseases to humans (3).

Although pesticides have long been used to control the population and spread of hazardous pests, such as cockroaches, bed bugs, termites, ticks, and rats, they further control the outbreak of diseases such as malaria, plague. However, most pesticides are considered toxic to humans and harmful to the environment (4).

Pesticides are classified into two main categories based on their harmful effects on human health: short-term and long-term impacts (5). Many studies suggest that human pesticide exposure may be related to chronic effects such as cancer, asthma, diabetes, leukemia, brain tumors, and Parkinson disease. There are some short-term pesticide hazards due to human exposure, such as skin and eye irritation, headaches, dizziness, nausea, congenital defects, vomiting, abortion, and impaired immune functions.

Also, exposure to pesticides is a significant factor in people's poisoning (3). The USA Environmental Protection Agency estimates that approximately 10000 to 20000 pesticide poisonings occur annually, according to physician-diagnosed (6). Additionally, pesticides are known as urban pollutants (3).

In this study, we only present and discuss the findings of recent investigations on the risk of leukemia and brain tumors in children due to the pesticides used in the household. Also, we reviewed the different common pesticides that are used in homes and focused on pesticide classification based on the target pest, acute toxicity hazard categories, and chemical structure. Finally, we introduced some approaches to reduce the side effect of pesticides in households.

2. Evidence Acquisition

Electronic databases such as Google Scholar, PubMed, and Scopus were searched using the following search terms: "Children", "Pesticide residues", "Risks," "Leukemia", and "Brain neoplasms". This review was designed to identify the relevant electronic studies published from January 2000 to February 2020.

A total of 692 potentially relevant articles were identified. Following the exclusion of 602 citations, 90 full-text papers were retrieved for detailed examination. A total of 15 articles matched the eligibility criteria. All papers included in this systematic review were written in English.

3. Results

Classification of pesticides based on the target pest

Pesticides can be classified according to the type of target pests (5, 7). Table 1 provides the classification of pesticides based on the target pest. Figure 1 shows the location of some main pests in houses and the surrounding environment (8, 9).

Classification of pesticides based on acute toxicity hazard categories

The World Health Organization (WHO) has classified pesticides into five levels based on toxicity level and median lethal dose (LD_{50}) of oral and dermal routes for rats (Table 2) (10).

Classification of pesticides based on chemical structure

In general, pesticides are classified into five main groups based on their chemical structure: organochlorines, organophosphates, carbamates, neonicotinoids, and pyrethroids. As shown in Table 3, some main pesticides are commonly used in urban households (11, 12).

Table 1. Type of pests and pesticides used against them

Pest Type	Pesticide
Acari	Acaricides
Algae	Algicides
Birds	Avicides
Bacteria	Bactericides
Fungi	Fungicides
Weeds	Herbicides
Mites	Miticides
Insect	Insecticides
Snails	Molluscicides
Nematodes	Nematicides
Rodent	Rodenticides
Virus	Virucides
Fish	Piscicides
Tree	Silvicides
Vertebrate	Perdicides

Journal of Pediatrics Review

Pesticide residue in household

The possibility of people's exposure to pesticides in houses is more than outside. The amount of pesticide residue inside dust of household is 10 to 100 times higher than in ambient or soil surfaces (13, 14). When households are exposed to pesticides spraying several times to exterminate the pests, they contain more pesticide residues than other households. After pesticide spraying, these chemicals have become part of many household products, such as paints, furniture, wall hangings, carpets, and building materials (14).



Journal of Pediatrics Review

Figure 1. Some main pests in houses and the surrounding environment

Children sensitivity to pesticide

Epidemiologic studies have suggested that pesticide usage in households can have serious side effects on children under 15 years and may cause some diseases such as leukemia and brain tumors (15, 16). Children are more susceptible to pesticides because their metabolic processes are not fully developed, and they cannot detoxify chemicals that enter into their bodies (17). According to WHO report, over 30% of children's diseases are due to environmental factors, including pesticides (18). Children are more susceptible to pesticide exposure because their immune systems are not fully developed (17). Children are exposed to pesticides in two ways: direct and indirect (Figure 2). In direct exposure to pesticides, children do hand-to-mouth behavior during their play and eat food from the surfaces and the ground (4, 19). In general, children absorb more pesticides from their environment than adults (19). Besides, they spend most of their time indoors and consequently absorb household pesticides. In indirect exposure to pesticides, children can be exposed to pesticides due to their parents' work in hazardous and pesticide-related environments (20). Moreover, exposure to pesticides

Table 2. Classification of pesticides according to WHO

Toxicity Level	LD ₅₀ for the Rat (mg/kg Body Weight)*	
	Oral	Dermal
Extremely hazardous (Ia)	<5	<50
Highly hazardous (Ib)	5-50	50-200
Moderately hazardous (II)	50-2000	200-2000
Slightly hazardous (III)	Over 2000	Over 2000
Unlikely to present an acute hazard (U)	5000 or higher	-

*Lethal Dose where 50% of the population dies.

Journal of Pediatrics Review

during pregnancy is another indirect way of exposing children to pesticides (21).

Pesticides exposure and pregnancy

The exposure of pregnant women to indoor pesticides is worrying. In general, all pesticides, especially domestic pesticides, are toxic and can be hazardous. Exposure of pregnant mothers to pesticides can impair the fetus's development in the uterus and neurodevelopment of children (21). Due to the rapid growth of the nervous system of the fetus during the first trimester of pregnancy, pregnant women should avoid contact with any

pesticide during this time. The results of animal experiments show that exposure to pesticides during pregnancy may have adverse effects on the fetus, such as miscarriages, preterm births, low birth weight, congenital disabilities, and learning problems in children. Also, maternal household exposure to pesticides during fetal life can be contributed to the development of some diseases in adult life, such as cancer (20, 22).

Leukemia and Brain tumors in children

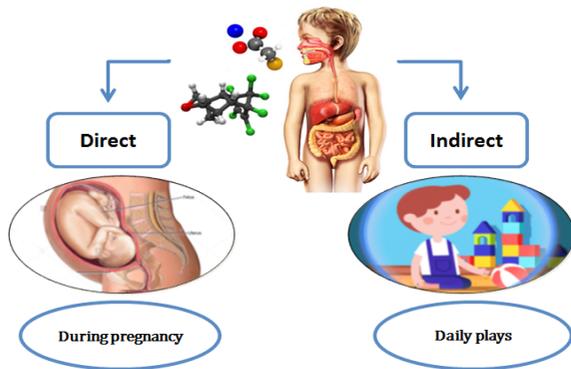
Leukemia is one of the most common cancers in children and accounts for about 30% of all cancers in chil-

Table 3. Some main pesticides in common use in urban households

Variables	Pesticides	LD ₅₀ Oral*	LD ₅₀ Dermal
Phenylpyrazole	Fipronil	336	382
	Diazinon	300-400	3600
Organophosphates	Malathion	5500	>2000
	Chlorpyrifos	92-276	2000
	Dichlorvos	56-80	75-210
	Propoxur	800-1000	90-128
Carbamates	Carbaryl	250-850	>2000
	Pirimicarb	147	>500
Neonicotinoids	Imidacloprid	450	>5000
	Cyfluthrin	500	>5000
Pyrethroids	Cypermethrin	250	2000
	Deltamethrin	431	>2000
	Permethrin	>4000	>4000

* LD₅₀ for the rat (mg/kg body weight).

Journal of Pediatrics Review



Journal of Pediatrics Review
Figure 2. Exposure pathways of children to pesticides

dren under 15 years (23). Moreover, leukemia is the third leading cause of death among children less than 15 years and comprises one-third of all cancers diagnosed in children less than 15 years in high-income countries. Childhood leukemia is a heterogeneous phenotypic and genetic disease. Acute Leukemia (AL) comprises more than 95% of all childhood leukemia, including acute lymphoid/lymphoblastic leukemia (ALL) and Acute Myeloid Leukemia (AML), with frequent type higher than 75% and 16%, respectively (15). Brain tumors are the second leading cause of cancer after leukemia in developed countries. In general, brain tumors are the second leading cause of cancer-related death among children and adolescents less than 19 years in the United States and Canada. Approximately 11000 to 13000 Americans die from the primary tumors of the central nervous system each year. Also, brain tumors are the second most lethal childhood tumor in children under 14 years in Europe. Approximately the primary tumors of the central nervous system account for 20% of childhood cancers and 25% of all childhood deaths related to cancer (16).

Exposure to the residential pesticide as the risk factor for leukemia and brain tumors

There are risks for leukemia and brain tumors in children exposed to the pesticide, including exposure to pesticides during pregnancy, indoor pesticide exposure, and prenatal pesticide exposure. Based on the results, there is a statistically significant association between residential pesticide exposure and childhood leukemia and brain tumors (Table 4).

Approaches to reduce the side effects of pesticides on children in the houses

In general, the best way to reduce the risk of pesticide exposure to children is never to use pesticides during

pregnancy. Below, we consider some of the best approaches to reduce the risks of pesticides on children.

Integrated Pest Management (IPM)

The first approach is the Integrated Pest Management (IPM) to reduce household pests. Recently, the IPM approach is considered a safe strategy for humans and the environment. Furthermore, IPM programs have been more environmentally friendly for managing urban pests such as cockroaches and bed bugs (37). In a recent study, Wang et al. (2019) revealed that the IPM implementation could significantly reduce the insecticide residue concentrations and the number of detected insecticides in floor dust samples (37). According to the definition, the IPM approach is defined as the simultaneous usage of both chemical and non-chemical strategies to control pests. In general, IPM refers to a wise combination of physical, environmental, mechanical, biological, and chemical controlling methods to minimize the risk of exposure to pesticides and prevent pests (38). The IPM strategy uses various non-chemical techniques, including heat treatment, vacuuming, laundering, freezing, and heat steam, to reduce household pests (2).

Green pesticides

One way to minimize exposure to pesticides is the use of green pesticides regarding household pests. These are suitable and safe methods for humans and the environment. According to the definition, green pesticides are pesticides derived from organic sources that are considered environmentally friendly and are causing less harm and low toxicity to human and animal health, habitats, and the ecosystem (39). Some Essential Oils (EOs) are green pesticides that are safe for applicators and residents can be used against household and structural pests. EOs can be applied to the skin and even ingested with impunity (40). Recently, essential oils are used as an alternative method to control insect pests, and is a pest control technology, although some study used of essential oil-based pesticides (41, 42), to control pests.

Educational workshops

Increasing knowledge and awareness of people about household pests by holding workshops is one way to improve people's skills in preventing and controlling pests in the household. One of the most critical factors to increase the pest's infestation is a general lack of public knowledge about these pests. In general, the knowledge and awareness of people regarding the biology, morphology, and behavior of urban pests can help detect primary

Table 4. Summary of the results of studies about the exposure of children and adolescents to pesticides and the risk of leukemia and brain tumors

Study Design	Cancer Type	Sample Size	Country of Study	Result	Reference
Case-control study	Leukemia	Cases (n=136) Controls (n=266)	International	A strong association was found between the use of pesticide and leukemia	Alexander et al. 2001 (24)
Case-control study	Brain tumors	Cases (n=66) Controls (n=236)	The USA	A strong association was found between children whose mothers reported chemical treatment of the home for pests during pregnancy or childhood and brain tumors.	Nielsen et al. 2005 (25)
Case-control study	Leukemia	Cases (n=41)	The USA	A strong association was found between the use of pesticides and leukemia.	Soldin et al. 2009 (26)
Case-control study	Brain tumors	Cases (n=526)	The USA	A weak association was observed between the use of pesticides and brain tumors.	Shim et al. 2009 (27)
Case-control study	Brain tumors	Cases (n=201) Controls (n=285)	The USA	A strong interaction was observed between genotype and insecticide exposure during childhood.	Nielsen et al. 2010 (28)
Case-control study	Leukemia	Cases (n=85) Controls (n=85)	Colombia	A strong association was observed between the mother's houses exposure to pesticides during pregnancy and childhood acute lymphoid leukemia	Castro-Jiménez, et al. 2011 (29)
Case-control study	Leukemia	Cases (n=443) Controls (n=324)	The USA	Any exposure to petroleum products during the preconception or prenatal period was significantly associated with infant leukemia.	Slater et al. 2011 (30)
Case-control study	Leukemia	Cases (n=176) Controls (n=180)	China	Pyrethroid may be associated with the risk of childhood acute lymphoid leukemia.	Ding et al. 2012 (31)
Case-control study	Leukemia	Cases (n=252) Controls (n=423)	Brazil	Associations with the ever use of pesticides during pregnancy were observed for acute lymphoid leukemia.	Ferreir et al. 2012 (32)
Case-control study	Brain tumors	Cases (n=730) Controls (n=3624)	Australia	Pesticide exposure and possibly exposure during pregnancy are associated with increased brain tumors risk in children	Greenop et al. 2013 (33)
Case-control study	Leukemia	Cases (n=85)	Iran	Exposure to indoor pesticides was seen among many cases.	Zakerinia et al. 2015 (34)
Case-control study	Leukemia	Cases (n=12717) Controls (n=25294)	International	There was an association between the use of pesticides and leukemia.	Bailey et al. 2015 (35)
Case-control study	Leukemia	Cases (n=248) Controls (n=111)	China	The household use of mosquito repellent was significantly associated with an increased risk of childhood acute leukemia.	Zhang et al. 2015 (36)
Case-control study	Leukemia	Cases (n=251) Controls (n=577)	Costa Rica	There are associations between more frequent maternal insecticide use inside the home and increased odds of acute lymphoid leukemia among boys and girls combined.	Hyland et al. 2018 (23)
Case-control study	Leukemia	Cases (n=116) Controls (n=162)	Italy	Increased risk for acute childhood leukemia was associated with prenatal maternal use of insecticides/rodenticides.	Ferri et al. 2018 (20)

Journal of Pediatrics Review

infestations and resurgence (43). Furthermore, knowledge of pesticide application in the household should be increased to reduce their side effects. Overall, easy access to pesticides and also lack of control rules for the application of pesticides are the common problems in the developing countries (44). Altogether, holding workshops about the application of pesticides is useful and can be done by different organizations such as health centers, veterinary organizations, and medical universities.

Using mobile applications

Today many mobile health applications have been designed to increase the knowledge and awareness of people regarding household pests. On the other hand, mobile applications can improve pest control skills in

people, which is a good way because of the current advanced software technology. Alizadeh et al. (2019) designed a mobile health application to identify, prevent, and control bed bugs as an urban nuisance pest. The findings showed that learning with mobile software can improve the health condition of infested people. Also, the participants reported the usefulness and applicability of this software (45).

4. Conclusion

There is a positive association between pesticide exposure in households and leukemia and brain tumors in children under 15 years old. This paper recommends limiting the use of household pesticides to reduce the risks of leukemia and brain tumors in children. It is nec-

essary to increase knowledge and awareness among people about household pests. In conclusion, there are some approaches to reduce urban pests and, consequently, the risks of pesticide side effects on children. Some of these approaches include integrated pest management and green pesticides. Also, educational methods such as local government education programs can increase the knowledge and awareness of people regarding household pests. Besides, holding workshops and using mobile applications can improve people's skills in preventing and controlling pests.

Ethical Considerations

Compliance with ethical guidelines

This is a review study and does not need ethical consideration.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflicts of interest

The authors declared no conflict of interest.

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