Pesticide exposure conditions on Parkinson's disease patients followed at a neurology clinic of a university hospital and perception of the relationship of exposure with illness

Condições da exposição a agrotóxicos de portadores da doença de Parkinson acompanhados no ambulatório de neurologia de um hospital universitário e a percepção da relação da exposição com o adoecimento

Paula Renata Olegini Vasconcellos[1], Maria Lucia Frizon Rizzotto[1], Gicelle Galvan Machineski[1], Rose Meire Costa[1]

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ABSTRACT The objective of this research was to investigate, from the work history of patients with Parkinson's disease, followed at the neurology outpatient clinic of a university hospital, the occurrence and conditions of exposure to pesticides, as well as the perception of the relationship between exposure and illness. This is an exploratory and descriptive study with a quantitative and qualitative approach, carried out at the Hospital Universitário do Oeste do Paraná, in Cascavel, Paraná, Brazil. Thirty-two subjects, the user or family members, with Parkinson's disease were interviewed by telephone interview using a semi-structured script. Of these, 16 (50%) were men; most of them retired elderly (87.48%), with low education (53.13%); 25 (78.11%) worked in agriculture, living in rural areas from 11 to 30 years old; 24 (74.98%) stated that they had direct or indirect contact with pesticides; the most cited form of pesticide application was with costal spray; Most (75%) did not use personal protective equipment and learned to handle pesticides with family members. It is concluded that a significant number of individuals with Parkinson's disease had some labor activity in agriculture during life, many of them with direct contact with pesticides, either in the preparation and application or even in the washing of clothes.

KEYWORDS Pesticides. Parkinson's disease. Occupational exposure. Public health.

RESUMO *O objetivo desta pesquisa foi investigar, a partir da história laboral de portadores da doença de Parkinson acompanhados no ambulatório de neurologia de um hospital universitário, a ocorrência e as condições da exposição a agrotóxicos, bem como a percepção da relação da exposição com o adoecimento. Trata-se de estudo exploratório e descritivo, com abordagem quantitativa e qualitativa, realizado no Hospital Universitário do Oeste do Paraná, em Cascavel, Paraná, Brasil. Foram entrevistados 32 sujeitos, o usuário ou familiares, com doença de Parkinson, por meio de entrevista telefônica a partir de roteiro semiestruturado. Desses, 16 (50%) eram homens; a maioria idosos aposentados (87,48%), com baixa escolaridade (53,13%); 25 (78,11%) trabalharam na agricultura, residindo na área rural de 11 anos a 30 anos; 24 (74,98%) afirmaram ter tido contato com agrotóxicos de forma direta ou indireta; a forma mais citada de aplicação dos agrotóxicos foi com pulverizador costal; a maioria (75%) não utilizou equipamentos de proteção individual e aprendeu a manipular os agrotóxicos com familiares. Conclui-se que um número expressivo de indivíduos com doença de Parkinson teve alguma atividade laboral na agricultura durante a vida, muitos deles com contato direto com agrotóxicos, seja no preparo e aplicação ou mesmo na lavagem das roupas.*

PALAVRAS-CHAVE *Agroquímicos. Doença de Parkinson. Exposição ocupacional. Saúde pública.*

[1] Universidade Estadual do Oeste do Paraná (Unioeste) – Cascavel (PR), Brasil.
paula.vasconcellos@hotmail.com

Introduction

After the Second World War, what is known as a 'green revolution' or contemporary agricultural revolution was observed, initially in the central countries, but, from the 1950s, in developing countries with large territorial dimensions such as Brazil, India and Mexico. This 'revolution', whose ideological discourse was to combat world hunger, promoted a process of high mechanization in the countryside, selection of plants with strong profitability potential and wide use of fertilizers, modifying the classic agricultural production process to increase production, in particular, rice, corn, wheat and soybeans for export. As a result, the extensive use of pesticides has grown to control production deficit caused by agricultural diseases and increase productivity[1].

In Brazil, this started in the 1960s, with government support, aiming to increase productivity, modernize agriculture, facilitate activities in the field with the use of machines (tractors, harvesters), chemicals (fertilizers and pesticides) and modified seeds, sold by multinationals that entered the Country. As an outcome of this modernization process, latifundia and monoculture production were formed mainly in the Midwest, South and Southeast regions[2,3].

Since 2008, Brazil has been occupying a prominent position in the world in the consumption of pesticides in parallel with the dissemination of studies that reveal its negative impacts on human health. The ability to disperse and transform pesticides in the environment favors their mobility in various ecosystems with a wide range of territories, exposing different population groups to their toxic effects, such as workers in various activities related to production and consumption, residents who live close to pesticide factories and farms, in addition to eating contaminated food. These impacts are related to the current development model, focused on the production of commodities for export[4,5].

The adverse effects of exposure to pesticides depend on the chemical characteristics, the amount absorbed or ingested, the time of exposure and the general health conditions of the exposed person, being divided into acute and chronic[6-8]. The acute effects appear soon after the worker contact with the pesticide and within 24 hours, presenting defined characteristics. Chronic effects are perceived in a matter of weeks, months or years after contact with these products, which makes it difficult to associate this phenomenon with the development of pathologies such as those that affect the Central Nervous System (CNS) and the Peripheral Nervous System (PNS). This is because the causes can also be related to genetic, environmental, food, immunological factors, among others[8-10].

In addition, the damage associated with the health of rural workers has been masked by the discourse of the relevance of increased productivity, since the effects of pesticides on human health, especially chronic ones, have not been adequately identified[10,11].

Among the pathologies that affect the CNS, there is Parkinson's disease (PD), first described in 1817, in London, by the British physician James Parkinson[12]. It is a neurological disease, which affects the individual's movements, giving rise to tremors associated with slow movement (bradykinesia), muscle stiffness and postural instability[13].

The PD occurs due to the degeneration of the black substance in the brainstem, which synthesizes dopamine, a neurotransmitter that has the function of transmitting information in the form of electrical signals from one neuron to another. The reduction of dopamine levels causes an imbalance in the systems involved in the control of movements[13-15].

The disease is considered to be of multicausal origin, and, currently, the relationship between exposure to pesticides associated with increased risk of PD worldwide is being considered, especially among those who report agricultural work, as observed by Rugbjerg et al.[16] in a study conducted in Canada; Tüchsen

and Astrup[17], in Denmark; and Liew et al.[18], in the United States of America (USA).

The association of the PD with labor exposure to pesticides is already confirmed and made official in France. The French government, after analyzing numerous scientific reports, added to Decree nº 2012-665, of May 4, 2012, PD as a disease of agricultural workers who used pesticides in their crops[19,20].

There are still few Brazilian studies that measure chronic diseases and evaluate the effects of the use of pesticides on human health. In addition, there are still few studies that discuss the agricultural models in dispute, such as family farming, agroecology as opposed to the model of intensive use of pesticides in Brazil[9-11,21].

Research that analyzes the consequences of prolonged exposure to pesticides can and must go beyond the quantitative approach, also needing to consider the narrative of the individuals involved in the agricultural work process. Qualitative studies are important to assist the discovery of new elements about the problem raised, which are, often, invisible in certain types of research designs, contributing little to the debate on the use of pesticides in the Country and to the formulation of public policies[10].

Thus, the objective of the research was to investigate, based on the labor history of PD patients followed up at the neurology outpatient clinic of the University Hospital of Western Paraná (Huop), the occurrence and conditions of exposure to pesticides, as well as the perception of the relationship exposure with illness.

Material and methods

Exploratory, descriptive research, with a quantitative and qualitative approach, developed with PD patients and/or family members attended at the neurology outpatient clinic of Huop.

From research in the medical records of that service, 48 users diagnosed with PD were identified, of which 32 (66.66%) were included in the study for meeting the inclusion criteria, that is, having a diagnosis of PD performed by a neurologist; being over 18, having attended the service at least once in the last 5 years and accepting to be part of the research.

The collection of information was carried out from March to May 2018 through Computer-assisted Telephone Interviewing (Etac) using a form based on the Protocol for the Evaluation of Chronic Intoxications by Pesticides[22], being adapted for PD; validated by five judges with knowledge in the field of this disease or pesticides; and pilot test for final adjustments. The interview was conducted with those who agreed to participate in the research, the Free and Informed Consent Term (ICF) was replaced by verbal consent, whose agreement was given through recording after presenting the research objectives and reading the term. The interviews were recorded and transcribed in full and used to complement the quantitative data. Each interviewee was identified by the letter E, followed by a number from the entry in the database.

The project was approved by the Human Research Ethics Committee of the State University of Western Paraná (Unioeste) under opinion nº 2.414.998 of 2017, and the ethical aspects were respected according to Resolution nº 466/2012 CNS[23].

Results and discussion

Among the participants, 50% (16) were male, 87.48% (28) over 60; 81.24% (26) were retired, 87.48% (28) lived in an urban area; 43.74% (14) had less than 4 years of study and 9.39% (03) said they were illiterate.

Santana et al.[24] reported in their study with farmers that 55.3% had a low level of education and that 24.5% were illiterate, with 64% using pesticides. The low level of education can make it difficult to read and understand the harmful effects of pesticides, but it cannot be considered as an isolated factor for its incorrect use.

When asked about reading the label on the packaging of pesticides, among the participants who had direct contact, only one stated that he always read the labels. The others did not know how to read or learned from family members how to use the product, one stated that he did not even know if it had a label *"But I don't even remember if it had a label... after a while others started coming... yeah... they said it was poison, but then he had already been poisoned"* (E15).

When asked about the possible causes for the development of PD, the majority (59.35%) did not know how to identify any aspect and/or determinant for PD, as expressed in the speech of an interviewee *"[...] I have no idea. So, in fact, I didn't even ask the doctor what causes this Parkinson's disease, you know"* (E5).

Seven respondents said they believed that emotional aspects, such as nervousness (E23), stress (E30) or even alcoholism, were related to the possible causes of the disease: *"He was an alcoholic, look according to what I read, we, it's a possibility, although I don't know the causes that Parkinson's can occur"* (E17).

In the literature, the risk for PD is associated with factors such as: exposure to pesticides, consumption of dairy products, history of melanoma and traumatic brain injury[25].

One interviewee cited rural work as a possible cause:

> *The mother was very hardworking in the field, she was very harmed in the field, right? The mother did all the heavy work, even pregnant, went to the farm with us! Pregnant with us and she was going to work in the fields!* (E7).

At least two respondents associated PD with exposure to pesticides, one as a suspect:

> *[...] because we are children and adolescents, we may have had some contact, but working with it, dealing directly with the poison, no. We could smell it, but it was normal, there was no way to avoid it.* (E10).

And another more directly:

> *... I've been working with agricultural poison for a while [...] yes today they say that there are people who worked a lot with insecticide and developed Parkinson's.* (E15).

Dardiotis et al.[26], through a literature review, showed several studies that investigated the association between genetic factors, exposure to pesticides and the emergence of PD. Results were found in which neuronal loss may predispose to the development of the disease, therefore, it is important to consider these interactions to better understand the pathogenic mechanism of PD. Studies conducted by Fitzmaurice et al.[27] revealed that environmental exposure to the pesticide benomyl, a fungicide used in Brazil, interferes with the metabolic activity of the enzyme Aldehyde Dehydrogenase (ALDH); and as a result, Dopal toxin (3-4-Dihydroxyphenylacetaldehyde), naturally produced by the brain, accumulates and causes damage to dopaminergic neurons, which increases the risks of PD. The authors further argue that even with the genetic involvement of PD, environmental factors are relevant in their origin.

Pavlou and Outeiro[28] state that the epigenetic modulation of gene expression by environmental factors, which cause changes in gene expression or function without changes in the DNA (Deoxyribonucleic Acid) sequence, is emerging as an important mechanism in PD. They conclude that PD can be caused by the combination of genetic mutations, environmental toxins and mitochondrial dysfunction, and epigenetic modification acts as a mediator between environmental exposure and genes, contributing to PD-related neurodegeneration.

Regarding the labor activity exercised by the research subjects during their lifetime, 78.11% (25) worked in agriculture and lived in the rural area for an average time of 11 years to 30 years, in several states of the federation (Minas Gerais, Paraná , Pernambuco, Rio

Grande do Sul, Rondônia, Santa Catarina and São Paulo). Three participants lived their entire lives in the rural area:

> *Look, he always worked in agriculture, you know. He has always been part of agriculture. From childhood. Even after he retired he kept working.* (E5).

Some women claimed to have worked in farming and domestic care their whole lives (E7, E8, E9).

A review by Mostafalou and Abdollahi[29] on human exposure to pesticides and their toxicity, with risk analysis to develop PD, found that occupational exposure to pesticides increases the risk of developing the disease from 1,3 to 5,6 times.

Among the participants, 74.98% (24) stated that they had direct or indirect contact with pesticides. The statement that follows exposes a routine of exposure very common in the field to the present day:

> *He worked in the agrochemical sector! Even I got intoxicated with this, the father put poison on the cotton and put us to work in the middle, I ended up in the hospital! [...] He* [the father] *applied the poison and we were already there in the farm, right? Cotton was very poisonous! Do you believe that even today he applies poison, and it can't be right? Because he already had cancer in his mouth, and he still applies it near home [...] and the smell comes all inside the house!* (E7).

Data obtained in an agricultural region in the USA revealed that long-term exposure, since childhood, increases the risk of developing PD in adulthood by four to six times[30].

A study carried out in France – including male agricultural workers with clinically identified PD cases –, which used an occupational questionnaire with indicators such as duration, cumulative exposure and intensity, found that high-intensity exposure to pesticides was positively associated with PD, as well as exposure pesticides in specialized vineyard farms has been associated with PD[31].

The use of pesticides, to eliminate vectors such as malaria, in public services is still a common practice in Brazil, exposing the product to both the general population and the agents that apply it.

> *[...] she lived for many years in Rondônia and by the time she got there, there was a lot of malaria, so Sucam* [Superintendence of Public Health Campaigns] *used to come every 15/20 days, a month, spraying everything. The houses, the farms, everything [...] on the walls of the houses was a little 'white', from applying that so much [...] the boys who worked at Sucam carried that barrel on their backs, it was not like the truck has today , it was all manual.* (E16).

DDT (Dichlorodiphenyltrichloroethane) is a type of organochlorine insecticide that was widely used in Brazil in health campaigns to combat the mosquito of the genus *Anopheles*, which transmits malaria. The application of the pesticide took place within the households to end outbreaks of disease transmission. As it is an acute and chronic neurotoxic organochlorine for humans, it can cause changes in behavior and balance disorders[32].

The use of this pesticide in crops was banned in 1985; and in 1998, it was banned for use in health campaigns. However, only in 2009, with Law nº 11.936, of May 14, 2009, its commercialization for any purpose was prohibited in the Country[33,34].

Some participants reported environmental exposure, due to the perception of the smell that remained in the air after the application of the pesticide.

> *[...] we could smell it, but it was normal, there was no avoiding it [...].* (E10).

> *[...] there was a time when he rented a lot, but as he had a little house right there in the middle to*

take care of everything, so he was close, he used to stay in the house all day. (E14).

[...] the house was in the middle of the fields, so we could smell it, right? That smell from afar, no matter how much it closed the doors and windows, there was still that smell [...]. (E27).

Costello et al.[30] concluded that the application of two types of pesticides (maneb and paraquat), over a distance of 500 meters from homes in California, exponentially increased the risk of developing PD, demonstrating the effects of indirect exposure to the pesticide.

The list of activities developed in agriculture and Parkinson's was studied in France, in which it was possible to observe that the incidence of the disease increased with the highest proportion of land that was dedicated to agriculture, especially the production of vineyards. This association was also confirmed in individuals who were not farmers, but lived in rural areas[35]. Likewise, studies conducted by neurologists at the University of California, Los Angeles, USA, showed evidence of the association between PD and pesticides, which expose not only the rural worker but also workers and individuals in the vicinity of agricultural areas or who inhaled their particles from the drift[36].

Among the participants who claimed to have contact with the pesticide, directly or indirectly, the most reported way of applying the product was the use of costal pulverizer by 45.84% (11) of the subjects.

He applied it with those manual machines, which he puts on his back, then there was a powder poison on the cotton too [...] he applied it on that machine and the smoke came up... then he applied that and that stayed in the air. (E7).

The concern with health due to the application of pesticides through spraying was reported in the study by Conceição et al.[37]. Farmers who handled the product said that, with pulverization, they were more exposed; and the wind direction also increased exposure and contact with the pesticide.

It is also important to highlight the environmental contamination by pulverization, the dispersion of pesticides by wind or water in the environment, that is, the 'technical drift'. The pesticide does not only reach the crop in which it was applied, as it also ends up being disseminated through the air and its surroundings with at least 30% of the product, and can exceed up to 70%, even following all the guidelines and technical standards of application. This indicates that there is no use of pesticides without contaminating the environment, as well as without affecting the health of workers or residents of the rural area[38].

With regard to the use of Personal Protective Equipment (PPE), of the individuals who reported direct contact in the application of the pesticide, 75% (9) said they did not use any part of the PPE.

The poison came in powder, we took it in a bucket and threw it with our hands, directly with our hands. We applied it without a mask, without anything, without a glove, without any protection, without any guidance, it was poison and poison, and ... they said it was not dangerous. (E15).

In the case of these individuals, most of them, contact with pesticides occurred in the 1970s and 1980s, when regulations practically did not exist. Regulatory Norm (RN) 6, the first that deals with the use of PPE, occurred in 1978, which made it difficult to access information and recommendations on its use[39].

However, the recommendation of using PPE, in most cases, is ineffective, both for not using all the items necessary for the work activity in question and for the option of not using it, given the discomfort that the equipment causes, such as excess of heat, disrupting the work process. It is also known that PPE does not fully protect workers, and can often become a means of contamination[37,40,41].

No participant, who was also often exposed due to farming activities and environmental contamination, reported the use of PPE for washing clothes used in the application of the pesticide. This activity is considered an action of direct contact of exposure to pesticides by NR 31[42].

Abreu and Alonzo[43] point out in their review of rural work and health risks that, often, the clothes that were used in the application of pesticides are handled in the same tank as other clothes of individuals in the family; or even done, in that place, the cleaning of the equipment used for the application of the pesticide.

The participants reported that, in indirect contact with the pesticide, in most cases, the application of the product was carried out by parents or spouses, and that these, in several reports, they did not read the labels on the packages, because they learned how to use with other family members or neighbors

> *[...] I remember that he asked, you know, the neighbors also said: I'm passing this, the bottle yields so many liters. Information from neighbors, where he also bought, at the vet like that, but he was not a label reader.* (E16).

In the study by Santana et al.[24], farmers who claimed to work with pesticides reported that information on the use of the product, in 44.2%, was obtained through neighbors, as well as through television and radio. A portion said they received guidance from professionals, however, 18.6% never had any information on how to correctly use the pesticide.

Some interviewees reported the planting of tobacco, a culture that uses a lot of pesticides, as a way of supporting the family (E7, E16, E18, E30). *"[...] there in the city where we used to live to get money was tobacco. It's just like soybeans today, back then, were tobacco"* (E18). The use of pesticides in tobacco growing is intense; and, in general, the work is done manually.

> *[...] I worked with tobacco, then they said that I had to put poison, otherwise I would fill it with bugs there, and since it was a greenhouse, I had to select leaf by leaf to dry it in the shed. So they handled that tobacco when they removed it from the field, it had to dry like that in the shade, they had contact with it all day.* (E16).

> *[...] I had contact with the poison, because we planted tobacco. [...] We used to plant everything we ate there. But the poison was only in the tobacco that we sold to make money. At that time, we didn't need to put poison* [in food]. *Only in smoke because the bugs used to gnaw.* (E18).

A study by Murakami et al.[44] with tobacco growers on small rural properties in Paraná shows low education and poor sanitation and health, in addition to high exposure to toxic agents causing psychiatric disorders, hearing loss and late organophosphate-induced polyneuropathy.

The South region has the highest concentration of tobacco production in the Country, being generally cultivated by families on small rural properties[45]. The cultivation of tobacco, according to Pignati et al.[46], had the highest amount of pesticides used by hectares in Brazil in recent years.

Currently, as an alternative to correct the harmful effects to the ecosystem of the conventional agriculture model, the agroecology model has been proposed as a way to reduce environmental impacts and to generate new forms of sustainable rural development. It seeks the interaction of knowledge, techniques and practices respecting the ecological, economic, technical and cultural conditions of each region and population. Through this, an ecological balance can be created worldwide guaranteeing food security. By striving for biodiversity, agroecology maintains a global ecological balance, guaranteeing food security[47,48].

Due to the long period between exposure to pesticides and the time of the interview, many participants did not remember the name of the pesticides used, characterizing a memory bias.

It is important to note that, since PD has a late onset, pesticides that have been intensely used in the past may no longer be used and commercialized today, and it is important to carry out additional studies with more recent pesticides[20].

It is considered relevant to evaluate rural populations exposed to pesticides with regard to the diagnosis of PD, since this happens years after the first symptoms of the disease, and studies on environmental risk factors are of great value. Thus, exposure to pesticides in low doses for long periods should be an alert for health services and society, aiming to reduce the consequences for future generations.

Conclusions

Most interviewees diagnosed with PD had some work activity in agriculture during their lifetime; lived in the rural area on average between 11 years and 30 years, had contact with pesticides, either in the preparation and application or even in the washing of contaminated clothes.

It is worth mentioning the little knowledge of the toxicity of the product as well as the incorrect handling and the low adherence to the use of PPE, due to the fact that most individuals are elderly and, at the time of contact with the pesticide, do not have access to information. A low perception of the association between PD and exposure to pesticides was also identified, despite the fact that a large part of the interviewees reported prolonged exposure to various types of pesticides and the fact that, some years ago, this relationship was recognized in European countries.

Thus, knowing that the association of genetic and environmental factors can trigger PD, and that the onset of symptoms occurs late after the origin of this disease, it is extremely important to conduct studies to assess environmental factors, especially in the rural population.

In such a way, additional investigations on this risk factor through the interaction of several areas of knowledge in the sociocultural, political-economic and environmental contexts, and with other methodological possibilities, will contribute to the reflection and to the implementation of prevention practices of the PD in future generations, with evaluative actions and control of the harmful effects of pesticides.

In this way, scientific productions can provide relevant data to draw the attention of managers and professionals of the SUS to the theme in order to promote new health practices and policies.

Collaborators

Vasconcellos PRO (0000-0003-0984-1458)* and Rizzotto MLF (0000-0003-3152-1362)* contributed in all stages of this study. Machineski GG (0000-0002-8084-921X)* and Costa RM (0000-0002-5344-5076)* contributed to the correction and final elaboration of the study. ■

*Orcid (Open Researcher and Contributor ID).

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