



EVALUATION OF PESTICIDES EXPOSITION: FIVE YEARS OF TOXICOLOGICAL ANALYSIS

Claudia Regina dos Santos

Universidade Federal de Santa Catarina
 crs0805@gmail.com

Angela Somavilla Higioka

Universidade Federal de Santa Catarina
 angelahigioka@gmail.com

Raquel Cardoso de Souza

Universidade Federal de Santa Catarina
 raquel.cardoso.souza@gmail.com

Eliza Bianchini de Paula

Universidade Federal de Santa Catarina
 eliza.bdp@hotmail.com

Virginia Coldebella

Universidade Federal de Santa Catarina
 virginia.coldebella@gmail.com

Synthia Campos

Universidade Federal de Santa Catarina
 titafc@hotmail.com

Mariah Bonelli Rossenq Neves

Universidade Federal de Santa Catarina
 mariahbrn123@gmail.com

Maryá Nunes Fusinato

Universidade Federal de Santa Catarina
 marya.fusinato@gmail.com

Lauren Bauermann

Universidade Federal de Santa Catarina
 laurenbauermann@gmail.com

Abstract

This study aimed to present results from 5 years of toxicologic analysis of acute intoxications suspicious of pesticides, and evaluation of occupational exposition of Endemic Agents of the state of SC. Were realized Paraquat identification analysis on urine and the cholinesterase activity determination, both related to cholinesterase inhibitors exposition. Were analysed 82,9% of intoxication cases related to Paraquat. Regarding the intoxications by cholinesterase inhibitors, the butyrylcholinesterase activity was the most requested for suspects of acute intoxications. For Endemic Agents were realized 2.120 analysis for both enzymes. It is considered that this activity had a wide reach, since the samples come from all over the state for both situations. Also, the inclusion of students in the activity reinforces the importance of disponibilizate the analysis for the community and on the formation of human resources.

Keywords: Laboratorial Analysis. Pesticides. Acute Intoxication. Occupational Monitoring.

AVALIAÇÃO DA EXPOSIÇÃO A AGROTÓXICOS: CINCO ANOS DE ANÁLISES TOXICOLÓGICAS

Resumo

O presente trabalho teve como objetivo apresentar os resultados de 5 anos de análises toxicológicas para as suspeitas de intoxicação aguda por agrotóxicos, e na avaliação da exposição ocupacional dos Agentes de Endemias do estado de SC. Foram realizadas análises para identificação de paraquat em urina e a determinação da atividade das colinesterases, relacionadas à exposição a inibidores da colinesterase. Foram analisados 82,9% dos casos de intoxicação relacionados ao paraquat. Com relação às intoxicações por inibidores da colinesterase, a atividade da butirilcolinesterase foi a mais solicitada para as suspeitas de intoxicações agudas. Para os Agentes de Endemias foram realizadas 2.120 análises para ambas as enzimas. Ainda que o monitoramento tenha tido grande alcance, uma vez as amostras foram provenientes de todo o estado para ambas situações. Ainda a inserção de alunos na atividade reforça a importância na disponibilização da análise à comunidade e na formação de recursos humanos.

Palavras-chave: Análises Laboratoriais. Agrotóxicos. Intoxicação Aguda. Monitoramento Ocupacional.

EVALUACIÓN DE LA EXPOSICIÓN A LOS PLAGUICIDAS: CINCO AÑOS DE ANÁLISIS TOXICOLÓGICO

Resumen

El presente estudio tuvo como objetivo presentar los resultados de 5 años de análisis toxicológicos para la sospecha de envenenamiento agudo por pesticidas, y en la evaluación de la exposición ocupacional de trabajadores de control endémico en el estado de SC. Se realizaron análisis para identificar el paraquat en la orina y determinar la actividad de la colinesterasa relacionada con la exposición a los inhibidores de la colinesterasa. Se analizó el 82,9% de los casos de intoxicación relacionada con el paraquat. En cuanto a las intoxicaciones por inhibidores de la colinesterasa, la actividad de la butirilcolinesterasa fue la más solicitada por sospecha de intoxicación aguda. Para los trabajadores, se realizaron 2.120 análisis para ambas enzimas. Aunque el monitoreo tuvo un amplio alcance, una vez que las muestras vinieron de todo el estado para ambas situaciones. Además, la inclusión de estudiantes en la actividad refuerza la importancia de poner el análisis a disposición de la comunidad y en la capacitación de recursos humanos.

Palabras clave: Análisis de Laboratorio. Pesticidas. Intoxicación Aguda. Monitoreo ocupacional.



INTRODUCTION

Brazil is one of the biggest food producers and exporters of the world, and the agribusiness represents one of the most important foundations of Brazilian Gross Domestic Product (GAZZIERO, 2015). The term pesticides refer to chemical products used with the purpose to control weeds, insects, mites, nematodes, mollusks, fungi, bacteria and virus, those who can compromise cultivation. These substances received this denomination in 1989 starting from the decree of Law N° 7.802 from July of 1989, highlighting the toxicity of these products to the environment and the human health. According to the decree, pesticides are products and agents of physical, chemical or biological processes, intended for use in production departments, storage and processing of farm products, on pastures, on forests protection, being them natives or implanted, and for others ecosystems and urban, hydric and industrial areas, which have the purpose to change the fauna and flora composition, in order to protect them from the damage of harmful living beings (BRASIL, 1989).

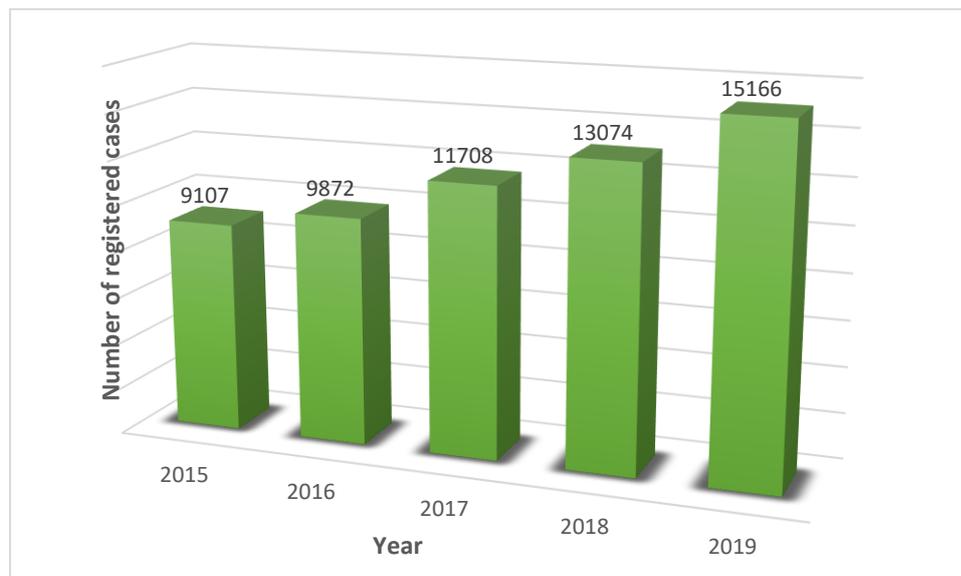
They are classified in many ways, and as for toxicity, in 2019 it started to count on 6 categories: from extremely toxic to unclassified product, having included this last category and a previous one, unlikely to cause acute damage, changing the classification criteria. Besides that, at the same year, the number of legal pesticides went to 474 (BRASIL, 2019a). The country ranks the 44th position of United Nations on pesticides use for Food and Agriculture Organization (BRASIL, 2019b).

In Santa Catarina, agriculture is described as strongly marked by family work, with a predominance of small and medium farms and great diversity on cultivation. According to historical analysis by Carvalho, Nodari and Nodari (2017), the use of pesticides on the area is old, starting in 1957 and totalizing more than 50 years.

Once the pesticides circulation on the state is large, the risk of exposure and possible intoxication also becomes more present. Between the years of 2015 and 2019, the Information Center and Toxicological Assistance of Santa Catarina (CIATox/SC) registered 58.927 cases of intoxications by various agents in Santa Catarina, being this an increasing number over the years, as shown in Figure 1:

Evaluation of pesticides exposition: five years of toxicological analysis

Figure 1. Number of intoxication cases for year, registered by CIATox/SC between the years 2015 to 2019.



Source: CIATOX, (2020)

Among these intoxications, the pesticides accounted for a total of 3.124 cases recorded during the last 5 years. During this period, paraquat intoxications totaled 181 cases, while intoxications by cholinesterase inhibitors (carbamates and organophosphates) totaled 417 cases. Table 1 details the number of cases per year related to pesticides intoxications recorded by CIATox/SC in the same period.

Table 1. Number of pesticides intoxications recorded between the years of 2015 and 2019 registered by CIATox/SC.

| Toxic agent / Year | 2015 | 2016 | 2017 | 2018 | 2019 |
|--------------------------|------------|------------|------------|------------|------------|
| CholinesteraseInhibitors | 94 | 89 | 88 | 79 | 67 |
| Paraquat | 33 | 39 | 41 | 35 | 33 |
| Total | 127 | 128 | 129 | 114 | 100 |

Source: CIATox/SC, (2020)

Pesticides comprise a group of chemicals widely used in the daily lives of people who live in both rural and urban areas. Therefore, are compounds known for the population in general. When someone has a single multiple contact with a toxic agent for a period of up to 24h, which signals and symptoms manifest immediately or up to two weeks, there is an acute intoxication. However, if the toxic agent exposure is long (over then three months) and cumulative, chronic intoxication may occur (OGA; CARVALHO; BATISTUZZO, 2014). Usually individuals with an acute intoxication or look for attendance or they are taken to one

almost immediately after exposure. However, those with possible chronic intoxication are almost never able to correlate the toxic agent exposure to the clinical manifestations (PARANA, 2018).

The intoxications may happen in various circumstances, for an example, if it's premeditated, then it's called an intentional intoxication. If it occurred as a result of circumstances that cannot be controlled, there is an accidental intoxication. Another possible situation is one that occurs in the workplace. However, this one can be controlled through security measures such as personal protective equipment (PPE), collective protective equipment, reduced workday, among other measures established by the regulations. Yet, the exposure control does not mean the absence of it, thus, many of the occupationally exposed professionals may suffer chronic intoxication. Between the workers that can be exposed to their workplaces are the farmers and endemic control workers (EWCs), being the pesticides the main toxic agents responsible for these intoxications (CARVALHO *et al.*, 2017).

Paraquat is a bipyridyl compound used as an herbicide being used a lot in Brazil, for the efficiency of the control of weed and for the low cost. However, the National Health Surveillance Agency (ANVISA) resolutions RDS n° 177, from 21 of September of 2017 and RDC n° 190, from 30 of November of 2017, deal about the ban of the active compound paraquat in agrochemical products in Brazil. The ban was made based on the conclusions of Technical Review n° 08/GGTOX/ANVISA, from 13 of June of 2016, and aims to reduce the risk of chronic exposure of farmers and workers to the product (ANVISA, 2016; ANVISA, 2017a, b).

In intact skin paraquat is practically not absorbed due to its polarity, however prolonged contact or high concentrations may cause ulcerations or dermatitis that facilitate the absorption of the product. Despite this characteristic, after ingesting even small amounts, a serious evolution is possible. Even if less than 10% of the total ingested is absorbed in the gastrointestinal tract, this absorption is rapid, and a decrease in absorption may occur if there was a recent diet. Paraquat is quickly eliminated by kidneys, with a half-life around 5h. However, because it is nephrotoxic it starts to compromise the functioning of the kidneys, increasing the half-life and causing the accumulation on the body, mainly in the lung tissue, followed by the kidneys, muscles, heart and liver (SCHMIDT, 2006; DINIS-OLIVEIRA *et al.*, 2008; CDC, 2018).

Acute oral intoxications are more frequently recorded and usually evolve to more severe cases than those dermal or inhaled. The early symptoms are pain and burning in the mouth, pharynx, esophagus and stomach, nausea, vomiting, diarrhea, and ulcer site and tissue

Evaluation of pesticides exposition: five years of toxicological analysis

necrosis. The evolution of the case can lead to renal injury and pulmonary fibrosis, characterized by cough, dyspnea, tachypnea, drop in hemoglobin saturation, peripheral cyanosis and hypoxemia. Exposure of the skin can lead to irritation, dryness, dermatitis, erythema, blisters and ulcers. Contact nails, can cause discoloration, softening and deformation. Inhaling paraquat can lead to nosebleeds. (SCHMITT et al., 2006; CDC, 2018).

As for the ways to assess exposure, confirmation of exposure includes qualitative and quantitative analyzes, and the colorimetric method with 1% sodium dithionite is widely used and effective. This conventional screening technique has a Limit of detection of 1 mg.L⁻¹ and should be performed during the first 24 hours after exposure to paraquat, with a better visual response in the first 12 hours after exposure. The method is applied to urine samples and/or gastric lavage, which must be added to a 1% (w/v) sodium dithionite solution, freshly prepared in alkaline medium with 1 mol/L sodium hydroxide (MOFFAT; *et al.*, 2011). Considering the kinetics of these compounds, a detected result indicates that the individual ingested the substance.

Another class of pesticides that can trigger intoxications that also evolve in a serious way, are cholinesterase inhibitors, which can be divided into two groups: organophosphates and carbamates (CCIn, 2000). In the care of a patient intoxicated by cholinesterase inhibitors, treatment is effective when it is possible to identify the toxic agent, besides the amount absorbed and the time elapsed after exposure, as it directs the treatment to a better prognosis (BRASIL, 2018).

Cholinesterase inhibitors act by phosphorylating cholinesterases, acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), inhibiting the degradation of acetylcholine, resulting an accumulation of this compound that is a chemical mediator for the synapses of the Central Nervous System and Peripheral Nervous System which lead to toxic manifestations. (BRASIL, 2018). The main symptom presented in an acute intoxication by these agents is due to the excessive stimulation of the secretory organs, which leads to an increase in secretions in the bronchial, lacrimal, salivary, dermal, intestinal and pancreatic sites; other symptoms presented are miosis, bradycardia, seizures, hyperthermia and respiratory failure (POPE, KARANTH, LIU, 2005).

The measurement of cholinesterase activity is used to confirm acute intoxications when they are below the reference value and to monitor occupational exposure (BRASIL, 2018). In addition to cholinesterases being considered validated biomarkers for occupational and environmental exposure, some studies demonstrate other potentials for measuring cholinesterase activity in samples such as saliva (LIONETTO, 2013).

Evaluation of pesticides exposition: five years of toxicological analysis

In Brazil, the only parameter for monitoring occupational exposure to pesticides is related to cholinesterase inhibitors. So, according to the Regulatory Norm 7 of Ordinance 1.892 of 1978 of the Ministry of Labor, the activity of AChE or BChE must be determined at least every 6 months. The Limit Permissible for AChE is 30% inhibition, while for BChE it is 50% inhibition, based on the individual's pre-occupational values. Inhibition values higher than those described indicate excessive exposure and requires removal from work activities, however, lower values may already indicate the need for attention to the health of the worker on service. (BRASIL, 1978).

The Toxicology Sector of the Clinical Analysis Laboratory Unit of the University Hospital Professor Polydoro Ernani de São Thiago (HU/UFSC), created in 2015, aims to meet the demands of toxicological analysis, including the cases registered at CIATox/SC, for diagnostic assistance and confirmation of suspected poisoning. Also, since 2016, a partnership was established between this Sector and the Central Public Health Laboratory (LACEN), of the State Department of Health of Santa Catarina in order to carry out toxicological analyzes that are not carried out by LACEN, specifically the monitoring of the occupational exposure of ECWs. This demand is related to the fact that the agents involved in the control of outbreaks of dengue use cholinesterase inhibitors and thus are exposed occupationally.

Therefore, the present study shows the results of laboratory support used to elucidate diagnoses of suspected cases of acute poisoning by pesticides in patients treated by CIATox/SC, as well as the biological monitoring of ECWs in the state of SC, over 5 years of carrying out these laboratory analyzes.

MATERIALS AND METHODS

This study reflects an extension project carried out over 5 years, between 2015 and 2019. Samples from two different origins were evaluated: individuals with suspicion of acute intoxication by paraquat or by cholinesterase inhibitors (carbamates and organophosphates) and individuals with occupational exposure history (ECWs) from counties of the state of Santa Catarina, focusing on monitoring the exposure through the AChE and BChE activity evaluation.

The samples were sent to CIATox/SC for cases with suspicion of acute intoxication and by the counties of the state through LACEN for the cases of occupational exposure evaluation.

Evaluation of pesticides exposition: five years of toxicological analysis

Were received blood/serum/plasma samples for evaluation of effect biological indicators already recommended (cholinesterases), and urine to paraquat identification. The samples were received from the whole state of Santa Catarina, since in Santa Catarina these exams are realized only on the Clinical Analysis Laboratorial Unity of HU/UFSC.

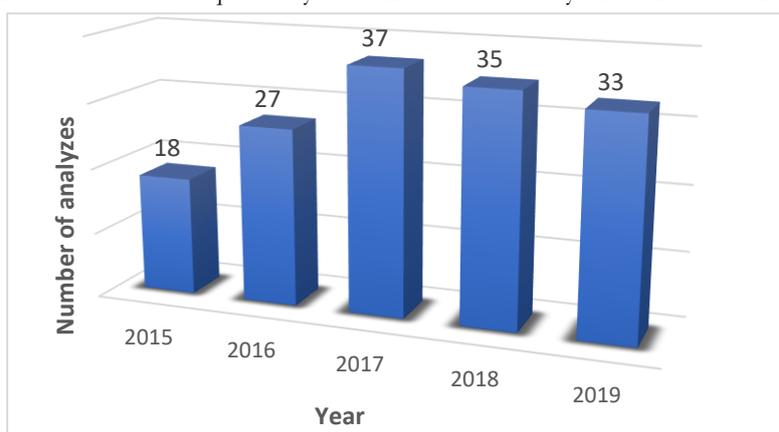
The analysis was realized by colorimetric methods for detection of paraquat or spectrophotometric for the measure of cholinesterase activities, the technique was properly validated and they're part of the routine analysis of the involved sectors. It was conducted by sector's pharmaceutical-biochemical and by academics of Pharmacy Graduation Course who are part of the project as volunteers or interns, always under the project Coordinator supervision.

The obtained results were delivered directly to the requesters in the form of a laboratory report in order to confirm diagnostic and help on the necessary therapeutic condictions in cases of acute intoxication suspects and evaluate the necessity of establishing protection measures to the occupationally exposed individuals.

RESULTS AND ANALYSIS

In the period of 2015 to 2019, were analyzed 1,374 samples related to paraquat and cholinesterase inhibitors suspect of intoxications or expositions. For paraquat detection, was realized 150 colorimetric analysis (Figure 2), all of them to attend the emergency demand of CIATox/SC.

Figure 2. Distribution of Paraquat analysis fulfilled between the years of 2015 and 2019 (n=150)



Source: Author, (2020)

According to Figure 2, the analysis distribution between 2015 and 2019 showed a considerable increase between 2015 and 2017, remaining constant in the last 3 years, even with the ban of the substance in 2017 (ANVISA, 2017b). An important aspect is that between 1984

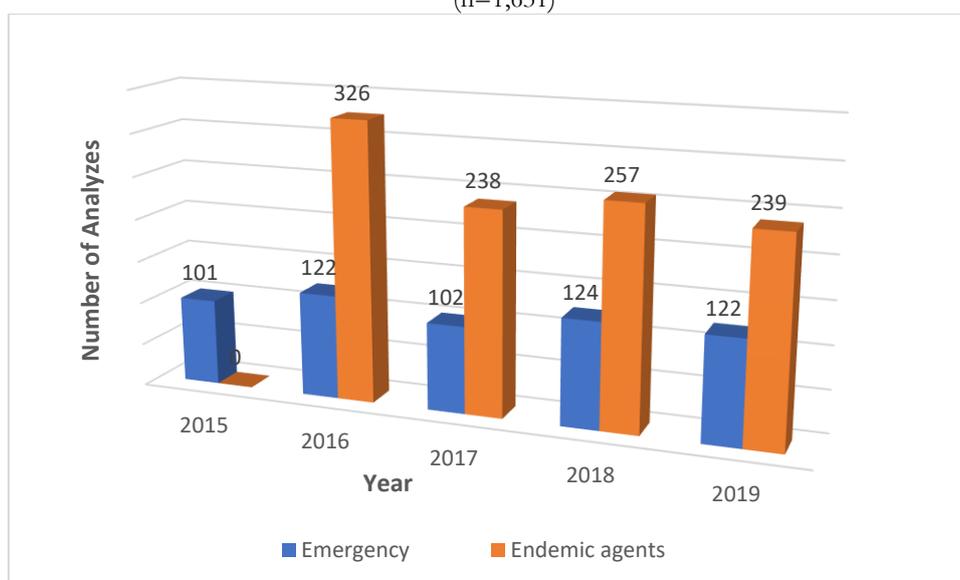
Evaluation of pesticides exposition: five years of toxicological analysis

and 2002, that is in 18 years 19 cases were registered, with an average of 12 cases/year (BIGOLIN, 2004). In this study, besides the little variation observed between the years, the annual average was 36 cases. The RDC n° 190 of 2017 (ANVISA, 2017b) which ban the use and sale of paraquat in Brazil was published in September of 2017 and establish a 3 years term for a total extinction of the substance on the country, thus, it is expected that throughout 2020, these occurrences will decrease.

Despite the laboratory analysis having been realized only with samples from HU/UFSC patients or samples sent from counties, when comparing with the number of cases registered by CIATox/SC in the same period (181 cases), samples from 82.9% of cases were analyzed. Thus, even with the complex logistics transport, which sometimes end up complicating the receivment of the samples, the existence of the service, the disclosure of the sector and the possible severity of the intoxication support the importance of carrying out these analyses.

The cholinesterase activity determinations (Figures 3 and 4) of emergency character presented a total of 735 analysis on the period of 2015 to 2019. Of these, 571 were Butyrylcholinesterase activity determination (BChE) and 164 of acetylcholinesterase activity (AChE). The discrepancy may be attributed to the fact that the BChE activity determination provides the result more quickly, been therefore more applicable to acute intoxications.

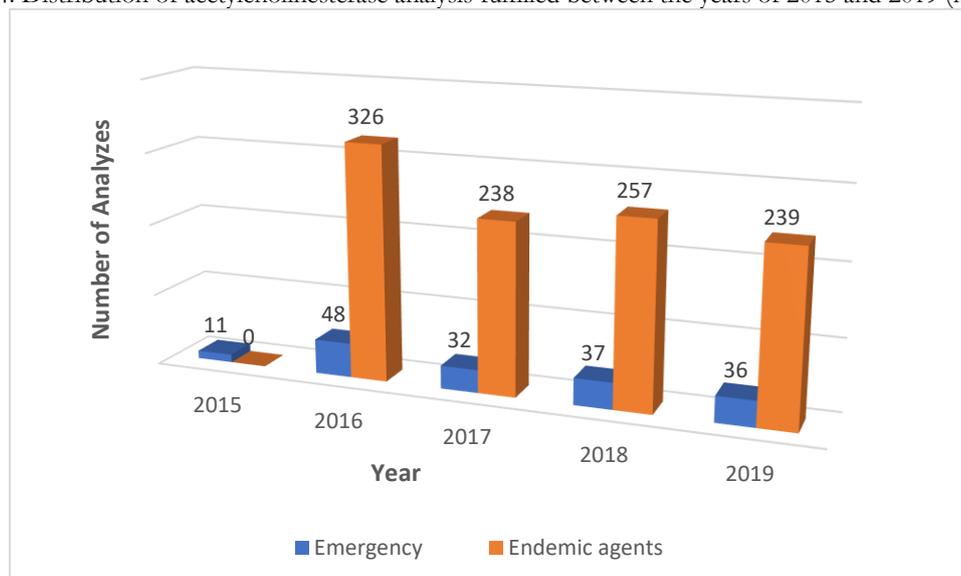
Figure 3. Distribution of butyrylcholinesterase analysis fulfilled between the years of 2015 and 2019 (n=1,631)



Source: Author, (2020)

Evaluation of pesticides exposition: five years of toxicological analysis

Figure 4. Distribution of acetylcholinesterase analysis fulfilled between the years of 2015 and 2019 (n= 1,222).



Source: Author, (2020)

When the cholinesterase activities determinations are fulfilled for de ECWs, both enzymes are evaluated concomitantly as recommended by NR 7. Between 2015 and 2019, 2,120 samples were analyzed, 1,060 from each of the cholinesterase, BChE and AChE. These determinations were realized for about 400 endemic control workers of the state. It shows that, as determined by the labor legislation, these analyzes are carried out periodically, that is, they must occur repeatedly throughout working time. As can be seen, no determinations were made related to ECWs, because the partnership with LACEN was signed in 2016.

Despite the total number of analyzes versus the number of ECWs diseases seems to be expressive, the average number of analyzes was 5.3 analyzes per individual, almost one a year, and is therefore much lower than recommended. The Legislation provides, for example, that for those endemic agents who apply and works with malathion the control must be fortnightly. It is worth mentioning that the analysis by average does not refer to reality, for example of the total number of individuals evaluated since 2016, only 16 maintained revaluations until 2019 (NEVES, *et al.*, 2019). The others are reevaluated over a very long interval between collections or they have only performed one collection, it's not known if the periodic examination is not being carried out, or if these individuals were disconnected from this activity.

The opportunity to monitor the exposure to pesticides for these professionals reflects the importance that this partnership has in the scope of workers' health. Each year the number of notifications of diseases such as dengue and yellow fever has significantly increased throughout Brazil including the Santa Catarina state. According to data from the Dengue

Evaluation of pesticides exposition: five years of toxicological analysis

Control Program of the Epidemiological Surveillance of Santa Catarina, in 2020, in January and February, 8,597 outbreaks of dengue were identified in the State, the cities with the highest number of outbreaks reported Joinville (1.273), Camboriú (487) and Concórdia (452). It is worth mentioning that *Aedes aegypti* is a vector not only of dengue and yellow fever, but also of chikungunya. Thus, the efforts to combat the existing focus has enjoyed the active participation of endemic agents. So, the control of the exposure of these workers to the pesticides used to extinguish the outbreaks of *Aedes aegypti* and other vectors that causes diseases is extremely important to monitor the health of this exposed worker (SANTA CATARINA, 2020).

In the research carried out by Lima et al (2015), the normal activity of cholinesterase levels of endemic agents from two Health Micro-regions in Ceará was assessed. The authors found that 11.1% of the monitored agents had their cholinesterase levels altered and that in 25% of the cases the values were close to the lower limit of normality, indicating the importance of this type of monitoring.

In Santa Catarina, the Joint Technical Note DIVS, DIVE, and LACEN of 2016 establishes the rules regarding the collection, conditioning and analysis of samples regarding the determination of cholinesterases of SC endemic control workers (SANTA CATARINA, 2016). This note reflects the concern of the state in relation to the health of these workers, as well as, it allows the analysis of the data to be used as an indicator in the management of the exposure of these workers. Currently, the Clinical Analysis Laboratory Unit of the HU/UFSC carries out the analyzes and forwards the results to the requesting Units, which are responsible for interpreting the results. Although, the interpretation and appropriate referrals are not the subject of this study, it is very important to keep available the possibility of this monitoring, which exists only after 2016 and is conducted exclusively at UFSC.

It is recognized that there is a need to increase the number of individuals included in this monitoring process and carry out evaluations as recommended by law. As so, the continuity of this activity is essential for this group that has no other possibility of evaluation.

CONCLUSION

In the present study, the results were presented over 5 years of execution of the related extension project. During this period, 181 cases were registered at CIATox/SC with suspected paraquat poisoning and in 82.9% of the cases in the laboratory analysis confirmed or discarded the situation. Another analysis offered through this project was the measurement of

Evaluation of pesticides exposition: five years of toxicological analysis

cholinesterase activity to assess acute or occupational exposure to cholinesterase inhibitor poisoning. Among these analyzes it was observed that for suspicions of acute poisoning, butyrylcholinesterase activity was the most requested since it has a good correlation with acute exposure and the result is released in within hours. In order to monitor the exposure of endemic agents, 2,120 analyzes were carried out on about 400 endemic agents.

It is known that despite efforts, analyzes are not carried out for all suspected paraquat poisoning or cholinesterase inhibitors, neither it is monitoring of 100% of endemic agents. However, considering what has been done so far, the possibility of offering the community the tests described here help to confirm the diagnosis of acute intoxications, safely guiding the appropriate treatment in addition to decreasing expenses with hospital stay in cases of acute intoxication. For workers, periodic assessment makes it possible to monitor occupational exposure and assess whether control measures or changes in the way the work is performed are necessary.

It is also worth mentioning the importance of this project in the training of academics who experience the activities, accompanying the importance of toxicological analyzes, both in situations of acute exposure/intoxication, and in chronic exposures, in this case occupationally. Despite existing a subject that deals with the theme, the opportunity to apply toxicological analysis provides the consolidation of knowledge and sensitize future professionals to the importance of this field.

REFERENCES

AGÊNCIA NACIONAL DE VIGILÂNCIA SANITÁRIA - ANVISA. Parecer Técnico de Reavaliação nº 12/GGTOX/Anvisa, de 05 de outubro de 2016. Propõe medidas transitórias de descontinuação do uso do Paraquate no país até sua proibição total. Brasília, DF, 05 de outubro de 2016. Disponível em: <http://portal.anvisa.gov.br/documents/10181/2871639/08.+Parecer+12-2016+-+complementar+-+Paraquate.pdf/7a2f4f5c-90c1-4a7c-817a-83e1861ec16b>. Acesso em: 10 fev. 2020.

AGÊNCIA NACIONAL DE VIGILÂNCIA SANITÁRIA - ANVISA. Resolução de Diretoria Colegiada - RDC nº177, de 21 de Setembro de 2017. Dispõe sobre a proibição do ingrediente ativo Paraquate em produtos agrotóxicos no país e sobre as medidas transitórias de mitigação de riscos. **Diário Oficial da União**, Brasília, DF, nº 183, de 22 de setembro de 2017a. Disponível em: http://portal.anvisa.gov.br/documents/10181/2871639/RDC_177_2017_COMP.pdf/d182599c-e61a-4edf-9044-1fb0a72b2fe7. Acesso em: 10 fev. 2020.

AGÊNCIA NACIONAL DE VIGILÂNCIA SANITÁRIA - ANVISA. Resolução de Diretoria Colegiada - RDC nº190, de 30 de Novembro de 2017. Altera a Resolução da

Diretoria Colegiada nº 177, de 21 de setembro de 2017, que dispõe sobre a proibição do ingrediente ativo Paraquate em produtos agrotóxicos no país e sobre as medidas transitórias de mitigação de riscos. **Diário Oficial da União**, Brasília, DF, nº 230, de 1º de dezembro de 2017b. Disponível em:

http://portal.anvisa.gov.br/documents/10181/2871639/RDC_190_2017_.pdf/eb2f6c7f-c965-4e76-bed9-ea9842e48b5c. Acesso em: 16 maio 2017.

BIGOLIN, R. C. **Intoxicações provocadas pelo herbicida Paraquat**: estudo de 219 casos. 2004. 53f. Trabalho de Conclusão de Curso (Graduação) – Curso de Graduação em Medicina, Universidade Federal de Santa Catarina. Florianópolis, 2004.

BRASIL. Ministério da Agricultura, Pecuária e Abastecimento. Portal de Notícias. Mesmo com aumento do registro de defensivos agrícolas, venda caiu nos últimos anos. Brasília, 04 de julho de 2019a. Disponível em: <http://www.agricultura.gov.br/noticias/mesmo-com-aumento-do-registro-de-defensivos-agricolas-venda-do-produto-caiu-nos-ultimos-anos>. Acesso em: 16 fev. 2020.

BRASIL. Ministério da Agricultura, Pecuária e Abastecimento. Portal de Notícias. Ranking da FAO mostra que uso de defensivos no Brasil é menor que em diversos países da Europa. Brasília, 26 de junho de 2019b. Disponível em: <http://www.agricultura.gov.br/noticias/ranking-da-fao-mostra-que-uso-de-defensivos-no-brasil-e-menor-que-em-diversos-paises-da-europa>. Acesso em: 16 fev. 2020.

BRASIL. Ministério da Agricultura, Pecuária e Abastecimento. Portal de Notícias. Em 2019, 94,5% dos defensivos agrícolas registrados foram produtos genéricos. Brasília, 27 de dezembro de 2019. Disponível em: <http://www.agricultura.gov.br/noticias/em-2019-94-5-dos-defensivos-agricolas-registrados-foram-produtos-genericos>. Acesso em: 16 fev. 2020.

BRASIL. Ministério da Saúde. Comissão Nacional de Incorporação de Tecnologias no SUS – CONITEC. Diretrizes Brasileiras para Diagnóstico e Tratamento de Intoxicações por Agrotóxicos: Capítulo 2. **Relatório de Recomendações**, n. 407. Brasília, dez. 2018. 206p. Disponível em: http://conitec.gov.br/images/Relatorios/2018/Recomendacao/Relatorio_DiretrizAgrotoxico.pdf. Acesso em: 16 fev. 2020.

BRASIL. Ministério do Trabalho e Emprego - MTE. Portaria nº 3.214, de 06 de junho de 1978. Aprova as Normas Regulamentadoras - NR - do Capítulo V, Título II, da Consolidação das Leis do Trabalho, relativas a Segurança e Medicina do Trabalho. **Diário Oficial da União**, Brasília, DF, p. 5.203, 06 de julho de 1978. Disponível em: https://enit.trabalho.gov.br/portal/images/Arquivos_SST/SST_NR/NR-07.pdf. Acesso em: 16 maio 2017.

BRASIL. Presidência da República. Lei nº 7.802, de 11 de julho de 1989. Dispõe sobre a pesquisa, a experimentação, a produção, a embalagem e rotulagem, o transporte, o armazenamento, a comercialização, a propaganda comercial, a utilização, a importação, a exportação, o destino final dos resíduos e embalagens, o registro, a classificação, o controle, a inspeção e a fiscalização de agrotóxicos, seus componentes e afins, e dá outras providências. **Diário Oficial da União**, Brasília, DF, p. 11.459, 12 de julho de 1989. Disponível em: https://www.planalto.gov.br/ccivil_03/LEIS/L7802.htm. Acesso: 16 de maio de 2018.

CENTRO DE CONTROLE DE INTOXICAÇÕES DE NITERÓI - CCIn. **Intoxicações exógenas agudas por carbamatos, organofosforados, compostos bipiridílicos e piretróides**. Niterói: CCIn, 2000. 43 p. Disponível em:

<http://www.cvs.saude.sp.gov.br/zip/intoxicacoes%20agudas%20-%20carbamatos%20e%20organoclorados.pdf>. Acesso em: 07 fev. 2020.

CARVALHO, L. V. B. *et al.* Exposição ocupacional a substâncias químicas, fatores socioeconômicos e Saúde do Trabalhador: uma visão integrada. **Saúde Debate**. Rio de Janeiro, v. 41, n. Especial, p. 313-326, jun. 2017. Disponível em: <http://www.scielo.br/pdf/sdeb/v41nspe2/0103-1104-sdeb-41-spe2-0313.pdf>. Acesso em: 01 mar. 2020.

CARVALHO, M. M. X.; NODARI, E. S.; NODARI, R. O. “Defensivos” ou “agrotóxicos”? História do uso e da percepção dos agrotóxicos no estado de Santa Catarina, Brasil, 1950-2002. **Hist. Ciênc. Saúde-Manguinhos**, Rio de Janeiro, v. 24, n. 1, p.75-91, jan./mar. 2017. DOI: <http://dx.doi.org/10.1590/s0104-59702017000100002>.

CENTERS FOR DISEASE CONTROL AND PREVENTION - CDC. Emergency Preparedness and Response. Facts About Paraquat. Atlanta, Abr. 2018. Disponível em: <https://emergency.cdc.gov/agent/paraquat/basics/facts.asp>. Acesso em: 10 fev. 2020.

CENTRO DE INFORMAÇÃO E ASSISTÊNCIA TOXICOLÓGICA DE SANTA CATARINA - CIATox/SC. Estatísticas: 2015 a 2019. Florianópolis, 2020. [Acesso restrito].

DINIS-OLIVEIRA, R. J. *et al.* Paraquat poisonings: mechanisms of lung toxicity, clinical features, and treatment. **Crit. Rev. Toxicol.**, London, v. 38, n. 1, p. 13-71, jan. 2008. DOI: <http://dx.doi.org/10.1080/10408440701669959>

GAZZIERO, D. L. P. Misturas de agrotóxicos no tanque nas propriedades agrícolas do Brasil. **Planta Daninha**, Viçosa, v. 33, n. 1, p. 83-92, mar. 2015. Disponível em: http://www.scielo.br/scielo.php?pid=S0100-83582015000100083&script=sci_abstract&tlng=pt. Acesso em: 16 fev. 2020.

LIMA, E. P. *et al.* Níveis de colinesterase como marcador de risco de distúrbios neurológicos em agentes de endemias. **J. Health Biol. Sci.** Fortaleza, v. 3, n. 2, p. 73-76, 2015. DOI: [10.12662/2317-3076jhbs.v3i2.187.p73-76.2015](http://dx.doi.org/10.12662/2317-3076jhbs.v3i2.187.p73-76.2015).

LIONETTO, M. G. *et al.* Acetylcholinesterase as a biomarker in environmental and occupational medicine: new insights and future perspectives. **BioMed Res. Int.**, New York, v. 2013, Art. ID n. 321213, 8p, 2013. DOI: [10.1155/2013/321213](http://dx.doi.org/10.1155/2013/321213).

MOFFAT, A. C. *et al.* **Clarke’s analysis of drugs and poisons**: in pharmaceuticals, body fluids and postmortem material. 4. ed. Chicago: Pharmaceutical Press, 2011. 2v.

NEVES, M. B. R. *et al.* Evaluation of the adherence to biological monitoring in endemic agents of the State of Santa Catarina (2016 to 2019). *In*: CONGRESSO BRASILEIRO DE TOXICOLOGIA (CBTOX), XXI; ENCONTRO REGIONAL LATINO-AMERICANO DE TOXICOLOGIA FORENSE (TIAFT), XV, de 28 a 31 de outubro de 2019, Águas de Lindoia/SP. **Abstract book**, p. 256. Disponível em: http://www.cbtox-tiaft.org/book/file/AbstractBook_CBTOX.pdf. Acesso em: 01 mar. 2020.

OGA, S.; CARVALHO, M. M. A.; BATISTUZZO, J. A. O. **Fundamentos de Toxicologia**. 4. ed. São Paulo: Atheneu, 2014.

PARANÁ. Secretaria de Estado da Saúde. Centros de Controle de Envenenamento (CCE). **Intoxicações agudas por agrotóxicos: atendimento inicial do paciente intoxicado**. Curitiba: SES/PR, 2018. Disponível em:
<http://www.saude.pr.gov.br/arquivos/File/IntoxicacoesAgudasAgrotoxicos2018.pdf>.
Acesso em: 01 mar. 2020.

POPE, C.; KARANTH, S.; LIU, J. Pharmacology and toxicology of cholinesterase inhibitors: uses and misuses of a common mechanism of action. **Environ. Toxicol. Pharmacol.** [online], Amsterdam, v. 19, n. 3, p.433-446, may 2005. DOI: 10.1016/j.etap.2004.12.048.

SANTA CATARINA. Secretaria de Estado da Saúde. Superintendência de Vigilância em Saúde. Diretoria de Vigilância Epidemiológica – DIVE. Programa de Controle de Dengue, 2020. **Relatório**. Disponível em:
http://vigilantos3.dive.sc.gov.br/vigilantos3/dengue_relatorio_programa/dengue_relatorio.pdf?ano=2020&type=pdf. Acesso em: 16 fev. 2020.

SANTA CATARINA. Secretaria de Estado da Saúde. Superintendência de Vigilância em Saúde – SVS. **Nota Técnica Conjunta DIVS, DIVE e LACEN, de 30 de agosto de 2016**. Orienta sobre o fluxo de coleta, acondicionamento e transporte das amostras biológicas para monitoramento da colinesterase nos agentes de saúde que utilizam inseticidas organofosforados e carbamatos nas atividades de controle vetorial. Disponível em:
http://www.dive.sc.gov.br/conteudos/agrivos/notas_tecnicas/NotaTecnicaConjuntaSUV_exames%20colinesterase.pdf. Acesso em: 01 mar. 2020.

SCHMITT, G. C. *et al.* Aspectos gerais e diagnóstico clínico laboratorial da intoxicação por paraquat. **J. Bras. Patol. Med. Lab.**, Rio de Janeiro, v. 42, n. 4, p. 235-243, ago. 2006. Disponível em: <http://www.scielo.br/pdf/jbpm/v42n4/a03v42n4.pdf> Acesso em: 01 mar. 2020. DOI:<http://dx.doi.org/10.1590/s1676-24442006000400003>.

Recebido em: 15/03/2020

Aceito em: 24/03/2020