The Association between Pesticide Exposure and Neurological Signs and Symptoms in Farmers in Magelang District, Central Java, Indonesia

Ismail Setyopranoto¹, Ibnu Widya Argo¹, Aulia Fitri Ramadhani¹, Ery Kus Dwianingsih², Whisnu Nalendra Tama¹, Abdul Gofir¹, Cempaka Thursina Srie Setyaningrum¹, Andre Stefanus Panggabean¹, Sri Susanti¹, Rusdy Ghazali Malueka*¹

¹Department of Neurology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Dr. Sardjito General Hospital, Yogyakarta, Indonesia; ²Department of Anatomical Pathology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Dr Sardjito General Hospital, Yogyakarta, Indonesia

Abstract

BACKGROUND: Excessive use of pesticides is known to cause neurotoxicity. Chronic effects of pesticide poisoning include neuropathy and tremors.

AIM: This study aimed to determine the association between pesticide exposure and the occurrence of neurological signs and symptoms, especially neuropathy and tremor, in farmers.

METHODS: This was a cross-sectional study. The study location was Seloprojo Village, Ngablak District, Magelang Regency, Central Java Province. Farmers as subjects were recruited to determine neuropathy using Diabetic Neuropathy Symptom (DNS) and Diabetic Neuropathy Examination (DNE) scoring. Tremor events were measured with Tremor Rating Scale (TRS). Cholinesterase levels were examined using venous blood samples to determine the level of pesticide poisoning.

RESULTS: Of the 120 farmers studied, 68.3% experienced pesticide poisoning with cholinesterase levels below normal values. Weakness of the upper limb was found in 10 subjects (8.33%), while weakness of the lower limbs was found in 6 subjects (5%). There were 59.2% farmers who met the neuropathy criteria from the DNS score and those who met the neuropathic criteria from the DNE score were 6.7%. Tremor symptoms were found in 71.7% of the farmers. There was no significant association between cholinesterase levels and DNS score (p = 0.737), but there were significantly lower levels of cholinesterase (p = 0.046) in the neuropathy group measured with DNE score. There was no significant association between cholinesterase levels and TRS (p = 0.204).

CONCLUSION: Cholinesterase levels were significantly associated with neuropathy incidence measured with DNE criteria but statistically not related to tremors in farmers exposed to pesticides.

Introduction

Pesticides had been used widely in agricultural fields to increase crop and food production in Indonesia. Farmers have been using it to control pests and diseases of the crops. In the last three decades, pesticide uses have been increasing extensively [1]. These overuses could lead to many medical problems, including neurological problems [2]. Cholinesterase inhibitors pesticide (i.e., organophosphates and carbamates) are known to reduce the activity of acetylcholinesterase (AChE) [3]. This will result in the increase of acetylcholine concentration in the synapse, which will lead to some nicotinic and muscarinic symptoms and central–peripheral nervous system toxicity [4].

One area known to have significant pesticide poisoning problems is Ngablak, a district in Magelang Regency, Central Java, Indonesia. A previous study showed that 99.8% of farmers in this area had pesticide intoxication ranged from mild to severe [5]. Another study performed in the region showed that 76.47% of farmers classified as having pesticide poisoning by cholinesterase examination. Almost 90% of the farmers (75%) did not handle the pesticide correctly [6].

Exposure to pesticide during their application usually causes reversible neurotoxic effects but can also be deadly. The influence of pesticides on the nervous system may be involved in acute toxicity, or it can also contribute to chronic neurodegenerative disorders, especially Parkinson’s disease [7], [8], [9]. Some of the chronic effects of pesticide poisoning are weight loss, anorexia, amnesia, tremors, headache, dizziness, anxiety, psychological disorders, chest pain, irritability, and cognitive impairment. Organophosphate pesticides that
enter the human body affect nerve function by blocking the enzyme cholinesterase, an essential chemical in delivering impulses along nerve fibers. Thus, one of the effects of pesticide poisoning is the occurrence of disorders of the nervous system, including the central and peripheral nervous system [9]. Pesticides, including organophosphate and organochlorine, have also been shown to be associated with tremor [10].

The objective of this study was to evidence the role of pesticide exposure on the emergence of neurological signs and symptoms, especially neuropathy and tremor, in farmers in Ngablak District, Magelang Regency, Central Java Province.

Methods

Subject selection

This study was an observational analytic study with a cross-sectional design to identify the effect of pesticide exposure, measured through blood cholinesterase levels, on the emergence of neurological signs and symptoms in farmers in Ngablak District, Magelang Regency, Central Java Province, Indonesia. One of the villages in the region, Seloprojo Village, was randomly selected as a study location. The inclusion criteria in this study were: (1) Farmers aged at least 21 years in Seloprojo Village who use pesticides in their agricultural practices and (2) willing to be the subject of research by signing an informed consent after getting an explanation from the research team. Meanwhile, the exclusion criteria in this study were: (1) Having a history of diabetes mellitus, (2) suffering from Parkinson’s disease, (3) dementia patients, and (4) chronic alcoholic drinkers.

Measurement of variables

This study used a structured interview questionnaire regarding demographic data, clinical conditions of neuropathy, and risk factors for neuropathy due to exposure to pesticides. Assessment of exposure to pesticides was determined using a questionnaire. A medical examination was done once with the main focus being a neurological examination. The neurological examination consisted of history taking and examination of sensory function, motor strength, physiological reflexes, pathological reflexes, diabetic neuropathy symptom (DNS) score, diabetic neuropathy examination (DNE) score, and tremor rating scale (TRS). Although DNS and DNE were originally developed to detect neuropathy in diabetics, it can also be used to detect neuropathy caused by other reasons. Cholinesterase levels were examined using venous blood samples, which were processed in a private laboratory to determine the level of pesticide poisoning in the research subjects’ blood.

Statistical analysis

All data were validated, encoded, recapitulated, and tabulated with means and standard deviation (SD), then entered in the computer using a statistical program. The study received approval from the Health Research Ethics Committee, Faculty of Medicine, Universitas Gadjah Mada.

Results

Subject characteristics

In total, 120 subjects were included in this study with an average age of 48.1 ± 13.6 years. According to gender groups, 93 subjects (77.5%) were male. Most subjects were elementary school graduates (60.8%). Subjects with normal nutritional status (BMI = 18.5–22.5) were 46.7%, overweight (BMI > 22.5) were 46.7%, and only 6.7% had underweight nutritional status (BMI < 18.5). Of all subjects, the average length of work as a farmer was 24.05 ± 15.6 years, with the number of working hours of 6.3 ± 2.3 h/day (Table 1).

Of the 120 farmers studied, 68.3% experienced pesticide poisoning with cholinesterase levels below normal values. Most of the farmers in this study were not in compliance with the use of personal protective equipment (PPE); there were 67 subjects (55.8%) who never used PPE, and only 30 subjects (25%) sometimes used PPE. While according to the duration of using pesticides, there were 82 subjects (68.33%) who used pesticide sprays over 10 years. The majority of farmers (78.3%) spray pesticides routinely with a frequency of 1–2 times/week (Table 1).

Neurological disorders with weakness of the upper limb were found in 10 subjects (8.33%), weakness of the lower limbs was found in 6 subjects (5%). To determine the incidence of neuropathy in subjects, DNS and DNE scoring was used. From the 120 farmers, there were 59.2% who met the neuropathy criteria from the DNS score and those who met the neuropathic criteria from the DNE score were 6.7%. The presence or absence of tremors was measured by the Tremor Rating Scale. Of the 120 farmers, 71.7% had tremor symptoms.

Statistical analysis

Table 2 shows the factors that influence DNS score. It was found that some of the behaviors related to the application spraying of pesticides did
Table 1: Descriptive data of research subjects (n = 120)

| Variable                          | n (%)       | Mean (SD)     |
|-----------------------------------|-------------|---------------|
| Age (years)                       | 48.1 (13.6) |               |
| Sex                               |             |               |
| Male                              | 93 (77.5)   |               |
| Female                            | 27 (22.5)   |               |
| Level of education                |             |               |
| No school                         | 17 (14.2)   |               |
| Graduated from elementary school  | 73 (60.8)   |               |
| Graduated from junior high school | 22 (18.3)   |               |
| Graduated from senior high school | 8 (6.7)     |               |
| Length of work as farmers, years  | 24.05 (15.6)|               |
| Number of hours of work, hours/day| 6.3 (2.3)   |               |
| Nutritional status                |             |               |
| Underweight                       | 8 (6.7)     |               |
| Normal                            | 56 (46.7)   |               |
| Overweight                        | 56 (46.7)   |               |
| Compliance using PPE              |             |               |
| Never                             | 67 (55.8)   |               |
| Sometimes                         | 30 (25)     |               |
| Always                            | 23 (19.2)   |               |
| Duration of using pesticides:     |             |               |
| < 1 year                          | 8 (6.6)     |               |
| 1–5 years                         | 14 (11.7)   |               |
| 5–10 years                        | 15 (12.5)   |               |
| >10 years                         | 82 (68.3)   |               |
| Frequency of spraying/week        |             |               |
| ≥2 times                          | 6 (5)       |               |
| 1–2 times                         | 94 (78.3)   |               |
| <1 time                           | 20 (16.7)   |               |
| Duration of spraying/day          |             |               |
| <5 h                              | 108 (90)    |               |
| >5 h                              | 12 (10)     |               |
| Upper limb weakness               | 10 (8.33)   |               |
| Lower limb weakness               | 6 (5)       |               |
| Cholinesterase levels             |             |               |
| Normal                            | 38 (31.7)   |               |
| Below normal                      | 82 (68.3)   |               |
| Upper limb weakness               | 10 (8.33)   |               |
| Lower limb weakness               | 6 (5)       |               |
| DNS examination                   |             |               |
| Neuropathy                        | 71 (59.2)   |               |
| No neuropathy                     | 49 (40.8)   |               |
| DNE examination                   |             |               |
| Neuropathy                        | 8 (6.7)     |               |
| No neuropathy                     | 112 (93.3)  |               |
| Tremor examination                |             |               |
| Tense                              | 86 (71.7)   |               |
| Non-tense                          | 34 (28.3)   |               |
| Blood cholinesterase levels       |             |               |
| Normal                            | 38 (31.7)   |               |
| Below normal                      | 82 (68.3)   |               |

Table 2: Factors that affect neuropathy as assessed by DNS score

| Variable                          | DNS results | Ratio (95% CI) | p-value | Average difference (95% CI) |
|-----------------------------------|-------------|----------------|---------|-----------------------------|
| Mean age, years (SD)              |             |                |         |                             |
| Sex                               |             |                |         |                             |
| Male                              | 51          | 42             | 0.740 (0.554–0.989) | 0.073 |                      |
| Female                            | 20          | 7              |         |                             |
| Smoking status:                   |             |                |         |                             |
| Non-smoker                        | 28          | 13             | 0.338   |                             |
| Former smoker                     | 4           | 3              |         |                             |
| Smoker                            | 39          | 33             |         |                             |
| Mean BMI, years (SD)              | 22.9 (3.57) | 22.8 (3.25)    | 0.979   |                             |
| Nutritional status                |             |                |         |                             |
| Underweight                       | 5           | 3              | 0.911   |                             |
| Normal                            | 32          | 24             |         |                             |
| Overweight                        | 34          | 22             |         |                             |
| Level of education                |             |                |         |                             |
| No school                         | 10          | 7              | 0.542   |                             |
| Graduated from elementary school  | 40          | 33             |         |                             |
| Graduated from junior high school | 15          | 7              |         |                             |
| Graduated from high school        | 6           | 2              |         |                             |
| Mean length of work as farmers, years (SD) | 23.86 (15.27) | 24.32 (16.29) | 0.924 | -6.25–5.34                             |
| Mean number of hours of work, hours/day (SD) | 6.04 (2.43) | 6.77 (2.21) | 0.065 | -1.59–0.133                             |
| Spraying frequency /week           |             |                |         |                             |
| <1x                               | 12          | 10             |         |                             |
| ≥1x                               | 59          | 39             | 0.804   |                             |
| Duration of spraying/day          |             |                |         |                             |
| <5 h                              | 66          | 42             | 0.161   |                             |
| >5 h                              | 5           | 7              |         |                             |
| Compliance using PPE              |             |                |         |                             |
| Never                             | 37          | 30             | 0.480   |                             |
| Sometimes                         | 18          | 12             |         |                             |
| Always                            | 16          | 7              |         |                             |
| Mean cholinesterase Levels, U/L (SD) | 8.74 (1.89) | 8.86 (1.66) | 0.737 | -0.69 – 0.63                             |
| Cholinesterase levels             |             |                |         |                             |
| Normal                            | 22          | 16             | 0.847   |                             |
| Below normal                      | 49          | 33             |         |                             |

* Significant (p < 0.05): DNS: Diabetic neuropathy symptom; BMI: Basal metabolic index; CI: Confidence interval
The use of pesticides has become commonplace for Indonesian farmers to maintain the quality of crops. However, improper methods of use and a lack of knowledge about pesticides result in excessive exposure of farmers. Of the 120 farmers studied, 68.3% of farmers experienced pesticide poisoning with cholinesterase levels below normal values. This is similar to the Prijanto study [5] performed in the same region showing 71.02% of farmers had been poisoned. Many studies had shown significantly lower cholinesterase levels in pesticide users compared with non-pesticide users [11, 12, 13]. A new study found that the reduction of cholinesterase was not only caused by organophosphate or carbamate [14]. Farmers who used pesticides other than organophosphate or carbamate also had lower cholinesterase levels compared with the unexposed group [15]. The proposed mechanism was organophosphate and organochlorine inhibits pseudocholinesterase in plasma, cholinesterase in red blood cells, and in the synapse, which at certain levels cause poisoning.

In this study, 59.2% of subjects had symptoms of neuropathy identified by DNS. This is higher than

Table 3: Factors that affect neuropathy as assessed by DNE score

| Variable                              | DNE results             | Ratio (95% CI) | p-value | Average difference (95% CI) |
|---------------------------------------|-------------------------|----------------|---------|-----------------------------|
|                                       | Neurpathy               | Normal         |         |                             |
| Mean age, years (SD)                  | 53 (19.3)               | 47.75 (13.15)  | 0.577   | −10.94–21.44                |
| Sex                                   |                         |                |         |                             |
| Male                                  | 6                       | 87             | 0.871 (0.186–4.070) | 1.000 |
| Female                                | 2                       | 25             |         |                             |
| Smoker status                         |                         |                |         |                             |
| Non-smoker                            | 2                       | 39             | 0.646   |                             |
| Former Smoker                         | 1                       | 6              |         |                             |
| Smoker                                | 5                       | 67             |         |                             |
| Mean BMI, years (SD)                  | 22.3 (2.19)             | 22.9 (3.51)    | 0.788   | −3.03–1.95                  |
| Nutritional status                    |                         |                |         |                             |
| Underweight                           | 0                       | 8              | 0.736   |                             |
| Normal                                | 4                       | 52             |         |                             |
| Overweight                            | 4                       | 52             |         |                             |
| Level of education                    |                         |                |         |                             |
| No school                             | 0                       | 17             | 0.553   |                             |
| Graduated from elementary school      | 6                       | 67             |         |                             |
| Graduated from junior high school     | 1                       | 21             |         |                             |
| Graduated from high school            | 1                       | 7              |         |                             |
| Mean length of work as farmers, years (SD) | 33 (22.91)             | 23.4 (14.92)   | 0.279   |                             |
| Mean number of hours of work, hours/day (SD) | 7.37 (2.66)             | 6.27 (2.33)    | 0.203   |                             |
| Spraying frequency/week               |                         |                |         |                             |
| <1x                                   | 7                       | 91             | 1.000   |                             |
| ≥1x                                   | 1                       | 21             |         |                             |
| Duration of spraying/day              |                         |                |         |                             |
| <5 h                                  | 8                       | 100            | 0.714   |                             |
| ≥5 h                                  | 0                       | 12             |         |                             |
| Compliance using PPE                  |                         |                |         |                             |
| Never                                 | 4                       | 67             | 0.903   |                             |
| Sometimes                             | 2                       | 28             |         |                             |
| Always                                | 2                       | 21             |         |                             |
| Mean cholinesterase Levels, U/L (SD)  | 7.63 (0.805)            | 8.83 (1.82)    | 0.046*  | −1.92–0.48                  |
| Cholinesterase level                  |                         |                |         |                             |
| Normal                                | 0                       | 38             | 0.046*  |                             |
| Below normal                          | 8                       | 74             |         |                             |

*Significant (p < 0.05); DNS: Diabetic neuropathy symptom, BMI: Basal metabolic index, CI: Confidence interval, PPE: Personal protective equipment

Table 4: Bivariate analysis of the results from the tremor rating scale

| Variable                              | Tremor rating scale       | Ratio (95% CI) | p-value | Average difference (95% CI) |
|---------------------------------------|---------------------------|----------------|---------|-----------------------------|
|                                       | Non-tremor                |                |         |                             |
| Mean age, years (SD)                  | 48.17 (13.58)             | 47.91 (13.86)  | 0.896   | −5.21–5.17                  |
| Sex                                   |                          |                |         |                             |
| Male                                  | 69                       | 24             | 1.178 (0.862–1.612) | 0.254 |
| Female                                | 17                       | 10             |         |                             |
| Smoker status                         |                          |                |         |                             |
| Non-smoker                            | 29                       | 12             | 0.697   |                             |
| Former Smoker                         | 6                        | 1              |         |                             |
| Smoker                                | 51                       | 21             |         |                             |
| Nutritional status                    |                          |                |         |                             |
| Underweight                           | 8                        | 0              | 0.083   |                             |
| Normal                                | 42                       | 14             |         |                             |
| Overweight                            | 36                       | 20             |         |                             |
| Level of education                    |                          |                |         |                             |
| No school                             | 14                       | 3              | 0.300   |                             |
| Graduated from elementary school      | 52                       | 21             |         |                             |
| Graduated from junior high school     | 13                       | 9              |         |                             |
| Graduated from high school            | 7                        | 1              |         |                             |
| Compliance using PPE                  |                          |                |         |                             |
| Never                                 | 46                       | 21             | 0.660   |                             |
| Sometimes                             | 22                       | 8              |         |                             |
| Always                                | 18                       | 8              |         |                             |
| Mean cholinesterase Levels, U/L (SD)  | 8.60 (1.64)              | 9.13 (2.11)    | 0.204   | −1.25–0.17                  |
| Cholinesterase level                  |                          |                |         |                             |
| Normal                                | 24                       | 14             | 0.159   |                             |
| Below normal                          | 62                       | 20             |         |                             |

CI: Confidence interval, PPE: Personal protective equipment

Discussion

The use of pesticides has become commonplace for Indonesian farmers to maintain the quality of crops. However, improper methods of use and a lack of knowledge about pesticides result in excessive exposure of farmers. Of the 120 farmers studied, 68.3% of farmers experienced pesticide poisoning with cholinesterase levels below normal values. This is similar to the Prijanto study [5] performed in the same region showing 71.02% of farmers had been poisoned. Many studies had shown significantly lower cholinesterase levels in pesticide users compared with non-pesticide users [11, 12, 13]. A new study found that the reduction of cholinesterase was not only caused by organophosphate or carbamate [14]. Farmers who used pesticides other than organophosphate or carbamate also had lower cholinesterase levels compared with the unexposed group [15]. The proposed mechanism was organophosphate and organochlorine inhibits pseudocholinesterase in plasma, cholinesterase in red blood cells, and in the synapse, which at certain levels cause poisoning.

In this study, 59.2% of subjects had symptoms of neuropathy identified by DNS. This is higher than
a previous study that showed 37% of farm sprayers complained of sensory symptoms. Other studies from the US and UK showed that intermittent sensory symptoms, mainly in the form of the glove and stocking, were found in 2 to 31% of exposed cases. Signs of neuropathy as assessed by DNE were found in 6.7% of subjects in this study. This is lower compared to a previous study which showed 16% of the subjects had sensory signs. Our study showed that 8% of the farmers have upper extremity weakness and 5% have lower extremity weakness. This is in line with previous studies showing that 0 to 21% of farm sprayers complained of motor weakness [16].

This study showed that blood cholinesterase level, a stable marker of pesticide poisoning, was significantly associated with neuropathy incidence measured with DNE criteria. Cholinesterase inhibitors pesticide (i.e., organophosphates and carbamates) are known to reduce the activity of acetylcholinesterase (AChE) [3]. This will result in the increase of acetylcholine concentration in the synapse which will lead to some nicotinic and muscarinic symptoms and central–peripheral nervous system toxicity [4]. These effects on acetylcholine in synapse could release a high number of glutamate and causing neuronal death because of glutamate excitotoxicity [17]. The mechanism of neuropathy by organophosphate and carbamate usually begins with axonal degeneration followed by secondary demyelination [18]. Organophosphate can also cause delayed neuropathy, which is called Organophosphate-induced Delayed Neuropathy (OPIDN). It is caused by a progressive distal axonopathy of peripheral nerves and spinal cord [19]. The most common cause of OPIDN was acute high-dose intoxication [19]. A chronic low-dose effect on neuropathy has also been proposed.

Pesticide poisoning occurs due to a lack of awareness in the use of PPE and low knowledge concerning the risks of pesticides. One factor that plays a role in causing a decrease in the level of cholinesterase is the length of work as a farmer. In general, the longer working time as a farmer, the greater the level of exposure to pesticides [20]. The duration of exposure to pesticides is also influenced by the frequency of spraying and the use of PPE. If spraying is done with high frequency without being equipped with the use of PPE, then it can affect blood cholinesterase levels in farmers even though the duration of spraying is less than 5 h/day [20]. According to Samosir et al., farmers who worked longer than 5 h/day had 2.6 times higher risk to experience balance disorders compared to farmers who worked less than 5 hours per day [21]. Our study did not show an association between duration of exposure, length of spraying per day, and frequency of spraying with the incidence of neuropathy. This will require further study.

Pesticides, including organophosphate and organochlorine, have also been shown to be associated with tremor [10]. However, our study did not show this association. This will also need further study.

Conclusion

This study showed that pesticide poisoning as measured by blood cholinesterase level is associated with neuropathy incidence measured with DNE criteria but statistically not related to tremors in farmers exposed to pesticides.

Acknowledgment

The authors would like to thank all of the residents at the Department of Neurology, Universitas Gadjah Mada, for their help during the study.

References

1. Abang AF, Kouame CM, Abang M, Hanna R, Photos AK. Assessing vegetable farmer knowledge of diseases and insect pests of vegetable and management practices under tropical conditions. Int J Vegetable Sci. 2014;20(3):240-53. https://doi.org/10.1080/19315260.2013.800625
2. Munoz-Quezada MT, Luco BA, Iglesias VP, Muñoz MP, Cornejo CA, Achu E, et al. Chronic exposure to organophosphate (OP) pesticides and neuropsychological functioning in farm workers: A review. Int J Occup Environ Health. 2016;22(1):68-79. https://doi.org/10.1080/10773525.2015.1123848
3. Suarez-Lopez JR, Checkoway H, Jacobs DR Jr., Al-Delaimy WK, Ghagah SC, Potential short-term neurobehavioral alterations in children associated with a peak pesticide spray season: The mother’s day flower harvest in Ecuador. Neurotoxicology. 2017;60:125-33. https://doi.org/10.1016/j.neuro.2017.02.002
4. Perwitasari DA, Prasasti D, Supadmi W, Jaikishin SA, Wiriaangi IA. Impact of organophosphate exposure on farmers’ health in Kulon Progo, Yogyakarta: Perspectives of physical, emotional and social health. SAGE Open Med. 2017;5:1-6. https://doi.org/10.1177/2050312117719092
5. Prihadi P, Faktor-Faktor Yang Berhubungan Dengan Efek Kronis Keracunan Pestisida Organofosfat Pada Petani Sayuran di Kecamatan Ngablak Kabupaten Magelang, Masters Thesis, Universitas Diponegoro; 2008.
6. Prihadi P, Faktor-Faktor Yang Berhubungan Dengan Efek Kronis Keracunan Pestisida Organofosfat Pada Petani Sayuran di Kecamatan Ngablak Kabupaten Magelang, Masters Thesis, Universitas Diponegoro; 2008.
7. Ascherio A, Chen H, Weisskopf MG, O’Reilly E, McCullough ML, Calle EE, et al. Pesticide exposure and risk of Parkinson’s disease. Ann Neurol. 2006;60(2):197-203. https://doi.org/10.1002/ana.20904
8. Smeiney RJ, Jackson-Lewis V. The MPTP model of Parkinson’s disease. Brain Res Mol Brain Res. 2005;134(4):57-66. https://doi.org/10.1016/j.molbrainres.2004.09.017
9. Colosio C, Tiramani M, Maroni M. Neurobehavioral effects of pesticides: State of the art. Neurotoxicology. 2003;24(4-5):577-91. https://doi.org/10.1016/s0161-813x(03)00055-x PMid:12900071

10. Nerilo SB, Martins FA, Nerilo LB, Salvadego VE, Endo RY, Rocha GH, et al. Pesticide use and cholinesterase inhibition in small-scale agricultural workers in Southern Brazil. Braz J Pharm Sci. 2014;50(4):783-91. https://doi.org/10.1590/s1984-82502014000400014

11. Louis ED, Factor-Litvac P, Parides M, Andrews L, Santella RM, Wolff MS. Organochlorine pesticide exposure in essential tremor: A case-control study using biological and occupational exposure assessments. Neurotoxicology. 2006;27(4):579-86. https://doi.org/10.1016/j.neuro.2006.03.005 PMid:16620996

12. Kori RK, Hasan W, Jain AK, Yadav RS. Cholinesterase inhibition and its association with hematological, biochemical and oxidative stress markers in chronic pesticide exposed agriculture workers. J Biochem Mol Toxicol. 2019;33(9):e22367. https://doi.org/10.1002/jbt.22367

13. Pothu UK, Thammisetty AK, Nelakuditi LK. Evaluation of cholinesterase and lipid profile levels in chronic exposed persons. J Fam Med Prim Care. 2019;8(6):2073-8. https://doi.org/10.4103/jfmpc.jfmpc_239_19 PMid:31334182

14. Lozano-Paniagua D, Gomez-Martín A, Gil F, Parron T, Alarcon R, Requena M, et al. Activity and determinants of cholinesterases and paraoxonase-1 in blood of workers exposed to non-cholinesterase inhibiting pesticides. Chem Biol Interact. 2016;259(B):160-7. https://doi.org/10.1016/j.cbi.2016.04.008 PMid:27062891

15. Pathak MK, Fareed M, Bihari V, Reddy MM, Patel DK, Mathur N, et al. Nerve conduction studies in sprayers occupationally exposed to mixture of pesticides in a mango plantation at Lucknow, North India. Toxicol Environ Chem. 2011;93(1):186-96. https://doi.org/10.1080/02772248.2010.496587

16. Boostani R, Mallat A, Afsari R, Derakhshan S, Saeedi M, Rafeemanesh E, et al. Delayed polyneuropathy in farm sprayers due to chronic low dose pesticide exposure. Iran Red Crescent Med J. 2014;16(5):e5072. PMid:25031861

17. Figureiredo TH, Apland JP, Braga MF, Marini AM. Acute and long-term consequences of exposure to organophosphate nerve agents in humans. Epilepsia. 2018;59 Suppl 2:92-9. https://doi.org/10.1111/epi.14500 PMid:30159887

18. Lotti M, Moretto A. Organophosphate-induced delayed polyneuropathy. Toxicol Rev. 2005;24(1):37-49. https://doi.org/10.2165/00139709-200524010-00003 PMid:16042503

19. Albers JW, Garabrant DH, Schweitzer SJ, Garrison R, Richardson R, Berent S. The effects of occupational exposure to chlorpyrifos on the peripheral nervous system: A prospective cohort study. Occup Environ Med. 2004;61(3):201-11. https://doi.org/10.1136/oom.2003.008847 PMid:14985514

20. Budiawan AR. Risk factors associated with cholinesterase in shallot farmers in Nguresiti Pati. Unnes J Public Health. 2014;3(1):353.

21. Samosir K, Setiani O, Nurjazuli N. Association between pesticide exposure and disturbance of body balance of horticultural farmers in Ngablak Sub-district, Magelang Regency. J Kesehatan Lingkungan Indones. 2017;16(2):63-9.