

A systematic review and meta-analysis

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Introduction

Organophosphate and pyrethroid pesticides:
Most common types of insecticides used globally

Organophosphate (OP) pesticides:
Chlorpyrifos, malathion, parathion and diazinon

Pyrethroid (PY) pesticides:
Pyrethrin, cypermethrin, permethrin, deltamethrin, transfluthrin

Neurological effects: Exposure to these pesticides are known to effect neurological status

Synergistic effect: Exposure to both the OP and PYR pesticides is largely common, due to their synergistic mechanism of pest control

Additive exposure: Additive neurotoxic effects on exposure to these pesticides have been reported

Mechanism of neurotoxicity: OP pesticides
Blocking the β -cholinesterase enzymes acetyl cholinesterase (AChE) and butyryl cholinesterase (BChE), resulting in the accumulation of acetylcholine, causing neurological and cholinergic manifestations

Mechanism of neurotoxicity: PYR pesticides
Targeting the sodium channels in the nervous system and modulating the nerve potentials

Need of the study:
Combined study of the neurological effects of OP and PYR pesticides is lacking

Objective

To analyse the neurotoxic effects of combined exposure to OP and PYR pesticides, in view of their neurological and neurobehavioral manifestations, through:

- ✓ Systematic Review
- ✓ Meta-analysis

Materials and Methods

PubMed and Scopus

Studies assessing the neurological symptoms and/or neurobehavioral manifestations among the patients who were exposed to combination of OP and PYR pesticides.

Inception to February, 2024

Population (P) Exposure (E) Outcome (O)
MeSH terms: "organophosphate", "pyrethroid", "neurological manifestations"

Author; year; Study Region; Design; Participants; age; sex; The categorical results from individual studies for each group, with respect to the neurological symptom: seizures, along with other neurological symptoms: 'feeling depressed', 'difficulty in concentration', 'difficulty in understanding', 'troubles in remembering', 'feeling irritable' and 'headache' were collected in terms of frequency or percentage

Risk of Bias by JBI and New Castle Ottawa scale

Evidence synthesis Methods

The categorical results from individual studies were collected in terms of frequency with percentage and the continuous data was collected as mean with standard deviation or median with interquartile range

The evidence was synthesized narratively from the available data and it was presented in tabular form

Cochrane Review Manager Software (RevMan web) was used for conducting the meta-analysis

Pooled data was presented as Risk Ratio (RR) with a 95% Confidence Interval (CI).

Statistical heterogeneity of data was assessed using the I2 statistic and Cochrane P-value.

Publication bias was not conducted due to less than three studies in each pooled analysis.

Results

Records identified from:

- Databases (N = 730)
- PubMed (n = 27)
- Scopus (n = 309)
- Embase (n = 394)

Records **Screened** (N = 695)

Reports sought for **Retrieval** (N = 108)

Reports assessed for **Eligibility** (N = 108)

Studies included in **Systematic Review** (N = 8)

Studies included in **Meta-analysis** (N = 4)

Duplicate Records Removed (N = 35)

Records Excluded (N = 587)

Records Excluded (N = 100) Reasons:

- Animal Study (n = 13)
- Method development (n = 2)
- Not outcome of interest (n = 11)
- Either OP or PYR, not a combination (n = 20)
- Duplicate (n = 5)
- Book chapter (n = 3)
- Plant study (n = 2)
- Review (n = 12)
- Pesticides other than OP and PYR (n = 32)

Results

The eight included studies (Callender, 1994; Iyyadurai, 2014; Fiedler, 2015; Motsoeneng, 2015; Srinivasan 2016; Ismail, 2017; Yusuf, 2022 and Wu, 2023) were published between the years 1994 to 2023 and originated from India (n=2), United states (n=1), South Africa (n=1), Egypt (n=1), Malaysia (n=1) Thailand (n=1) and Taiwan (n=1). Three studies were prospective observational cohort studies, one study was a retrospective cohort study, two studies were analytical cross-sectional studies, and two were case reports.

Study or Subgroup	Exposed group		Non-exposed group		Weight	Risk ratio		Risk ratio	
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI		
Ismail, 2017 (2005)	13	41	2	38	27.1%	6.02	[1.45, 24.97]		
Ismail, 2017 (2009)	4	21	1	20	16.4%	3.81	[0.46, 31.23]		
Motsoeneng, 2015	62	121	30	90	56.5%	1.54	[1.09, 2.16]		
Total (95% CI)	79	183	33	148	100.0%	2.58	[0.95, 7.01]		
Total events: 79 Heterogeneity: Tau ² = 0.43; Chi ² = 4.23, df = 2 (P = 0.12); I ² = 53% Test for overall effect: Z = 1.85 (P = 0.06) Test for subgroup differences: Not applicable									

(a)

Study or Subgroup	Exposed group		Non-exposed group		Weight	Risk ratio		Risk ratio	
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI		
Ismail, 2017 (2005)	12	41	2	38	31.5%	5.56	[1.33, 23.25]		
Ismail, 2017 (2009)	1	21	0	20	10.6%	2.86	[0.12, 66.44]		
Motsoeneng, 2015	34	121	20	90	57.8%	1.26	[0.79, 2.04]		
Total (95% CI)	47	183	22	148	100.0%	2.20	[0.72, 6.76]		
Total events: 47 Heterogeneity: Tau ² = 0.51; Chi ² = 4.06, df = 2 (P = 0.13); I ² = 51% Test for overall effect: Z = 1.38 (P = 0.17) Test for subgroup differences: Not applicable									

(b)

Study or Subgroup	Exposed group		Non-exposed group		Weight	Risk ratio		Risk ratio	
	Events	Total	Events	Total		M-H, Fixed, 95% CI	M-H, Fixed, 95% CI		
Ismail, 2017 (2005)	11	41	2	38	9.7%	5.10	[1.21, 21.53]		
Ismail, 2017 (2009)	2	21	1	20	4.8%	1.90	[0.19, 19.40]		
Motsoeneng, 2015	31	121	16	90	85.5%	1.44	[0.84, 2.47]		
Total (95% CI)	44	183	19	148	100.0%	1.82	[1.12, 2.95]		
Total events: 44 Heterogeneity: Chi ² = 2.68, df = 2 (P = 0.26); I ² = 25% Test for overall effect: Z = 2.41 (P = 0.02) Test for subgroup differences: Not applicable									

(c)

Study or Subgroup	Exposed group		Non-exposed group		Weight	Risk ratio		Risk ratio	
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI		
Ismail, 2017 (2005)	12	41	1	38	25.9%	11.12	[1.52, 81.50]		
Ismail, 2017 (2009)	4	21	1	20	24.5%	3.81	[0.46, 31.23]		
Motsoeneng, 2015	32	121	16	90	49.6%	1.32	[0.79, 2.20]		
Total (95% CI)	48	183	20	148	100.0%	2.98	[0.72, 12.31]		
Total events: 48 Heterogeneity: Tau ² = 0.99; Chi ² = 5.34, df = 2 (P = 0.07); I ² = 63% Test for overall effect: Z = 1.51 (P = 0.13) Test for subgroup differences: Not applicable									

(d)

Study or Subgroup	Exposed group		Non-exposed group		Weight	Risk ratio		Risk ratio	
	Events	Total	Events	Total		M-H, Fixed, 95% CI	M-H, Fixed, 95% CI		
Ismail, 2017 (2005)	11	41	1	38	3.8%	10.20	[1.38, 75.26]		
Ismail, 2017 (2009)	4	21	1	20	3.8%	3.81	[0.46, 31.23]		
Motsoeneng, 2015	59	121	22	90	92.4%	1.99	[1.33, 3.00]		
Total (95% CI)	74	183	24	148	100.0%	2.37	[1.60, 3.51]		
Total events: 74 Heterogeneity: Chi ² = 2.94, df = 2 (P = 0.23); I ² = 32% Test for overall effect: Z = 4.33 (P < 0.0001) Test for subgroup differences: Not applicable									

(e)

Study or Subgroup	Exposed group		Non-exposed group		Weight	Risk ratio		Risk ratio	
	Events	Total	Events	Total		M-H, Fixed, 95% CI	M-H, Fixed, 95% CI		
Ismail, 2017 (2005)	15	41	9	38	15.7%	1.54	[0.77, 3.11]		
Ismail, 2017 (2009)	4	21	2	20	3.4%	1.90	[0.39, 9.28]		
Motsoeneng, 2015	105	121	42	90	80.9%	1.86	[1.48, 2.34]		
Total (95% CI)	124	183	53	148	100.0%	1.81	[1.45, 2.26]		
Total events: 124 Heterogeneity: Chi ² = 0.25, df = 2 (P = 0.88); I ² = 0% Test for overall effect: Z = 5.24 (P < 0.0001) Test for subgroup differences: Not applicable									

(f)

Risk of occurrence of other neurological symptoms (a) 'feeling depressed' (b) 'difficulty in concentration' (c) 'difficulty in understanding' (d) 'troubles in remembering' (e) 'feeling irritable' and (f) 'headache' between the exposed group compared to the non-exposed group

Discussion

Strength:

- the first systematic review and meta-analysis to systematically investigate the neurological effects of the combined exposure to OP and PYR pesticides.

Limitation:

- Limited research in the area of combined occupational exposure to OP and PYR pesticides. However, through our systematic analysis we have attempted to strengthen the limited evidence available in this area.

Conclusion

Neurological symptoms were found to be more prevalent in individuals exposed to the combination of OP and PYR pesticides, compared to non-exposed individuals. However, neurobehavioral performance was observed to be largely unaffected by the exposure of these pesticides in most of the studies. Occupational exposure to combination of OP and PYR pesticides significantly increased the risk of developing headaches, difficulty in comprehension and irritability.

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