Case Report

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Intermediate Syndrome After Organophosphate Poisoning: Clinical Course and a Case of Delayed Neuromuscular Dysfunction

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Abstract

Intermediate Syndrome (IMS) is a delayed neuromuscular complication of organophosphate poisoning, typically occurring 24–96 hours post-exposure and often leading to respiratory failure. The author reports a 39-year-old male who ingested 40% chlorpyrifos and developed IMS on day 4 post-ingestion, presenting with proximal muscle weakness, neck flexor involvement, and respiratory compromise. Laboratory tests revealed markedly decreased serum cholinesterase, and electromyography confirmed postsynaptic receptor desensitization with early proximal involvement. Pralidoxime was initially administered but discontinued after 48 hours due to early receptor desensitization. The patient received supportive care, including mechanical ventilation for eight days, physiotherapy, and structured follow-up. He regained independent walking by day 10 and was discharged on day 11. By integrating clinical, laboratory, electrophysiological, and follow-up data, this case highlights IMS progression and recovery, emphasizing the critical role of supportive care in resource-limited settings and providing valuable insights into its management.

Keywords: organophosphate poisoning; intermediate syndrome; cholinesterase inhibition; neuromuscular paralysis; respiratory failure

Introduction

Organophosphate (OP) poisoning is a major public health threat worldwide due to the widespread use of agricultural pesticides [1]. Globally, approximately three million pesticide poisonings occur each year, resulting in more than 30,000 deaths [2]. In Sub-Saharan Africa, OP poisoning is a significant health concern; Uganda reported 6,314 cases per year (2017–2022) with a 4.2% fatality rate [3]. In Ethiopia's Harari Region, 11% of OP-poisoned patients died during hospitalization [4]. Intermediate Syndrome (IMS) develops in about 20% of OP poisoning cases, typically 24–96 hours after exposure [5]. IMS is distinct from the acute cholinergic crisis, which is characterized by muscarinic signs such as bronchorrhea, bradycardia, and miosis. It is also distinct from Organophosphate-Induced Delayed Polyneuropathy (OPIDP), which appears 2–3 weeks later and mainly affects distal muscles [6]. Mortality among IMS patients with respiratory failure can reach 28.4% [7].

IMS results from persistent acetylcholine accumulation at the neuromuscular junction, causing nicotinic receptor desensitization and structural changes that impair muscle contraction and may lead to respiratory failure [8]. Diagnosis is often challenging because early symptoms can overlap with residual cholinergic effects [5]. Therefore, early recognition and timely supportive management, are essential for improving outcomes [2]. This case report highlights the practical challenges of managing IMS in a low-resource setting. It demonstrates the successful use of prolonged mechanical ventilation and comprehensive supportive care, emphasizing the real-world application of these management strategies. It also serves as a critical reminder for clinicians to remain vigilant for

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delayed complications of organophosphate poisoning, ensuring timely recognition and intervention to improve patient outcomes.

Case Presentation

A 39-year-old male farmer presented to the emergency department with acute respiratory distress, excessive salivation, sweating, and vomiting, three and a half hours after ingesting an unknown quantity of 40% emulsifiable chlorpyrifos in a suicide attempt. He was diagnosed with acute cholinergic toxicity and promptly treated with atropine and pralidoxime: atropine was given as 2 mg IV boluses every 10 minutes until signs of atropinization were achieved, followed by a continuous infusion of 0.02 mg/kg/hr; pralidoxime was administered as a 20 mg/kg IV loading dose over 30 minutes, followed by a continuous infusion of 10 mg/kg/hr. The acute cholinergic crisis resolved within 36 hours, at which point both atropine and pralidoxime were discontinued. However, he subsequently developed IMS, characterized by progressive proximal muscle weakness, neck flexor involvement, and respiratory muscle paralysis, peaking around 96 hours post-ingestion.

He had no prior medical or neurological conditions but had long-term occupational exposure to organophosphate pesticides due to agricultural work without protective equipment. He occasionally smoked and consumed alcohol. On presentation, his vital signs were: blood pressure 112/74 mmHg, heart rate 101 bpm, axillary temperature 37.2 °C, and respiratory rate 26 breaths/min. On examination, the patient had Medical Research Council (MRC) grade 2–3 weakness in proximal and distal limbs, indicating movement possible only when gravity is eliminated (grade 2) and movement against gravity but not resistance (grade 3). Lower limb reflexes were diminished. He demonstrated increased respiratory effort with wheezing and bilateral crepitations, mild cyanosis, hyperactive bowel sounds with mild abdominal tenderness, and tachycardia. Pupils were 2 mm and reactive. His mental status was altered, with a Glasgow Coma Scale (GCS) of 8/15 (E3V2M3). Laboratory findings after the onset of intermediate syndrome are summarized in the table below (Table 1).

Table 1. Laboratory Findings After the Onset of Intermediate Syndrome.

Test		Result	Normal Range	Notes
Arterial Blood Gas	pH	7.288	7.35–7.45	Mixed acidosis, hypoxia
	$PaCO_2$	41.9 mmHg	35–45 mmHg	
	PaO_2	65 mmHg	75–100 mmHg	
	O_2 Sat	87%	95–100%	
Hematology	WBC	26,980/mm³	4,000–11,000/mm³	Leukocytosis with neutrophilia, slightly low Hg
	Neutrophils	89%	40-70%	
	Hemoglobin (Hg)	11.7 g/dL	13.5–17.5 g/dL	
Biochemistry	Serum cholinesterase	2,570 U/L	4,900–11,900 U/L	Low cholinesterase, elevated liver enzyme, mild hypokalemia, elevated serum lipase
	ALT	151 U/L	7–56 U/L	
	Potassium (K^+)	3.0 mmol/L	3.5–5.0 mmol/L	
	Serum lipase	770 U/L	0–160 U/L	

Peripheral blood smear showed normocytic, slightly hypochromic red blood cells. Urine analysis was positive for organophosphate metabolites, confirming exposure. Chest X-ray revealed mild pulmonary infiltrates and areas of lung collapse, while computed tomography of the head showed no acute abnormalities. Electromyography (EMG) of proximal (biceps brachii) and distal (extensor digitorum) muscles showed reduced compound muscle action potentials (CMAP) amplitudes (2.1–2.5 mV; normal 5–10 mV), prolonged distal latencies (7.2–7.8 ms; normal 4–6 ms), and a >10% decrement on repetitive nerve stimulation at 3 Hz, confirming postsynaptic receptor desensitization. No spontaneous fibrillation potentials were observed. The patient was diagnosed with IMS, supported by markedly decreased serum cholinesterase, positive urine analysis, and EMG findings.

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The patient was treated with atropine and pralidoxime. Atropine was administered as an IV bolus of 2 mg every 10 minutes until clinical signs of atropinization were achieved (resolution of bronchorrhea, stabilization of heart rate, and pupil dilation), followed by a continuous IV infusion at 0.02 mg/kg/hr, titrated according to clinical response. Pralidoxime was given as a 20 mg/kg IV loading dose over 30 minutes, followed by a continuous infusion of 10 mg/kg/hr for 48 hours, after which it was discontinued due to ongoing acetylcholine receptor desensitization limiting its efficacy during the IMS phase. The patient developed respiratory failure and received mechanical ventilation and oxygen therapy. Intravenous fluids (0.9% normal saline at 2 mL/kg/hr) were administered to maintain hydration and electrolyte balance. Supportive care, including physiotherapy, was provided to prevent complications and promote neuromuscular recovery. As cholinergic symptoms improved, the atropine infusion was gradually tapered over five days.

By day 4, the patient showed early signs of muscle recovery and improved respiratory function. He was successfully weaned off mechanical ventilation on day 8 and regained independent walking by day 10. Neuromuscular function and cholinesterase levels stabilized. He was discharged on day 11 with monthly outpatient and psychiatric follow-up, counseling to prevent self-harm, advice to avoid further organophosphate exposure, and ongoing physiotherapy.

Discussion

Organophosphate poisoning is a significant public health concern, particularly in agricultural settings where these pesticides are widely used [6]. According to the World Health Organization (WHO), approximately three million pesticide poisonings occur worldwide each year, resulting in more than 40,000 deaths [5]. IMS is a delayed neuromuscular complication that usually arises 24–96 hours post-exposure [9]. It is characterized by proximal muscle weakness, respiratory muscle involvement, and cranial nerve dysfunction, often requiring intensive care and mechanical ventilation in severe cases. The severity of OP poisoning varies according to the type, dose, and route of exposure [10]. In this case, a 39-year-old male farmer developed IMS four days after chlorpyrifos ingestion, consistent with previously reported timelines.

Patients with IMS commonly present with proximal limb weakness, difficulty lifting the arms or climbing stairs, ocular symptoms such as ptosis and ophthalmoplegia, and respiratory compromise that may require ventilatory support [11]. Deep tendon reflexes are often diminished. IMS can be classified into classic (generalized proximal weakness with cranial nerve involvement), respiratory (predominant respiratory muscle weakness requiring oxygen or ventilation), and neurological (rare, with altered consciousness or seizures) subtypes [3,6]. This patient exhibited both classic and respiratory IMS features, requiring mechanical ventilation for eight days until recovery.

Diagnosis relies on clinical assessment, a history of OP exposure, and the delayed onset of neuromuscular symptoms [2,5]. Laboratory evaluation revealed markedly decreased serum cholinesterase, confirming exposure [1,6,7]. EMG of proximal and distal muscles demonstrated reduced CMAP amplitudes, prolonged distal latencies, and a >10% decrement on repetitive stimulation, indicating postsynaptic receptor desensitization and early proximal muscle involvement [12]. Compared with previous cases, the findings were similar—particularly the critical 72–96-hour window when EMG changes in IMS first appear [13]. In our patient, strong clinical suspicion and EMG testing within this period provided objective confirmation of neuromuscular dysfunction, supporting the diagnosis and guiding timely management.

The pathophysiology of IMS involves persistent acetylcholinesterase inhibition, leading to acetylcholine accumulation at neuromuscular junctions, receptor desensitization, impaired transmission, and proximal muscle weakness [2,5]. Prolonged overstimulation can deplete neurotransmitter stores and exhaust muscle energy, potentially resulting in respiratory failure if not recognized [2,7].

Management is primarily supportive, including close respiratory monitoring, mechanical ventilation, physiotherapy, and structured follow-up [7,9]. Anticholinergics such as atropine alleviate residual cholinergic effects but have limited efficacy during IMS. In this patient, pralidoxime was

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initially administered but discontinued after 48 hours due to early receptor desensitization [2,11,13]. This aligns with prior IMS cases, in which continued acetylcholinesterase reactivation proved ineffective. Recovery depended mainly on supportive measures rather than prolonged antidotal therapy.

The prognosis of OP poisoning varies from days to weeks, with potential long-term deficits [8]. In this patient, early recognition, EMG-guided monitoring, and timely supportive care enabled neuromuscular recovery, confirming and extending observations from previous IMS reports. This case report is compared with prior studies in table below (Table 2).

Table 2. The comparison between previously published studies and the finding of this manuscript.

Findings from some earlier published literature (review) studies							
No	Author/Year	OP Compound	Time to IMS Onset	Key Clinical Features	Mechanical Ventilation	Duration of Ventilation	Outcome
1	Asraf, 2019 [2]	Chlorpyrifos 50%	4 hours	Proximal muscle weakness, respiratory difficulty	Yes	5 days	Recovered with atropine + ventilation.
2	Kaeley, 2021 [14]	50 ml of organophosphorus insecticide	Six hours	Respiratory failure, neck and proximal limb weakness	Yes	7 days	Recovered with ventilation + atropine + pralidoxime.
3	Setia, 2023 [7]	500 mL monocrotophos + ethanol	2 days	Severe neuromuscular weakness, respiratory compromise	Unspecified	Not reported	Recovered with antibiotics + atropine + pralidoxime.
4	Lageju, 2022 [5]	an unknown quantity of Chlorpyrifos	Not reported	Profound muscle weakness, respiratory failure	Yes	48 hours	Recovered with ventilation + atropine + pralidoxime.
Finding of this manuscript							
1	Bereda, 2025	40% chlorpyrifos (unknown amount)	36 hours	Progressive proximal weakness, respiratory muscle paralysis, altered mental status	Yes	8 days	IMS	Full recovery with ventilation, IV fluids, atropine; pralidoxime discontinued due to early receptor desensitization.

Strengths and Limitations

This case highlights the need for continued monitoring after acute organophosphate poisoning and provides a practical management protocol in a resource-limited setting, emphasizing prolonged ventilation, supportive care, and timely interventions. The limitations of this study include its single-case design, unclear long-term outcomes, and limited generalizability to all cases of organophosphate poisoning.

Conclusion

IMS is a serious delayed complication of organophosphate poisoning, typically occurring 24–96 hours post-exposure. This case highlights the onset of proximal muscle weakness and respiratory compromise four days after chlorpyrifos ingestion, confirmed by EMG and markedly decreased serum cholinesterase. Early recognition, EMG-guided diagnosis, and supportive management—including mechanical ventilation, physiotherapy, and timely discontinuation of pralidoxime due to receptor desensitization—enabled recovery. This report underscores the importance of careful

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monitoring, evidence-based interventions, and individualized care in resource-limited settings, providing practical insights into IMS management.

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