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Original Article

A Randomized Controlled Clinical Trial to Compare the Efficacy of Pralidoxime When Given in Continuous Infusion Versus Intermittent Dose in Terms of Symptomatic Improvement Over a Given Time Scale

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ABSTRACT

Background: Organophosphorus pesticide poisoning produces potentially fatal cholinergic toxicity, but the optimal pralidoxime maintenance regimen remains uncertain. Objective: To compare early clinical recovery following intermittent pralidoxime administration and continuous pralidoxime infusion in patients with acute organophosphorus poisoning. Methods: This parallel-group randomized controlled clinical trial included 104 patients treated at Aziz Bhatti Shaheed Teaching Hospital, Gujrat, Pakistan, between 2024 and 2025. All patients received an initial 2-g intravenous pralidoxime dose. Group A received 1 g every six hours for 48 hours, whereas Group B received a continuous infusion of 8 mg/kg/hour for 48 hours. Clinical response was assessed at 24 and 48 hours. Categorical outcomes were compared using two-sided Fisher's exact tests, with risk ratios and 95% confidence intervals calculated. Results: At 24 hours, clinical response occurred in 17 of 45 patients (37.8%) in Group A and 35 of 59 patients (59.3%) in Group B (RR, 1.57; 95% CI, 1.02–2.41; p=0.047). At 48 hours, response occurred in 40 patients (88.9%) and 58 patients (98.3%), respectively (RR, 1.11; 95% CI, 0.99–1.23; p=0.083). Treatment extension was required in 11.1% and 1.7% of patients, respectively (p=0.083). No deaths occurred. Conclusion: Continuous pralidoxime infusion was associated with faster clinical recovery at 24 hours, although later response differences were not statistically significant. Keywords: Organophosphorus poisoning; Pralidoxime; Continuous infusion; Intermittent dosing; Cholinergic toxicity; Pesticide poisoning; Randomized controlled trial.

INTRODUCTION

Primary biliary cirrhosis is a chronic cholestatic liver disease characterized by progressive immune-mediated destruction of the small intrahepatic bile ducts. It predominantly affects middle-aged women and may eventually result in fibrosis, cirrhosis, portal hypertension, and hepatic decompensation. Histopathological findings commonly include portal inflammation, bile duct injury, and granuloma formation, supporting the proposed autoimmune basis of the disease (1,2). Primary biliary cirrhosis may also coexist with extrahepatic autoimmune disorders, including Sjögren syndrome, systemic sclerosis, autoimmune thyroid disease, and other rheumatological conditions (3,4).

Pulmonary complications are well recognized in advanced chronic liver disease. These may arise from ventilation–perfusion mismatch, intrapulmonary vascular dilatation, anatomical right-to-left shunting, pulmonary vascular disease, or alterations in the alveolar–capillary membrane. In patients with primary

biliary cirrhosis, respiratory abnormalities may additionally be related to coexisting autoimmune disorders, interstitial pulmonary involvement, airway disease, or granulomatous inflammation. Pulmonary granulomas and fibrotic changes have been described in selected patients, although their frequency, clinical importance, and relationship with the severity of hepatic disease remain uncertain (5,6).

Previous studies have reported reductions in diffusing capacity for carbon monoxide, abnormalities in lung volumes, airway obstruction, and impaired exercise performance among patients with primary biliary cirrhosis. However, these findings have not been consistent, and their interpretation has frequently been complicated by smoking, anaemia, asthma, emphysema, Sjögren syndrome, systemic sclerosis, and other coexisting disorders (7). It also remains unclear whether measurable pulmonary dysfunction occurs in patients without overt respiratory symptoms or whether such abnormalities are more frequent among patients with clinically symptomatic liver disease (7-11).

Patients with primary biliary cirrhosis may be categorized clinically as asymptomatic or symptomatic according to manifestations such as pruritus, jaundice, xanthoma, xanthelasma, hyperpigmentation, hepatomegaly, and splenomegaly. Although this clinical classification does not replace biochemical or histological staging, it may help identify patients with a greater burden of clinically apparent disease (8,9). Evaluating pulmonary function across these clinical groups may therefore improve understanding of the frequency and pattern of respiratory involvement and help determine whether pulmonary assessment should form part of the broader clinical evaluation of affected patients (12-16).

The present study aimed to assess pulmonary-function abnormalities in patients with primary biliary cirrhosis compared with healthy individuals and to examine whether pulmonary-function parameters differed between symptomatic and asymptomatic patients. Particular attention was given to lung volumes, airflow indices, diffusing capacity for carbon monoxide, exercise capacity, arterial oxygenation, and anatomical right-to-left shunting.

MATERIALS AND METHODS

A prospective comparative observational study was conducted in the Department of Medicine, Lahore General Hospital, Lahore, Pakistan, from January 2021 to January 2023. Consecutive patients with a diagnosis of primary biliary cirrhosis who were evaluated or managed by the department during the study period were considered for inclusion. The diagnosis was based on a compatible clinical presentation and laboratory findings and was supported by liver histopathology where biopsy was clinically feasible. Patients in whom the available clinical, biochemical, or histopathological findings did not support the diagnosis were not included in the analysis.

A total of 26 patients with primary biliary cirrhosis were included. Patients were classified as symptomatic when they had one or more clinically apparent manifestations, including pruritus, jaundice, xanthoma, xanthelasma, hyperpigmentation, hepatomegaly, or splenomegaly. Patients without these manifestations were categorized as asymptomatic. On this basis, 19 patients were classified as symptomatic and seven as asymptomatic. Clinical information, duration of disease, smoking status, serum bilirubin, serum alkaline phosphatase, and other available laboratory and histopathological findings were recorded for subsequent comparisons (17-19).

A healthy comparison group was selected from individuals participating in an epidemiological assessment. Twenty-eight potentially eligible individuals were approached, of whom 19 agreed to participate. The control group comprised 16 women and three men aged 42–67 years, with a mean age of approximately 56 years. Controls were selected to provide an age- and sex-comparable reference group and underwent the same clinical respiratory assessment and core pulmonary-function testing as the patient group.

All patients and healthy controls were evaluated by the same chest physician to reduce interobserver variability. The assessment included clinical examination, posteroanterior and lateral chest radiography, dynamic spirometry, measurement of lung volumes, and assessment of pulmonary diffusing capacity. Exercise testing and estimation of anatomical right-to-left shunting were undertaken in the subgroup of patients for whom these measurements were available (16).

Dynamic spirometry was performed using a Bernstein spirometer. Recorded indices included vital capacity, forced expiratory volume in the first second, the expiratory volume ratio reported as FEV%, and maximum voluntary ventilation. Functional residual capacity was determined using the closed-circuit helium-dilution technique, from which total lung capacity and residual volume were calculated. Pulmonary-function measurements were expressed as percentages of the predicted values appropriate to the participant's demographic characteristics. Obstructive, restrictive, and hyperinflation patterns were classified according to the recorded combinations of expiratory airflow and lung-volume measurements.

Diffusing capacity for carbon monoxide was determined using the single-breath technique and was expressed as a percentage of the predicted value. A value below 70% of the predicted value was classified as reduced in accordance with the threshold applied in the original analysis. Haemoglobin concentration was considered when interpreting reduced diffusing capacity because anaemia may lower the measured value. Ventilation distribution was assessed using a modified single-breath nitrogen test. The phase III alveolar plateau slope was measured and reported relative to the predicted nitrogen concentration gradient. Nitrogen concentration was analysed using an Ohio 700 nitrogen analyser.

Arterial blood gases were measured using standard electrodes with a Radiometer ABL 1 analyser. Anatomical right-to-left shunting was assessed from arterial blood samples obtained before and after 20 minutes of breathing 100% oxygen. A shunt fraction greater than 7.5% of cardiac output was considered increased according to the threshold used in the study.

Exercise capacity was evaluated using an electronically braked bicycle ergometer. Workload was progressively increased in six-minute stages until the participant reached symptom-limited maximal exertion. Maximum working capacity was calculated using the reference procedure applied in the study. A 12-lead electrocardiogram was recorded before and after exercise, and six-lead electrocardiographic monitoring was undertaken during the exercise test.

Keratoconjunctivitis sicca was assessed using the Schirmer test and rose Bengal staining. It was considered present when the Schirmer test result was less than 5 mm over five minutes in association with rose Bengal evidence of corneal or conjunctival epithelial damage. The presence of keratoconjunctivitis sicca was examined in relation to pulmonary-function abnormalities and reduced diffusing capacity. The available findings from the Kveim test, liver histopathology, serum immunoglobulin M, alkaline phosphatase, bilirubin, antimitochondrial antibodies, C1q binding, and alpha-1 antitrypsin phenotyping were also examined in exploratory analyses.

Data were analysed using IBM SPSS Statistics version 22.0. Continuous variables were summarized as mean ± standard deviation, and categorical variables were presented as frequencies and percentages. Student's independent-samples t-test was used to compare continuous pulmonary-function measurements between groups when the assumptions of parametric testing were satisfied. Associations between categorical variables were assessed using the chi-square test, with consideration of the small group sizes when interpreting the results. Linear regression and correlation analysis were used to examine the relationship between diffusing capacity for carbon monoxide and maximum working capacity. Statistical tests were two-sided, and a p-value below 0.05 was considered statistically significant.

The study was conducted after approval from the relevant ethics committee of Ameer-ud-Din Medical College, Lahore. Participant information was handled confidentially, and the study procedures were undertaken in accordance with applicable institutional ethical requirements.

RESULTS

Twenty-six patients with primary biliary cirrhosis and 19 healthy controls were included in the comparative analysis. Among the patients, 19 were classified as symptomatic and seven as asymptomatic. Fourteen of the 26 patients had at least one abnormal pulmonary-function finding, corresponding to an overall prevalence of 53.8%. Abnormal pulmonary-function findings were observed in 13 of 19 symptomatic patients (68.4%) compared with one of seven asymptomatic patients (14.3%; Fisher's exact p=0.026).

Table 1. Pulmonary-Function Parameters in Symptomatic and Asymptomatic Patients With Primary Biliary Cirrhosis

Pulmonary-function parameter, % predicted	Asymptomatic PBC (n=7), mean ± SD	Symptomatic PBC (n=19), mean ± SD	Mean difference (95% CI)	p-value
Total lung capacity	91.9 ± 12.9	100.9 ± 10.0	9.0 (−3.2 to 21.2)	0.130
Vital capacity	91.5 ± 9.7	97.9 ± 10.7	6.4 (−3.2 to 16.0)	0.173
Maximum voluntary ventilation	93.5 ± 14.0	92.1 ± 15.5	−1.4 (−15.3 to 12.5)	0.830
Residual volume	92.5 ± 23.1	106.9 ± 16.5	14.4 (−7.4 to 36.2)	0.167
Expiratory volume ratio	103.1 ± 8.9	93.7 ± 8.0	−9.4 (−18.0 to −0.8)	0.035
Forced expiratory volume in 1 second	98.0 ± 13.5	95.5 ± 13.5	−2.5 (−15.7 to 10.7)	0.682
Phase III nitrogen slope	109.9 ± 52.0	146.9 ± 95.0	37.0 (−24.3 to 98.3)	0.222
Diffusing capacity for carbon monoxide	84.5 ± 13.8	70.9 ± 14.6	−13.6 (−27.2 to 0.0)	0.050

CI: confidence interval; PBC: primary biliary cirrhosis; SD: standard deviation. Mean differences were calculated as symptomatic minus asymptomatic values. P-values were derived using Welch's independent-samples t-test.

Symptomatic patients showed a lower mean expiratory volume ratio than asymptomatic patients, with a between-group mean difference of −9.4 percentage points (95% CI, −18.0 to −0.8; p=0.035). Mean diffusing capacity was also lower in symptomatic patients by 13.6 percentage points, although the confidence interval approached the null value (95% CI, −27.2 to 0.0; p=0.050). Symptomatic patients had numerically higher total lung capacity, residual volume, and phase III nitrogen slope, but these differences were not statistically significant. Vital capacity, forced expiratory volume in 1 second, and maximum voluntary ventilation were broadly comparable between the two patient groups.

Table 2. Pulmonary-Function Parameters in Patients With Primary Biliary Cirrhosis and Healthy Controls

Pulmonary-function parameter, % predicted	All PBC patients (n=26), mean ± SD	Healthy controls (n=19), mean ± SD	Mean difference (95% CI)	p-value
Total lung capacity	97.9 ± 10.8	98.1 ± 9.1	−0.2 (−6.2 to 5.8)	0.947
Vital capacity	96.1 ± 18.3	98.5 ± 8.4	−2.4 (−10.7 to 5.9)	0.559
Maximum voluntary ventilation	93.4 ± 15.1	98.1 ± 14.0	−4.7 (−13.5 to 4.1)	0.289
Residual volume	102.7 ± 19.1	93.8 ± 12.3	8.9 (−0.6 to 18.4)	0.065
Expiratory volume ratio	97.2 ± 10.1	100.3 ± 5.9	−3.1 (−7.9 to 1.7)	0.203
Forced expiratory volume in 1 second	97.1 ± 13.4	102.9 ± 10.2	−5.8 (−12.9 to 1.3)	0.107
Phase III nitrogen slope	139.1 ± 82.2	108.5 ± 7.7	30.6 (−2.7 to 64.0)	0.070
Diffusing capacity for carbon monoxide	76.1 ± 16.1	88.1 ± 12.1	−12.0 (−20.5 to −3.5)	0.007

CI: confidence interval; PBC: primary biliary cirrhosis; SD: standard deviation. Mean differences were calculated as PBC minus control values. P-values were derived using Welch's independent-samples t-test.

Compared with healthy controls, patients with primary biliary cirrhosis had a significantly lower mean diffusing capacity for carbon monoxide. The mean difference was −12.0 percentage points of the predicted value (95% CI, −20.5 to −3.5; p=0.007). Residual volume was numerically higher among patients, with a mean difference of 8.9 percentage points, but the confidence interval included no difference (95% CI, −0.6 to 18.4; p=0.065). The phase III nitrogen slope was also higher among patients, although the comparison did not reach statistical significance (mean difference, 30.6 percentage points;

95% CI, −2.7 to 64.0; p=0.070). No statistically significant differences were found for total lung capacity, vital capacity, maximum voluntary ventilation, forced expiratory volume in 1 second, or the expiratory volume ratio.

Table 3. Frequency and Pattern of Abnormal Pulmonary-Function Findings in Patients With Primary Biliary Cirrhosis

Pulmonary finding	n/N (%)
Any abnormal pulmonary-function finding	14/26 (53.8)
Abnormal pulmonary-function finding among symptomatic patients	13/19 (68.4)
Abnormal pulmonary-function finding among asymptomatic patients	1/7 (14.3)
Reduced diffusing capacity for carbon monoxide	9/25 (36.0)
Obstructive spirometric pattern	5/26 (19.2)
Hyperinflation	2/26 (7.7)
Restrictive spirometric pattern	1/26 (3.8)
Bronchial asthma among patients with abnormal pulmonary findings	3/14 (21.4)
Pulmonary emphysema among patients with abnormal pulmonary findings	1/14 (7.1)

The denominator for reduced diffusing capacity was 25 because this measurement was unavailable for one patient with emphysema. Categories were not mutually exclusive because some patients had more than one pulmonary-function abnormality.

Reduced diffusing capacity was the most frequent specific abnormality and was documented in nine of the 25 patients with an available measurement (36.0%). All nine patients with reduced diffusing capacity were from the symptomatic group. Four were current smokers, one was a former smoker, and four were nonsmokers. Three patients with reduced diffusing capacity had mild anaemia, although the manuscript indicated that haemoglobin adjustment did not fully account for the reduction.

Five patients demonstrated an obstructive spirometric pattern, including patients with known bronchial asthma or emphysema. Hyperinflation was identified in two patients, while one asymptomatic patient demonstrated a restrictive pattern. Chest radiography showed hyperinflation in the patient with severe emphysema but did not identify corresponding abnormalities in the remaining patients or healthy controls.

Table 4. Individual Pulmonary-Function Profiles of Patients With Abnormal Findings

Clinical group	VC, % predicted	TLC, % predicted	RV, % predicted	Expiratory volume ratio, % predicted	DLCO, % predicted	Pulmonary-function pattern
Asymptomatic	75	75	74	110	73	Restrictive
Symptomatic	83	86	94	87	62	Reduced DLCO
Symptomatic	111	119	137	90	55	Reduced DLCO; hyperinflation
Symptomatic with asthma	87	88	91	78	84	Obstructive
Symptomatic with asthma	102	125	183	93	77	Hyperinflation
Symptomatic	104	160	112	95	67	Reduced DLCO
Symptomatic	87	94	109	96	50	Reduced DLCO
Symptomatic	108	106	103	79	64	Reduced DLCO; obstructive
Symptomatic	87	102	134	81	58	Reduced DLCO; obstructive
Symptomatic	100	93	75	96	65	Reduced DLCO
Symptomatic with emphysema	58	107	198	43	—	Obstructive
Symptomatic with asthma	83	93	112	83	83	Obstructive
Symptomatic	97	102	115	93	65	Reduced DLCO
Symptomatic	113	110	104	97	69	Reduced DLCO

DLCO: diffusing capacity for carbon monoxide; RV: residual volume; TLC: total lung capacity; VC: vital capacity. All measurements are expressed as percentages of predicted values.

Among the 14 patients with abnormal pulmonary-function findings, 13 were symptomatic and one was asymptomatic. Nine had a DLCO below 70% of the predicted value, with measured values ranging from 50% to 69%. Five showed an obstructive pattern, two showed hyperinflation, and one demonstrated a restrictive pattern. Some patients had overlapping abnormalities, particularly reduced DLCO combined with obstruction or hyperinflation.

In the subgroup that underwent both exercise testing and measurement of diffusing capacity, DLCO showed a strong positive relationship with maximum working capacity (r=0.74), indicating that lower gas-transfer capacity was associated with lower exercise performance. Abnormal pulmonary-function findings were identified in four of six patients with keratoconjunctivitis sicca; however, no statistically significant association was found between keratoconjunctivitis sicca and either overall pulmonary dysfunction or reduced DLCO.

Arterial oxygen tension was within the normal range in all assessed patients except the patient with severe emphysema, whose arterial oxygen tension was 7.3 kPa. An increased anatomical right-to-left shunt was identified in eight of 19 evaluated patients (42.1%). The mean shunt fraction was 6.5%, with values ranging from 3.9% to 10.0%. No statistically significant relationships were observed between increased shunt or abnormal pulmonary function and serum bilirubin, serum alkaline phosphatase, serum immunoglobulin M, liver-biopsy stage, alpha-1 antitrypsin phenotype, C1q binding, or antimitochondrial-antibody findings.

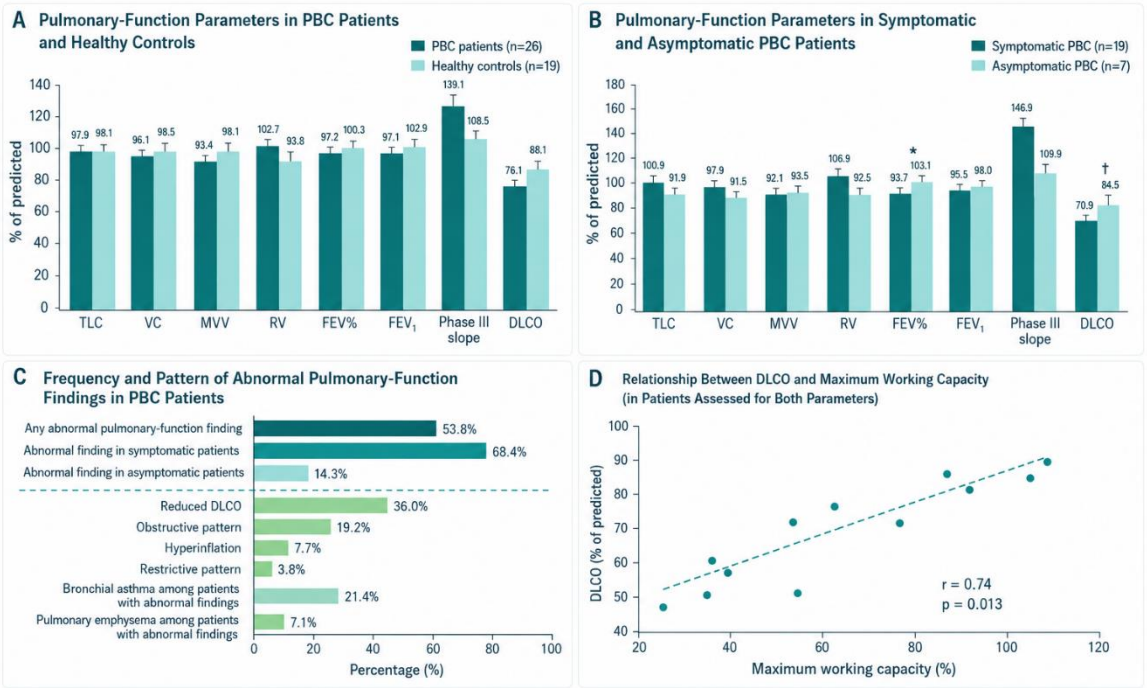

Figure 1 The multipanel figure shows that patients with primary biliary cirrhosis had lower DLCO than healthy controls, while symptomatic patients demonstrated more pronounced reductions in DLCO and expiratory volume ratio than asymptomatic patients. Overall, 53.8% of patients had abnormal pulmonary-function findings, rising to 68.4% among symptomatic patients, with reduced DLCO being the most common abnormality. DLCO also showed a strong positive correlation with maximum working capacity (r=0.74, p=0.013), indicating that impaired gas transfer was associated with poorer exercise performance.

DISCUSSION

The present study compared intermittent pralidoxime administration with continuous infusion in patients treated for acute moderate-to-severe organophosphorus pesticide poisoning. Continuous infusion was associated with a higher probability of achieving the predefined clinical response within 24 hours. A desirable response occurred in 59.3% of patients receiving continuous infusion compared with 37.8% receiving intermittent treatment, corresponding to an absolute difference of 21.5 percentage points and a relative risk of 1.57. By 48 hours, clinical response had occurred in most patients in both

groups. Although the response rate remained numerically higher with continuous infusion, the difference was not statistically significant when analysed using the two-sided Fisher's exact test. Similarly, treatment extension beyond 48 hours was less frequent with continuous infusion, but the estimate was imprecise and did not reach statistical significance (4, 17, 20).

The earlier response observed with continuous infusion is pharmacologically plausible. Pralidoxime reactivates organophosphorus-inhibited acetylcholinesterase before the enzyme–toxin complex undergoes aging, but its clinical effectiveness depends on the pesticide involved, time from exposure to treatment, circulating toxin burden, and maintenance of an adequate oxime concentration (2–4). Intermittent dosing may produce relatively high post-dose concentrations followed by declining concentrations between doses. In contrast, continuous administration following an initial loading dose may maintain more stable systemic exposure during the period in which the organophosphorus compound continues to be absorbed or redistributed (8). This mechanism could explain why a greater proportion of patients receiving continuous infusion achieved clinical recovery within the first 24 hours.

The present findings are generally consistent with those of Pawar et al., who reported improved outcomes with a high-dose continuous pralidoxime regimen compared with repeated bolus administration in patients with organophosphorus poisoning (5). Kaur et al. also reported more favourable clinical recovery with continuous infusion than with repeated bolus treatment (9). However, differences in pralidoxime formulation, loading and maintenance doses, poisoning severity, type of ingested pesticide, treatment delay, atropine administration, respiratory support, and outcome definitions limit direct comparison between studies. The observed benefit should therefore be interpreted as applying to the complete treatment regimens evaluated rather than to infusion pattern alone (13-16).

The comparison of regimens is particularly important because the two study groups may have received substantially different cumulative pralidoxime doses. A continuous infusion of 8 mg/kg/hour over 48 hours would ordinarily deliver a considerably larger maintenance dose than 1 g administered every six hours, depending on patient weight. Consequently, the faster early response may reflect the combined effects of sustained exposure and a higher total pralidoxime dose. The study cannot independently determine whether the observed difference resulted from continuous delivery, cumulative dose intensity, or both. Future comparative trials should either use equivalent cumulative doses or evaluate dose intensity and mode of administration as separate treatment factors.

The reported respiratory findings also suggested earlier improvement with continuous infusion. Bronchorrhoea and bronchospasm were reported to improve within 12 hours in 92% of patients receiving continuous infusion, whereas improvement was reported after approximately 30 hours in 75% of patients receiving intermittent treatment. Respiratory manifestations are clinically important because excessive pulmonary secretions, bronchoconstriction, central respiratory depression, and neuromuscular weakness contribute to respiratory failure in acute organophosphorus poisoning (2,3). Nevertheless, the respiratory comparison should be interpreted cautiously because exact numerators, common assessment times, recovery-time distributions, and time-to-event analyses were unavailable. The findings therefore indicate a clinically relevant pattern but do not provide a precise comparative estimate of respiratory recovery time (4, 9, 13).

The higher 24-hour response rate with continuous infusion may have practical implications in emergency and critical-care settings. Earlier control of cholinergic manifestations could potentially reduce the duration of intensive monitoring, repeated rescue treatment, respiratory vulnerability, and demand on critical-care resources. However, these outcomes were not directly measured in the present study. Total atropine exposure, intubation, mechanical ventilation, intensive-care stay, hospital stay, treatment cost, and adverse reactions should be included in future trials to determine whether earlier symptomatic improvement translates into meaningful patient-centred and health-system benefits.

No deaths occurred in either treatment group during the reported observation period. This finding should not be interpreted as evidence of equivalent or superior survival because the study was not adequately powered to detect mortality differences, and the follow-up period was not fully characterized. Larger trials have reported inconsistent effects of pralidoxime on mortality and other major outcomes. Eddleston et al. found no consistent survival advantage from pralidoxime in a randomized trial, while subsequent systematic evaluation continued to identify considerable uncertainty because of heterogeneity in treatment regimens, pesticide compounds, illness severity, and study quality (6,7). A recent meta-analysis of adjunctive treatments has also emphasized the need for better-standardized clinical trials in organophosphorus poisoning (10).

The study had several strengths. It directly compared two clinically used pralidoxime regimens in a public-sector hospital where organophosphorus poisoning represents an important emergency-care problem. Both groups received the same initial pralidoxime loading dose and were assessed at clinically relevant early time points. The use of exact statistical testing and effect estimates provided a more informative interpretation than reliance on threshold p-values alone.

The study also had important limitations. It was conducted at a single centre and included a relatively small sample with unequal group sizes. Details of sequence generation, allocation concealment, assessor blinding, protocol deviations, and intention-to-treat analysis were not available. The composite desirable-response outcome was based on clinical manifestations and was not supported by a validated scoring system or biochemical measurement of red blood cell acetylcholinesterase activity. Atropine dosage and other co-interventions were not quantified, although atropine directly affects salivation, bronchorrhoea, bronchospasm, and several components of the clinical endpoint. The type and quantity of pesticide ingested, time from exposure to treatment, baseline poisoning severity, ventilation requirement, and adverse drug effects were not reported. In addition, the two treatment regimens differed in both method of administration and probable cumulative dose, preventing isolation of the independent effect of continuous infusion.

Further multicentre randomized trials should use clearly concealed allocation, standardized poisoning-severity criteria, equivalent or explicitly compared cumulative pralidoxime doses, objective clinical endpoints, and blinded outcome assessment where feasible. Future studies should also report atropine requirements, cholinesterase activity, ventilation, intensive-care and hospital stay, adverse events, recurrence of toxicity, intermediate syndrome, mortality, and treatment costs. These measures would clarify whether the earlier symptomatic response associated with continuous infusion translates into sustained clinical and economic benefits.

CONCLUSION

Continuous pralidoxime infusion was associated with a higher probability of achieving clinical improvement within 24 hours than intermittent six-hourly administration in patients with acute organophosphorus pesticide poisoning. By 48 hours, response rates were high in both groups, and the differences in clinical response and treatment extension were not statistically significant under exact testing. The findings suggest that the continuous regimen may accelerate early symptomatic recovery; however, the effects of administration pattern and cumulative pralidoxime dose could not be separated, and confirmation in larger, methodologically rigorous multicentre trials is required.

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