

Research Article,

Clinical consequences of Hypotension in patient with organophosphate poisoning

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Abstract:

Objective: Aim of study is to describe the clinical consequences of hypotension in patient with organophosphate poisoning.

Method: In the retrospective cohort study, we analyzed data of 66 patients with organophosphate poisoning who were treated at Bir Hospital, Nams Kathmandu. Data from those with hypotension and normal blood pressure were compared to identify significant clinical consequences.

Results: All together 66 patients were enrolled in this study out of which 44(66.7%) were female and 22(33.3%) were male. After analyzing data, we found 18.2% of case with severe poisoning (ACHE < 700 U/L). Among all, 41(62%) were found to have normal blood pressure and 25(37.9%) were found to have low blood pressure. Among those with hypotension, around 56% were found to have prolonged QTc interval, $p < 0.003$ and there was statistically significant association between QTc prolongation and vasopressor requirement, $X^2(1) = 22.98$, $P < 0.001$. Patients requiring higher dose to reach atropinization had statistically significant hypotension, $P < 0.001$. Those with low blood pressure were found to require more days of hospital admission, $P < 0.001$. Patients with hypotension were found to have severe poisoning both on the basis of POP Score severity grading, 16(64%) $P < 0.002$ and ACHE Severity scale, 7(28%) $P < 0.05$. In comparison with normal blood pressure group, low blood pressure group had significantly more chance of developing complications like septic shock (2), aspiration pneumonia (5), ARDS (1) and bed sore, $P = 0.002$. Vasopressor requirement was significantly more among those with low blood pressure, $P < 0.001$. Most of hypotensive patients were needing ICU care, found to have higher WBC count $P = 0.002$ and lower GCS Score at admission $P < 0.001$. There was positive correlation between hypotension and POP Score at admission $P < 0.001$.

Conclusion: Hypotension is a common complication in patient with organophosphate poisoning and is associated with higher POP Score, lower ACHE level, lower GCS Score, increased vasopressor requirement, more hospital stays, increasing ICU admission, more chance of developing septic shock and aspiration pneumonia.

Introduction:

Organophosphate ingestion is the most common cause of self-harm encountered here in Nepal. It usually affects young populous. Organophosphates are found in various forms and formulations that are easily accessible to general public. These compounds are extremely potent poison causing

rapid clinical deterioration with minimal ingestion or exposure¹².

Acute cholinergic crisis includes signs and symptoms resulting from hyperstimulation of muscarinic receptors causing bradycardia, hypotension along with bronchorrhea, bronchoconstriction, miosis and abdominal cramps. Organophosphate found to cause QTc

prolongation resulting into torsade de pointes¹⁻³. Other mechanism of hypotension in organophosphate poisoning suggested are dose dependent reduction in heart rate and decrease in peripheral vascular resistance via peripheral vasodilatation⁷.

Over 40% of patients dying from dimethoate and organophosphate compound present with systolic blood pressure of less than 80 mm of Hg⁵. Despite adverse prognostic consequences of hypotension, its clinical correlates and outcomes have not been studied in large study. In our country specially in rural area, prevalence of organophosphate poisoning is common on the other hand vitals monitoring is very poor due to lack of good center and trained man power.

Methods:

Study design

This was a retrospective cohort study of patient with organophosphate poisoning who were treated at Bir Hospital, Kathmandu Nepal from December 2018 to December 2019. Bir Hospital is central government hospital one among best referral centers in Nepal.

Diagnostic criteria of organophosphate poisoning: Diagnosis is made on the basis of clinical suspicion, the characteristic of clinical signs, smell of pesticides or solvent and reduced serum acetylcholinesterase level⁶. Patient with POP Score 0-3 is regarded as having mild poisoning, 4-7 as having moderate poisoning and 7-11 as having severe poisoning⁷. On the basis of plasma acetylcholinesterase activity, ACHE level of 0-700 U/L regarded as severe poisoning, 701-1400 U/L as moderate poisoning and 1401-3500 U/L as having mild poisoning⁷.

Management of organophosphate poisoning:

After ABCD evaluation on arrival of patient in emergency department, give a bolus of 0.6-3mg atropine iv rapidly and administer doubling dose every 5 min until the patient is fully atropinized (HR>80bpm, SBP>80 mm of Hg, pupils are fully dilated and clear lungs)⁸. Once atropinized, give an infusion of 10-20% of total dose required to atropinized the patient each hour in 0.9% normal saline with intermittent bolus whenever required. If patient has symptoms of atropine toxicities (tachycardia, hyperthermia, delirium, urinary retention) then reduce infusion by 20%. Give loading dose of pralidoxime at 20-30 ml/kg over 30min and then repeated every 6-8hrly.

Inclusion criteria

- Patient with definite history suggestive of organophosphate poisoning below age 75y.
- Patient with alleged history of organophosphate poisoning presented within 24hr.
- Patient or relatives who gave written consent.

Exclusion criteria

- Patients age more than 75y.
- Patients under anti-hypertensive medication.
- Patients with definite history suggestive of coronary heart disease.
- Patients having history suggestive of heart failure.
- Patients under diuretic therapy.

Data collection

All data were collected from stores where all files of patients were kept after they were discharged. Parameters like age, sex, address, blood pressure, underlying comorbidities, date of admission and discharge, complications developed during admission, POP Score at admission, ACHE Level at admission, GCS score at admission, lab parameters (LFT, RFT, ECG, CBC etc.). Patients were categorized into two group; one with hypotension at admission or within 24 hour of admission and other with no hypotension.

Statistical methods

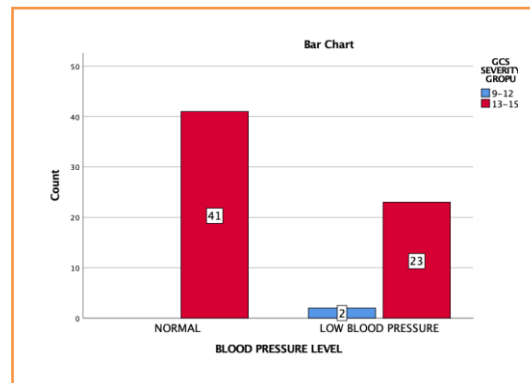
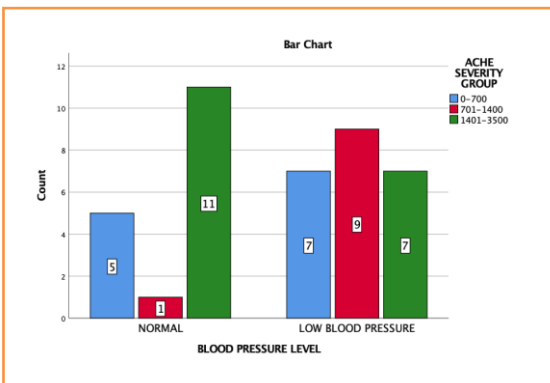
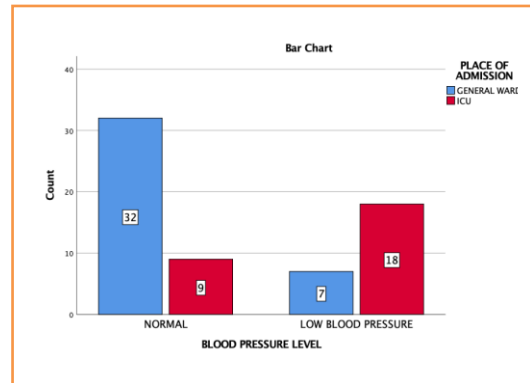
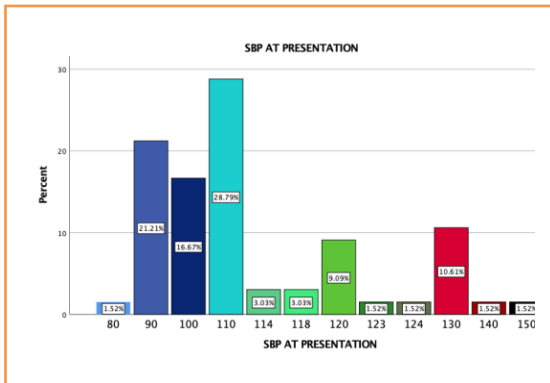
Data were analyzed using IBM SPSS statistic 25. Descriptive data were summarized using standard technique and reported as percentage with 95% confidence interval. Continuous data were presented as mean +/- SD and categorized data as absolute number and percentage. The student t-test and chi-square tests were used for comparison of continuous and categorical variables between groups respectively. Fisher's exact test used for analyzing difference between two groups when there were cells < 5. Correlation between continuous variable were assessed using Pearson's correlation. Predictive values of hypotension and

clinical outcomes was assessed by logistic regression.

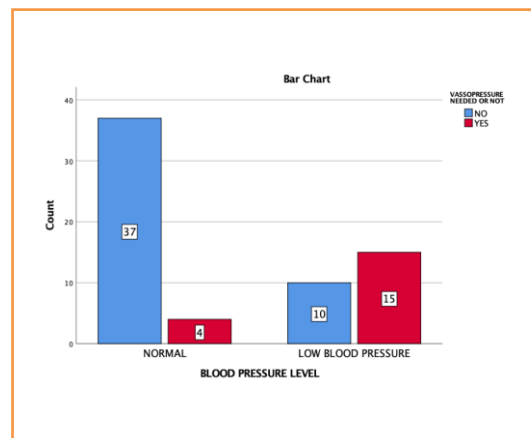
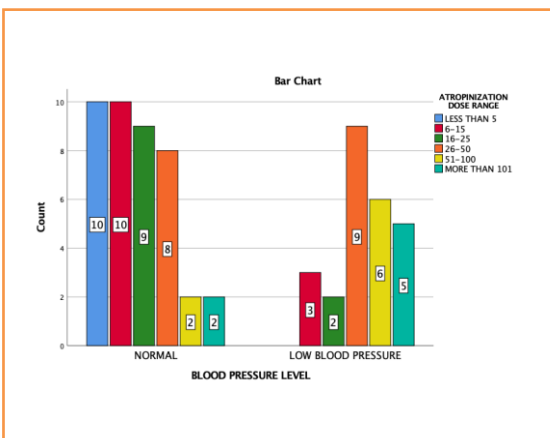
Observations and results:

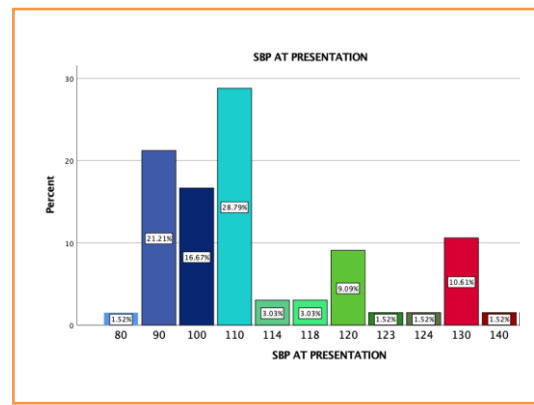
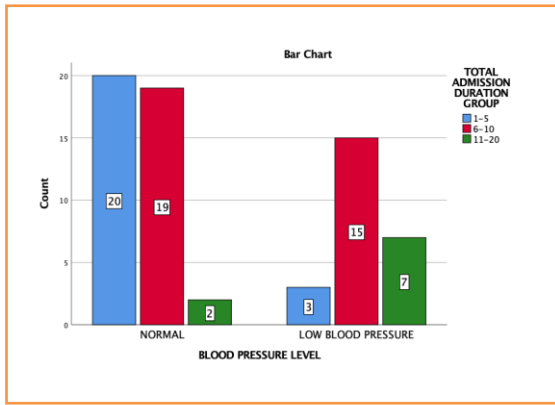
All together 66 patients were enrolled in this study, out of which 44(66.7 %) were female and 22(33.3%) were male. During study, 50% of patient were found to have ingested chlorpyrifos

(50%) + cypermethrin (5%) a combination of diethyl compound. Among all patients, 41(62%) were having normal blood pressure and 25(37.9%) were found to have low blood pressure. Among those with hypotension, 13(52%) were female and rest 12(48%) were male.

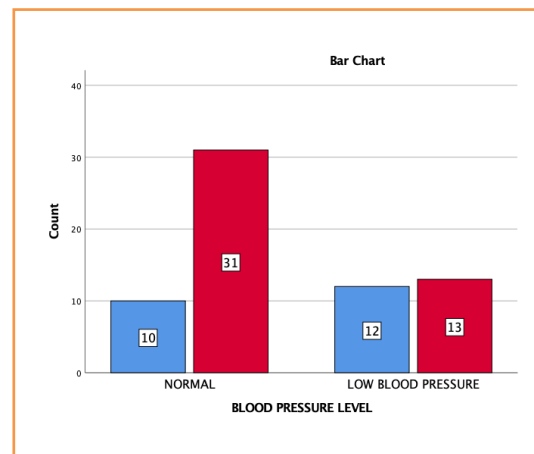
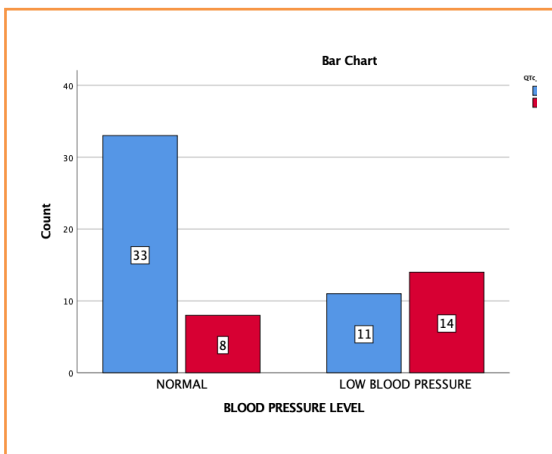
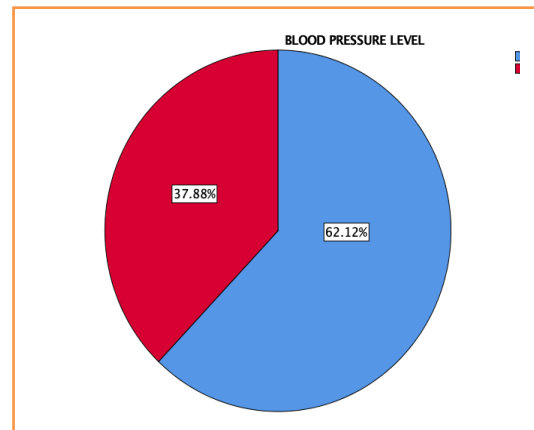
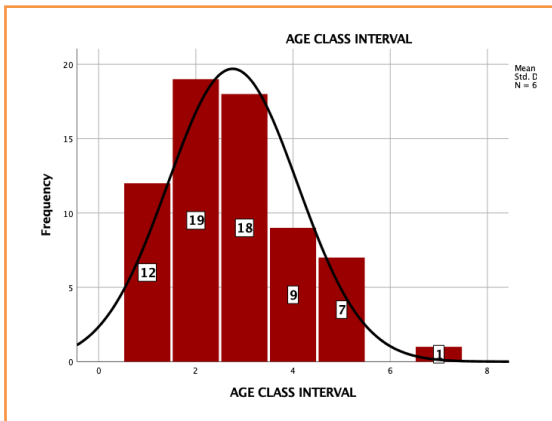


Requirement of vasopressor among diethyl compound consumer were significantly higher (16.6% vs 4.5%, P = 0.035). There is statistically significant association between QTc prolongation and vasopressor requirement; $X^2(1) = 22.98, P < 0.001$. Age had no effect on blood pressure; $X^2(5) = 3.331, P = 0.649$ however patients requiring higher dose to reach atropinization has statistically significant hypotension; Fisher's exact test, $P < 0.001$. Patients with low blood pressure were found to have severe poisoning on the basis of POP score at admission $P = 0.002$ and ACHE level at admission $P = 0.005$. In comparison to normal blood pressure group, low blood pressure group had significantly more chance of developing complications like septic shock (2), aspiration pneumonia (5), ARDS (1) and bed sore (1); $P = 0.002$. Even vasopressor requirement was significantly higher among low blood pressure group; $P < 0.001$.





Among low blood pressure group, most of them were requiring ICU 18(72%) however requirement of mechanical ventilation was insignificant. Around 56% of patient were found to have prolonged QTc interval as calculated by Bazet’s formula; P = 0.003. However renal function and liver function were not affected. When performing independent sample t-test, we found low blood pressure group had significantly higher dose of atropine requirement for atropinization; t (64) = -3.908, P = 0.002 and lower GCS score at admission; t (64) = 1.847, P < 0.001. There was positive correlation between low blood pressure and POP score at admission; rs (66) = -0.602, P < 0.001 and total dose of atropine required for atropinization.



A. Histogram showing age wise distribution of patients B. Percentage of patients with normal blood pressure and low blood pressure. C. Bar chart showing comparison of QTc interval among those with normal and low blood pressure. D. Bar chart showing sex distribution among normal and low blood pressure group.

Discussions:

We did study at center where all the referred cases from all over Nepal used to come. In our study, we found 37.9% of patients developing hypotension

significantly higher than other study where they found hypotension in only 10.9% cases⁹. In our study, Age had no significant effect on outcome regarding development of hypotension; P = 0.69

however in some study, age was associated with higher incidence of hypotension (geriatric group vs non geriatric group; 38.6% vs 21.1%, $P = 0.032$ ¹³. In another study, electrocardiographic abnormalities like prolonged QTc interval were seen in 31(67%) and hypotension in 8(17%) cases¹⁰ however in our study, we found statistically significant QTc prolongation in 56%; $P = 0.003$ and hypotension in 25(37.9%) cases.

In our study, incidence of hypotension in patient with prolonged QTc interval was significantly higher than that in patient with normal QTc interval (56% vs 44%, $P = 0.003$) which is comparable to study done by Shou-Hsuan Liu et al¹¹. Patient with severe organophosphate poisoning typically died due to irreversible cardiovascular failure, acidosis and respiratory failure¹⁷. With advance in respiratory management and intensive care, it is possible to maintain the respiratory function of patients with organophosphate poisoning however management of hypotension is challenging despite adequate administration of atropine. There is no specific treatment protocol for management of hypotension in organophosphate poisoning. There is limited evidence available to treat irreversible hypotension in organophosphate poisoning.

In patient with severe organophosphate poisoning, hypotension usually develops due to overstimulation of muscarinic acetylcholine receptors in CNS, NM junction and peripheral nervous system⁹. In previous study, patients with severe organophosphate poisoning complicated by hypotension showed reduced total peripheral resistance and maintained cardiac output^{4,5}. However, the use of vasopressor like catecholamines found to be ineffective⁵. This may be attributable to impaired cardiovascular regulation by CNS through a complex mechanism. For example, microinjection of mevinphos in rostral ventrolateral medulla of anesthetized rats induced progressive hypotension that was accompanied by an increased phase I followed by a decrease phase II in the experimental index of baroreflex mediated sympathetic tone resulting into fatality of rat in 35%²¹. These findings highlight the importance of CNS in the development of hypotension in acute severe organophosphate poisoning.

We want to highlight the need of further study on the standards pertaining to atropinization in severe organophosphate poisoning. Although atropine shows moderate penetration in the CNS, it is the

mainstay of therapy. For patients with hypotension in severe organophosphate poisoning, excess dose of atropine may be required to reverse their hypotension, this should take precedence over control of other muscarinic symptoms⁴. The correct standard of atropinization is to provide early and sufficient atropine to prevent hypotension. Further studies should evaluate the fundamental of atropinization in patients with severe organophosphate poisoning.

Study limitations

This type of retrospective cohort study may miss some data. We did not take dose and type of organophosphate compounds ingested into consideration during analysis. We also do not take consideration of comorbid condition in analysis. Our sample size is small, broad and large study is needed to further evaluate these findings. As study was conducted at referral center, so many patients found to receive vasopressor before arrival.

Conclusions:

Hypotension is a common complication in patient with organophosphate poisoning and is associated with higher POP Score, lower ACHE level, lower GCS Score, increased vasopressor requirement, more hospital stays, increasing ICU admission, more chance of developing septic shock and aspiration pneumonia.

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