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Original Article

Cholinesterase and Liver Enzymes in Patients with Organophosphate Poisoning

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Abstract

Background

Insecticide poisoning is the main cause of organophosphorus compounds poisoning worldwide, leading to high degree of morbidity and mortality especially in the developing countries like Nepal. The liver is the main organ that metabolizes various compounds including toxins, chemicals and drugs and eventually excretes from the body. Few studies have been done in Nepal to see the level of liver enzymes among the organophosphorus compounds poisoning. This may helps in early diagnosis of acute hepatic failure and reduces OP poisoning related death.

Materials and Methods

After approval from Institutional Review Committee of Kathmandu University School of Medical Sciences, retrospective chart review study was done with organophosphate poisoning cases admitted at Dhulikhel Hospital, Kathmandu University Hospital from April 2014 to September 2017. Out of total 68 cases admitted 54 cases that meet the inclusion criteria were chosen for the study. Laboratory data was extracted from laboratory software, MIDAS version 3.2. and statistical analysis was carried out using Statistical Package for Social Sciences (SPSS) version 21 software.

Results

Majority of the patients with organophosphate poisoning were female with 64.8% and the majority (31.5%) of patient were of age group 16-25. Plasma cholinesterase level was found to be significantly decreased in the patients with organophosphate poisoning and random blood sugar was raised significantly (125.77±52.3), p-value 0.04. Among all liver enzymes, there is a significant negative correlation of Cholinesterase with Aspartate aminotransferase (r = -0.35; p-value<0.05).

Conclusion

This study suggests some level of negative correlation between serum cholinesterase and liver enzymes in OP poisoning and a significant negative correlation with serum Aspartate aminotransferase.

Keywords: *Cholinesterase, Poisoning, Liver*

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Introduction

Organophosphate not only causes environmental pollution but also is a major causes of acute and chronic OP poisoning [1]. Self-poisoning by organophosphate is estimated to kill around 200,000 people per year, largely in the Asia-Pacific region and the mortality rate varies from 10-20% [2]. Poisoning with over use and misuse of various pesticides, drugs and other toxic compounds frequently occur in Nepal. Poisoning is a common cause of emergency department visits and medical admissions in various hospitals, suggesting it as a major health problem in the country. In the year 1999-2000, the nationwide suicidal death due to poisoning was reported to be 31% [3-5]. In India, the incidence of OP poisoning is around 1.26 lakhs during the period of 12 months in 2007, as reported by Ravi et al [6].

Organophosphates compounds are commonly used in the agriculture as an insecticide, but were also used as chemical warfare agents [7]. In a multi-centered study done by Gupta SK et. al. in five major hospital of Nepal, OP compound was found to be a major cause of poisoning in Nepal comprising 52% of total poisoning cases [8].

Cholinesterase is an enzyme. Cholinesterase enzyme exists in two forms as pseudocholinesterase and cholinesterase. Pseudocholinesterase is present in the liver and plasma, whereas acetylcholinesterase is present in the RBCs and nervous tissue [9]. Cholinesterase hydrolyses acetylcholine, mainly located in the nervous system, skeletal muscle motor end plates and human erythrocytes [9]. Organophosphate poisoning results from exposure to organophosphates. It causes inhibition of acetylcholinesterase, resulting in the accumulation of acetylcholine and overstimulation of cholinergic synapses, producing symptoms like miosis, bradycardia, emesis, sweating, salivation, lacrimation, blurred vision, urination and defecation [10-11]. Complications of OP poisoning are cardiac arrhythmias, aspiration, acidosis, acute renal failure, respiratory paralysis, coma and Death. Death may results due to any of the above mentioned complication and combination of any one of the above complications [12]. Low serum cholinesterase supports the diagnosis and also used for the monitoring of organophosphate poisoning. Therefore serum cholinesterase level is commonly measured [12] in the laboratories.

The liver enzyme shows broad substrate specificity, including a variety of pesticide oxidations. The toxicity of organophosphorus compounds is mediated by generation of free radicals which may alter the liver metabolism and is evidenced by changes in level of its enzymes [13]. Many researchers have shown increase level of liver enzymes and decrease level of serum cholinesterase in OP poisoning, [14] but very little work has been done in Nepal that study the correlation between serum cholinesterase and liver enzymes in OP poisoning. Therefore, this study is done to find out the correlation between cholinesterase and liver enzymes in OP poisoning cases admitted in the Dhulikhel hospital.

Materials and Methods

Retrospective chart review study was done. Prerecorded, patient centered data was used for data collection among the patients with OP poisoning attending Emergency Department followed by admission to Medicine ward or ICU of Dhulikhel Hospital from April 2014 to September 2017.

After approval from Institutional Review Committee of Kathmandu University School of Medical Sciences, study was done in Dhulikhel Hospital. Data were collected from the patient's record file which records the personal history of patient such as name, age, sex and clinical records. Data of patients meeting inclusion criteria was recorded in the proforma. Laboratory data was extracted from laboratory software, MIDAS version 3.2. Out of total 68 cases admitted 54 cases that meet the inclusion criteria were chosen for the study. Incomplete record file with missing information were excluded from the study. Similarly, cases below 16 years of age, patients with any other cause of poisoning and patients with chronic disease such as diabetes and chronic renal failure were excluded from the study. Confidentiality of data was maintained while recording. Descriptive statistics was presented in percentage, frequency, mean, median and Standard Deviation. Spearman's Correlation Coefficient was done and p value less than 0.05 were considered significant.

Results

Table 1: Demographic details of patients with OP poisoning

Characteristics		Number (n = 54)	Percentage (%)
Gender	Male	19	35.2
	Female	35	64.8
Age	16-25	17	31.5
	26-35	7	13
	36-45	10	18.5
	46-55	12	22.2
	>55	8	14.8
Ethnicity	Tamang	20	37
	Brahmin	14	25.9
	Danuwar	6	11.1
	Chettri	4	7.4
	Newar	5	9.3
	Others ?	5	9.3

? Magar, Majhi, B.K., Pariyar, Mizar, Thakuri

The statistics in Table 1 portrays the demographic characteristics of the sample subjects in a one-way frequency/percent distribution.

Demographic Details

Out of 54 cases with OP poisoning, majority of the patients were female with 64.8% and the rest 35.2% were Male. The age group varies with a maximum of 31.5% in the age group 16-25, followed by 22.2% in the age group 46-55 to a low of 13% in the age group 26-35. The minimum age recorded in the study was 16 years and the maximum age was 78 years. Tamang people are mostly affected with OP poisoning accounting 37% of total cases followed by Brahmin 25.9%. Chettri 7.4%. Other ethnicity includes Magar, Majhi, B.K., Pariyar, Mizar, Thakuri. Plasma cholinesterase level was found to be significantly decreased in the patients with OP poisoning.

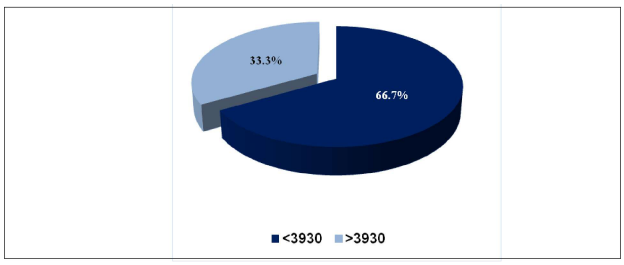

Figure 1: Level of plasma Cholinesterase in patients with OP poisoning

Table 2: Descriptive statistics of laboratory parameters of the patients with OP poisoning

Parameters	Mean±SD	Median (Per 25, Per 75)
Cholinesterase (U/L)	2705.3±2913.36	825 (493,5660)
AST (IU/L)	48.30±26.10	42 (30,59)
ALT (IU/L)	36.70±28.62	29 (22,36)
ALP (IU/L)	109.5±33.17	105.5 (81.75,130.25)
RBS (mg/dl)	125.77±52.3	118 (89.5, 142.5)
Total Bilirubin (mg/dl)	0.93±0.39	0.8 (0.6,1.1)
Direct Bilirubin (mg/dl)	0.3±0.14	0.3 (0.2,0.4)
Creatinine (mg/dl)	0.78±0.25	0.75 (0.6,0.9)
Urea (mg/dl)	24.35±8.48	24 (18,19)
Albumin (g/dl)	4.31±0.59	4.4 (3.9,4.7)

The statistics in Table 2 portrays the descriptive statistics of laboratory parameters of the patients.

Table 3: Level of Cholinesterase with liver enzymes out of 54 cases

Liver Function Test in serum		Serum Cholinesterase level <3930 U/L (low) No. of patients	Serum Cholinesterase level >3930 U/L (Normal) No. of patients
AST	>40 IU/L	21	7
ALT	>40 IU/L	8	4
ALP	>128 IU/L	12	3
RBS	>110 mg/dl	9	0
Total Bilirubin	>1.4 mg/dl	5	4
Direct Bilirubin	≥0.5 mg/dl	5	4

The statistics in Table 3 shows the level of serum cholinesterase and liver enzymes. AST level is elevated in majority of the patients with decreased serum cholinesterase level.

Among all liver enzymes, there is a significant negative correlation between serum Cholinesterase and AST. Spearman's Correlation Coefficient: -0.351; p-value<0.05

Discussion

OP poisoning is associated with high degree of morbidity and mortality among patients admitted

Table 4: Correlation of serum cholinesterase with liver enzymes

	Serum Cholinesterase	
Parameters	Correlation coefficient 'r'	p-value
AST IU/L	-0.351	0.009*
ALT IU/L	-0.04	0.77
ALP IU/L	-0.15	0.28
RBS mg/dl	-0.233	0.09
Total Bilirubin mg/dl	-0.15	0.29
Direct Bilirubin mg/dl	-0.086	0.55

to the emergency department [15]. OP compounds cause irreversible inhibition of Acetyl cholinesterase and shows symptoms collectively referred to as cholinergic crisis. This is due to the accumulation of Acetylcholine at the synapse which over stimulates the central and the peripheral nervous system [11]. The resulting muscarinic and nicotinic symptoms usually continue for days and months until the Acetylcholine Esterase (AchE) enzyme forms again [16].

As shown in the Table 1, among the fifty four patients with OP poisoning, female were found to be mostly affected comprising 64.8% of total cases. This result is much similar with the study done by Khadka SB. which showed that 52.3% of total cases of poisoning were female [17]. A study done by Ramazan Amanvermez et. al. also showed that female were affected mostly than male accounting 52.74% of total cases [18]. This study also found majority of the patients with OP poisoning were between the age group of 16-25 years followed by individuals belonging to 46-55 years old with mean age group of 39.46±16.9. This result was consistent with the study done by Khadka SB [17] and Al Jumaan MA et al [19]. The study done by Khadka SB. showed that the most commonly affected age group was 21-30 followed by the age group of 11-20 years [17]. And the study done by Al Jumaan MA et al showed that the 20-30 age group was significantly more prone to suicide than other age groups [19]. In this study, we found significant decrease in serum cholinesterase level in patients with OP poisoning. As shown in the figure 1, about 66.7% of total cases of OP poisoning showed decreased level of serum cholinesterase. This result is consistent with the study done by Panda S et al [15].

Similarly, random blood sugar was significantly found to be raised in this study which is consistent with the study done by Panda S et al [15]. Previous studies have suggested that oral ingestion of several OP may results elevation of counter regulatory hormones reducing insulin sensitivity leading to increased blood sugar which is further accentuated by excessive adrenergic influence on glycogenolysis leading to hyperglycemia [20].

This study shows the elevation of serum AST, ALT and ALP among the cases of OP poisoning, mainly in the patients with decreased serum cholinesterase level (Table 2 and 3), which is similar to the study done by Ramazan Amanvermez et. al. [18] Similarly, other studies has also shown abnormal liver function tests, hepatic necrosis, and fatty changes in OP poisoning cases [21-22]. In this study negative correlation was seen between liver enzymes like AST, ALT and ALP with serum cholinesterase (Table 4), but was not significant except with enzymes AST (r = -0.351, p-0.009). This study suggests some level of correlation between serum cholinesterase enzymes and liver enzymes in OP poisoning. However, the present work was conducted on a relatively small number of patients, further studies with larger number of patients and case control study is required to support the present observations.

Conclusion

Serum cholinesterase was decreased and blood sugar level was raised in the majority of cases with OP poisoning but there was only significant negative correlation between serum cholinesterase and serum AST enzymes in OP poisoning.

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