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RESEARCH ARTICLE

"ANALYSIS OF EFFICACY OF FRESH FROZEN PLASMA TRANSFUSION IN ORGANOPHOSPHORUS POISONING IN INTUBATED PATIENTS -A RANDOMIZED CONTROL STUDY"

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Abstract

Aims &Objectives:-
To determine the reduction of length of ICU stay and mortality inorganophosphorus poisoning patients of intubated patients using Fresh frozen plasma as add on therapy.

Materials &Methods:-
Study design:
A case control study was conducted on ventilated organophosphorus patientsadmitted to Emergency Medicine of Bapuji Hospital.

Study period:
April 2024 to September 2024 (6 months)

Sample size:
sample size comes to be minimum of 22 in each group

Data analysis:
SPSS vers. 24.0 was used to do the analysis.

Exclusion Criteria:
1. Age < 18
2. Poisoning cases other than organophosphorus compounds.
3. Patients having serum cholinestarase level more than 2000 IU/L
4. Patients with comorbidities including diabetes, hypertension, malignancy etc

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Patients were divided into two groupsof 22 each. The control group received atropine and oximes only and the study group received atropine and oximes along with FFP 2 units (400 ml) on daily basis until patient is extubated or pseudocholinesterase level above 2000IU.

Results:-

Our study did show significant mortality benefit in FFP transfused patients (9.1% compared to control 31.8%). The mean number of days of hospital stay was 4.1 in cases with SD of 1.62 whereas it was 5.8 in control with SD of 2.00 and this was statistically significant p=0.004.

Conclusion:-

The use of FFP was found to have mortality benefit and also reduces length of hospital stay in our study.
Larger trials are required to determine the dosage and duration of FFP transfusion in order to add it to the standard therapy.

Introduction:-

Organophosphates are widely used as insecticides in agricultural practice. Due to its easy availability there is significant increase in the household incidence of occupational, accidental or homicidal consumptions.[1]
Organophosphorus compound poisoning is among one of the most common medical acute emergencies associated with high mortality rate. Organophosphates after entering into circulation binds to acetylcholinesterase & inhibit the enzyme, resulting in increased unbound acetylcholine. This manifests as cholinergic crisis, having both nicotinic and muscarinic actions. Muscle weakness and bronchorrhea lead to respiratory failure which is the leading cause of death in organophosphate poisoning.
Serum pseudocholinesterase levels to be checked for patient with organophosphorus poisoning. Patient presenting to the Emergency department with organophosphorus poisoning, airway, breathing, circulation should be managed first following which decontamination is done. Patient is then administered atropine which is a muscarinic and nicotinic antagonist;and pralidoxime which is acetylcholinesterase reactivator. Atropine is preferred over scopolamine and glycopyrrolate as it has both cental and peripheral antimuscarinic effects. Pralidoxime effectively reactivates red cell acetylcholinesterase inhibited by diethyl OP inhibited enzyme such as chlorpyrifos, quinalphos but only moderately reactivates dimethyl OP-inhibited enzyme such as dimethoate, fenthions.
FFP is now suggested as a useful therapy for Organophosphorus poisoning as it contains cholinesterase enzyme. The serum cholinesterase enzyme in FFP will confiscate freeorganophosphorous compound which is present in blood, thus preventing toxic effect on neuromuscular junction.
This study is done to analyse the effectiveness of FFP in ventilated patients of organophosphorus poisoning to compare mortality in atropine+ oxime group and atropine+ oxime+ FFP group. No study has been done to fill this gap hence the need for this study.

AIMS & OBJECTIVES:

To determine the reduction of length of ICU stay and mortality in organophosphorus poisoning patients of intubated patients using Fresh frozen plasma as add on therapy.

MATERIALS & METHODS:

- **Study design:** case control study
- **Study period:** April 2024 to September 2024 (6 months)
- **Sample size:** The study was conducted on all confirmed cases of organophosphorus pesticide poisoned patients admitted to Bapuji Hospital, Davangere during the study period of 6months.
  - $$n = \frac{2 (Z\alpha + Z\beta)^2 * S^2}{d^2}$$
- Where
- $Z\alpha$ =1.96 at 95% confidence level And $Z\beta$ =1.28 at 90% power
- S= combined standard deviation and
- d= Mean difference
- With 95% confidence level and 80% power with respect to (Dayananda VP et al[1]) sample size comes to be minimum of 22 in each group

Data analysis: Analysis will be done by descriptive statistics. Comparison between the groups was done by students unpaired t test or Mann Whitney U test as per the normality of the data. Chisquare test was used for qualitative data. A statistical package SPSS vers. 24.0 will be used to do the analysis. $p<0.05$ will be considered as significant

Inclusion criteria:

- All the OP poisoning intubated cases confirmed by history, circumstantial evidence of consumption, characteristic clinical examination and basic laboratory investigations.

Exclusion criteria:

- Age< 18
- Poisoning cases other than organophosphorus compounds.
- Patients having serum cholinestarase level more than 2000 IU/L
- Patients with comorbidities including diabetes, hypertension, malignancy etc

Data is collected from –

A case control study was conducted on ventilated organophosphorus patients admitted to Emergency Medicine of Bapuji Hospital. Patients with history and clinical picture suggestive of acute OP poisoning was studied. Thorough observation of poison container was done and sent for toxicology analysis. Institutional Ethical Committee approval was taken. Written consent was obtained after explaining to patient/relatives in their language.

Patients were divided into two groups of 22 each who fulfill the inclusion – exclusion criteria

- Control group received atropine and oximes only.
- Study group received atropine and oximes along with FFP 2 units (400 ml) on daily basis until patient is extubated.
- Patients wereatropinized and atropine infusion given to maintain a state of atropinization with 20% of atropinized dose and titrated accordingly. Injection oximes will be given 30 mg/kg intravenous (IV) bolus followed by 10 mg/kg/h depending up on clinical improvement.
- Gastric lavage and decontamination was done and activated charcoal added.
- Hemodynamic parameters, saturation, muscle power, and CNS status was continuously monitored and recorded regularly. Arterial blood gas (ABG) analysis done once in 24 h and also when required.
- Plasma cholinesterase level was measured on daily basis until extubated
- Ventilation done with synchronized intermittent mandatory ventilation and settings was managed according to ABG status. Antibiotic prophylaxis was given to both groups according to institutional protocol.
- Patients were weaned from ventilator according to clinical assessment of muscle power and respiratory effort.
- Patients were extubated when they achieved extubation criteria and monitored in ICU for respiratory distress for 24 h, and later shifted to stepdown ward.
- Patients were analyzed for increase in serum cholinesterase level, length of ICU stayand mortality rate.

Methodology:

After getting informed consent from the patient / bystander, 2 units FFP was transfused on a daily basis to op poisoning patients until extubation. And 2ml blood drawn daily and serial pseudo cholinesterase levels was monitored.

Statistical analysis:

- Relevant data was collected, tabulated and analysis was done using SPSS software (latest version).
- Relevant statistical tests was applied.

RESULTS

AGE				
Group	**N**	**Mean**	**Std. Deviation**	**t**
Control	22	33.591	8.645	.843
Cases	22	36.619	14.344	p=0.404 ns

GENDER				
		Group		**Total**
		Control	**Cases**	
F	Count	3	6	9
	%	13.6%	27.3%	20.5%
M	Count	19	16	35
	%	86.4%	72.7%	79.5%
Total	**Count**	**22**	**22**	**44**
	%	**100.0%**	**100.0%**	**100.0%**
a. X2=1.257 p=0.262 ns				

MANNER				
		Group		**Total**
		Control	**Cases**	
Suicidal	Count	22	22	44
	%	100.0%	100.0%	100.0%
Total	**Count**	**22**	**22**	**44**
	%	**100.0%**	**100.0%**	**100.0%**

COMPOUNDS				
		Group		Total
		Control	Cases	
Chlorpyrifos	Count	8	6	14
	%	36.4%	27.3%	31.8%
Dimethoate	Count	1	0	1
	%	4.5%	0.0%	2.3%
Monocrotophos	Count	6	2	8
	%	27.3%	9.1%	18.2%
Unknown Op compound (diagosed by toxicological analysis	Count	4	9	13
	%	18.2%	40.9%	29.5%
Prophenophos	Count	2	5	7
	%	9.1%	22.7%	15.9%
Quinalphos	Count	1	0	1
	%	4.5%	0.0%	2.3%
Total	**Count**	**22**	**22**	**44**
	%	**100.0%**	**100.0%**	**100.0%**
a. X2=7.495 p=0.186 ns				

REASON				
		Group		Total
		Control	Cases	
Low GCS	Count	5	5	10
	%	22.7%	22.7%	22.7%
Low GCS with respiratory failure	Count	11	6	17
	%	50.0%	27.3%	38.6%

Type 1 Respiratory failure	Count	2	8	10
	%	9.1%	36.4%	22.7%
Type 2 respiratory failure	Count	4	3	7
	%	18.2%	13.6%	15.9%
Total	**Count**	**22**	**22**	**44**
	%	**100.0%**	**100.0%**	**100.0%**
a. X2= 5 .213 p=0.157 ns-				

	PSEUDOCHOLINEESTERASE LEVELS			
		Groups		**Total**
		Control	**Cases**	
	< 200	13	13	26
	%	59.09%	59.09%	59.09%
	200-500	7	5	12
	%	31.81%	22.72%	27.27%
	500-2000	2	4	6
	%	9.09%	18.18%	13.6%
Total	**Count**	**22**	**22**	**44**
	%	**100.0%**	**100.0%**	**100.0%**

STATUS					
			Group		**Total**
			Control	**Cases**	
Status	DAMA	Count	7	6	13
		%	31.8%	27.3%	29.5%
	Death	Count	7	2	9

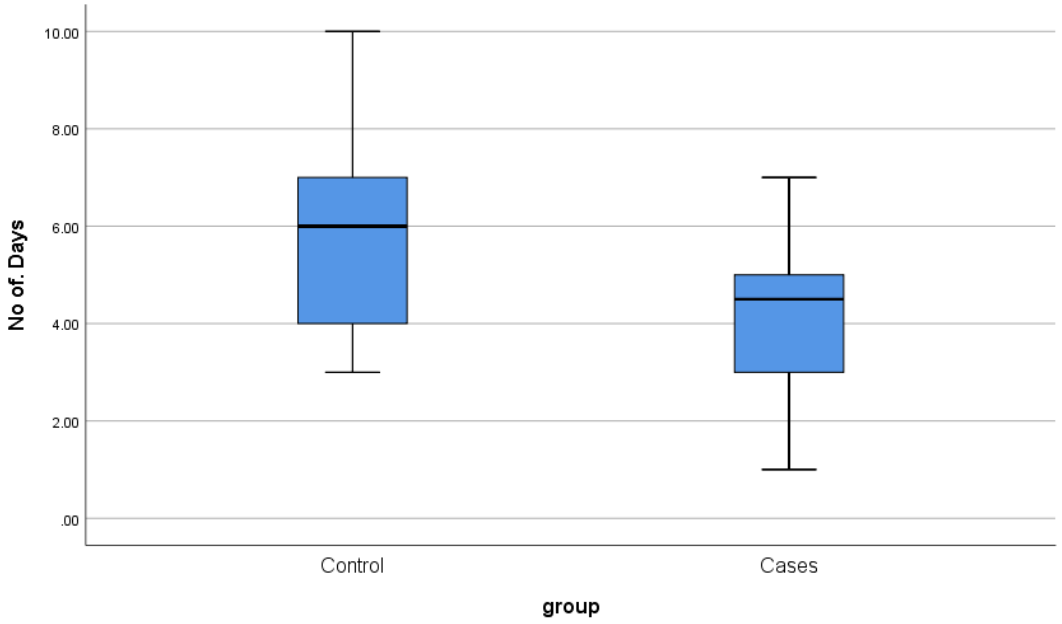
		%	31.8%	9.1%	20.5%
	Improved	Count	8	14	22
		%	36.4%	63.6%	50.0%
Total		**Count**	**22**	**22**	**44**
		%	**100.0%**	**100.0%**	**100.0%**
a. X2=5.752 p=0.042 ns					

NO OF. DAYS				
Group	**N**	**Mean**	**Std. Deviation**	**t**
Control	22	5.864	2.007	3.057
Cases	22	4.182	1.622	p=0.004 hs

PSEUDOCHOLINEESTERASE LEVEL PRIOR TO EXTUBATION		
		Cases
	<300	11
	%	50.00%
	300- 1000	3
	%	13.63%
	>1000	8
	%	36.36%
Total	**Count**	**22**
	%	**100.0%**

In our study mean age of case was 36years and control was 33years. Male predominance was observed in both the groups with 72.7% in cases and 86.4% in control. Manner of consumption of all cases were suicidal. The compound consumed in our study was Chlorpyrifos (31.8%), unknown organophosphorus compound (29.5%), Monocrotophos (18.2%) and profenofos (15.9%) of cases. The most common reason for intubation in our study was low GCS with respiratory failure in 38.6% of cases followed by low GCS and type 1 respiratory failure which accounted for 22.7% of cases each. Pseudocholineesterase level at presentation was less than 200 in 59.9 percent of cases, between 200 to 500 in 27.27% of total cases and 500 to 2000 in 13.6% of total cases. 63.6% cases who received FFP showed improvement while 9.1% of cases expired whereas in control 36.4% showed improvement and 31.8% had expired. The mean number of days of hospital stay was 4.1 in cases with SD of 1.62 whereas it was 5.8 in control with SD of 2.00 and this was statistically significant p=0.004. The pseudocholinesterase level prior to extubation, 50 percent of ffp transfused case have pseudocholineesterase level by 200 to 300, 36.36% have levels between 300 to 1000 and 13.63% have levels above 1000.

No of. Days



DISCUSSION

In our study we had observed that there was significant decrease in mortality (to 9%) in cases who received 2 units of FFP daily compared to control where FFP was not given (i.e 36.4%). Similar findings were observed in study conducted by Dayananda V. et al and Güven M et al where they reported 0% mortality rate in FFP transfused cases.[1,2] Guven M et al further showed that transfusion of FFP prevents intermediate syndrome[2].

It was also observed that the mean number of days of hospital stay was 4.1±1.69 in cases whereas 5.8±2.0 in control the improvement seen was consistent with the study conducted by Dayanand V et al which also showed significant decrease in ICU stay.[1]

Low pseudocholineesterase level corresponds to severity of poisoning[3]. Majority of our cases presented with severe Organophosphorus poisoning with 59.09% of cases with pseudocholinesterase less than 200. The pseudocholinesterase level prior to extubation in our cases is less than 300 in 50% of cases. The raise of the pseudocholinesterase value in our study with FFP transfusion couldn't be assessed adequately with every 2 units of FFP transfused as the value was less than 200 and not measureable according to our lab reports. Acc to study conducted by StovnerJevery two units of FFP increases serum cholinesterase by 461.7±142.1 IU/L, approximately.[4]

Furthermore due to severe degree of organophophate poisoning in our study a large amount of it which was proteins bound were probably released and neutralized in daily basis by FFP.

Interestingly in a case by Pazooki S, 4 units FFP were only given on presentation showed no significance in clinical course[5]. The FFP tranfused at presentation sequesters only a certain amount of enzyme. In case of severe toxicity large amount of enzyme which is unbound or gradually released from the bound proteins is left free which requires further amount of cholinesterase enzyme present in FFP to be neutralized. This dose of FFP to be determined is inconclusive and further studies need to be done to determine the same.

Conclusion:

- The use of FFP was found to have mortality benefit and also reduces length of ICU stay.

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