

ORIGINAL RESEARCH

Study of Serum Creatine Phosphokinase (CPK) level in Organophosphate Poisoning and Its Correlation with severity of poisoning in the patients attending tertiary care Centre, North India

Ram Bhagyawant¹, Shilpa Karande²

¹Assistant Professor, Department of Neurology, Sarojini Naidu Medical College, Agra

²Associate Professor, Department of General Medicine, TNMC & BYL Nair Hospital, Mumbai

Corresponding author

Ram Bhagyawant

Department of Neurology, SNMC, Agra- 282002, U.P., India.

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ABSTRACT

Background: The issue of organophosphorus (OP) poisoning remains a significant global health concern, especially prevalent in developing nations. In OP poisoning, elevated levels of Sr. CPK (creatine phosphokinase) are often observed due to rhabdomyolysis. This elevation can serve as an effective and cost-efficient marker to evaluate poisoning severity.

Aims and Objective: This current investigation endeavors to assess serum creatine phosphokinase (CPK) level in OP poisoning and to find out its correlation with the severity of OP poisoning

Methodology: A retrospective and prospective study spanning a duration of one and half year was carried out on patients with OP poisoning at a tertiary-level medical college.

Results: Throughout the study duration, a total of 40 patients presented themselves. Instances of intentional self-poisoning (95%) outweighed those of accidental exposure (5%). The preponderance of patients were identified as housewives (32.5%), succeeded by individuals in occupations such as private job, farmers, studentship, sweepers and some were unemployed (5%). Among the toxins ingested by patients, Dichlorvas (42.5%) emerged as the predominant choice (35.74%). The mean duration of hospital stays varied among the different severity level. In terms of outcomes, 75% of patients survived without the need for mechanical ventilation and the mortality rate documented in our study stood at 10%. Mean CPK levels were 143, 497.25, and 1806.80 IU/L for mild, moderate, and severe cases of poisoning. Our study showed a significant positive correlation between serum CPK levels and the severity of acute OP poisoning, as determined by the PERADENIYA ORGANOPHOSPHORUS POISONING (POP) score. We observed a negative correlation between serum CPK and serum pseudocholinesterase levels. Furthermore, our study revealed that high CPK is associated with severe poisoning and mortality.

Conclusion: Serum CPK level can be used as an alternative, equally effective and cost-efficient biomarker for assessing the severity of acute OP poisoning. However, the main disadvantage with this marker is its non-specificity.

Keywords – Serum CPK level can be used as an alternative, equally effective and cost-efficient biomarker for assessing the severity of acute OP poisoning. However, the main disadvantage with this marker is its non-specificity.

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Introduction

Organophosphorus compounds find extensive use as pesticides in agriculture for safeguarding crops and controlling pests. These compounds have served as chemical warfare nerve agents. Their widespread availability, coupled with over-the-counter sales, has led to a steady rise in poisoning incidents involving these agents.^{1,2,3}

Organophosphate compounds are one of the most common causes of poisoning worldwide. According to various Indian reports, the rates of poisoning as a suicidal method range from 20.6% to 56.3% out of which organophosphates range from 10.3% to 43.8%.^{4,5}

An Indian study recorded 92,000 deaths attributed to OP compounds in 2010, with a mortality rate ranging from 15% to 30%. The high fatality can be attributed to the toxicity of OP poisoning and the lack of suitable medical facilities.^{6,7}

OP compounds serve as potent inhibitors of acetyl and pseudocholinesterase. To gauge poisoning severity, the levels of serum pseudocholinesterase and erythrocyte cholinesterase are assessed. These markers reveal exposure, acute toxic effects, and actual activity at cholinergic nerve terminals. While the measurement of erythrocyte cholinesterase is intricate and not commonly conducted in most labs,

the estimation of pseudocholinesterase levels is more widespread, albeit less dependable.^{8,9}

The muscle twitching and excessive activity during the cholinergic crisis of acute OP poisoning, as well as the subsequent paralysis due to muscle overactivity resembling ischemia-reperfusion, can both result in the production of free radicals and muscle damage and subsequently leading to elevated levels of Serum CPK (Creatine Phosphokinase).^{10,11} This elevation can serve as an equally effective and cost-efficient marker to evaluate poisoning severity. However, in India, only a limited number of comprehensive studies have explored the potential of Sr. CPK as a superior severity marker for OP poisoning.¹²

Taking into consideration this context, we initiated a study to evaluate CPK's role as an alternative prognostic indicator and to establish a connection between CPK levels and the severity of OP poisoning.

Materials and Methods

SOURCE OF DATA:

Patients with history of OP poisoning admitted to medicine wards of tertiary care hospital, during the study period as per inclusion and exclusion criteria's.

DURATION OF STUDY:- 18 months

STUDY DESIGN – RETROSPECTIVE AND PROSPECTIVE OBSERVATIONAL STUDY

Method Of Collection Of Data:

Ethics committee approval was taken before initiating the study and 40 patients of OP poisoning based on history and fulfilling inclusion and exclusion criteria were obtained from general medical ward of the hospital. Patients with age more than 18 years, with history of exposure to OP poisoning within past 24 hours were included in study.

Following patients were excluded from the study- Patients with history of OP poisoning mixed with any other poison. History suggestive of Myopathy, Epilepsy, Schizophrenia, Autoimmune disease, Malignancy, Trauma, Sepsis, Renal disease, Myocardial infarction and Myocarditis, recent IM injection (within 3 days)¹³ History of drug intake like Statins, Fibrates, Dexamethasone, Frusemide, Amphotericin B, alcohol.

The baseline demographic data of every patient was recorded, including their age and gender. A thorough account of their exposure, duration, and history of seizures in non-epileptic patients following poison exposure, along with any associated medical conditions and drug histories, was documented. Comprehensive clinical examinations were conducted, encompassing pulse rate, respiratory rate, and pupil size. Furthermore, a detailed central nervous system examination was performed, assessing consciousness, response to verbal commands, fasciculation (generalized/continuous, spontaneous/induced), and neck muscle weakness.

On admission, venous blood sample was obtained from these patients & was evaluated for sr. CPK levels (Reference range- Up to 171 IU/L for male and Up to 145 IU/L in female) in medicine research lab in a tertiary care hospital by spectrophotometric methods.¹⁴ RBC Cholinesterase activity (Normal range- 10000-14000 IU/L) was measured by the procedure of Voss and Sachsse.¹⁵

Retrospective data was collected from medical record office of the hospital from registers the case files of eligible patients in study were taken out. Waiver of consent for expired patients was taken. Patients were categorized into mild, moderate and severe poisoning on the basis of PERADENIYA ORGANOPHOSPHORUS POISONING SCALE (POP) scale. (Table1)¹⁶

Data was tabulated and analyzed using SPSS (Statistical Package for Social Science, Ver.10.0.5) package. The results were averaged (mean + standard deviation) for continuous data and number and percentage for dichotomous data are presented in Table and Figure. Proportions were compared using

CHI-SQUARE (χ^2)

TEST OF SIGNIFICANCE.

SPEARMAN'S

CORRELATION

COEFFICIENTS - This was calculated to determine whether there is any correlation between the POP and CPK and Pseudo Cholinesterase. The Spearman's correlation coefficient is calculated to measure the strength of the linear relationship between two variables. In all the above test "p" value of less than 0.05 was accepted as indicating statistical significance.

TABLE 1: PERADENIYA ORGANOPHOSPHORUS POISONING (POP) SCALE

Parameters	Criteria	Score
Pupil size	≥2 mm	0
	<2 mm	1
	Pinpoint	2
Respiratory rate	<20/min	0
	>20/min	1
	≥20/min with central cyanosis	2
Heart rate	>60/min	0
	41-60/min	1
	<40/min	2
Fasciculation	None	0
	Present, generalized/continuous	1
	Both generalized and continuous	2
Level of consciousness	Conscious and rationale	0
	Impaired response to verbal commands	1
	No response to verbal commands	2
Seizures	Absent	0
	Present	1

Note: 0–3, mild poisoning; 4–7, moderate poisoning; 8–11, severe poisoning

Observations, Results and Discussion

This study was conducted in tertiary care hospital. Total 40 patients of OP poisoning admitted to the hospital were studied. The majority of patients fell within the 21–30-year age group (55%) in our study. These findings align with Bhattacharyya's study.¹⁷ In developing countries, the incidence of poisoning is higher among the young and economically active demographic. Male: Female ratio was found to be 3:2. (Table 2)

Concerning marital status, a substantial proportion of cases within our study were categorized as married individuals (75%), while 22.5% were unmarried, and 2.5% were divorced. A similar trend was evidenced in the work of Kora SA et al¹⁸, which demonstrated a higher incidence of poisoning among the married population (67%) compared to the unmarried (33%). In our study, the largest portion of cases pertained to housewives (32.5%), followed by laborers and individuals engaged in private jobs, each constituting

7.5%. Farmers accounted for 15% of the cases. However, divergent findings were presented by Mishra A et al., indicating that the majority were farmers (54.97%)¹⁹. Another study by Kora SA et al. revealed that the most common occupation was laborer (22.41%), trailed by housewives (17.81%) and farmers (15.51%)¹⁸.

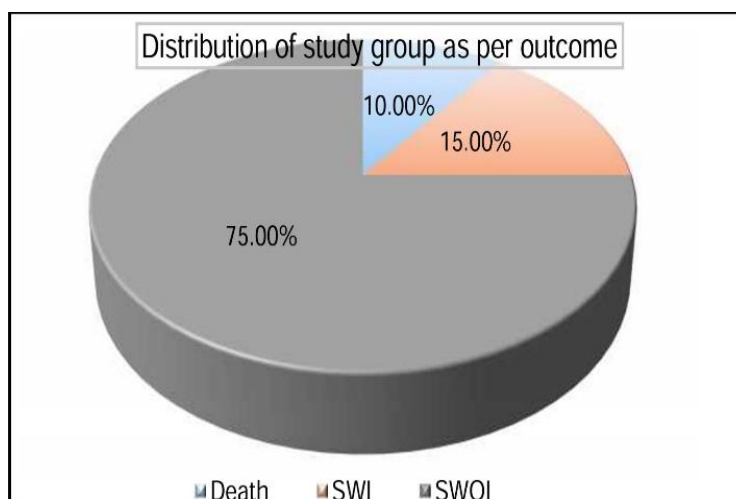
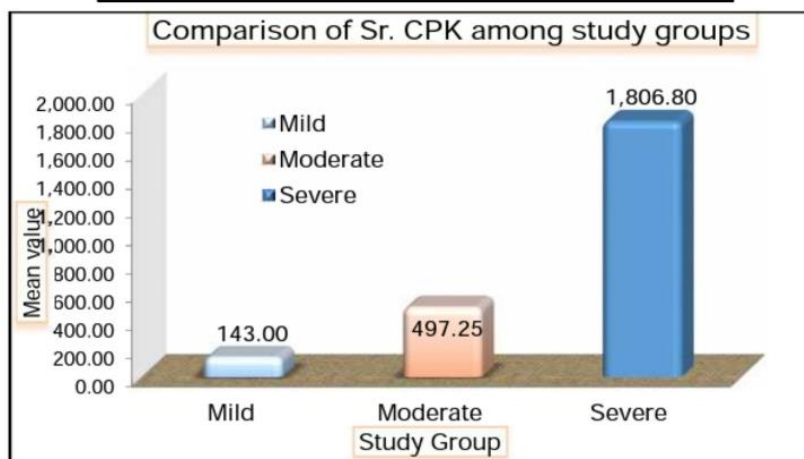
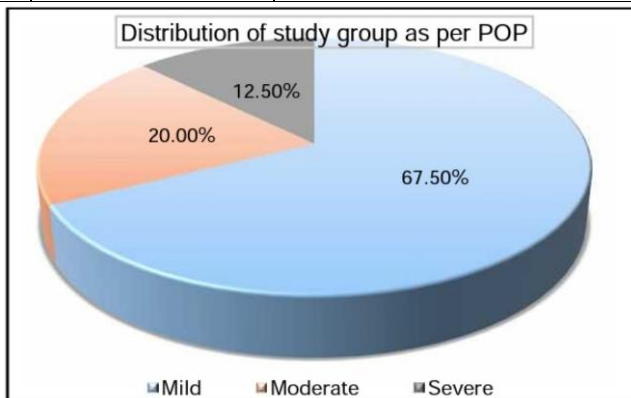
In our study, most used compound was Dichlorvas, which is a household insecticide (42.5%) followed by Chlorpyrifos, which is an agriculture pesticide (30%).

Our study revealed that the majority exhibited mild poisoning (67.5%), while 20% had moderate and 12.5% had severe poisoning. In Kuntal Bhattacharyya's¹⁷ research, mild, moderate, and severe cases comprised 27%, 50.8%, and 22.2% respectively, suggesting moderate poisoning is most common.

Table 2: Baseline demographic parameter of the patients of OP poisoning (n=40)

Parameter	Value	Percentage
Age (Years)	Mean±SD	27.35(±7.25)
Sex	M:F	1.5:1
Marital status	Divorced	2.50%
	Married	75.00%
	Unmarried	22.50%
Occupation	Farmer	15.00%
	Housewife	32.50%
	Labourer	17.50%
	Private job	17.50%
	Student	7.50%
	Sweeper	5.00%
	Unemployed	5.00%
Mode of poisoning	Accidental	5.00%
	Suicidal	95.00%

Type of poison consumed		
	Chlorpyrifos	30.00%
	Dichlorvas	42.50%
	Dimethoate	10.00%
	Methylparathion	7.50%
	Monocrotophos	2.50%
	Phorate	5.00%
	Thiomate	2.50%



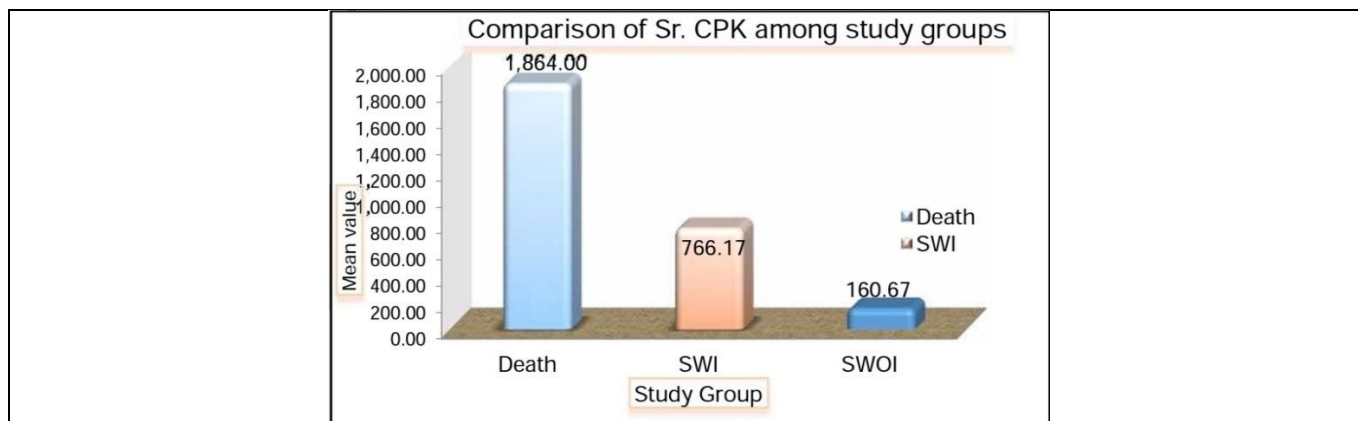


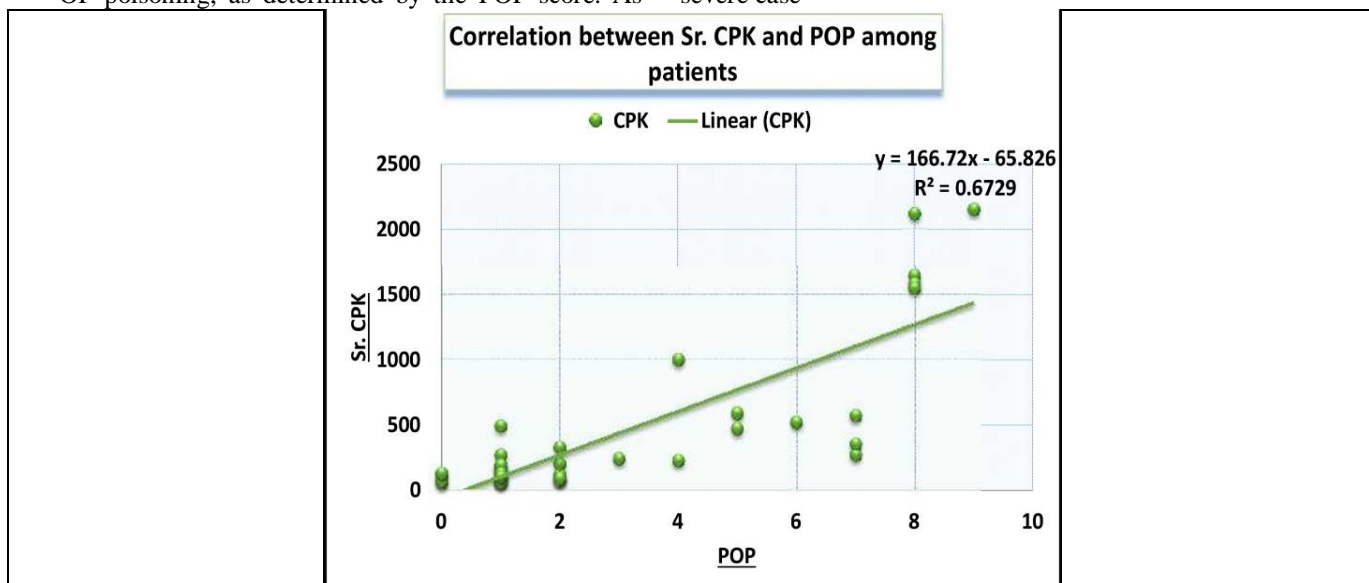
FIGURE 1: DISTRIBUTION OF STUDY GROUP AS PER POP
 FIGURE 2: COMPARION OF CPK AMONG STUDY GROUP
 FIGURE 3: DISTRIBUTION OF STUDY GROUP AS PER OUTCOME
 FIGURE 4: COMPARION OF SERUM CPK AMONG STUDY GROUP

In our study, mean CPK levels were 143, 497.25, and 1806.80 IU/L for mild, moderate, and severe cases of poisoning. Bhattacharyya's study¹⁷ reported mean CPK levels of 273.53, 456.06, and 1032.57 IU/L, and Narmeen's study found levels of 89.1, 273, and 688.8 IU/L respectively.

poisoning severity increased, serum CPK levels also increased.

Mean serum pseudo cholinesterase levels for mild, moderate, and severe cases were 2956, 1034.13, and 180.40 IU/L respectively in our study. In Narmeen's study, these levels were 5834.8, 2077.2, and 607.4 IU/L. Bhattacharyya's study¹⁷ measured erythrocyte cholinesterase (EchE) levels, which were 8783.53, 4770.19, and 2021.93 IU/L for mild, moderate, and severe case

Our study showed a significant positive correlation between serum CPK levels and the severity of acute OP poisoning, as determined by the POP score. As



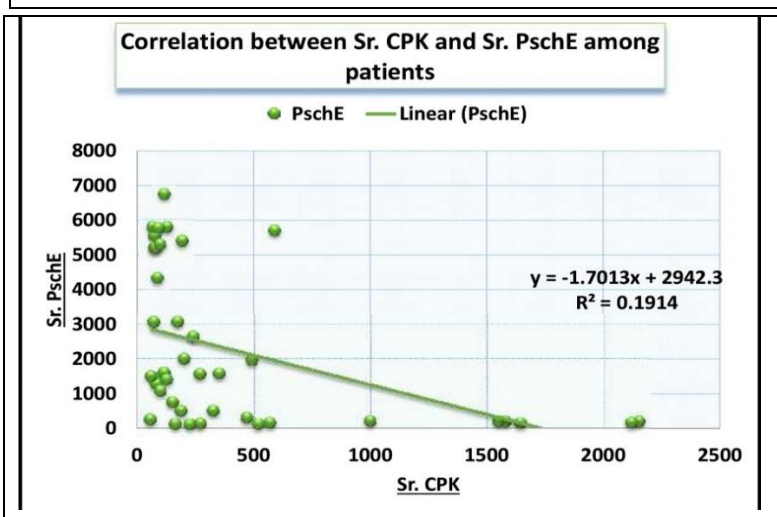
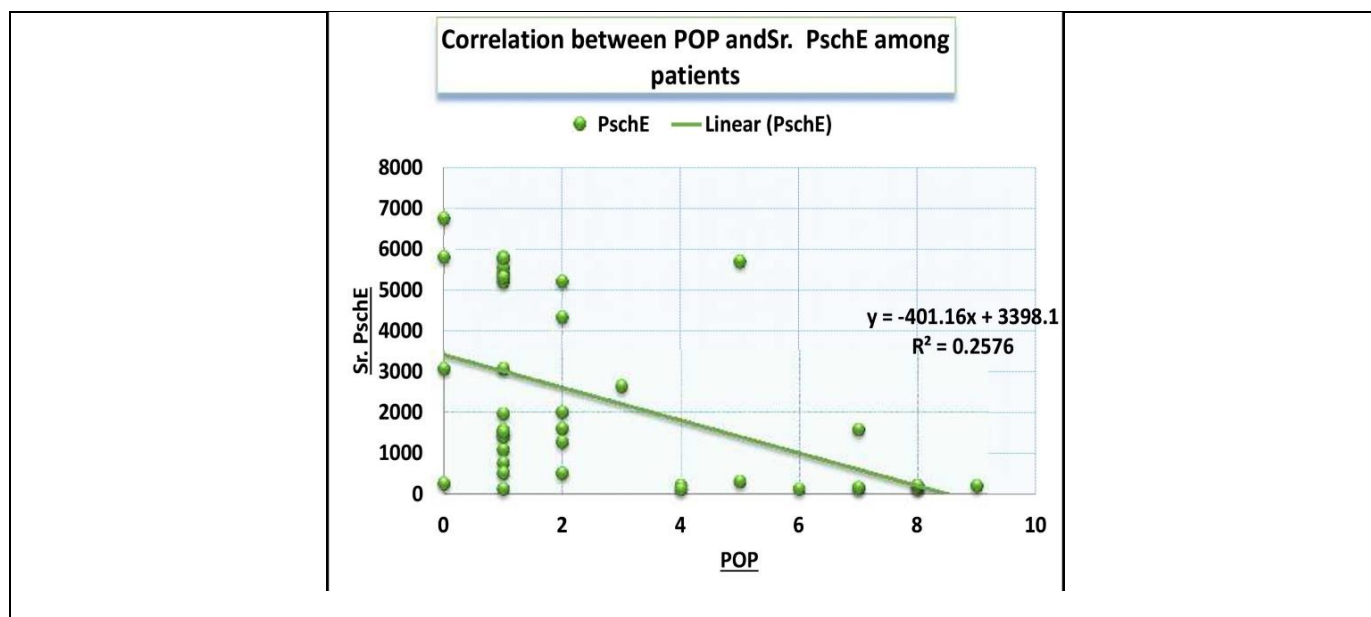


FIGURE 5: CORRELATION BETWEEN SERUM CPK AND POP AMONG PATIENTS

FIGURE 6: CORRELATION BETWEEN POP AND SERUM PschE AMONG PATIENTS

FIGURE 7: CORRELATION BETWEEN CPK AND SERUM PschE AMONG PATIENTS

We observed a negative correlation between serum CPK and serum pseudocholinesterase levels. Patients with high CPK had low pseudocholinesterase levels and vice versa, with statistically and clinically significant associations.

Bhattacharyya¹⁷ and Narmeen²⁰ reported a strong correlation between initial serum CPK and poisoning severity, supported by other studies. Elevated CPK indicates muscle injury, and its increase reflects the extent of acute muscle necrosis, as demonstrated by Calore et al's²¹ animal studies.

Our study found a link between high serum CPK levels and mechanical ventilation need and mortality. The highest mean CPK levels were in deceased patients and those requiring mechanical ventilation. Elevation in CPK levels predicts subsequent respiratory failure, as reported by Raddi and Sumathi.^{22,23}

Furthermore, our study revealed that high CPK is associated with severe poisoning and mortality.

negative correlation

Conclusion

Serum CPK level can be used as an alternative, equally effective and cost-efficient biomarker for assessing the severity of acute OP poisoning. However, the main disadvantage with this marker is its non-specificity. So, exclusion of other causes of raised CPK in a patient of acute OP poisoning is required.

Limitation

Since our study was conducted with a relatively small number of patients, further studies with greater number of patients are required to support our observation.

Source of Support: Nil.

Conflict of Interest: None

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