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CARDIAC AND HEPATIC TOXICITY IN PARAPHENYLENE DIAMINE (HAIR DYE) POISONING AMONG SUDANESE

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ABSTRACT

Accidental and deliberate PDD poisoning is not uncommon. The toxic effects of the dye on kidneys, liver and muscles are not fully understood and the cardiac toxicity is far poorly understood and ignored. A prospective descriptive cross sectional study was conducted in ENT hospital, Khartoum , Sudan to investigate the level of troponin, CKMB, CKtotal, LDH, AST, ALT and myoglobin in patients presented with parapheneylene diamine poisoning. A total of 40 patients were investigated. Levels were measured according to manufacturer protocols and normal values were taken accordingly. Among the study population the majority were females38 (95%) in the age group more than 32 years. The presenting symptoms were laryngeal edema, neck swelling and muscular swelling, the main presenting symptom was neck swelling which Was encountered in 22.5% of the population. There were 24 patients (40%) having no symptoms. The average values for troponin, CKMB, CKtotal, myoglobin, LDH, AST and ALT were found to be 0.018 (ng/ml), 566.8 (U/L), 1775 (U/L), 404.4 (ng/ml), 1800.5 (U/L), 636 (IU/L) and 305.4 (IU/L) consecutively. Troponin was found to be increased in 10% of the pateints, where lower reading was found to be 0.021 (ng/ml) and upper reading was 0.05 (ng/ml) normal value was taken up to 0.014. Thus in this study cardiac rhabdomyolysis in parapheneylene diamine poisoning was documented, the findings were not correlated with plasma level of the dye.

KEYWORDS: cardiac rhabdomyolysis, parapheneylene diamine (PPD) poisoning, Sudan.

INTRODUCTION

Paraphenylene diamine toxicity represents A main methods of suicide among Sudanese females according to the data of Omdurman teaching hospital from 17 cases of female suicide 15 were hair dye poisoning(88%)in the year 2012 **.** The first documentation of systemic PPD poisoning in 1924 described the case of a hairdresser who developed toxicity from handling the dye.[1]

Cases of PPD poisoning are frequently seen at the ENT causality and at the renal dialysis units, most of studies concentrate on the acute upper respiratory problems and renal complications, the nature of and severity of PPD induced cardiac toxicity was not well studied.

There is a high incidence of paraphenelylene diamine poisoning in our country beside wide contamination by the substance. Rhabdomyolysis and acute tubular necrosis are the two major corner stones in the pathogenesis of PPD toxication.[2][18][20] PPD causes contact dermatitis in susceptible individuals, but when ingested, it causes acute angioedema of Face and neck rhabdomyolysis and acute renal failure. PPD ingestion causes symptoms arising from involvement of different organs. Chemically, it is a derivative of paraphenylaniline.[3] Despite the fact that the causes of rhabdomyolysis are numerous, the final pathogenetic pathway is common, characterized by an increase in free ionized calcium in the cytoplasm.[12] [13] [14] [19] The increased [Ca2+]c initiates a chain of downstream reactions that eventually lead to the destruction of the muscle cell.[4] Myocarditis, myocardial rhabdomyolysis, and shock have also been described in PPD poisoning.[4][5][15][16][17]

Patients tend to present at the ENT department, causality, renal dialysis, dermatology and mortuary. There are very Limited published data about cardiac toxicity in PPD poisoning most of them were animal experimental work, none of them had been done in Sudan.

The current study was conducted to assess and validate the cardiac and hepatic toxicity in paraphenylenediamine poisoning (PPD), in terms of biochemical changes related to cardiac muscle damage and liver damage, special emphasis had been directed to cardiac toxicity.

MATERIALS AND METHODS

This is a prospective descriptive cross sectional study aimed at the investigation of The cardiac and hepatic toxicity due to paraphenelylene diamine among Sudanese patients. The study was Conducted at Omuderman teaching hospital and Khartoum ENT hospital during the period from may 2013 to December 2014.

Troponin, CKMB, CKtotal and myoglobin were measured using Cobas e 411 chemical analyzer was used. REF 04491815 190Roche diagnostic GmbH,D-68298 Manheim.

AST, LDH and ALT were measured by Chemical analyzer Mindray BS 200 P/N 0040-20-32482-(10.0)

Methods were according to the recommendations of the international federation of clinical chemistry (IFCC), heparinized serum was used within 24 hour at 20-25 oC.

Statistical analysis

Data obtained from this study were analyzed by using the statistical package for social science software (SSPS v. 13). A value of 0.05 was considered the value of statistical significance for all statistical tests in the present study. Chi square test was used to state the significance of the results.

Ethical clearance

A written consent had been obtained from all patients enrolled in this study, the aim of the study had been explained to patients.

Ethical approval was obtained from the ethical committee at the faculty of medicine university of Khartoum.

RESULTS

The characteristics of the studied population were shown in Table (1). The main presenting symptoms were laryngeal oedema, neck swelling and muscular swelling , the main presenting symptom was neck swelling which was found in 22.5% of the population. There were 24 patients (40%) having no symtoms. Table (2).

Troponin was found to be increased in 4 pateints, there as those for CKMB, CKtotal, myoglobin, LDH, AST and ALT were 37,30, 9,27,10 and 11 consecutively there were undetected values 1 for CKMB and 1 for LDH.

The upper readings, lower readings and average values were shown in table (4), for troponin the normal value was up to 0.014 (ng/ml), the lower reading was 0.021(ng/ml) and the higher reading was 0.015 (ng/ml), the average values for the increased was 0.018 (ng/ml).

CKMB the normal was up to 24 (U/L) while the lower reading was 31 (U/L), upper reading 4701 (U/L). The average was found to be 1775 (U/L).

The values for CKtotal were as followed upper reading 173 (U/L), lower reading 7810 (U/L) and the average was 1775 (U/L). The normal was taken up to 151 (U/L).

The values for myoglobin were 152 (ng/ml) lower reading, 680 (ng/ml) upper reading and the average was 404.4 (ng/ml). the normal was taken up to 70 (ng/ml).

The values for LDH, AST and ALT were as followed normal 207-414 (U/L), 1-50 (IU/L) and 10-50 (IU/L) consecutively. The upper readings were 70155 (U/L), 1452 (IU/L) and 606 (IU/L)

where as the lower readings were 416 (U/L), 72 (IU/L) and 83 (IU/L).
The average was 1800.5 (U/L), 636 (IU/L) and 305.4 (IU/L) for each.
Enzymes levels were not correlated the plasma levels of PPD.

Table (4.1): distribution of the study population by age and gender

Age groups	Gender		Total
	Male	Female	
1-16 years	0	8	8 (20%)
17-31	1	1	2 (5%)
□ 32 +	1	29	30 (75%)
Total	2 (5%)	38 (95%)	40 (100%)

Table (4.2): distribution of the study population according to symptoms.

symptoms	Frequency	Percent	Total
Laryngeal edema	1	2.5	
Neck swelling	9	22.5	
Muscular edema	6	15	
No symptoms	24	40	
Total	40	100	

Table (4.3): shows the values of troponin, CKMB, CK total, myoglobin, LDH, AST and ALT.

Parameter values	Troponin	CKMB	CKtotal	Myoglobin	LDH	AST	ALT
increased	4	37	30	9	27	10	11
normal	36	2	10	31	12	30	29
undetectable	1	1	0	0	1	0	0

Table (4.4): Shows increased upper and lower values of troponin, CKMB, CK total, myoglobin, LDH, AST and ALT.

Variable values	Troponin (ng/ml)	CKMB (U/L)	CKtotal (U/L)	Myoglobin (ng/ml)	LDH (U/L)	AST (IU/L)	ALT (IU/L)
Normal	Up to 0.014	Up to 24	Up to 151	Up to 70	207-414	10-50	10-50
lower reading	0.021	31	173	152	416	72	83
Upper reading	0.015	4701	7819	680	70155	1452	606
average	0.018	566.8	1775	404.4	1800.5	636	305.4

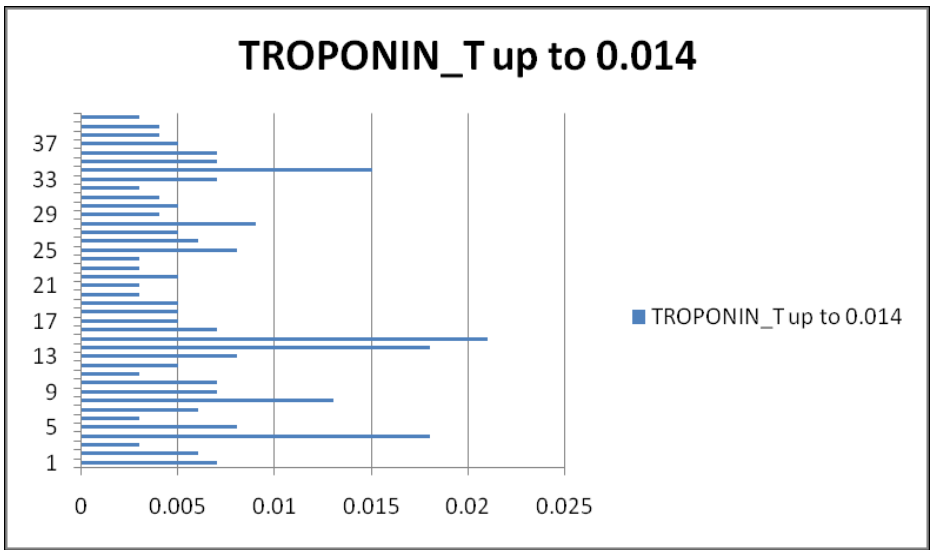

Figure (1): Shows the distribution of troponin values taking up to 0.014 as normal.

DISCUSSION

In the current study it was documented that there was significant cardiac rhabdomyolysis in PPD toxicity as well as more marked rhabdomyolysis. The fact was supported by an increase in troponin which is cardio specific and incomparable increase in CKMB, CK total and myoglobin.

This is the first study investigating the cardiac enzymes in this number of paients.

Common features of Para-phenylene diamine poisoning are orofacial oedema, angio-neurotic oedema, rhabdomyolysis, myoglobinuria, acute renal failure. In the study done on 13 patients 11 were females having mean age 27.2 years, the predominant clinical features were cervicofacial oedema and pain, cola-coloured urine and oliguria. Laboratory investigations revealed elevated hepatic transaminases (100%), leucocytosis (92.3%), elevated creatinine phosphokinase (92.3%).[5]

Omdeman hospital mortuary registration revealed almost comparable ages with the previous study from south India.

The present study is in agreement concerning the clinical presentation since all patient 40 patients presented with cevicofascial oedema. The previous study had the limitation of low number of cases. Even in the present study clinical presentation was not correlated with plasma level of PPD.

Almost all previous studies concentrated on the renal involvement in PPD toxicity and causes of renal failure and now it is well known in the treatment protocols to take measures to minimize the renal insult. Apart from few case reports and animal experimental work the cardiac manifestations were ignored.

In the experimental design by Abdelzaher et al. 2012.[7] which was done in Albino rats a case control design the level of CKMB and LDH was found to be CKMB ranges

157.1 to 575.5 (U/L) according to doses applied to skin, where as the figures for LDH were 256.8 to 1375.2 (U/L), troponin was not taken as a measure of cardiac injury in the study. The figures are in agreement with our study where the average of CKMB 566.8(U/L) and that for LDH 1800.5 (U/L).

The present study documented the cardiac injury associated with PPD toxicity and it explains cases of sudden death observed with toxcicity. Mundav et al (1989) concluded that the toxic effects of PPD are related with high doses causing rhabdomyolysis, acute renal failure and sudden death, the work was done On rats and tissue damage was attributed to increased free radical formation.[8]

In the present study such correlations can not be done since the PPD concentration was not measured.

A Case report showed normal troponin and cardiac enzymes corresponding with normal troponin value in 90% of patients. CKMB was increased in 37 patient representing 92.5% compatible with the literature.[8] [10] [11] Indicating the rhabdomyolysis involving the cardiac muscle.

CK total was increased in 30 patients representing 75 % of patients, results were compatible with PK Jain et al.[9] where 521 cases (51.08%) showed raised serum CPK levels. Maximum value of serum CPK level was reported as 2,81,000 IU/L.

All cases of increased CKMB levels show more than 4% CKMB\CK ratio indicating myocardial damage.

Serum myoglobin was increased in 9 representing 22.5%, Myoglobin is released from muscle tissue by cell destruction and alterations in the permeability of the skeletal muscle cell membrane. Causes of elevation include myocardial infarction, rhabdomyolysis ,myopathies and renal failure. Thus, the precipitation of myoglobin in the renal tubules with secondary obstruction, tubular toxicity, or both constitutes the primary causes for acute kidney injury during myoglobinuria.

The present study documented the acute cardiac damage following PPD ingestion evidenced by high CKMB level in 92.5% of patients, elevated CK total in 75% of patients, all patients with elevated CKMB show CKMB/CK ratio more than 4% and all cases of elevated CKMB show CK elevation (p value.05).

CONCLUSION: The current study documented cardiac rhabdomyolysis in para pheneylene diamine toxicity, but failed to correlate the values of cardiac enzymes with the plasma level of PDD.

Competing interests

The authors declare that they have no competing interests.

Authors contributions

AMM and IA coordinated and carried out the study. AB and ME participated in the statistical analysis. MA participated in the clinical work and laboratory work.

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