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Biochemistry

A Retrospective Study on the Biochemical Profile of Self Poisoning with a Popular Indian Hair Dye

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ABSTRACT

Background: The use of Supervasmol 33 ®, a commonly used hair dye, with a suicidal intention, is associated with significant morbidity and mortality. The Clinical Biochemistry laboratory can play an important role in the management of the patients who have consumed this dye, since a better understanding of the biochemical changes with respect to the quantity of dye which has been consumed, can lead to an early identification of the complications.

Aim: The present study was thus taken up to compare the biochemical profile of the patients with Supervasmol 33 ® dye poisoning and to check whether a dose-toxicity relationship existed.

Materials and Methods: Eighty one individuals, who consumed Supervasmol 33® during a period of two years, were retrospectively considered for the study. They were divided into two groups based on the amount of dye which was consumed (group I ≤50ml and group II >50ml). The biochemical parameters of these patients were analysed by using a Beckman CX9 Auto-analyser and commercial kits.

Results: The renal function parameters like urea, creatinine and potassium were significantly higher in the group II patients as compared to the group I patients ($p<0.001$). The enzymes, creatine phosphokinase (CPK), aspartate transaminase (AST) and alanine transaminase (ALT) were elevated in the group II patients as compared to the group I patients, though this difference was statistically insignificant. The group II patients had more adverse clinical outcomes in the form of a longer duration of hospital stay, more number of patients requiring haemodialysis and mortality. The consumption of Supervasmol 33® > 50ml was associated with serious complications like rhabdomyolysis, acute renal failure and adverse clinical outcomes.

Conclusion: Biochemical changes are related to the severity of the organ damage and can thus help in the early diagnosis of the complications as well as in the follow-up of the organ damage.

Key Words: Acute renal failure, Biochemical changes, Hair dye poisoning, Paraphenylenediamine, Rhabdomyolysis

INTRODUCTION

Hair dye poisoning is widely reported in the underdeveloped and developing countries such as Asia and Africa [1-7]. Case reports have also been published from India [3-6]. Poisoning with Supervasmol 33 ®; a commonly used hair dye, in South India have been reported [4-6]. This dye is composed of paraphenylenediamine (PPD), ethylene diamine tetra acetic acid (EDTA), propylene glycol, liquid paraffin, cetostearyl alcohol, sodium laurylsulphate and resorcinol. Its main constituent, PPD, is widely used for dyeing furs as well as for oxidizing hair dyes, while in India, it is used in combination with *henna* (*Lowsonia inermis*). Henna is used traditionally to colour the palms and to dye hair. PPD accelerates the dyeing process. PPD produces local toxic effects in the form of skin irritation, contact dermatitis, chemosis, lacrimation, exophthalmos or even permanent blindness. The direct toxic effects of PPD on the mucous membranes cause severe oedema of the face and neck, which frequently require emergency tracheostomy [8]. This is followed by rhabdomyolysis and acute renal failure which often culminate in death, if they are not treated aggressively [9,10]. Propylene glycol, another constituent of Supervasmol 33 ®, is a phenol derivative and is commonly used as a solvent. Resorcinol, being a phenol, has been postulated to cause renal failure, while EDTA which may be present may cause hypocalcaemia.

Over the past few years, we have been observing a number of cases which were being admitted to the emergency ward at our tertiary care centre, of ingestion of Supervasmol 33 ® with a suicidal intention. The poisoning with this product has increased because of its extensive usage for dyeing purposes. Also, it is widely available across the counter. The Clinical Biochemistry laboratory can play an important role in the management of these patients. This has been pointed out in one of the case reports of Gandhe et al (2009) [11]. There are very few reports [5, 6, 8] on the changes in the biochemical profile in patients who have consumed the Supervasmol 33® hair dye. The biochemical changes reflect tissue damage. The most common cause of death in these patients is acute renal failure, which occurs as a result of the nephrotoxic components of this hair dye, as well as due to rhabdomyolysis. The early identification of rhabdomyolysis can help the clinicians in initiating renoprotective measures and in thus decreasing the morbidity and the mortality. The degree of the tissue damage is related to the dose of the poison; hence, an understanding of the biochemical changes with respect to the quantity of the dye which has been consumed, can lead to an early identification of the possible complications like acute renal failure and can lead to a better management of these patients. The present study was thus taken up to compare the biochemical profile of the patients, based on the amount of the Supervasmol 33 ® dye which was consumed and to investigate whether a dose-toxicity relationship existed.

MATERIALS AND METHODS

We retrospectively included 81 consecutive patients of self-poisoning with Supervasmol 33 ®, who were brought to the emergency ward of Sri Venkateswara Institute of Medical Sciences (SVIMS), Tirupati, between May 2008 and April 2010. Most of the patients received preliminary care at other centres before being referred to our hospital, which is a tertiary care centre. The demographic data and the clinical presentations were retrieved from the patient's medical records which were available with the medical records section of our institute. One patient was excluded due to death on the day of admission due to cardio-respiratory arrest. To check whether a dose-toxicity relationship existed, we divided the remaining patients into two groups based on the amount of dye which was consumed, from the case history which was given in the patient records. Seventeen patients who had consumed ≤ 50 ml of the dye were assigned to group I, while 22 patients who had consumed more than 50ml were assigned to group II. The history of the amount of dye which was consumed was not available in 41 patients.

This division was based on the availability of the Supervasmol 33® hair dye in the market in two pack sizes; 50ml and 100ml, and for each application 10-15ml of the dye was required, as per the oral questioning of the dye users. Hence, the exact amount of consumption could not be ascertained, since the dye was usually in use. Hence, the grouping of the patients was as follows: ≤ 50 ml (group I) and >50ml (group II). The amount of PPD which was present in 100ml of the Supervasmol 33® dye was 4g (4%) as was mentioned on the bottle and similarly in a 50ml bottle, the dye amount was 2g (4%).

The biochemical findings were retrieved from the hospital information system from day 2 to day 4 after the consumption of the dye. Though the data for these patients was available from day 1 of their admission to the day of discharge (average hospital stay – 9.21 days; range:2-33 days), day 3 was selected, based on the observation of the data which showed a peak around day 3. Also, our hospital being a tertiary care centre, the patients were referred here from other hospitals after receiving primary care there. Once admitted, the treatment was initiated and the investigations were sent for further management. This incidentally also was found to be the third day on an average in most of the cases.

ASSAYS

The biochemical parameters such as serum urea, creatinine, sodium, potassium, total bilirubin, conjugated bilirubin, Aspartate transaminase (AST), Alanine transaminase (ALT), Lactate dehydrogenase (LDH) and Creatine phosphokinase (CPK) were measured by using a Beckman CX9 fully automated analyser and commercially available kits.

STATISTICAL ANALYSIS

The data were reported as means ± SD for the normally distributed variables and as median (range) for the skewed variables. The comparison of the variables between the groups I and II was done by using the 't' test for the normally distributed variables and the Mann-Whitney U test for the skewed variables by using a Microsoft Excel spread sheet and SPSS for Windows, version 11.5. p values which were <0.05 were considered as statistically significant.

RESULTS

As shown in [Table/Fig-1], the patients with Supervasmol 33® poisoning had elevated renal parameters i.e urea and creatinine levels. Similarly, they showed elevated levels of the enzymes AST, ALT, LDH and CPK.

As shown in [Table/Fig-2], the renal function parameters i.e. urea, creatinine and potassium were significantly higher in the group II patients as compared to the group I patients (p<0.001). The enzymes, LDH and CPK were higher in the group II patients as compared to the group I patients, but the difference was not statistically significant. Similarly, the levels of AST and ALT were higher in the group II patients as compared to the group I patients, but the difference was statistically insignificant.

Adverse clinical outcomes were predominant in the group II patients as compared to the group I patients, as was seen by the requirement for the dialysis and the longer duration of the hospital stay. The mortality in group I was 1 out of 17 (5.88%), while in group II, it was 2 out of 22 (9.09). This was based on the period of the follow-up from the day of admission till the date of the discharge (2-33days).

DISCUSSION

A number of case reports and series have been published on hair dye poisoning with a suicidal intention. These studies were focussed on the clinical presentation, as well as on the biochemical changes. The Supervasmol 33® hair dye has been shown to produce systemic toxicity which has been attributed to its main component, PPD, the lethal dose of which has been shown to be 3g%. PPD produces local toxic effects in the form of skin irritation, contact dermatitis, chemosis, lacrimation, exopthalmos or even permanent blindness. Laryngeal oedema occurs even with 5-10ml of Supervasmol 33® due to the direct toxic effects of PPD on the mucous membranes, which often require an emergency tracheostomy [8]. Another common finding which has been seen in patients with Supervasmol 33® poisoning, is rhabdomyolysis. PPD promotes calcium release and the leakage of calcium ions from the smooth endoplasmic reticulum, thus causing continuous contraction and irreversible change in the muscle structure [12]. Rhabdomyolysis is the main cause of acute renal failure and the morbidity and mortality are high once renal failure develops.

An early recognition of the rhabdomyolysis is crucial, since intravenous bicarbonate and saline have been shown to ameliorate the development of acute renal failure[5]. Rhabdomyolysis results in the release of muscle cell contents like potassium, phosphorus and myoglobin, as well as enzymes like CPK, AST, ALT and LDH into the circulation. As shown in [Table/Fig-1], the patients with Supervasmol 33® poisoning showed rhabdomyolysis, as was evidenced by the elevated levels of serum potassium, and enzymes like AST, ALT, CPK, and LDH. The elevated renal parameters suggested the development of acute kidney injury due to rhabdomyolysis.

To check whether a dose-toxicity relationship existed for Supervasmol 33® poisoning, the biochemical markers were compared, based on the amount of dye which was consumed, in patients in whom the history of the amount which was consumed was available. As shown in [Table/Fig-2], the group II patients i.e those who had consumed > 50 ml of the Supervasmol 33® hair dye showed significantly higher potassium levels along with higher levels of the enzymes, CPK, AST, ALT, and LDH as compared to the group I patients i.e those who had consumed ≤ 50ml of the Supervasmol 33® hair dye. This showed that the amount of the dye did contribute to the cell damage, thereby releasing contents from the RBCs and the myocytes, thus contributing to the severity of the rhabdomyolysis.

Variables	(Mean ± SD) (n=80)	Reference values
Urea (mg/dL)	62.54 ±59.27	15 – 40
Creatinine (mg/dL)	2.55 ± 2.85	0.7 – 1.4
Sodium (mmol/L)	138.14 ± 5.35	130 – 150
Potassium (mmol/L)	4.37± 0.77	3.0 – 5.0
Total bilirubin (mg/dL)	1.30± 0.54	0.2 – 1.2
Direct bilirubin (mg/dL)	0.28± 0.23	0.2 – 0.4
AST (SGOT))† (IU/L)	208 (17-1340)	< 40
ALT (SGPT)† (IU/L)	138.5 (14-1180)	< 35
LDH (IU/L)†	905.00 (80-15400)	200 – 400
CPK (IU/L)†	11240.00 (80-78500)	< 200

[Table/Fig-1]: Biochemical Profile of patients with Supervasmol 33 ® poisoning
SD = Standard deviation; † = Median values.

Variables	Group I (Mean ± SD) ≤ 50 ml (n=17)	Group II (Mean ± SD) > 50 ml (n=22)	P value
Urea (mg/dL)	41.68 ±38.61	90.40 ± 64.46	<0.01*
Creatinine (mg/dL)	1.34 ± 1.62	3.75 ± 3.31	<0.01*
Sodium (mmol/L)	139.47 ± 4.51	136.13 ± 7.51	NS
Potassium (mmol/L)	4.02 ± 0.55	4.75 ± 0.93	<0.01*
Total bilirubin (mg/dL)	1.38 ± 0.69	1.40 ± 0.51	NS
Direct bilirubin (mg/dL)	0.27 ± 0.18	0.33 ± 0.31	NS
AST (SGOT))†, (IU/L)	176.00 (31-1880)	188.00 (83-1340)	NS
ALT (SGPT)† (IU/L)	88.00 (14-735)	156.00 (62-1180)	NS
LDH (IU/L)†	1320.00 (840-7400) (n=6)	740.00 (287-12970) (n=13)	NS
CPK (IU/L)†	6775.00 (80-10120) (n=6)	11400.00 (798-48700) (n=13)	NS

[Table/Fig-2]:Comparison of Biochemical parameters between two groups *= statistically significant; †= Median values; SD = Standard deviation; n = Number of patients.

Outcome	Group I (≤50 ml) (n=17)	Group II (> 50ml) (n=22)
Patients requiring haemodialysis	1 (5.88%)	9(40.9%)
Patients requiring ventilatory support	8 (47.05%)	8 (36.36%)
Duration of hospital stay (Days)	8.87± 6.08	12.95 ± 9.37
Recovered	16	20
Death	1(5.88%)	2(9.09%)

[Table/Fig-3]: Outcome of patients

Though, CPK, AST, ALT and LDH are representative of the degree of muscle injury as myoglobin, they do not predict the development of renal failure [13]. Elevated potassium levels serve as a sole prognostic indicator of rhabdomyolysis. In vivo experiments in cats have shown that for every unit (mmol/L) of increase in the initial potassium concentration, there is a 57% decrease in the chance of survival [14]. Elevated potassium levels can lead to fatal arrhythmias. Given the high risk of acute renal failure (ARF) in rhabdomyolysis, potassium has been suggested as an important marker of renal function [15]. The early recognition of ARF and prompt treatment with dialysis are crucial to prevent fatal complications. Hence, the serum potassium levels were taken as an indicator of rhabdomyolysis, although the data for the serum CPK levels were also available in some patients, to support our findings of rhabdomyolysis.

Myoglobin, which was released as a result of rhabdomyolysis, has been implicated in heme induced renal damage, mainly by causing oxidative damage to the renal tubules. However, renal failure can also occur as a result of other nephrotoxic chemicals which are present in the Supervasmol 33® dye. Apart from PPD, propylene glycol and resorcinol which are present in the Supervasmol 33® dye can result in acute tubular necrosis. The histological change of acute tubular necrosis has been described in PPD poisoning [16]. Propylene glycol which is present in the Supervasmol 33® dye, is associated with hyperosmolality, raised anion gap metabolic acidosis, central nervous system depression, arrhythmias and less commonly, renal dysfunction [17]. A proximal renal tubular cell swelling and vacuole formation have also been seen in propylene glycol poisoning cases [18]. But the characteristic features of rhabdomyolysis and laryngeal oedema which typify PPD are absent with propylene glycol.

The group II patients had significantly elevated urea, creatinine and potassium levels as compared to the group I patients. One patient in group I and 14 patients in group II developed renal failure, of which one patient of group I and 9 patients of group II required dialysis support. This showed that the dose of the dye was related to end organ damage.

Hence, the results of our study suggest that the ingestion of more than 50ml of the Supervasmol 33® dye was associated with significant rhabdomyolysis and acute renal failure, which required haemodialysis. The only supportive evidence in the form of urine myoglobin levels was however lacking.

The adverse clinical outcomes also show the dose-outcome relationship. The patients in group II, who had consumed > 50 ml of the dye, had a poor clinical outcome, with more number of patients requiring dialysis support and a longer hospital stay as compared to the group I patients. Mortality was seen in two patients in group II as against one in group I. This sole mortality in group I was probably due to the late presentation of this patient (11th day). The lethal dose of PPD has been shown to be 3g [10], which was the dose which was associated with the consumption of > 50 ml of the dye.

A number of case reports have been published, which have reported rhabdomyolysis and acute renal failure as the consequences of hair dye consumption [3-5]. However, to the best of our knowledge, no one has evaluated the biochemical changes which are associated with hair dye poisoning in a large group of patients with respect to the amount of dye which was consumed. Chrispal et al (2010) [6], in a retrospective study, have evaluated the clinical and the laboratory profile of the patients with Supervasmol 33® poisoning and have found no dose toxicity relationship in their study (n=13). However, the number of patients was too less in their study, to draw any solid conclusion.

An early diagnosis and intervention are the cornerstones for the management in the cases of rhabdomyolysis and acute renal failure. In cases where the amount which is consumed is not known, the biochemical changes can give a clue to this and guide the physicians to manage the patients accordingly. The results

of the present study showed that the biochemical changes were related to the severity of the organ damage. Hence, biochemical investigations can help in the early diagnosis of the complications, as well their follow-up. Supervasmol 33® is available quite freely across the counter and is used extensively. There should be regulations and restrictions on the sale of PPD containing products (Hair dyes) like Supervasmol 33®.

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