Toxicology: Open Access

Research Article Open Access

Correlation between Demographic Variables, Treatment Modalities and Outcome in Acute Copper Sulphate Poisoning in a Tertiary Care Hospital in Bangladesh

Debasish Dutta[1], Richmond Ronald Gomes*[2], FM Monjur Hasan[3], Seema Saha[4] and Md. Mamun Newaz[5]

[1]Departments of Medicine, Ad-din Women's Medical College Hospital, Dhaka, Bangladesh
[2]Department Medicine, Jashore Medical College Hospital, Jashore, Bangladesh
[3]Department of Medicine, Ad-din Sakina Women's Medical College Hospital, Jashore, Bangladesh
[4]Department of Microbiology, Jashore Medical College Hospital, Jashore, Bangladesh
[5]Department of Medicine, Rajshahi Medical College Hospital, Rajhshahi, Bangladesh

Abstract

Background: Ingestion of copper sulphate is a common mode of poisoning in the Indian subcontinent. Cases are mainly suicidal in nature. The clinical course of the copper sulphate intoxicated patient is often complex involving intravascular hemolysis, jaundice and renal failure. The treatment is mainly supportive. Mortality is quite high in severe cases if treatment is not adequate and prompt.

Methods and materials: This cross sectional, observational, prospective studywas conducted on 50 patients with acute copper sulphate poisoningattended in Medicine department of Khulna Medical College Hospital from January 2020 to June 2020.

Result: The study showed that age frequency 25(50%) were from 11-20 years,15(30%) were from 21-30 years, 5(10%) were from 31-40 years, 3(6%) were from 41-50 years, 1(2%) were from 51-60 years, and 1(2%) were from 61-70 years of age. Out of 50 patients, 17(34%) were male and 33(66%) were female patients. poisoning is more common in married (68%) person than unmarried (32%); among low educational background population as 37(74%) of the study population having educational qualification of primary or below primary; among housewife 23(46%), student 12(24%) and farmer/day labour 8(16%); among rural population 33(66%) than urban 17(34%); among poor people 40(80%) than solvent 10(20%). History of familial disharmony/stress 36(72%) and depressive illness 13(26%) are common than others. Moderate to severely raised serum ALT (p-value=0.05), presence of hemolysis on peripheral blood film(p-value=0.035) and raised serum creatinine (p-value=0.035) demonstrated significant statistical association with the outcome of patients. All the patients were treated conventionally. With supportive treatment, 48(96%) of patients were improved and 2(4%) of patients had died where penicillamine was used as chelating agent in about all patients 49(98%).

Conclusion: Acute copper sulphate poisoning is common in our country which is mainly suicidal in nature. As death occurs due to multi organ failure, while gastrointestinal, intravascular haemolysis, hepatic and renal toxicities significantly contribute to it. Management in High dependency unit is also required.

Keywords: Intravascular hemolysis, Jaundice and Renal failure, Penicillamine

Introduction

Copper sulphate forms bright blue crystals containing five molecules of water [$CuSO_4.5H_2O$]. It is commonly known as "Blue Vitriol" or "Blue Stone". Usually The people of the southern region of Bangladesh uses copper sulphate as a fungicidal agent [1]. It is used chiefly for agricultural purposes as a pesticide and in leather industry. It was also being used as a precipitator in heavy metal poisoning and was used to treat gastric and topical exposure to phosphorous. It has a nauseous and metallic taste. Solutions are acid to litmus, freely soluble in water [2,3]. It is consumed mainly with suicidal intentions. Accidental poisonings have been reported from children as well [4,5].

Approximately 30% of ingested copper is absorbed from the gastrointestinal tract [6]. In blood, copper is initially albumin-bound and transported via the hepatic portal circulation to the liver where it is incorporated into ceruloplasmin. Copper is present in serum in two forms; 93% is tightly bound to ceruloplasmin and 7% is loosely bound to albumin [7]. The copper-albumin complex represents the toxicological active portion of the serum copper [2]. Systemic transport of copper from liver is primarily as ceruloplasmin, which appears to donate copper to tissues. Copper is distributed to all tissues with the highest concentrations in liver, heart, brain, kidneys and muscle. Intracellular copper is predominantly bound to metallothionein. Fecal and biliary excretion accounts for 80 percent of excreted copper. Approximately four percent is excreted in the urine [6].

In acute poisoning, albumin, rather than ceruloplasmin, binds the excess copper. The liver is the major site of deposition of copper following large ingestion.Lethal dose is about 10-20 g [7]. The copper

***Corresponding author:** Richmond Ronald Gomes, Departments of Medicine, Ad-din Women's Medical College Hospital, Dhaka, Bangladesh, E-mail: rrichi.dmc.k56@gmail.com

Received: 26-Oct-2021, Manuscript No. tyoa-21-45690; **Editor Assigned:** 09-Nov-2021; PreQC No. tyoa-21-45690(PQ); **Reviewed:** 13-Jan-2022, QC No: tyoa-21-45690, **Revised:** 17-Jan-2022, Manuscript No: tyoa-21-45690(R); **Published:** 24-Jan-2022, DOI: 10.4172/2476-2067.1000170

Citation: Dutta D, Gomes RR, Hasan FMM, Saha S, Newaz M (2022) Correlation between Demographic Variables, Treatment Modalities and Outcome in Acute Copper Sulphate Poisoning in a Tertiary Care Hospital in Bangladesh. Toxicol Open Access 8: 170.

content in normal adult liver ranges from 18-45 mg/g dry weight. When the concentration of hepatic copper is greater than 50 mg/g dry weight, liver cell necrosis occurs with release of large amount of copper into the serum. This released copper is rapidly taken up by erythrocytes and results in oxidative damage and may result in hemolysis of RBCs [2]. It is proposed that free reduced copper in the cell binds to sulfhydryl groups and inactivates enzymes such as glucose-6-phosphate dehydrogenase and glutathione reductase [8]. Intravascular hemolysis appears 12-24h following ingestion of copper sulphate.

Jaundice in copper sulphate poisoning is partly hepatic in origin in addition to hemolysis [9]. Jaundice appears on the second or third day following ingestion. Liver damage has been attributed to liver mitochondrial dysfunction due to oxidized state. Intravascular hemolysis plays a major role in the pathogenesis of renal failure [8,10]. The heam pigment released due to hemolysis and direct toxic effect of copper released from lysed red cells contribute to tubular epithelial damage of the kidney. Severe vomiting, diarrhea, lack of replacement of fluid and gastrointestinal bleed, leading to hypotension could also contribute to renal failure [10]. Renal complications are usually seen on the third or the fourth day and onwards after the poisoning [11].

The incidence of copper sulphate poisoning varies at different geographical areas depending on the local use of copper sulphate and the availability of other suicidal poisons. Diagnosis is based on history of exposure. Mainstay of treatment is supportive, including careful fluid therapy and vasopressors as needed, blood transfusion if needed and methylene in symptomatic methemoglobinemia. Chelation therapy given in most cases. The role of dialysis is limited to the management of associated renal failure. High mortality is noted in severe cases due to methemoglobinemea, hepatotoxicity and renal failure.

Method and material

This cross sectional, observational, prospective study was carried out in Medicine department of Khulna Medical College Hospital(KMCH) from Januray, 2020 to June 2020. Total 50 cases of acute copper sulphate poisoning were selected. Data were processed and analyzed using SPSS (Statistical Package for Social Science) 15.0.

Inclusion criteria

- All patients with acute copper sulphate poisoning admitted in Medicine wards of KMCH.
- Voluntarily given consent.

Exclusion criteria

- Not willing to give informed consent.
- Patient is suffering from Wilsons disease, chronic liver disease and chronic kidney disease.

Results

Table- 1 shows that copper sulphate poisoning most commonly occurs under the age of 30 years (80%) and less common in old age group between 50-70 years(4%). Their age frequency 25(50%) were from 11-20 years, 15(30%) were from 21-30 years, 5(10%) were from 31 -40years, 3(6%) were from 41-50 years, 1(2%) were from 51-60 years, and 1(2%) were from 61-70 years of age.

Copper sulphate poisoning is more common in female than male. Table -2 shows that among 50 cases, 17(34%) were male and 33(66%) were female.

Table -3 shows that copper sulphate poisoning is more common in married (68%) person than unmarried (32%).

Table -4 shows that copper sulphate poisoning is more common among people with low educational background. 74% of the study population having educational qualification of primary or below primary level.

Table -5 shows that copper sulphate poisoning is more common among housewife 23(46%), student 12(24%) and farmer/day labour 8(16%).

Table -6 shows that copper sulphate poisoning is more common among rural population 33(66%) than urban 17(34%).

Table -7 shows that copper sulphate poisoning is more common among poor people 40(80%) than solvent 10(20%).

Table -8 shows that copper sulphate poisoning is more common

Table 1: Showing frequency of age of the respondent.

Age group	Frequency	Percent
11-20	25	50.0
21-30	15	30.0
31-40	5	10.0
41-50	3	6.0
51-60	1	2.0
61-70	1	2.0
Total	50	100.0

Table 2: Showing frequency of sex of the respondent.

Sex	Frequency	Percent
Male	17	34.0
Female	33	66.0
Total	50	100.0

Table 3: Showing distribution on the basis of marital status.

Marital status	Frequency	Percent
Married	34	68.0
Unmarried	16	32.0
Total	50	100.0

Table 4: Showing distribution on the basis of educational status.

	Frequency	Percent	Cumulative Percent
Primary	37	74	74
SSC	10	20	94
HSC	3	6	100
Total	50	100	

Table 5: Showing distribution on the basis of occupation.

Occupation	Frequency	Percentage (%)
Housewife	23	46.0(%)
Student	12	24.0(%)
Farmer/ day labour	8	16.0(%)
Service	1	2.0(%)
Others	6	12.0(%)
Total	50	100.0(%)

Table 6: Showing distribution on the basis of location of residence.

location of residence	Frequency	Percentage (%)
Rural	33	66.0(%)
Urban	17	34.0(%)
Total	50	100.0(%)

Table 7: Showing distribution on the basis of Socio-economic condition.

Socio economic status	Frequency	Percentage (%)
Poor	40	80.0(%)
Solvent	10	20.0(%)
Total	50	100.0(%)

Table 8: Showing relevant Psychiatric/ Family /Personal History.

Relevant Psychiatric/Family/Personal History	No. of Patient	Percentage (%)
Familial disharmony/stress	36	72%
Previous suicidal attempt	15	30%
H/O depressive illness	13	26%
H/O suicidal attempts in family members	6	12%
H/O schizophrenia	2	4%
Suicidal death in family members	1	2%

Table 9: Modalities of Treatment.

Modalities of Treatment		No. of patients	Percentage(%)
Induced vomiting at home/ hospital	Done	40	80.00%
	Not done	10	20.00%
Stomach wash with plain water/1% potassium ferrocyanide	Given	46	92.00%
	Not given	4	8.00%
Cap. penicillamine	Given	49	98.00%
	Not given	1	2.00%
Inj. Dimercaprol	Given	1	2.00%
	Not given	49	98.00%

among patients suffering from familial disharmony /stress 36(72%) and depressive illness 13(26%), than others

Table- 9 shows that all the patients were treated conventionally. 40(80%) patients were forced to vomit by artificial means (induced vomiting). 46(92%) patients received Stomach wash with plain water or 1% potassium ferrocyanide. Penicillamine was used as chelating agent in 49(98%) patients.

Table- 10 shows that with the above treatment, 48(96%) patients improved and 2(4%) patients died.

Among 16 patients of raised serum creatinine, 14 patients improved and 2 patients died. Among 34 patients of normal serum creatinine, all of them(100%) improved. There is statistically significant association (p-value=0.035) between raised serum creatinine and outcome of treatment of patients in acute copper sulphate poisoning (Table- 11).

Chi-square ($\chi 2$) Test was employed to analyze the data. P-value <0.05 was considered statistically significant.

Among 13 patients of Moderate to severely raised (>80 u/l) serum ALT, 11 patients had improved and 2 patients had died. among 4 patients of Mildly raised (41-80 u/l) serum ALT and 33 patients of normal serum creatinine, all of them(100%) had improved. There is statistically significant association (p-value=0.05) between raised serum ALT and outcome of patients in acute copper sulphate poisoning **(Table- 12).**

Chi-square ($\chi 2$) Test was employed to analyze the data. P-value <0.05 was considered statistically significant.

Among 16 patients with features of hemolysis on peripheral blood film, 14 patients improved and 2 patients died. Among 34 patients with normal peripheral blood film, all patients(100%) improved. There is

Table 10: Outcome of treatment of the patients under study.

Outcome of treatment	No. of patients	Percentage (%)
Improved	48	96.00%
Death	2	4.00%
Total	50	100.00%

Table 11: Co-relation between serum creatinine and outcome of treatment.

	Serum creatinine			
Outcome of treatment of patient	increased (>1.2 mg/dl)	Normal (upto 1.2 mg/ dl)	Total	**P-Value**
Improved	14	34	48	
Death	2	0	2	**0.035**
Total	16	34	50	

Table 12: Co-relation between serum alanine aminotransferase (ALT) and outcome of treatment of patient.

	Outcome of patient			
Serum alanine aminotransferase (ALT)	Improved	Death	Total	**P-Value**
Moderate to severely raised (>80 u/l)	11	2	13	
Mildly raised (41-80 u/l)	4	0	4	0.05
Normal (upto 40u/l)	33	0	33	
Total	48	2	50	

Table 13: Co-relation between features on peripheral blood picture and outcome of patient.

	Outcome of patient			
Peripheral blood picture	Improved	Death	Total	**P-Value**
Features of hemolysis	14	2	16	
Normal study	34	0	34	**0.035**
Total	48	2	50	

statistically significant association (p-value=0.035) between presence of features of haemolysis on peripheral blood film and outcome of patients in acute copper sulphate poisoning **(Table-13).**

Chi-square ($\chi 2$) Test was employed to analyse the data. P-value <0.05 was considered statistically significant.

Discussion

Acute copper sulphate poisoning is a common mode of poisoning in southern region of Bangladesh which are mainly suicidal in nature.1Usually The people of this region use copper sulphate as a fungicidal agent. The incidence of acute copper sulphate poisoning varies at different geographical areas depending on the local use of copper sulphate and the availability of other suicidal poisons.

The lowest dose copper sulphate that is toxic when ingested is 11mg /kg 12. Akintonwa et al,199613 claimed 10-20 gm copper sulphate to be a “definitely fatal” dose. In a review of 123 cases Ahsan et al, 19941 observed an “unpredictable” outcome in those consuming less than 50 gm while 100 gm was “invariably” fatal.

In our study, age of the patient range from 13 to 65 years and the incidence of poisoning varies in different age groups. The poisoning most commonly occurs under the age of 30 years (80%) and less common in older age group between 50-70 years(4%). This study is similar to the previous study, SH Mollick et al 201114 in whichmaximum (62.5%) patient were in the young age group of 16-25 yr&Mital VP et al,199615, which stated , copper sulphate poisoning is more common in adults.

Copper sulphate poisoning is more common in female 33(66%) than male17(34%). In previous study, SH Mollick et al 201114(57.5%) &Chowdhury FR et al 201116 stated female are mostly affected.Most of the patients are married(68%). copper sulphate poisoning is more commonly occurs in married female (24 person out of 33 person). In the previous study, Howlader MAR et al 2008 17 shows that highest number 62 (62%) of the patients were married. More common among people with low educational background. 74% of the study population having educational qualification of primary or below primary level. In previous study, Howlader MAR et al 200817, shows that majority(53%) of the patients having educational qualification up to secondary.

Housewife 23(46%), student 12(24%) and farmer/ day labours 8(16%) commonly used copper sulphate for poisoning, which is consistent with the previous studies [Azhar et al 199218 and Khan et a1 198319].80% of affected population were poor where only 20 % were solvent, which is consistent with the previous study [Howlader MAR et al 200817]Most of the patients lived in rural area 33(66%), which is consistent with the previous study [SH Mollick et al 201114 (85%),Howlader MAR et al 200817]Most of the poisoning occurs as result of familial problem like familial disharmony / stress 36(72%), and depressive illness 13(26%), than others.

Among 13 patients of Moderate to severely raised (>80 u/l) serum ALT, 11 patients improved and 2 patients died. Among 4 patients with mildly raised (41-80 u/l) serum ALT and 33 patients with normal serum ALT, all of them(100%) had improved. There is statistically significant association (p-value=0.05) between raised serum ALT and outcome of patients in acute copper sulphate poisoning (Table- 12).

Intravascular hemolysis can start as early as within the first 24 hours since ingestion and is due to the direct oxidative damage to erythrocyte membranes. The hemolysis can be rapid and severe with drastic drops in the hemoglobin level.Among 16 patients with features of hemolysis on peripheral blood film, 14 patients improved and 2 patients died. Among 34 patients of normal peripheral blood film, all of them(100%) improved. There is statistically significant association (p-value=0.035) between presence of features of hemolysis on peripheral blood film and outcome of patients in acute copper sulphate poisoning (Table- 13).

Among 16 patients with raised serum creatinine, 14 patients improved and 2 patients died. Among 34 patients with normal serum creatinine, all of them(100%) improved. There is statistically significant association (p-value=0.035) between raised serum creatinine and outcome of patients in acute copper sulphate poisoning (Table-11).

In our study, case fatality was 4% (2 out of 50 cases) and almost all of them developed GIT , hepatic , intravascular hemolysis and renal toxicities. In previous studies, fatality rate were 20% in SH Mollick et al 201114, 24.2% in Agarwal et al 1975 20 and 18.75% chuttani et al 1965 21.

All the patients were treated conventionally. 40(80%) patients were forced to vomit by artificial means (induced vomiting). 46(92%) patients received Stomach wash with plain water or 1% potassiumferrocyanide. All patients received intravenous fluid, antibiotic and diuretics. Penicillamine was used as chelating agent in 49(98%) patients and used at a dose of 1.5 g/d in 3 divided doses. One patient (2%) received injdimercaprol as chelating agent. All patients tolerated oral penicillamine without any side effects.In a previous study, Nelson LS et al 2002 22 , stated that penicillamine is commonly used as a chelating agent in acute copper sulphate poisoning and intramuscular administration of dimercaprol or British anti-Lewisite (BAL) is recommended when oral administration of penicillamine is difficult or contraindicated (severe corrosive injury in alimentary tract).

Conclusion

Copper sulphate is a common form of suicidal agent with significant mortality. It is a readily available substance and can be taken easily. Acute copper sulphate poisoning is a rare event and uncommon worldwide except Indian subcontinents. It is most prevalent in southern region of Bangladesh. Copper sulphate poisoning is common in female than male and young age. Oral copper sulphate ingestion has significant effects on gastrointestinal, hematological, hepatic and renal system.Mainstay of treatment is supportive, including careful fluid therapy and chelation therapy.Although death occurs due to multi organ failure, gastrointestinal, intravascular hemolysis, hepatic and renal toxicities significantly contribute to it.

Limitations of study

The sample size was relatively small. No follow-up could be carried out to repeat the investigations.Actual measurement of dose of copper sulphate is not possible. Advanced investigations facilities are limited. No advanced life supports were available.

Funding

Self funded.

Conflict of Interests

None declared.

References

1. Gupta PS, Bhargava SP, Sharma ML (1962) Acute copper sulphate poisoning with special reference to its management with corticosteroid therapy. J Assoc Physicians India 10: 287-292.
2. Sharma NL, Singh RN, Natu NK (1967) Accidental poisoning in infancy and childhood. J Indian Med Assoc 48: 20-25.
3. Blundell S, Curtin J, Fitzgerald D (2003) Blue lips, coma and haemolysis. J Paediatr Child Health 39: 67-68.
4. Dash SC (1989) Copper sulphate poisoning and acute renal failure. Int J Artif Organ 12: 610-610.
5. Singh M, Singh G (1968) Biochemical changes in blood in cases of acute copper sulphate poisoning. J Indian Med Assoc 50: 549-554.
6. Chugh KS, Sharma BK, Singhal PC, Das KC, Datta BN, et al. (1977) Acute renal failure following copper sulphate intoxication. Postgrad Med J 53: 18-23.
7. Mehta A, Patney NL, Bhati DP, Singh SP (1985) Copper sulphate poisoning-Its impact on Kidneys. J Indian Med Assoc 83: 108-10.
8. Akintonwa A, Mabadeje AF, Odutola TA (1989) Fatal poisonings by copper sulfate ingested from" spiritual water". Vet Human Toxicol 31: 453-454.
9. Mollick SH, Mollick KA, Bakar A, Miah M (2011) Burden and outcome of acute copper sulphate poisoning in a teaching hospital. Bangl Med J Khulna 44: 7-10.
10. Mital VP, Wahal PK, Bansal OP (1966) Study of erythrocytic glutathione in acute copper sulphate poisoning. Ind J Pathol Bacteriol 9: 155-162.
11. Chowdhury FR, Rahman AU, Mohammed FR, Chowdhury A, Ahasan HAMN, et al. (2011) Acute poisoning in southern part of Bangladesh The case load is decreasing. Bangladesh Med Res Council Bull 37: 61-65.
12. Howlader MAR, Sardar MH, Amin MR, Morshed MG, Islam MS, et al.Khttps://ccforum.biomedcentral.com/articles/10.1186/s13054-016-1208-6
13. Azhar MA (1992) Poisoning cases in a district hospital of Bangladesh. JOPSOM 11: 69-72.
14. Khan NI, Sen N, Haque NA (1985) Poisoning in a medical unit of Dhaka medical college hospital in 1983. Bangladesh Med J 14: 9-11.
15. Agarwal SK, Tiwari SC, Dash SC (1993) Spectrum of poisoning, requiring haemodialysis in a tertiary care hospital in India. Int J Artif Organ 16: 20-22.