

Endosulfan-toxicity: Is seizure a criterion for mortality?

Fakhar Alam^{#1}, Umer Bin Abdul Aziz¹, Ahmad Nadeem Aslami²

ABSTRACT

Endosulfan is a chlorinated insecticide that causes CNS hyper-stimulation state. Mortality and morbidity rates are high and there is no specific treatment for this toxicity. A retrospective study of endosulfan poisoning cases was conducted in the NIMS Medical College & Hospital, Jaipur, Rajasthan to assess endosulfan poisoning cases and to find out the association between seizures and mortality. Data was retrieved from clinical records and laboratory files. Diagnosis was based on history and clinical findings. Blood samples of all the patients were sent for toxicological analysis. Out of 42 cases, 36 (85.71%) were males and 6 (14.29%) were females. Mean age of the victims was 34 years. 76.19% patients were farmers. The most common mode of poisoning was suicidal (95.24%). The total mortality rate was 78.57%. Generalized Tonic Clonic (GTC) type seizure was recorded in 83.33% cases. The association between mortality and GTC Seizure was found to be significant ($p < 0.0001$). This study seeks special attention from government and implementation of strict legal guidelines to curb the menace of endosulfan poisoning.

Keywords: endosulfan poisoning; insecticide; seizures; mortality.

INTRODUCTION

Endosulfan is an organochlorine insecticide and acaricide. All routes of exposure can be hazardous (stomach, lungs, skin). India is currently touted the world's largest user of endosulfan.¹ Poisoning by chlorinated hydrocarbon insecticides is well known. One such insecticide is endosulfan and has been widely used in agriculture since 1960.² Accidental and suicidal poisoning with endosulfan is reported sparsely in literature.³ Endosulfan is a widely used insecticide that is associated with a high fatality rate in humans when ingested accidentally or with the purpose of suicide. Endosulfan is a very lethal poison that produces CNS stimulation and status epilepticus.⁴ The commonest manifestations are neurological along with other organ dysfunctions. There is no specific therapy for this poison and management of endosulfan poisoning is only supportive. Especially, in the rural areas, cases with acute generalized seizure shall suggest intoxication when etiology is unclear even in absence of signs of intoxication.⁵ As there are limited studies done on endosulfan poisoning, present study was aimed to assess endosulfan poisoning cases coming to a tertiary care teaching hospital in Rajasthan and to find out the association between seizures and mortality due to endosulfan.

MATERIAL AND METHODS

A retrospective study was conducted in the emergency department of our Medical college & Hospital at Jaipur, Rajasthan after approval from institutional ethical committee. Data was retrieved from clinical records and laboratory files. The patients presenting with endosulfan poisoning from January 2013 to December 2015 were enrolled for the analysis. Diagnosis was based on history and clinical findings. Blood samples of all the patients were sent for toxicological screening. The data regarding demographic characteristics such as age and gender were recorded. Etiology of poisoning whether suicidal or accidental was also noted. Clinical characteristics such as nausea, vomiting, diarrhea and seizures were also noted. Biochemical parameters (Blood urea, serum creatinine, serum electrolyte, Liver function test, serum bilirubin levels) and complete blood counts (CBC) was also noted.

RESULTS

In total, 42 case records were analyzed. Among them, 36 (85.71%) were males and 6 (14.29%) were females, giving a male: female ratio of 6:1. Mean age of the victims was 33.97 ± 10.76 years (range 18 to 61 years). The age group affected most (73.80%) was 20-40 years. According to occupation, 32 (76.19%) patients were

#Corresponding Author : drfakhar786@gmail.com

¹Department of Forensic Medicine, NMCH, Sasaram, Bihar-821305

²Department of Community Medicine, NMCH, Sasaram, Bihar-821305

farmers, 6 (14.28%) were students while 4 (9.52%) were unemployed. The patients presented with initial symptoms of nausea (66.67%) and vomiting (64.29%) while 4.76% complained of diarrhea. The most common mode of poisoning was suicidal (95.24%) followed by accidental (4.76%) [Table 1]. All the 36 male victims committed suicide by ingesting endosulfan. All patients died within 6-36 hours after ingestion of endosulfan. We recorded 33 (78.57%) deaths among them, giving a total mortality rate of 78.57% due to endosulfan poisoning. Seizure was noted in 35 (83.33%) cases, all of which was of Generalized Tonic Clonic (GTC) type. Out of these, 31 (88.6%) died while only 2 (28.6%) patients died who had no seizures on presentation. The association between mortality and GTC Seizure was found to be significant ($p < 0.0001$). [Table 2] According to time of initiation of symptoms, 57% of the patients had complained of symptoms within one hour of ingestion of endosulfan while 38% developed symptoms within two hours. [Figure 1] Complete blood count (CBC), Blood sugar, Urea, Creatine and electrolytes were normal except Liver Function Test in the form of aspartate amino transferase (AST) and alkaline amino transferase (ALT), which were abnormal in 30 (71.42 %) patients. Tonic-clonic convulsions were treated with Diazepam, Phenytoin and Phenobarbital. Supportive care to these patients was provided that included decontamination of skin, gastric lavage, active charcoal, lidocaine for arrhythmia. Almost all significant complications including shock, hepatic toxicity, acute renal failure (ARF), Rhabdomyolysis and cardiac injury developed in these patients which led to their deaths. All the patients were admitted in Intensive care units (ICU) and ventilator support was provided to them. An important postmortem finding in nearly all deceased was marked congestion of meningeal vessels.

DISCUSSION

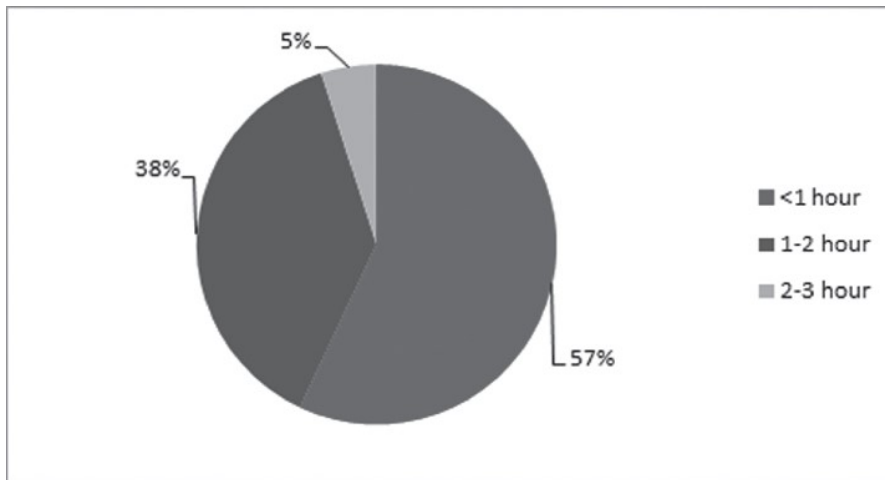
Endosulfan toxicity could precipitate enormous jeopardy and may result in irreversible and fatal damage. The spectrum of involvement may range from mild nausea, vomiting and anxiety to convulsions and multi-organ damage resulting in death.⁶ In this study 85.71% were males who ingested endosulfan. A study done by Karatas AD *et al* showed that out of total cases of endosulfan poisoning, 78.3% were males.⁷ We observed that most of the patients in our study were young male farmers who committed suicide by ingesting endosulfan. In India, it is estimated that nearly 16,000 farmers die due to suicide

each year, and at rates far above those of the general populations. Socio-economic factors are associated with farmer suicides, with increase indebtedness playing the predominant role. It has led to agrarian crisis affecting the most vulnerable farmers.⁸ Deliberate self poisoning by ingesting pesticides is serious health problem among farmers. Pesticide storage in households is unsafe and this may lead to associated self injury, both unintentional and intentional.⁹ The patients presented with initial symptoms of nausea (66.67%) and vomiting (64.29%) while 4.76% complained of diarrhea. The most common mode of poisoning was suicidal (95.24%) followed by accidental (4.76%). Nausea and vomiting were the most common symptoms experienced by the patients in this study, similar to other studies.¹⁰ Endosulfan, being an organochlorine readily crosses the intestinal barrier (oral absorption > 90%) and the blood brain barrier (log BB > 0.4), causing prompt symptoms in patients.¹¹ The predominant toxicological effect in endosulfan poisoning is over-stimulation of CNS. Most of the patients had symptoms within an hour of ingestion. The seizures were of GTC type in all the cases. Other studies also showed similar results.^{7,12-14} Liver function results were abnormal in 71.42 % patients. Liver function test in the form of AST or ALT could be abnormal in endosulfan toxicity.¹⁵ The mainly affected organ in endosulfan toxicity is liver. Gross examination in endosulfan poisoning showed swollen and pale liver.¹⁶ The association between mortality and GTC Seizure was found to be significant ($p < 0.0001$). This study showed a significant association between development of seizures and mortality. Seizures were the most common cause of death in endosulfan poisoning, as seen in other studies. Seizures may lead to status epilepticus. Post mortem examination carried out on the individuals who died due to status epilepticus confirmed that the deaths were due to asphyxia.^{15,17,18} Endosulfan can cause cerebral edema along with other complications including heart failure, acute renal failure and disseminated intravascular coagulation (DIC). It may also cause liver, kidney and lung toxicity.¹⁹⁻²¹

CONCLUSION

Poisoning is a very common health menace in this part of country, Endosulfan being one of the main culprits. Most often poisoning is either suicidal or may be accidental. Commonest manifestations of endosulfan poisoning are neurological along with other associated

Fig 1: Showing the duration of onset of symptoms after ingestion of Endosulfan



organ dysfunctions. This retrospective study analyses 42 suspected endosulfan poisoning cases. Most of the cases in our study had GTC seizures, majority of them expired in less than 36 hours. Endosulfan is banned in most of the developed and developing countries whereas it's still used in India extensively. Though a ban on Endosulfan exists in the south Indian state of Kerala (imposed through a court order), it still awaits a pan India ban. Endosulfan use should be banned under strict legislation and steps

be taken to educate and create awareness regarding the use of pesticides in agricultural community as well as the population in general. Moreover healthcare personnel should be specifically trained to provide immediate remedial measures to combat emergency situations arising out of pesticide use in high risk areas.

Conflict of interest : Declared none.

Funding source : Nil

Table 1: Showing the Association of seizures with mortality, demographic profile and clinical characteristics

Characteristics	N	%
Age (years)		
<19	1	2.38
20-40	31	73.80
41- 60	8	19.05
>60	2	4.76
Gender		
Male	36	85.71
Female	6	14.29
Profession		
Farming	32	76.19
Student	6	14.28

Unemployed	4	9.52
Aetiology		
Suicidal	40	95.24
Accidental	2	4.76
Clinical		
CNS		
• Seizue (GTC)	35	83.33
General		
• Nausea	28	66.67
• Vomiting	27	64.29
• Diarrhea	2	4.76

Table 2: Showing the Association of seizures with mortality

Seizures	Mortality	Mortality Rate (95% CI)	Z	p	Rate Ratio (95% CI)
Yes (n=35)	31	88.6 (73.3-96.81)	1.737	0.08	3.1 (0.9551-10.0619)
No (n=7)	2	28.6 (3.68-70.98)	8.061	<0.0001	1
Total (N=42)	33	78.57 (63.19-8970)	4.886	<0.0001	

$\chi^2 = 12.5$; $df=1$; $p<0.0001$; Highly significant

REFERENCE

- Wang XP, Gong P, Yao TD, Jones KC. Passive air sampling of organochlorine pesticides, polychlorinated biphenyls, and polybrominated diphenyl ethers across the tibetan plateau. *Environ Sci Technol* 2010;44:2088-93
- Smith AG. Chlorinated hydrocarbon insecticides. In *Handbook of Pesticide Toxicology*. Hayes WJ, Laws ER, Eds. Academic Press; 1991:731-45.
- Bllano-Coronado JL, Repetto M, Ginestal RJ, Vicente JR, Yelamous F, Lardell A. Acute intoxication by endosulfan. *J Toxicol Clin Toxicol* 1992;30:575- 83.
- Yadav A, Alam F, Kothari NS, Gahlot RK. Suicidal Endosulphan Poisoning In a Pregnant Women A Case Report. *J Indian Acad Forensic Med* 2013;35:187-88.
- Kutluhan S, Akhan G, Gultekin F, Kurdoglu E. Three cases of recurrent epileptic seizures caused by Endosulfan. *Neurology India* 2003;51:102-3.
- Gude D, Bansal DP. Revisiting endosulfan. *J Family Med Prim Care*.2012;1:76-8.
- Karatas AD, Aygun D, Baydin A. characteristics of endosulfan poisoning: a study of 23 cases. *Singapore Med J* 2006; 47: 1030-2.
- Merriott D. Factors associated with the farmer suicide crisis in India. *J Epidemiol Glob Health* 2016;available on <http://dx.doi.org/10.1016/j.jegh.2016.03.003>
- Chowdhay AN, Banerjee S, Brahma, Welss MG. Pesticide practices and suicide among farmers of the sundarban region in India. *Food Nutr Bull*. 2007;28:381-91.
- Cebicci H, Bol O, Guzel MF, Vural A, Ceylan A. ENDUSULFAN POISONING:CASE SERIES. *Acta Medica Mediterranea* 2015;31:669.
- Escuder –Gllabert L, Villanueva- Camanas RM, Sagrado S, Medina-Hernandez MJ. Permeabilty and toxicological profile estimation of organochlorine compound by bio partitioning micellar chromatography. *Biomed Chromatogr* 2009;23:382-9.
- Ugur K, Cimen O, Hasan H, Sevda O, Ali G. Antioxidant Treatment With N-acetylsteine. In *ES Intoxication: Report of Two Cases*. The internet journal of Anesthesiology. 2006;11:1.
- Kuluhan S, Akhan G, Gultekin F, Kurdoglu E. Three cases of recurrent epileptic seizures caused by Endosulfan. *Neurol india* 2003;51:102-3.
- Okay C, Goksu E, Bozdemir N, Soyuncu S. Unintentional toxicity due to Endosulfan: a case report of two patients and characteristics of ES toxicity. *Vet Hum Toxicol* 2003;45:318-20.
- Venkateswarty K, Suryarno K, Srinivas V, Sivaprakash N, Jagannadharao NR, Mythilai A. Endosulfan poisoning- a clinical profile. *J Assoc Physicians India* 2000;48:323-5.
- Mor F, Ozmen O. Acute endosulfan poisoning in cattle. *Vet Hum Toxicol* 2003;45:323-4.
- Moon JM, Chun RJ. Acute endosulfan poisoning: a retrospective study. *Hum Exp Toxicol* 2009;28:309-16.
- Satar S, Sebe A, Alpay NR, Gumusay U, Guneyssel O. Unintentional endosulfan poisoning. *Bratisl Lek Listy* 2009;110:301-3.
- Battal D, Aktas A, Sungar MA, Bilgin NG, Ceekin N. Evaluation of poisoning deaths in the Cukurova Region, Turkey, 2007-2011. *Toxicol Ind Health* 2016;32:476-84.
- Yildiz M, Gurger M, Bozdemir MN, Basturk M, Atescelik M, Kilicarslan I et al .endosulfanzehirlenmesi:3 olgusunaumu.the Journal Of Academic Emergency Medicine 2008;7:44-6.
- Jain G, Singh DK, Yadav G. Malignant Hyperthermia in Endosulfan Poisoning. *Toxicol Int* 2012;19:74-6.