Original Research Paper

Endosulfan toxicity: A Retrospective Study and Review

[1]Fakhar Alam, [2]Umer Bin Abdul Aziz, [3]Ahmad Nadeem Aslami

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 (85.7%) were males and 6 (14.3%) were females. Mean age of the victims was 34 years. 76.2% patients were farmers. The most common mode of poisoning was suicidal (95.2%). The total mortality rate was 78.6%. Generalized Tonic Clonic (GTC) type seizures were recorded in 83.3% cases. The association between mortality and GTC Seizure was found to be significant ($p<0.0001$). This study seeks to draw special attention from the government and implementation of strict legal guidelines to curb the menace of endosulfan poisoning.

Key Words: Endosulfan poisoning, insecticide, seizures, mortality

Introduction:

Endusulfan is an organochlorine insecticide and aracicide. All routes of exposure can be hazardous (stomach, lungs, skin). India is currently touted the world's largest user of endosulfan.[1] Posioning by chorinated hydrocarban 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. It is a very lethal poison that produces CNS stimulation and status epilepticus[4]. The commonest manifestations are neurological along with other organ dysfunctions.

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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 suggest its intoxication when etiology is unclear even in absence of signs of intoxication.[5]

As there are limited studies done on endosulfan poisoning, the 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.

Materials and Methods:

A retrospective study was conducted in the emergency department of NIMS Medical college & Hospital, Jaipur, Rajasthan, after approval from the Institutional Ethics Committee. Data was retrieved from clinical records and laboratory files. 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 toxological screening.

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:

A total of 42 case records were analyzed. Among them, 36 (85.7%) were males, 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 (73.8%) was 20-40 years. According to occupation, 32 (76.2%) patients were farmers, 6 (14.3%) were students while 4 (9.5%) were unemployed. The patients presented with initial symptoms of nausea (66.7%) and vomiting (64.3%), while 4.8% complained of diarrhoea. The most common mode of poisoning was suicidal (95.2%), followed by accidental (4.8%) **(Table 1).** All the 36 male victims committed suicide by ingesting endosulfan.

All patients died within 6-36 hours after ingestion. We recorded 33 (78.6%) deaths among them, giving a total mortality rate of 78.6% due to endosulfan poisoning. Seizure was noted in 35 (83.3%) cases, which was of Generalized Tonic Clonic (GTC) type. Of these, 31 (88.6%) died while only 2 (28.6%) patients who died had no seizures on presentation. The association between mortality and GTC Seizure was found to be significant ($p<0.0001$). **(Table 2)**

According to the 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 Tests in the form of aspatrate amino transferase (AST) and alkaline amino transferase (ALT), which were abnormal in 30 (71.4%) 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, lidnocaine 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, 85.7% were males. A study done by Karatas AD, et al showed that of the 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. 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 lead 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 (66.7%) and vomiting (64.3%), while 4.8% complained of diarrhoea. The most common mode of poisoning was suicidal (95.2%), followed by accidental (4.8%). 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 tests were abnormal in 71.4 % patients. LFT, 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, ace 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 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 its 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. It's 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: None
Financial Assistance: None

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Table 1: The demographic and clinical characteristics of the cases

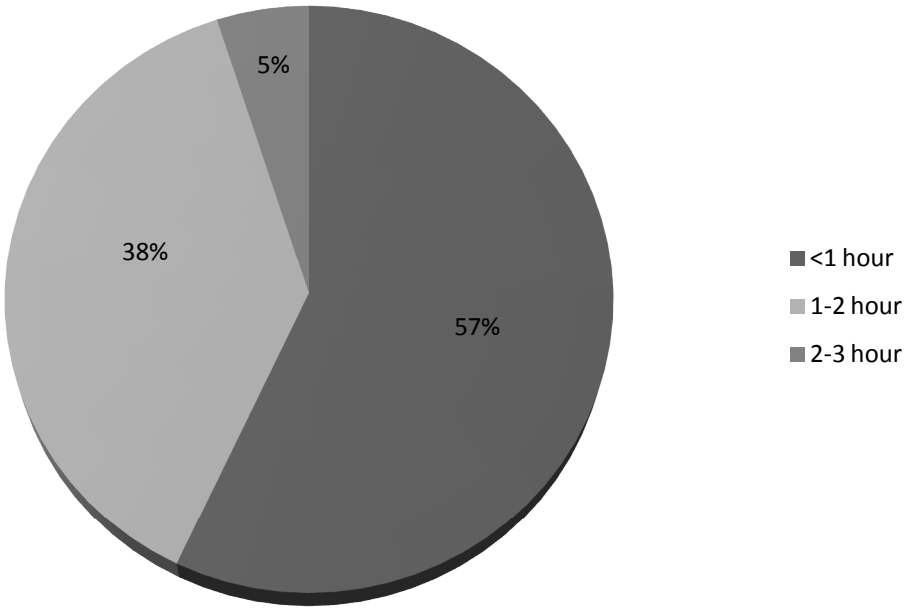
Characteristics	N	%
Age (years)		
<19	1	2.38
20-40	31	73.80
41- 60	8	19.05
>60	2	4.76
Gender		
Male	36	85.71
Female	6	14.29
Profession		
Farming	32	76.19
Student	6	14.28
Unemployed	4	9.52
Aetiology		
Suicidal	40	95.24
Accidental	2	4.76
Clinical		
CNS		
Seizue (GTC)	35	83.33
General		
Nausea	28	66.67
Vomiting	27	64.29
Diarrhea	2	4.76

Table 2: 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	

X^2= 12.5; df=1; p<0.0001; Highly significant

Figure 1: Time of initiations of symptoms after ingestion of Endosulfan



Original Article

Endosulfan-toxicity: Is seizure a criterion for mortality?

Fakhar Alam[#1], Umer Bin Abdul Aziz[1], Ahmad Nadeem Aslami[2]

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

Endusulfan 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] Posioning by chorinated hydrocarban 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 toxological 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

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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 aspatrate 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, lidnocaine 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.

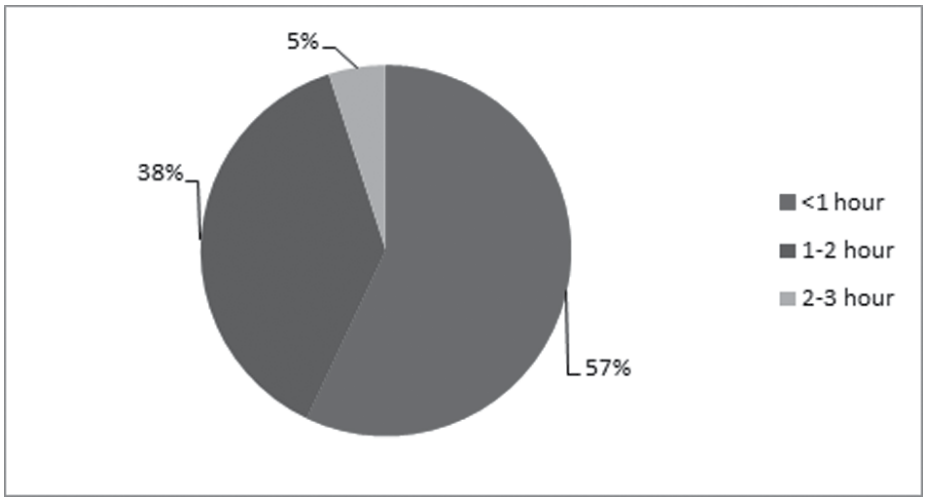
DISCUSSION

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 lead 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, ace 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
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Total (N=42)	33	78.57 (63.19-8970)	4.886	<0.0001	

X2= 12.5; df=1; p<0.0001; Highly significant

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