Alkaline Diuresis and Pre-emptive Hemodialysis as Treatment for 2,4-Dicholorophenoxy acid herbicide intoxication

Abstract

Introduction

Chlorophenoxy herbicides poisoning is very rare. It is used widely to control broad-leaved weeds. 2, 4-D is a Chlorphenoxy herbicide which has no antidote. The mission of this case report is to emphasize the role of accurate diagnosis and management of 2, 4-D herbicide intoxication.

Case report -19 year old male was admitted 6h after the deliberate ingestion of the contents of a half bottle(300ml) of weedkiller named Dallas contents of which were 59% w/w 2,4-D acid tech,30% w/w Di-methylamine. Soon after ingestion the patient gave history of vomiting, after which patient became unconscious.

On examination, RR was 35/min with a saturation of 90% on room air requiring 5-6L/min of oxygen. The pupils were small, 1.5mm in diameter, reactive. Arterial blood analysis showed mild Metabolic acidosis. Gastric aspiration and lavage were performed. Patient was unresponsive to deep painful stimulus. He was sweating profusely with a temperature of 39degree Celsius. Patient was electively intubated for airway protection.

Patient was admitted in the ICU.The total leukocyte counts were 17000/cmm. Liver function and kidney function tests were within normal limits. CPK total was 3150. Over the next 7 hours, patient's condition worsened and the blood pressure started dropping to 80/50mmHg. Patient was started on vasopressor support. Alkaline diuresis was started by giving 1meq/kg sodium bicarbonate in 0.9% normal saline, 100ml iv within the next 30 minutes and then added with 75meq of sodium bicarbonate and 25meq of potassium in 500ml 5% dextrose within 8 hours. Inj Furosemide 20mg was given every 12hours intravenously. On the second day, patient's laboratory investigations showed a rising trend in TLC, creatinine rose to 2.4mg/dl from 1.1mg/dl on the day of admission. Patient's metabolic acidosis also worsened. Patient's output dropped to 5-10ml/hr. Patient was then taken on Haemodialysis. Patient's urine output improved and GCS also improved. Three cycles of haemodialysis were done, the TLC showed a falling trend with normalising creatinine , metabolic acidosis also improved; pH normalised and patient was extubated on the fourth day. Patient was then shifted to ward and discharged subsequently on clinical improvement.

Conclusion-2,4-Dimethylamine intoxication is uncommon, doesn't have an antidote with very high morbidity and mortality. Alkaline diuresis as a life-saving treatment and must be supplemented by other therapies including decontamination of the gastrointestinal system, initial emergency resuscitation and supportive treatment with haemodialysis as and when required.

Key words: Alkaline Diuresis, Hemodialysis, Dicholorophenoxy acid, herbicide intoxication

Introduction

Chlorophenoxy herbicides poisoning is rare. It is used mainly for the control of broad-leaved weeds. These Compounds exhibit broad spectrum of mechanisms of toxicity which includes dose-dependent

cell membrane damage, uncoupling of oxidative phosphorylation, and disruption of acetylcoenzyme A metabolism (1). 2, 4-D is a Chlorphenoxy herbicide which doesn't have any antidote(2).Forced alkaline diuresis and Hemodialysis is the treatment of choice and if initiated on time may improve the otherwise very poor prognosis in severe intoxication with 2, 4-D and related weed killers. The mission of this study is to draw to attention the role of accurate diagnosis and the management of 2, 4-D herbicide intoxication.

Case report

19 year old male was admitted 6h after the deliberate ingestion of the contents of a half bottle(300ml) of weedkiller named Dallas contents of which were 59% w/w 2,4-D acid tech,30% w/w Di-methylamine,1% w/w lignin sulphonate. Soon after ingestion the patient gave history of vomiting, which was followed by aggressive behaviour and then a confused state. Within 1 hour patient became drowsy and was followed by unconsciousness.

Patient was brought to MGM in unconscious state. On examination in Casualty, the pulse rate and blood pressure were normal but the respiratory rate was 35/min with a saturation of 90% on room air requiring 5-6L/min of oxygen. The pupils were small, 1.5mm in diameter, reactive, muscle tone was normal and deep tendon reflexes were normal, plantars were flexors. Arterial blood analysis showed mild Metabolic acidosis and hypoxia (H+ 48 nmol/l, paCO2 37 kPa, bicarbonate 15 mmol/l and paO2 70 kPa). Patient was unconscious, not responding to Deep Painful Stimuli. Ryles tube no.14 was inserted and Gastric aspiration and lavage were performed. Over the next few hours his condition deteriorated. Patient still remained unresponsive to painful stimuli, the tendon reflexes disappeared, the pulse rate increased to 140/min and the temperature rose to 39 degree Celsius. He was vasodilated and sweating profusely. Cyanosis was evident despite a respiratory rate of 40-50/min and the Chest was clear clinically and radiologically. A normal arterial oxygen tension could only be maintained with 8L/min of oxygen through a mask and the temperature remained at 39degree Celsius despite cold sponging. Patient was electively intubated for airway protection.

Patient was admitted in the Intensive care unit, routine laboratory investigations were performed. The haemoglobin of the patient was 16.2g/dl, total leukocyte counts were 26250/cmm. Liver function and kidney function tests were within normal limits. Over the next 7 hours, the condition of patient deteriorated and the blood pressure started dropping to 80/50mmHg. Fluid resuscitation was given but blood pressure didn't reach the target and hence was started on vasopressor support to maintain systolic blood pressure >100mmHg. Pantoprazole was given in loading dose and was continued with maintenance dose via infusion. Alkaline diuresis was initiated by giving 1meq/kg sodium bicarbonate in 0.9% normal saline, 100ml iv within the next 30 minutes and then supplemented with 75meq of sodium bicarbonate and 25meq of potassium in 500ml 5% dextrose within 8 hours. Inj Furosemide 20mg was given every 12hours intravenously. Iv dexaamethsone was also given to treat cerebral edema. On the second day, patient's laboratory investigations showed a rising trend in total leukocyte count upto 30,000, creatinine rose to 2.4mg/dl from initial creatinine 1.1mg/dl on the day of admission. Patient's metabolic acidosis also worsened. Patient's output also dropped to 5-10ml/hr. A decision was then made to start the patient on Haemodialysis. Patient's urine output improved and GCS also improved. Three cycles of haemodialysis was done, patient was extubated on the fourth day, the total leukocyte

count showed a falling trend with normalising creatinine with metabolic acidosis also improved; pH normalised. Patient was then shifted to ward and discharged subsequently on clinical improvement.

Discussion

“Anticholinesterase compounds are the commenest method of poisoning in India but herbicide poisoning is also a method of suicide and is usually associated with high morbidity and mortality” (3). “Among different herbicidal poisonings we come across the most predominantly found poisonings are paraquat and glyphosate” (4). “The incidence of 2, 4-dichlorophenoxy acetic acid poisoning are few and rarely cases are reported from India” (5). “2, 4-dichlorophenoxy acetic acid commonly known as 2, 4-D is a plant herbicide. It is secondarily a plant growth regulator” (6). It was developed in the 1940s. It is the most commonly used pesticide in the non-agricultural sector at the same time one of the top ten most commonly used in the agricultural sec

“There is no discrete antidote available for 2,4-D dimethylamine intoxication. Chlorophenoxy is a weak acid (pKa 2.6 for 2,4-D) that is excreted in the urine in the same form. Intravenous sodium bicarbonate has its mechanism of action to act by increasing urine pH. Renal excretion is better in alkaline urine conditions (63 ml/min at pH 8.3) than in acidotic conditions (0.14 ml/min at pH 5.1) of urine” [2]. “For each unit increase in urine pH, the clearance of 2,4-D by the kidney is estimated to increase nearly five-fold” [3]. “Therefore its necessary to note that the administration of sodium bicarbonate with a target urine flow of 4–6 ml/minute increases the excretion of 2,4-D dimethylamine. In this scenario, urine pH after alkaline diuresis was not assessed , so the renal clearance and half time of 2,4-D in this patient could not be stated. Hypokalaemia may occur during alkaline diuresis, according to the literature, hence sodium bicarbonate should be followed by potassium injection" [2]. "Haemodialysis is more efficient than alkaline diuresis in that it can cause the release of hazardous chemicals without changing the pH of the urine or requiring huge volumes of intravenous fluids. However, the treatment strategy chosen is ultimately determined by the availability of facilities. There are case reports describing plasmapheresis as a therapy for intoxication in relation to haemodialysis, but there is very little evidence to support this strategy in the treatment of severe 2,4-D dimethylamine intoxication" [3, 4]. “In cases of mild intoxication, supportive therapy might be ample, but, in cases of severe intoxication, treatment with alkaline diuresis or haemodialysis is a necessity” [4]. “However, there is no severity classification as a reference to determine the most appropriate therapy. Shock and loss of consciousness in cases of 2,4-D dimethylamine intoxication are indicators of poor prognosis. However, timely and adequate administration of an alkaline diuresis can be life-saving. Recovery can be achieved in weeks to months despite initial severe toxicity” [2, 4,5].

Conclusion

2,4-Dimethylamine intoxication is uncommon, has no antidote, and has a significant morbidity and fatality rate. Alkaline diuresis is a life-saving therapy that needs to be combined with additional treatments such first emergency resuscitation, gastrointestinal system purification, and supportive care.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

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