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

Abstract

Introduction

Chlorophenoxy herbicides poisoning is uncommon. It is used widely for the control of broad-leaved weeds. 2, 4-D is a Chlorphenoxy herbicide which has no antidote. The goal of this case report is to emphasize 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. 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 deteriorated, the blood pressure started dropping to 80/50mmHg. Patient was started on vasopressor support. 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. 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 rare, does not have an antidote, and has high morbidity and mortality. Alkaline diuresis as a life-saving treatment must be accompanied by other therapies including initial emergency resuscitation, decontamination of the gastrointestinal system, and supportive treatment with haemodialysis as and when required.

Introduction

Chlorophenoxy herbicides poisoning is uncommon. It is used widely for the control of broad-leaved weeds. These Compounds exhibit a variety 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 has no antidote (2).Forced alkaline diuresis and Hemodialysis is the treatment of choice and if timely instituted may improve the otherwise very poor prognosis in severe intoxication with 2, 4-D and related weed killers. The goal of this study is to emphasize 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, patient's condition deteriorate the blood pressure started dropping to 80/50mmHg. Fluid resuscitation was given but blood pressure didn't reachthe 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 most common method of poisoning in India but herbicide poisoning is also a method of suicide and is associated with high morbidity and mortality (3). Among different herbicidal poisonings, the most predominantly found poisonings are paraquat and glyphosate (4). The incidence of 2, 4-dichlorophenoxy acetic acid poisoning is scanty and only few cases are reported from India (5). 2, 4-dichlorophenoxy acetic acid commonly known as 2, 4-D is a plant herbicide and secondarily a plant growth regulator (6). It was developed in the 1940s and is the most commonly used pesticide in the non-agricultural sector and one of the top ten most commonly used in the agricultural sec

There has been no specific antidote 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 acts by increasing urine pH. Renal excretion is better in alkaline urine conditions (63 ml/min at pH 8.3) than in acidic conditions (0.14 ml/min at pH 5.1) [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, the administration of sodium bicarbonate with a target urine flow of 4–6 ml/minute will increase the excretion of 2,4-D dimethylamine. In this case, urine pH after alkaline diuresis was not evaluated, so the renal clearance and half time of 2,4-D in this patient could not be determined. According to the literature, hypokalaemia may occur during alkaline diuresis and so sodium bicarbonate should be accompanied by potassium administration [2].Haemodialysis is more efficient than alkaline diuresis and can induce the release of toxic substances without manipulating urine pH and the requirement for large amounts of intravenous fluids. However, the treatment plan adopted is ultimately based on the availability of facilities. In addition to haemodialysis, there are case reports describing plasmapheresis as a therapy for intoxication, but there is limited evidence to support this approach in the treatment of severe 2,4-D dimethylamine intoxication [3, 4].In cases of mild intoxication, supportive therapy might be sufficient, but, in cases of severe intoxication, treatment with alkaline diuresis or haemodialysis is required [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 indicate a poor prognosis. However, timely administration of an alkaline diuresis can be life-saving. Recovery can be achieved in weeks to months despite initial severe toxicity [2, 4].

Conclusion

2,4-Dimethylamine intoxication is rare, does not have an antidote, and has high morbidity and mortality. Alkaline diuresis as a life-saving treatment must be accompanied by other therapies including initial emergency resuscitation, decontamination of the gastrointestinal system, and supportive treatment.

References

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