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An Incidence of Onion (*Allium cepa*) Toxicity in Cattle and Buffaloes

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Abstract

Toxicity was caused by the accidental ingestion of a large quantity onion (*Allium cepa*) by 6 cattle and 4 water buffalos. The animals exhibited the clinical signs of pale mucous membranes, lethargy, anorexia and voiding dark urine after 8-10 days of ingestion of onion. The post mortem showed the odor of onion and the rumen found several bits of onions. The kidneys were dark brown with urine. Microscopy demonstrated tubular degeneration and necrosis in the cytoplasm of renal tubular epithelial cells and tubular lumina with eosinophilic substance deposits.Hemorrhage and macrophages containing brown cytoplasmic pigment with centrilobular coagulative necrosis were found in liver. The ailing animals recovered with therapy with fluids, phosphorus, B-complex vitamins and vitamin C for five consecutive days.

Keywords: Biochemistry, Buffaloes, Cattle, Hematology, Onion, Toxicity, Treatment

1. Introduction

Poisonous plants and materials of domestic use cause greater financial losses to the animal husbandry sector in entire world. The cost will definitely increase due to the missed grazing opportunities, higher feed costs, increased health care costs, improvements in management, increased slaughter costs and missed weight gains[1].

More than a dozen obscure diseases are prevalent in Malnad region of Western Ghats. For some of these obscure diseases, toxic plant etiology has been suspected[1-2]. Onion, garlic, leek, kurrat, chives, shallots and scallions are included in the genus *Allium*[3]. Hemolytic anemia caused by accidental ingestion of onion (*Allium cepa*) has been previously reported in cattle, sheep, dogs, cats and horses[4-14]. Moreover, experimental induction of the toxicity also has been reported in sheep, dogs and cats[15-19]. The epidemiology of onion toxicities differs among species. In sheep, toxicity of onion occurs where it was grown commercially where as in horses toxicity occurs due to consumption of wild onions in grazing areas[17-22]. Domestic animals succumb to onion toxicity often. Toxicity episodes in cattle occur mainly where culled cultivated onions are inadvertently fed to livestock or where animals have access to onions which are stored or marketed and mishandled[6-7-12-23]. Dogs are usually affected by ingestion of home made food or when onions are used to improve the flavor of diets prepared for ill animals[5-10]. In cats, onion toxicosis can occur after the ingestion of some human baby foods, which are fed to anorexic animals because of higher palatability[8-15]. Onion toxicity is also recorded in captive tortoises.[24]. The incidences of the waste vegetable toxicity is also increasing day by day due to improper waste management practices. In the present study, the incidence of the accidental ingestion of onion by cattle and buffaloes and its toxicity is discussed.

2. Materials and Methods

2.1 Case History and Clinical Observation

In Agriculture Produce Market Committee (APMC) yard, Bhadravathi in Shivamogga District, Karnataka State, 10 animals (6 CB cows and 4 non descriptive buffaloes) aged between 4 to 9 years with clinical signs of passage of dark brown coloured urine were referred to Veterinary Hospital Bhadravathi and were examined. The history revealed that animals ingested discarded onions (*Allium cepa*) in APMC

yard during last 8-10 days. Affected animals were found anorectic, dull, depressed with tachycardia, tachypnoea and staggering gait. Few animals showed weakness, loss of appetite, dyspnea, lethargy, tensmus, frequent voiding of dark red urine pale or icteric skin and mucus membranes, onion odor on breath and a lowered body temperature(99-100^{0}F).

2.2 Postmortem Examination

Post mortem of two dead cross bred animals was conducted and the tissues were collected for histological examination in 10% Neutral Buffered Formalin (NBF) and processed for histopathology. The tissues were processed for histopathology by cutting sections of 4 µm thickness and stained with Haematoxylin and Eosin. Histopathological lesions observed in sections of tissues were recorded and photomicrographs were taken using Zeiss Axio Cam Erc5s microscope[57].

2.3 Hematology and Biochemistry

Haematological parameters like haemoglobin, WBC, DC and PCV, MCH etc. were estimated using Automatic Hemetology Analyser (Hycount 3 N, Hycel, Austria). Serum biochemical parameters like AST, ALT, creatinine, blood urea nitrogen, bilirubin, LPO, GSH, GPx, catalase etc were estimated using Semiautomatic Biochemical Analyser (HY-SAC, Hycel, Austria) with ready to use kits as per manufacturers leaflet. The rumen and intestinal contents were obtained for examination for the presence of cyanide and nitrate along with the intact onion[41]. The blood samples collected from normal healthy animals were served as control.

2.4 Treatment

The ailing animals were treated with administration of fluids (Intalyte Inj , Intas Animal Health Pvt Ltd, Ahmedabad, India, 1 litre, 10 ml/kg slow I/V per day), phosphorus (Tonophosphan Inj, MSD Animal Health, Pune, India 50 ml vial 15 ml IM per day), B-complex vitamins (Neuroxin-M Inj, Zydus Animal Health, Ahmedabad, India, 10 ml, IM per day), vitamin C (Tilodoxon inj, 500 mg vial, Tablets India Pvt. Ltd, Mumbai, 10 mg/kg, IM) for five consecutive days. In one animal in which there was severe anemia, blood transfusion was conducted. Two animals were also intraruminally administered with penicillin and streptomycin (Dicrysticin-S Inj, Zydus Animal Health, Ahmedabad, India, 2.5 g per day for 3 days, IR). The suspected samples of onions were collected and were sent for botanical identification.

2.5 Statistical Analysis

Data are expressed as the Mean ± Standard Error of Mean (SEM) and GraphPad Prism Trial Version 8.0.0 software for Windows was used as statistical tool and One-way ANOVA followed by Dunnett's multiple comparisons test was performed. Differences were deemed significant for values when $P<0.05$.

3. Results

The onions were identified botanically as *Allium cepa* by Dr. K. Gopalakrishna Bhat, Rtd Professor and head, Department of Botany, Purnaprajna College, Udupi, Karnataka State.

The visible mucus membranes of affected animals were pale. The animals were passing constipated faeces and dark brown coloured urine. The blood smear examination revealed negativity to hemoprotozoan parasites.

Table 1. Alteration in haematological parameters in cattle due to accidental ingestion of onion (*Alium cepa*)

Group	Control animals (n = 6)	Animals with onion toxicity (n = 6)	Reference values [56]
RBCs (10^6/µl)	7.15 ± 1.10	2.8 ± 0.48**	5.0-10.0
Hb (g/dl)	12 ± 0.20	5.77 ± 0.28 *	8-15
PCV (%)	32.15 ± 2.5	13.24 ± 0.78*	24-46
MCV (fl)	46.12 ± 5.4	54.63 ± 6.8*	40-60
MCH (pg)	13.10 ± 2.4	23.30 ± 4.2*	11-17
WBCs (10^3/µl)	11.50 ± 1.3	11.97 ± 4.38	4.0-12.0
Platelets (10^3/µl)	280.47 ± 66.57	253.26 ± 47.94	100-800
Lymphocytes (%)	58.15 ± 4.5	50.15 ± 4.30	62–63
Neutrophils (%)	28.1 7 ± 5.4	39.89 ± 1.7	15-33
Eosinophils (%)	11.79 ± 0.33	10.87 ± 0.43	0-20
Monocytes (%)	5.75 ± 0.5	4.77 ± 1.28	0-8

The values are expressed as Mean±SEM. The values indicated by asterisk are significantly different (*P<0.05, **P<0.01).
RBCs, Red blood cells; Hb, Hemoglobin; PCV, Packed cell volume; MCV, Mean corpuscles volume; MCH, Mean corpuscles hemoglobin; WBCs, White blood cells.

Table 2. Alteration in serum biochemical parameters in cattle due to accidental ingestion of onion (*Alium cepa*)

Parameter	Control animals (n = 6)	Animals with onion toxicity (n = 6)	Reference range [56]
Albumin (mg/dl)	3.82 ± 0.32	3.46 ± 0.30	2.5-3.8
ALT (U/l)	13.5 ± 0.33	38.2 ± 1.30*	6.9-35
AST (U/l)	48.15 ± 3.12	138.44 ± 13.27**	61-125
Bilirubin (mg/dl)	0.5 ± 0.03	12.2 ± 2.13*	0-1.6
Urea (mg/dl)	17.25 ± 1.25	59.34 ± 1.52*	6-22
CRT (mg/dl)	1.10 ± 0.05	2.58 ± 0.10*	1-2
Uric acid (mg/dl)	0.8 ± 0.04	3.78 ± 0.31*	0.4-1.2
Globulin (mg/dl)	3.23 ± 0.31	3.93 ± 0.44	3.0-3.5
Total protein (mg/dl)	7.42 ± 0.19	7.28 ± 0.46	7.5-7.6
GPx (U/mg protein)	188.7 ± 26.1	409.5 ± 20.5**	-
GR (U/mg protein)	938.2 ± 63.7	578.8 ± 38.2**	-
GSH (µmole/l)	7.51 ± 0.31	1.35 ± 0.47***	-
MDA (nmol/l)	10.49 ± 1.43	67.23 ± 5.28**	-
CAT (U/mg protein)	384.51 ± 19.18	114.1 ± 8.8**	-

The values are expressed as Mean±SEM. The values indicated by asterisk are significantly different (*P<0.05, **P<0.01).
ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; CAT, Catalase; GPx, Glutathione peroxidase; GR, Glutathione reductase; GSH, Reduced glutathione; MDA, Malondialdhyde.

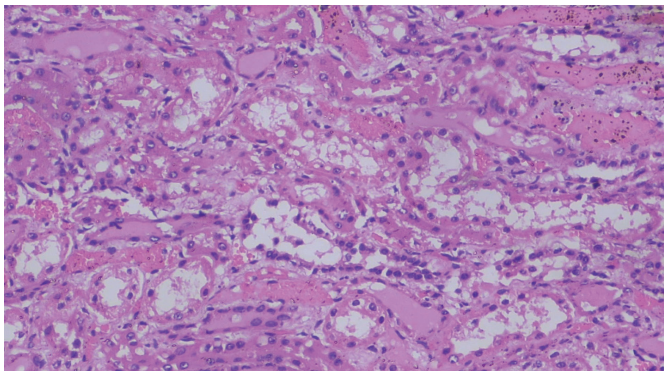


Figure 1. Degeneration and necrosis of tubular epithelial cells in kidney, H and E, 20X.

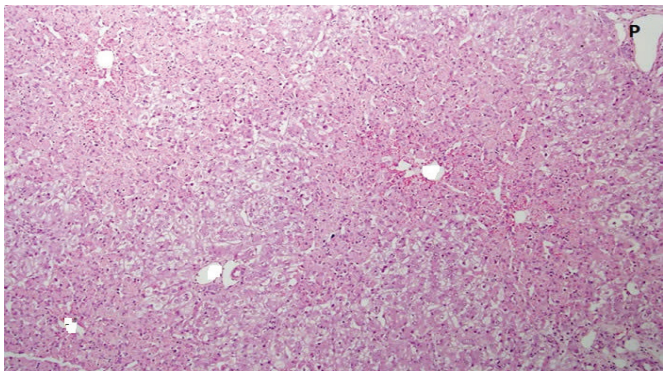


Figure 2. Moderate, multifocal, centrilobular, coagulative necrosis with hemorrhage in liver (H and E, 20 X).

Hematological examination revealed decrease in Total Erythrocyte Count (TEC), Hemoglobin concentration (Hb), Packed Cell Volume (PCV) and normal leukocyte count. Erythrocyte indices revealed elevated Mean Corpuscles Volume (MCV), Mean Corpuscles Hemoglobin (MCH) indicated tendency towards macrocytic hypochromic anemia (Table 1).

Serum biochemistry revealed increased ALT and AST, CRT, urea nitrogen, uric acid where as no consistent changes were observed in albumin, globulin and total protein concentrations (Table 2).

The rumen and intestinal contents were negative for the presence of cyanide and nitrate poisoning in the present study.

The post mortem examination revealed presence of partially digested onions in the rumen animals. In the postmortem, partially digested onions were found in the rumen. The mucous membrane was pale and also icteric. The characteristic smell of onion was evident there in from body and also the skeletal muscles of the dead animals. The skin revealed multi-focal petechiae and ecchymosis ecchymoses which were dominant in medial aspect of

the inner thigh. The blood was of diminished viscosity and decreased coagulation. The viscosity of the blood was diminished and the coagulation time was decreased. The color of the kidneys was dark brown. The bladder was full of urine with dark brown color. The gall bladder was enlarged with clotted bile.

The kidney microscopy revealed the degeneration and necrosis of tubular epithelial cells and also the hyaline droplets. In tubular lumina, deposits of eosonophilic material consistent with hemoglobin were found. There was degeneration and gangrene with deposits of white cell material within urinary organ cannular tissue cells and lumina. In liver, there was centrilobular clotting within the liver among hemorrhage and macrophages containing brown protoplasm pigment. [Figures 1 and 2].

In the present study, treatment regime was symptomatic as there is no specific antidote to the toxicity which included administration of fluids, phosphorus, B-complex vitamins and vitamin C for five consecutive days. All the treated animals recovered after a span of 10 days. They started taking the feed and water normally.

4. Discussion

The clinical signs observed in the present study were similar to those described in cattle,in sheep, horse and buffaoes[6–7–12–23–24].

The blood smear examination revealed negativity to hemoprotozoan parasites. This ruled out the diseases like babesiosis where will be hemoglobinuria[35]. The hemoglobinuria need to be differentiated in onion toxicity with other diseases such as babesiosis, postparturient hemoglobinuria and other causes of hemoglobinuria[12–36]. Similar change in the haematological parameters were reported by many workers in sheep in which hemoglobin concentration, packed cell volume, total erythrocyte count reduced than the reference range in onion toxicity[42–43]. Further the finding is supported by many who also observed the anaemia in the other domestic animals[16–25–26–28–34].

Serum biochemistry revealed increased ALT and AST, CRT, urea nitrogen, uric acid where as no consistent changes were observed in albumin, globulin and total protein concentrations. Similar changes in serum biochemical parameters observed as increased Aspartate Aminotransferase (AST), Creatinine (CRT) and bilirubin levels in sheep with onion toxicity indicative of the damage to liver and kidney[42–44]. This suggested there is existence of liver and kidney damage which is also observed by many who reported the onion toxicities in domestic animals like cattle, sheep, dog and cat[16–19–25–28–34–42–43–44]. The contents of onion like disulfides, n-propyl disulfate and S-methyl and S-prop(en)yl cysteine sulfoxides (SMCOs) derived from aminoacids might be responsible for the toxicity[28],

Compared to the control animals, the values of Malondialdhyde (MDA), a bio-indicator of lipid peroxidation was increased along with increase in values of Glutathione Peroxidase (GPx). The animals had decreased reduced Glutathione Levels (GSH), Glutathione Reductase (GR) and Catalase (CAT) enzymatic activities. In the present study, an increase in MDA was observed, suggesting the production and/or accumulation of Hydrogen Peroxide (H_2O_2) an active Reactive Oxygen Species (ROS) which is formed due to the degradation by CAT and the reduction of GR. Due to oxidative stress, denatured hemoglobin may precipitate, accumulate and bind to the erythrocyte membrane and accelerate the formation of Heinz bodies[4–6–10–15–29–30–32–51–52].

Lipid peroxidation also contributes to erythrocyte deformity leading to hemolytic anemia which may be due to intra or extravascular hemolysis[34]. Elevated levels may indicate liver damage or disease. Higher than normal levels of direct bilirubin in blood may indicate liver isn't clearing bilirubin properly. Further, there will be a fragility of erythrocytes which might be also due to production of H_2O_2[29–30–32–44–53]. The alternate mechanism of hemolysis may be attributed to damage to the erythrocytic plasma membrane, causing cellular lysis[29–34]. Cattle, horses, sheep and buffaloes are more resistant to onion toxicity compared to dogs and cats and this might be due to the differences in the structure of the hemoglobin and efficiency of protective enzyme systems[33–34]. Hemolytic anemia in the present episode of onion toxicity is a well known phenomenon. It is also shown that multiple toxic principles are involved in the toxicity. The ingredients of onion garlic and other *Allium* plants do cause toxicity due to the amino acid contents of them like n-propyl disulfate, disulfides,and S-methyl and S-prop(en)yl cysteine sulphoxides (SMCO)[16–19–25–28]. In the rumen, the SMCO are hydrolyzed by anaerobic bacteria to thiosulfonate. Further this is metabolized to dipropyl disulfides and dipropenyl disulfides[16–26–31]. It is said that oxidative damage in erythrocytes is caused by these disulfides[27–28–31]. In the affected animals, hemoglobin might be converted to oxidized ferric form methhemoglobin which is unable to transport oxygen and leading to death[17–19–27].. Heinz bodies are formed due to the aggregation of hemoglobin and its binding to cytoplasmic membrane due to the oxidative damage[29–30]. Extravascular hemolysis might be caused by intra erythrocytic nature of the Heinz bodies which are recognized by splenic and hepatic macrophages and get phagocytosed[30].

There was a characteristic methemobinemia with clinical sign of dark brown colored visible mucous membranes

which also evident in onion poisoning in many domestic animals. The hemolytic crisis in the particular incidence is similar to that reported in onion toxicosis in cattle, sheep and horses[4–11–12–17–18–27–37–39]. Consumption of onions can cause hemolytic anemia and methemobinemia which leads to increased respiration as inability to carry the oxygen by hemeoglobin as reported in many earlier studies resulting in secondary ischemic induced organ damage, nephrosis induced by hemoglobinuria and centrilobular necrosis in hepatic hepatic tissue as stated in this research[5–7–40].
The clinical examination of the ailing animals revealed that they have anorexia, tachycardia and polypnoea. This finding is in accordance with earlier toxicity reports of onion in small and large animals[25].

The rumen and intestinal contents were negative for the presence of cyanide and nitrate poisoning ruling out the possibility of other plant toxicities containing such ingredients with similar clinical signs[41–45].
The findings in post mortem like jaundice or pallor of tissues, dark brown kidneys and urine color, tissues with a strong odor of onion and fragments of onion seen within the rumen were common necropsy findings in other reported cases of onion toxicity in different species of domestic animals[6–12–34–37–43–45–54–55].
The histopathological lesions with a moderate, multifocal, centrilobular, coagulative necrosis with hemorrhage and macrophages containing brown cytoplasmic pigment similar to that of many such findings in earlier studies. Microscopic changes noticed in many other episodes in domestic animals were centrilobular necrosis and vacuolization of hepatocytes in midzonal areas of the liver and hemoglobinuric nephrosis in the kidneys. Earlier also many workers reported the similar PM changes. [6–7–9–22–23–35–37–44–54–55].
Administration of fluids is a good technique for dilution of the toxin as well as increased excretion of toxin from the body. The B-complex vitamins do have reversal effect of organ damage by toxin in many ways along with administration of vitamin C[46–49].

The severity of toxicity will be reduced by restriction of access to onions which is a standard method of access to more toxicant. In severely affected animals with anemia, blood transfusion is preferred method of speedy recovery as there will be low oxygen carrying capacity of hemoglobin as methhemoglobin does not have the oxygen carrying capacity[5–11–23–28].

In present study intra ruminal administration of penicillin and streptomycin made the speedy recovery. In reducing ruminal anaerobic bacteria that promote the formation of some oxidative substances, intraruminal antibiotic administration may be beneficial[16].

5. Conclusion

Toxicity was caused in cattle and buffaloes by accidental consumption of onion and the animals suffered with clinical signs of pale mucous membranes, lethargy, anorexia and voiding dark urine after 8-10 days. In post mortem, onionsmell in the carcass with dark brown urine and kidneys. Histopathology revealed the tubular epithelial cell degeneration and centrilobular coagulative necrosis in liver. Treatment to ailing was initiated with fluids, phosphorus, B-complex vitamins and vitamin for 5 days with good recovery rate.

6. Conflict of Interest

No conflict of interest.

7. Acknowledgements

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