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Original Research Article

Clinical Management of Drug Toxicity caused by combined administration of Diamenazene aceturate, Ivomectin and Oxytetracycline: Case Report in two Alsatians and one Caucasian Dogs

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Abstract

A four year old German shepherd female dog, Mig, was presented to the Veterinary Teaching Hospital (VTH) of the University of Nigeria, Nsukka (UNN) with primary complaints of in-appetence, vomition, weakness and progressive loss of weight. History of the case revealed that the anorexia had started five days before. The 18Kg dog had earlier been treated with Diamenazene aceturate and Ivermectin before referral to the VTH. Clinical examination of the dog revealed bilateral mydriasis, stiffness of the ear pinnea and muscle tremours. Physiological parameters showed tachycardia pyrexia and tachypnea and an imperceptible pulse. Differential diagnosis made included cerebral Trypanosomosis, Canine Distemper, Rabies and drug reaction. At the VTH, we routinely managed two other dogs with similar history of treatment with Diamenazene aceturate, Ivermectin and Oxytetracycline and clinical presentations of drug toxicity and intoxication using supportive therapy of dextrose saline, lactate ringers and normal saline and antidotes but these dogs died. This was the status quo prior to the findings reported herein. However, Mig, in addition to our a-fore mentioned routine therapy, was managed with Plasma Extender (Isoplasma), which is whole blood without cells. The recovery of Mig and the death of the other two dogs further emphasizes that inclusion of Isoplasma to the routine regimen is more effective for the management of drug toxicity and other forms of intoxication and this report advocates for its adoption in clinical practice. It is also worthy of note that whereas this case was handled in 2011, as at 2015, the time of reporting this case, Mig had whelped 4 other times; producing healthy puppies and Isoplasma has become a routine inclusion in the management of cases of intoxication in canine.

Keywords: Canine, Diamenazene aceturate, Ivomectin, Oxytetracycline, Toxicity

Abbreviations: INF: Infusion; **IV:** Intravenous; **IM:** Intramuscular**; Stat:** One Initial Dose

INTRODUCTION

The term toxin refers to poisons produced by bacteria, ticks and fungi and other biologic sources such as venoms and plant toxins (Kahn et al., 2005). Waste products, not removed from the body during liver or kidney failure, are also referred to as toxins (Boden, 2005). Toxicosis, poisoning and intoxication have been

used synonymously to refer to diseases produced by a toxicant (Kahn et al., 2005). Most cases of poisoning in domestic animals result from poisons being swallowed. In few instances poisons may be absorbed through a wound of the skin, or even through the unbroken skin, e.g. phenol preparations. Malicious poisoning is frequently encountered in dogs and cats (Boden, 2005). Dogs and Cats may also be poisoned if they have access to medicines (pills, tablets, etc.) intended for human use. Food poisoning has resulted from dogs consuming foods contaminated with rat poisons (Kahn et al., 2005). Administration of drugs in higher doses or use of drugs contra-indicated for a particular species or breed of animal, or administration of certain drugs to normal animals or animals sick of certain diseases can cause drug toxicity. Thus, a drug that is intended for therapeutic uses turns out lethal (Daniel et. al., 2005). Toxins, poisons and toxicants are used interchangeably in this report.

Toxicity could be acute (effects produced within 24-hours) or chronic (effects produced after prolonged exposure ≥ 3 months).Usually absorption occurs through the alimentary tract, skin, lungs, eye, mammary gland or uterus as well as from site of injection. Toxic effects may be local (surrounding affected cells) or generalized (involving the whole body systems). The primary factor affecting absorption is solubility. Insoluble salts are the least absorbable and lipid-soluble substance the most readily absorbable (*Kahn et al.,* 2005). Distribution or translocation of the toxicant follows via the blood stream to reactive sites, including storage depots. The liver receives the portal circulation and is the organ most commonly involved with detoxification. The highest concentration of a poison within an animal is not necessarily found in the organ or tissue on which it exerts its maximal effect (the target organ). Thus, knowledge of the translocation characteristics of poisons is necessary for proper selection of organs for analysis and management (Kahn et. al., 2005).

There are two phases of metabolism. Phase I includes oxidation, reduction and hydrolysis mechanisms. These reactions, catalyzed by hepatic enzymes, generally convert foreign compounds to derivatives of phase two. Some of the products are excreted. Phase two principally involves conjugation or synthesis reactions. Usually, a portion of this is excreted unchanged, and the rest is excreted or stored as metabolites. Significant differences in metabolic mechanisms exist between species. For example cats lack forms of glucuronyl transferase; their ability to conjugate morphine and phenols is compromised.

Excretion of most toxicants and their metabolites is by the kidneys. Many polar and high molecular-weight compounds are excreted through the bile. Milk is also a medium of excretion of some toxicants in some food animals. The route of administration, dose and condition of the animal can have a profound effect on excretion rates (Kahn et. al., 2005) and in turn the clinical consequences of a toxicant.

Factors affecting the activity and consequences of a toxicant can be exposure related factors. These are dose, time, frequency and duration of exposure, route of administration, and state of animal at time of exposure, time of administration relative to food intake, prevailing environmental conditions of temperature and humidity, etc. Biologic factors include; species and breed differences, age and size of animal, nutritional and dietary status of animal. Chemical factors are the nature of the toxicant (which determines its solubility) and the vehicle carrying the toxicants.

MATERIALS AND METHODS

Review of Cases

Case I: SHARON

On the 21st of May, 2011, a 3-year old male Alsatian (Sharon) was presented to the VTH. History showed that the dog had been managed with 2 ml of Diamenazene aceturate and 1.5 ml of Oxytetracycline. This treatment was believed to have worsened the condition of the dog.

The clinical signs during physical observation were copious stringy salivation from the mouth, mydriasis, stiffness of the ear pinnea, muscular tremours, and gapped mouth, with the tongue hanging out loosely. There were no ecto-parasites in the body. The animal at point of presentation assumed sternal recumbency but was sensitive to touch. Physiologic parameters across days are presented in Table 1 below.

Based on the history of drug administration before manifestation of signs, tentative diagnosis of Diamenazene aceturate toxicity was made. Other considerations included Snake bite and Hypersensitivity reaction.

Observations

Physiologic parameters

Day 2 Observation

The condition of the animal had worsened on day 2 as revealed by the parameters; see Table 1 below. The animal had become very weak with protruding tongue. There was paresis of the hind quarters, convulsion and opistotomus.

Day 3 Observation

Sharon's condition grew worse than on day 2, as revea-

Table 1. Showing physiologic parameters of case 1-Sharon

Parameters	Day 1	Day2	Day 3
Temperature	40.6.0°C	37.3° C	36.9° C
Pulse Rate	Unreadable	71	60 bpm
Respiratory Rate	60 bpm	33 bpm	30 bpm
Heart Rate	100 bpm	130 bpm	Unreadable
Weight	18kg	17kg	Unmeasured

led by physiologic parameters; see Table 1 above. The extremities were cold to near numb. Animal remained very weak with protruding tongue. There was paresis of the hind quarters, convulsion and opistotomus

Treatments

Day 1

Symptomatic treatments were:
1. Inj. Atropine Sulphate 1.2 mg/kg bwt, IV once
2. Inf. Dextrose saline, 500 ml , IV once
3. Inj. Dexamethasone 0.25mg\kg IM Stat (one dose)
4. Inj. Vitamin B-complex 2 ml, IM Stat (one dose)

Six hours later

5. Inf. Dextrose Saline 100 ml, IV stat
6. Inj. Calcium borogluconate, 15ml, IV stat
7. Inj. Chlorpromazine 2mg\kg bwt IV stat

Day 2

1. Inj. Streptopen (combined) 1ml\25kg body weight (bwt.) IM, stat (one dose)
2. Inj. Calcium borogluconate 15 ml administered through slow IV, stat (one dose**)**

DAY 3

1. Inj. Streptopen (combined) 1ml\25kg body weight (bwt.) IM, stat, (one dose)
2. Inj. Calcium borogluconate 15 ml administered through slow IV, Stat (one dose).
3. Inj. Vitamin B-complex 3ml IV stat

Case II: Target

On the 4th of June, 2011, a 1 year old male Caucasian called Target was presented to the VTH with a similar history of receiving 1.5 ml of Diamenazene aceturate and Oxytetracycline with attendant worsened condition. Prior to been referred to the VTH, Target had a history of in-appetence, febrile body temperature and a tentative diagnosis of Trypanosomosis for which aforementioned drugs were administered. Following this treatment, the dog grew weaker as the condition worsened. The animal at point of presentation was in sternal recumbency and sensitive to touch. The clinical signs observed were copious stringy salivation, mydriasis, stiffness of the ear pinnea, muscular tremours, and gapped mouth, with the tongue hanging out loosely. There were ecto-parasites in the body. Physiologic parameters across days have been presented in Table 2 below. Target which is ordinarily aggressive, like all Caucasian (Dog Breed Info Center, 2015), was docile and shy

A tentative diagnosis of toxicity was made based on history of concurrent Diamenazene aceturate and Oxytetracycline administration. Other conditions considered included Snake bite, Hypersensitivity reaction.

Observations

Physiologic parameters

Day 2

The condition of the animal got worse as revealed through physiologic parameters; see Table 2 above. Animal remained very weak with protruding tongue. There was paresis of the hind quarters, convulsion and opistotomus.

Day 3

The condition of the animal had worsened as revealed by the parameters; see Table 2 below. The animal was very weak. There was paresis of the hind quarters, convulsion and opistotomus.

Treatments

Day 1

Symptomatic treatment was based on the history of drug

Table 2. Showing the physiologic parameters for Target-case II

Parameters	Day 1	Day2	Day 3
Temperature	41.6.0°C	38.3° C	36.5° C
Pulse Rate	Unreadable	75	62 bpm
Respiratory Rate	65 bpm	30 bpm	30 bpm
Heart Rate	90 bpm	120 bpm	Not measured
Weight	15kg	12kg	Not measured

Table 3. Showing the physiologic parameters for Mig-case III

Parameters	Day 1 (9:00AM)	Day 1 (3:00PM)	Day2 (9:00AM)	Day 3	Day 4
Temperature	40.1° C	39.0°C	37.3° C	37.9° C	38°C
Pulse Rate	Unreadable	Unreadable	Unreadable	136 bpm	62 bpm
Respiratory Rate	100 bpm	64 bpm	34 bpm	42 bpm	34 bpm
Heart Rate	180 bpm	168 bpm	183 bpm	140 bpm	125 bpm
Weight	19kg	17kg	19kg	22kg	25kg
WBC	8300\mm		9600\mm		
PCV	32%		38%		
Hb	9.5g\dl		9.5g\dl		
RBC	$4.03X10^6$		$4.03X10^6$		

administration before manifestation of signs and observed symptoms. These treatments are:

1. Inj. Atropine Sulphate 1.2 mg/kg bwt, IM stat (one dose)
2. Inf. Dextrose saline 500 ml, IM, stat (one dose)
3. Inj. Dexamethasone 0.25mg\kg IM, stat (one dose)
4. Inj. Vitamin B-complex 2 ml, IM, stat (one dose)

Day 2

1. Inj. Streptopen (combined) 1ml\25kg bwt. IM stat, (one dose)
2. Inj. Calcium borogluconate 10 ml administered through slow intravenous route, one dose.
3. Inj. Vitamin B-complex 3ml IV stat

Day 3

1. Inj. Streptopen (combined) 1ml\25kg bwt. IM, stat (one dose)
2. Inj. Calcium borogluconate 15 ml administered through slow intravenous route, one dose.

Case III: MIG

On the 21st of June 2011, Mig, a 4 year old German shepherd bitch was presented to the VTH, UNN with the primary complaints of in-appetence, vomition, weakness and loss of weight. The dog had been off feed for 2 days. Consequently it was treated using 1.2ml of Diamenazene aceturate, 100mg of Oxytetracycline and 10mg of Ivomectin. Following this treatment the dog became weaker; after which it was referred to the VTH. Mig had up-to-date vaccination and de-worming record. The Client further reported that the dog was fed with little quantity of milk earlier that morning before she was brought to the VTH and had urinated twice the previous day but none on the day of presentation. Mig had whelped 14 puppies in a litter about 10 months ago

The clinical signs observed included bilateral mydriasis, stiffness of the ear pinnea, muscular tremors, marked mydriasis, torticollis, stiffness of the ear pinnea, swelling on the underbelly and dog screamed at touch. Also noticed was muscular tremours and inability to close mouth, loosely hanging out tongue with copious salivation. The pulse rate was imperceptible; thready-to-weak thus could not be obtained. However there was tachycardia, pyrexia and tachypnea with the animal preferring lateral recumbency.

Physiologic parameters across days are presented in Table 3 above.

The tentative diagnosis was drug intoxication following history of administration of Diamenazene aceturate, Oxytetracycline and Ivomectin. Other conditions considered included cerebral Trypanosomosis, Canine Distemper and Rabies.

Observations

Physiologic Parameters

Day 1 (3:00 PM)

The condition of the animal had worsened as revealed by

the parameters. Please see Table 1 above. The animal was weak; having erect pinnea, protruding tongue, but un-enlarged lymph nodes. Also noticed was paresis of the hind quarters, convulsion and opistotomus. Mydriasis had reduced.

Day 2 (9:00AM)

Observations

The animal showed great improvement with good body condition, she was quiet; not mooring like on day of presentation. Mydriasis of the pupil had subsided, the animal could rise on her own and the skin was lustre. There was presence of ecto-parasites.

Day 3 (9:00 AM)

Observations

By day 3 post-presentation, the physiologic parameters and heamogram were appreciably stable; please refer to table 3 above. Following this examination and because of the fleas, pour-on was administered on the dog.

Treatments

Day I

At the VTH, UNN the statutory treatment for treatment of drug toxicity was given to Mig. These are listed below:
1. Inj. Atropine Sulphate 1.2 mg/kg body weight IV, stat
2. Inf. Dextrose saline 250 ml, IV, stat
3. Inj. Dexamethasone at 0.25mg\kg IV, stat
4. Inf. Vitamin B-complex 3 ml IV, stat

Day 1 B: (6 Hours Later)

1. Inf. Dextrose Saline150 ml IV,
2. Inf. Dextrose saline 250 ml, IV,
3. Inj. Dexamethasone at 0.25mg\kg IV,
4. Inj. Vitamin B-complex 3 ml IV,
5. Inj. Calcium borogluconate 25 IV, stat
6. Inj. Chlorpromazine at dose of 2mg\kg body weight, IV , one dose

Day 1 C: (12 Hours Later)

Because of the Sonocardiogram and the heaemograph, that reveal tachycardia due to low volume of blood caused by anemia, a plasma extender was recommended for the dog.

1. Inf. Plasma Extender (Isoplasma®) 4% wt/vol. 500ml, IV, one dose
2. Inj. Streptopen (combined) 1ml\25kg body weight (bwt.) IM, one dose
3. Inj. Calcium borogluconate 25 ml, slow IV, one dose
4. Inf. Vitamin B-Complex 4 ml, IV, one dose

Day 2 (9:00 AM)

1. Inf. Darrow's solution 500ml IV, one dose
2. Inj. Streptopen (combined) 1ml\25kg body weight (bwt.) IM, one dose
3. Inf. Vitamin B-Complex 4 ml, IV, one dose

Day 2 (12:00 Noon)

1. Inj. Streptopen (combined) 1ml\25kg body weight (bwt.) IM, one dose
2. Inf. Vitamin B-Complex 4 ml, IV, one dose

Day 2 (6:00 PM)

1. Inf. Plasma Extender (Isoplasma®) 4% wt./vol. 500ml, IV, one dose
2. Inj. Streptopen (combined) 1ml\25kg body weight (bwt.) IM, one dose
3. Inj. Calcium borogluconate 30 ml, slow IV, one dose
4. Inf. Vitamin B-Complex 4 ml, IV, one dose

Day 2 Patient monitoring (8:00 PM)

1. Inf. Vitamin B-Complex 4 ml, IV, one dose

2. At about 8.30 pm the animal was fed with custard containing milk and sugar.

Day 3 (12:00 Noon)

At about 12.00 noon, the animal was fed with fish meal, meat broth and rice. The animal was alert and active thus, the animal was discharged with the instruction to repeat for follow-up treatments with antibiotics.

RESULTS

Case I

Laboratory Tests and Results

There were ova of helminthes in feces.

Death and Post-motern Examination

The dog died at about 2pm on the 3rd day of presentation. It was not posted because the owner obstructed the process; refusing to release the carcass to the Clinic.

CASE II

Laboratory Tests and Results

Blood screening revealed absence of haemo-parasites. Fecal examination revealed absence of helminthes ova

Death and Post-motern Examination

The dog died at about 5pm on day 3 of presentation. The dog was not posted because he died at the home of the owner and was not returned to the Clinic for post-mortem examination.

CASE III

Laboratory Tests and Results of Day 1

Sonography results revealed high heart rate, shallow depths and low peaks. Although the heart rate was high the beat was weak and the blood-filling capacity and volume was low suggesting hypo-volaemia sequel to dehydration. Blood heamogram WBC= 8300\mm, PCV 32%, Hb 9.5g\dl, RBC 4.03x 10^6.

Laboratory Tests and Results of Day 2 (9:00AM)

From this time on the physiologic parameters of the animal was monitored every 1\2 hourly and the dog showed progressive improvements. Again the heamogram was checked and the result showed WBC= 9600\mm, PCV= 38%, Hb 9.6\dl, RBC= 5.3x10^6.This result was an improvement on the last heamogram. However the PCV was still low and the animal had not started to eat any food.

Laboratory Tests and Results of Day 3 (12:00 Noon)

Result of urinalysis showed PH = alkaline, protein present, Ascorbic Acid, Blood, Bilirubin, urobilogin, nitrite glucose were not present in the urine of the animal. Examination showed that the animal was alert but hide-bound. She stood and walked with a tilted gait towards the right side. The dog cried due to body pain, settles down on sternal recumbency when petted, there was heavy flea infestation

Recovery and Discharge

The physiologic parameters of the patient (Mig) stabilized; the patient fed its self on commercial dog food, as well as showing full signs of recovery. Thus the animal was discharge to the owner.

DISCUSSION

Cerebral Trypanosomosis was one of the differentials in Mig because of the nervous and neurologic signs such as; muscular tremours and torticollis that were associated with the case. However, Trypanosomosis was ruled out because microscopic examination of the blood was negative for trypanosome parasite. There could be two other possibilities for the absence of Trypanosome parasite in the blood; the first being that Diamenazene aceturate that was earlier administered to the animal could have cleared the parasite from the peripheral circulation, since it has been reported that the effect of Diamenazene aceturate is remarkable within 24 hours of administration (Aliu, 2007). Secondly, the parasite may have crossed blood-brain barrier and be unavailable in the blood stream (Kahn, 2005).

Rabies was also suspected because of the stringy salivation and nervous sign. However, the history given by the owner did not reveal a prior animal bite exposure, neither incomplete record of vaccination nor were there observed, other accompanying nervous signs which are associated with Rabies. According to Barlough and Perterson (1995) absence of these characteristic symptoms of Rabies rules Rabies out from being a definitive diagnosis.

Canine Distemper (CD) was suspected because of ralves, fever, low grade in appetence, depression and nervous signs and a swelling on the underbelly. Other signs associated with CD such as diarrhea, neurologic signs (e.g. circling, nystagmus, convulsions) and skin papules and hyperkeratosis of the skin and dew pad were absent in this case. Besides the observed Papule in the under belly of Mig had existed in the dog for over one year; at time before Mig became sick

Ivermectin is most commonly used in monthly heartworm prevention. It is also used to treat ear mites as well as hair mites, which can cause mange. It is used to treat some internal parasites as well. Toxicity can occur if a dog is given an excessive dose of the medication (10 to 20 times the recommended dose). Additionally, certain dogs are genetically hypersensitive to the medication. In these dogs, Ivermectin can pass directly to the brain and be toxic or even lethal. Sensitivity to the drug can also be seen in dogs or puppies that have overdosed on a similar medication in the past. A genetic sensitivity to Ivermectin can be seen in several breeds, including the Caucasian, German shepherd and Collie (Pet Health Network, 2012) Adverse reactions to Ivermectin intoxication include;

Lethargy, Depression, Drooling, Vomiting, Dilated pupils, Loss of appetite, Disorientation, Tremors/Seizures, Blindness, Trouble standing, Slow heartbeat, Difficulty breathing and Coma (Pet Health Network, 2012; Coates, 2015).

Side effects of Diamidines a group to which Diamenazene aceturate (DA) belongs induce kidney damage, hepatic impairment, ataxia and convulsion as part of their adverse effect (Kahn, 2005). The underlining reason is the DA accumulates in the liver, kidneys and adrenal glands. Their excretion is slow, and remains largely unchanged for 2-4 weeks (Aliu, 2007). Literatures on recent studies do recommend use of DA in dogs (Kahn *et al*., 2005).

Generally, adverse reactions to drugs or medications include vomiting, fever etc (Aliu, 2007). It is often difficult to determine whether such signs are due to the medication or due to the disease being treated (Barlough and Pedersen 1995). It is probable that Alsatian and Caucasian breeds of dogs lack excretory and metabolic mechanisms to conjugate Diamenazene aceturate (Aiello *et. al.,* 1994).

Tetracyclines are relatively safe drugs except in horses and young animals (Aliu et. al., 2007). Most of the adverse effects of the group reported are associated with ability of the drug to suppress gut micro flora and to chelate metal ions, (Aliu, 2007). Rapid intravenous injection of the tetracyclines can cause hypotension, sudden collapse (Aiello *et. al.,* 1994) and hypersensitivity reactions in small animals (Aliu, 2007). These reactions were observed in the three case. Oxytetracycline can be occasionally nephrotoxic and should not be administered with other potentially nephrotoxic drugs (Snyder *et al,* 1994). It has also been reported that renal tubular necrosis (Aliu, 2007; Katzung, 1998) and other renal injury resulting in Nitrogen retention were associated with administration of tetracyclines that have lost their potency (Katzung, 1998). When used in combination with glucocorticoids, it often leads to significant weight loss particularly in anorectic animals (Aliu, 2007).

Samples collected included blood sample, in order to check presence of haemo-parasites particularly *Trypanosome sp.* This is routine in Tsetse endemic areas like Nigeria (Barlough and Pedersen 1995, Kahn et.al. 2005).

Atropine was given to case III as antidote to anticholinesterase dose (Aliu et. al., 2007). It acts to depress the peripheral nervous system by antagonizing acetylcholine effects by preventing acetylcholine from acting on the cholinergic receptor sites on the effector cells. Thus salivation, gastric juice and pancreatic secretion are depressed along with relaxation of smooth muscles of the intestinal tract etc dose (Aliu et. al., 2007). It also increases cardiac function and controls vomition in dogs (Aliu et. al., 2007). These effects of atropine may be responsible for recovery of Case III.

Dexamethasone is an adrenocortical steroid hormone and glucocorticoid anti-inflammatory synthetic analogue of prednisolone used as a corticosteroid to mitigate undesired inflammation. At some doses, it prevents extracellular fluid losses from dropping below what is lost during hemorrhage. It increases blood pressure and reestablishes urine output (Irvings 1994). This was particularly necessary to encourage urination and so aid detoxification in case III. Since inflammatory condition increase blood in circulation as well as the intoxicant being circulated to other organs and systems of the body, this drug was administered so as to reduce inflammation; therefore reducing the distribution of the toxicant.

Supporting Case III by administration of Dextrose and normal saline and Darrow's solution was necessary cause dilution of the intoxicant in the system. Fluid therapy also improves diuresis (Reasor and Davis ?). Fluid therapy was indicated to relief dehydration in case III being the animal was hide-bound. Normal saline was given to cater for the electrolyte losses of Na^- and replace fluid. However it does not contain energy thus dextrose saline, which is an energy source, was administered to provide additional fluid, Na^- and Cl^- and energy (Aliu 2007). In order to reverse metabolic acidosis that may be caused by dehydration, Darrow's solution was infused intravenously. Darrow's is known as a polyionic parenteral crystalloid solution containing NaCl, KCl and sodium lactate. The lactate is metabolized to bicarbonate (HCO_3^-) (Aliu et. al, 2007; Boden, et. al., 2005).

Penicillin a beta lactam narrow spectrum antibiotic was administered to check secondary infections due to Gram positive bacteria. It binds to and inhibits the transpeptidase. Streptomycin is an aminoglycoside antibiotic active against Gram negative and gram positive bacteria was administered to complement spectrum of activity of penicillin (Kahn et.al. 2005).

Calcium borogluconate is a soluble calcium salt that is used in prevention and treatment of hypocalcium, as observed in eclampsia in bitches and cardiac arrhythmias induced by hyperkalemia. Clinically calcium borogluconate has been adopted for the treatment of recumbency, hypocalcaemic tetany. Case III was recumbent and showed signs of convulsion at time of presentation. 10% Ca borogluconate at (1.2 mL/Kg) was administered to the dog through slow intravenous over a period of 20 minutes.

Flumethrine (Pouron®) was administered topically to case III to mitigate the fleas observed infestation. Pouron® was preferred to Ivomectin® because we considered that Mig might not handle the metabolism of Ivomectin® or any other systemic acaricide. Immediate relief was observed immediately the drug was administered topically to Mig. Isoflex a plasma extender was administered to Case III. Plasma extenders come in various forms, viz,, Dextran, Gelatin polypeptides etc. Dextran-40® is known to improve peripheral blood flow by lowering blood viscosity. It has osmotic effect and draws water into circulation. It also enhances shift of fluid into

vascular beds (Aliu 2007). Gelatin polypeptides on the other hand, are rapidly excreted by the kidneys and therefore exert a mild beneficial diuretic effect (Aliu 2007). This was used in management of case III

Isoplasma (Haemaccel®) This is a 3.5% colloidal infusion solution of polygeline with electrolytes for intravenous administration only. It is sterile and Pyrogen free Plasma volume extender. Haemoccel®, the trade name has a composition that each 100ml contains Polygeline, Polypeptides of degraded gelatin, cross-linked via urea bridges 3.5g; 0.85g of Sodium Chloride IP; 0.038g of Potassium Chloride IP; 0.070g o Calcium Chloride IP; injection water and electrolytes of sodium, potassium, calcium and chloride. The Haemoccel is prepared at a PH of 7.3. Therapeutically, Isoplasma is considered the same as Plasma (that is, whole blood without cells). It is used in conditions where the blood picture is severely distorted either by cases of intoxication, hemorrhage and acute loss of electrolyte

CONCLUSION

In each of three cases examined, their pulse was not perceptible at day 1 of presentation. It is probable that the observed fever caused a collapse of the blood vessels, thus making the pulse imperceptible. However, with administration of antibiotics (Streptopen. combined therapy), antidote (Atropine sulphate) and anti-inflammatory (Dexamethasone), the high temperature subsided and the pulse became perceptible on day 2. The changes in the heamogram observed in case 3, Mig, (improving PCV, Hb, Cell count, which occurred in course of the fluid therapy) can be explained by the fact the fluid therapy and plasma extender stabilized the hemodynamics.

At the VTH, as is also recommended and practiced by Pet Health Network (2012) and Coates (2015), we managed other dogs with similar history of treatment with Diamenazene aceturate, Ivermectin and Oxytetracycline and clinical presentations of drug toxicity and intoxication using routine approaches. These approaches are essentially symptomatic and supportive, viz;, decontamination, administration of activated charcoal, Intravenous fluid therapy (dextrose saline, lactate ringers and normal saline), endotracheal intubation, mechanical ventilation, extensive nursing care, seizure control, application of eye lubricants if the patient cannot blink, nutritional support and intravenous lipid emulsion therapy and antidotes (Coates 2015) but usually, these dogs die. However, Mig, in addition to our routine therapy, was managed with Isoplasma, which is whole blood without cells. The recovery of Mig and the death of the other two dogs further emphasizes that inclusion of Isoplasma to the routine regimen is more effective for the management of drug toxicity and other forms of intoxication and this report advocates for its adoption in Clinical practice.

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