Hum Exp Toxicol OnlineFirst, published on March 30, 2010 as doi:10.1177/0960327110362908

Human and Experimental Toxicology
000(00) 1–11

DOI: 10.1177/0960327110362908
het.sagepub.com

Hematological and biochemical profiles and histopathological evaluation of experimental intoxication by sodium fluoroacetate in cats

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Abstract

Sodium fluoroacetate (SFAC) is a potent rodenticide, largely used for rodent and domestic pest control. The toxic effects of SFAC are caused by fluoroacetate, a toxic metabolite, whose toxic action blocks the Krebs cycle and also induces the accumulation of citrate in the body, which is a serum calcium chelator. The most common clinical signs of this intoxication are the cardiac and neurological effects. However, the hematological, biochemical and histopathological findings occurring in intoxication are still unknown in different species. In the present study, 16 domestic cats were experimentally intoxicated with oral doses of fluoroacetate (0.45 mg/kg). The hematological and biochemical profiles and histopathological findings were made to look for auxiliary diagnosis methods in SFAC intoxications. The hematological profile showed transitory leucopenia and thrombocytopenia; in the biochemical profiles were detected hyperglycemia, increase of creatinequinase enzyme (CK) and creatinequinase cardiac isoenzyme (CK-MB), hypokalemia and hypophosfatemia. In the macroscopic and histopathological findings were observed lesions characteristic of degenerative and ischemic processes in heart, kidneys, liver, brain and lungs. These changes may be auxiliary to the diagnosis of intoxication by SFAC in cats, when associated with clinical signs described for the species. Thus, the complete blood count with platelet count, serum glucose, enzymes CK and CK-MB isoenzyme, as well as the electrolytes potassium and phosphorus, can facilitate the laboratory diagnosis during intoxication by SFAC, associated with the pathological findings in the case of death of the intoxicated animal.

Keywords

sodium fluoroacetate, cats, hematology, serum biochemistry, histopathology, diagnosis, intoxication

Introduction

The sodium fluoroacetate (SFAC) or Compound 1080 is a potent rodenticide used for rodents and vertebrate pest control.[1] It was prohibited in many countries because of its high toxicity. In Brazil, although prohibited by law, there is the illegal use, causing intoxication in children and domestic animals,[2] which continues to stimulate research about diagnostic methods by this intoxication.[3,4]

The toxic effects are caused by fluorocitrate, the fluoroacetate metabolite. This metabolite blocks body energy production by inhibition of Krebs cycle, resulting in neurological and cardiac signs, also metabolic acidosis and hypocalcemia due to increased citrate and its serum calcium chelation effect.[5]

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The clinical variability is evident in the fluoroacetate intoxication due to the individual and species sensibility differences.[4,6] The cardiotoxicity is manifested by cardiac arrhythmias, like ventricular tachycardia, ventricular fibrillation and cardiac arrest. The neurotoxicity is demonstrated by ataxia, hyperexcitation and convulsions.[7-9] Body system thermo-regulation is also affected because of energy production block, resulting in hypothermia in cats and hyperthermia in dogs.[9,10] Hypocalcemia and hypokalemia are common, as well as hypotension and metabolic acidosis.[9]

The oral toxic doses of SFAC in different species are 0.2–7 mg/kg in rodents, 0.5–2 mg/kg in human, 0.3–0.7 mg/kg in goats, 0.5–1.75 mg/kg horses, 0.3–0.4 mg/kg in pigs, 0.15–0.62 mg/kg in cattle, 0.25–0.5 mg/kg in sheep, 10–30 mg/kg in birds, 0.096–0.2 mg/kg in dogs and 0.3–0.5 mg/kg in cats.[8]

Glycerol monoacetate (Monoacetin®), an acetate donor, was proposed as an antidote by fluoroacetate intoxication. However, its effects against 'lethal synthesis' of fluoroacetate in fluorocitrate are effective only when used immediately after the toxic ingestion. The other therapeutic options include studies using 10% solution calcium gluconate, indicated as antagonist for hypocalcemia caused by SFAC; in addition, sodium succinate was experimentally selected as potent antidote in mice3 and cats,4 in an attempt to reverse hypocalcemia and metabolic acidosis.[3]

The assessment of laboratory parameters and necropsy findings are of great importance to determine the characteristics and the alterations resulting from intoxication by SFAC, to different species. This study evaluated hematologics and serum biochemical profiles and histopathological findings, in order to establish a protocol diagnostic laboratory as a routine in cases of intoxication in cats by SFAC.

Methods

The present study was approved by the Ethical Committee for Animal Research (CEEA – Comitê de Experimentação e Ética Animal) of the Faculty of Veterinary Medicine and Animal Science of the São Paulo State University – UNESP, Botucatu, Brazil.

The present study was conduced using a group of 16 domestic adult cats (male and female), with body weights between 2.5 and 5.0 kg. After 8 hours of fasting, the animals were experimentally intoxicated with 0.45 mg/kg by oral dose of the SFAC (Monofluoroacetic Acid Merck®). After the first clinical signs, all cats were anesthetized with pentobarbital (Hypnol 3% Cristalia®) up to 30 mg/kg, by intravenous route, a sufficient dose for convulsion controlling and to avoid cardiorespiratory depression.

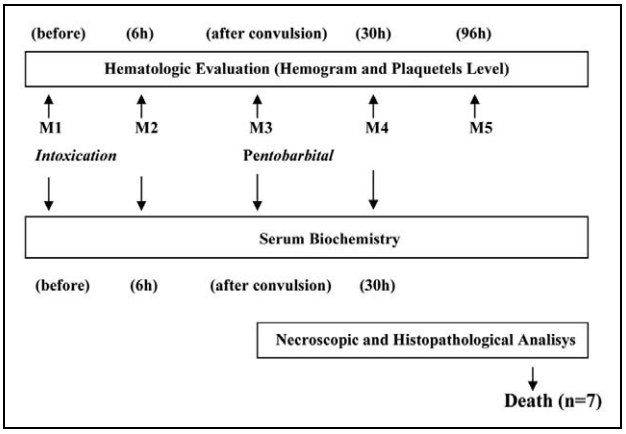

Figure 1. Experimental design for sodium fluoroacetate (SFAC) oral intoxication in cats.

The experimental design (Figure 1) contains the assessment times and samples collected during present study.

Proceeding for blood sampling and laboratorial analysis

Hemogram and platelet count. The cephalic and jugular veins were catheterized (BD Insyte ® catheter 24G) for harvest of blood samples for laboratory analysis at the times set out in the experiment (Figure 1). Blood samples for hemogram and platelet count were collected in syringes containing EDTA as anticoagulant (Becton Dickinson – BD ® – Dhihep Plus Kit – Vacutainer Brand).

Hematological assessment were performed before oral SFAC administration (M1), 6 hours after intoxication (M2), after seizure (M3), 30 hours after convulsion (M4), and 96 hours after intoxication (M5; Figure 1). The samples blood controls (M1) were harvested in all animals at the day before the intoxication. The last moment (M5) was set up to determine which of the period was necessary for the normalization of hematological values after the acute phase of intoxication.

There were analyzed hematocrit (Ht) – Centrifuge MH CELM®, plasma protein total (PPT) – refractometer Atago®, hemoglobin (Hb) – CELM-HB520®, the total count of erythrocytes and leukocytes total and differential – CELM electronic counter-

CC510®. The platelet count was performed manually in a Neubauer® chamber, using ammonium oxalate solution of 1% as the diluent.

Serum biochemistry. The biochemistry serum assessments were performed before oral SFAC administration (M_1), 6 hours after intoxication (M_2), after seizure (M_3), and 30 hours after convulsion (M_4; Figure 1).

Blood samples (4 mL) were harvested by jugular puncture and placed in a vacuum tube with gel separator and clot activator (Vacutainer®) and the samples were immediately centrifuged and frozen at –20°C. The blood samples, taken for determination of glucose, were packed in glass tubes containing 30 µL of sodium fluoride (Analytical Dynamics® Reagents) as anticoagulant and centrifuged immediately for analysis. Total volume of 300 µL of each sample was used, which was analyzed by the method selected according to the type of analysis. Were used dry chemistry devices (AVL® – Model OMNI Modular System) for analysis of sodium and potassium. For the other biochemical variables were used colorimetric methods, immunological or enzymatic of chemical wet (Kits CELM®, Technicon® – Model RA-XT). The blood samples for biochemical tests were analyzed as described in experimental design (Figure 1). Also were determined the serum concentrations or enzymatic activities of the following biochemical variables: glucose, urea, creatinine, alanine aminotransferase (ALT), lactate dehydrogenase (LDH), alkaline phosphatase (AP) and gamma glutamyltransferase (GGT), creatine kinase (CK) and cardiac fraction (CK-MB), calcium, phosphorus, chlorine, magnesium, sodium, and potassium.

Necroscopic and histopathological analysis

The seven cats that came to death during experimental intoxication were subjected to necropsy examinations and held the macroscopic descriptions of the injuries. Fragments of liver, heart, brain, lungs, kidneys, and spleen were harvested and fixed in formalin at 10% for further processing the material in paraffin blocks and stained with hematoxylin and eosin for histopathological analysis. The fixed material was cleaved and processed in paraffin and the blocks were cut on rotary microtome (Leica RM2025®), resulting in cuts of 4–5 µm. The sections were then stained with hematoxylin and eosin11 for observation under optical microscope (Carl-Zaiss Germany®).

Statistical analysis (Graph pad Instat®)

For each parametric variable evaluated in the experiment, the times were compared by analysis of variance (ANOVA) ($p < .05$) in a design into blocks, each characterized as an animal block.[12] The pathological findings were evaluated by descriptive analysis of the percentage of incidence of these findings between animals poisoned with SFAC.[12]

Results

Clinical signs

During the experimental intoxication in cats, the clinical signs were observed by the occurrence of convulsions and clinical parameter for the continuity of the experimental design with anesthesia of the animals and collection of biological samples at times thereafter. All animals experimentally poisoned by SFAC had gastrointestinal signs, episodes of vomiting with liquid bubbly, white to yellow in color, and soft stools with mucus or the presence of streaks of blood. Hypothermia, prostration, position of abdominal pain, transient tachypnea, irresponsibility bilateral mydriasis, agitation, hyperexcitability, and tremors were also clear signs of the appearance and progressive, leading to the occurrence of convulsions. These clinical signs observed in animals during experimental intoxication confirm the results of previous studies.[3,4]

Hematological profile

In the study of the hematological profile, the values of red blood cells did not change significantly ($p > .05$). However, average values of hemoglobin, in the animals intoxicated with MFAS, showed significant decrease 30 hours (M4) and 96 hours (M5) after intoxication ($p < .05$). The average values of the hematocrit showed a significant decrease ($p < .05$) from the convulsive episode (M3).

The leucocyte and platelet counts were the main hematological changes in experimental intoxication by SFAC in this study. The average values of total leukocytes (Figure 2), in the animals experimentally poisoned with SFAC, showed significant reduction ($p < .05$) 30 hours after intoxication (M4). The values of these decreases were transient, returning to the values of normality for the feline species, in the last evaluation at 96 hours after intoxication (M5). However, the total leukocyte count remained at lower values, if compared to the time control (M1). The relative and absolute values of segmented neutrophils

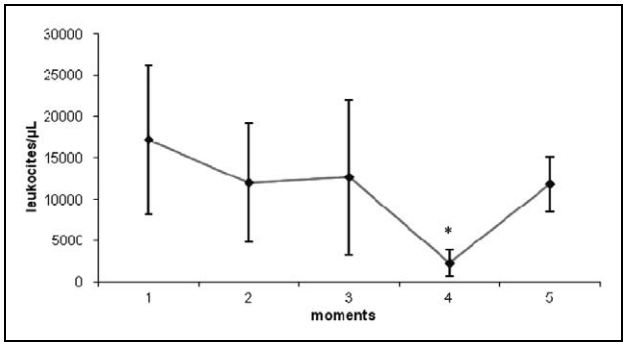

Figure 2. Average values of total leukocytes in sodium fluoroacetate (SFAC)-intoxicated cats in moments of evaluation. *Indicates significant difference ($p < .05$) at this time compared to M1.

decreased 30 hours after intoxication (M4). Moreover, the relative values of lymphocytes and eosinophils, in these animals, showed increase and decrease, respectively ($p < .05$), in the same period (M4). The absolute number of leukocytes had decreased ($p < .05$) from convulsive episode (M3), presenting with normal values at 96 hours after intoxication (M5). The relative number of monocytes showed a gradual increase after convulsion (M3), with significant ($P < .05$) 30h after intoxication (M4).

In platelet count, their average values showed a gradual and significant reduction ($p < .05$) from 6 hours after intoxication (M2), being more pronounced after 30 hours (M4), returning to normal values at 96 hours (M5) after the beginning of the experiment (Figure 3).

Serum biochemistry

In the study of the serum biochemistry, the glucose showed a significant increase ($p < .05$) from 6 hours (M2) after intoxication (Figure 4), returning to normal value 30 hours after intoxication (M4). The mean values of serum creatinine and urea showed no significant changes ($p > .05$) during the experiment.

The average values of LDH, in the animals intoxicated by SFAC, showed a gradual increase over time, with statistical significance ($p < .05$) after convulsions (M3), and returned to baseline 30 hours after intoxication (M4). Similarly, the mean values of CK and CK-MB also showed a gradual increase (Figure 5), however, the increases were significant ($p < .05$) only 30 hours after intoxication (M4). There were no relevant changes in the values of AP, ALT and GGT of animals intoxicated by SFAC ($p > .05$).

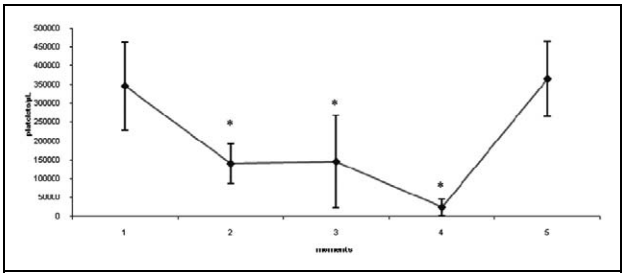

Figure 3. Average values of platelets in sodium fluoroacetate (SFAC)-intoxicated cats in moments of evaluation. *Indicates significant difference ($p < .05$) at this time compared to M1.

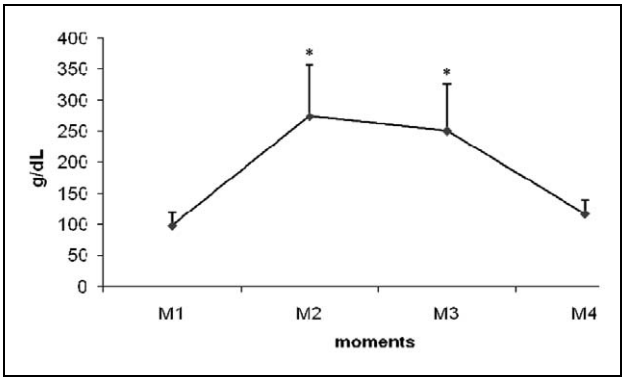

Figure 4. Average values of glucose (g/dL) in sodium fluoroacetate (SFAC)-intoxicated cats in moments of evaluation. *Indicates significant difference ($p < .05$) at this time compared to M1.

Among the electrolytes studied, the values of sodium showed significant reduction ($p < .05$) studied at the last moment (M4). Similarly, the potassium has decreased gradually ($p < .05$), early as 6 hours after intoxication, and remained so until the last moment (M4). The average values of total calcium showed a significant increase ($p < .05$) from 6 hours of intoxication (M2), however, the values of total calcium remained within the values of normality for the feline species in all the moments evaluated. The serum phosphorus also showed a significant decrease ($p < .05$) from 6 hours after intoxication, same happened with the values of magnesium. Furthermore, the chlorine showed no significant changes ($p > .05$).

Necroscopic and histopathological findings

The macroscopic findings showed hemorrhage, edema, ecchymosis, congestion and pulmonary emphysema (43%), right heart dilatation (43%), petechiae and suffusions of the endocardium and pericardium (57%),

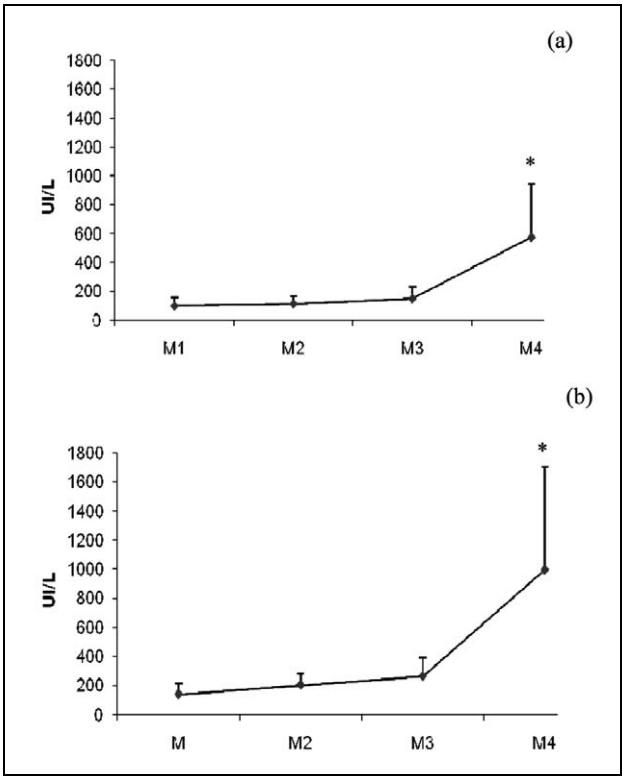

Figure 5. Average values of (a) CK (UI/L) and (b) CK-MB (UI/L) in sodium fluoroacetate (SFAC)-intoxicated cats in moments of evaluation. *Indicates significant difference ($p < .05$) at this time compared to M1.

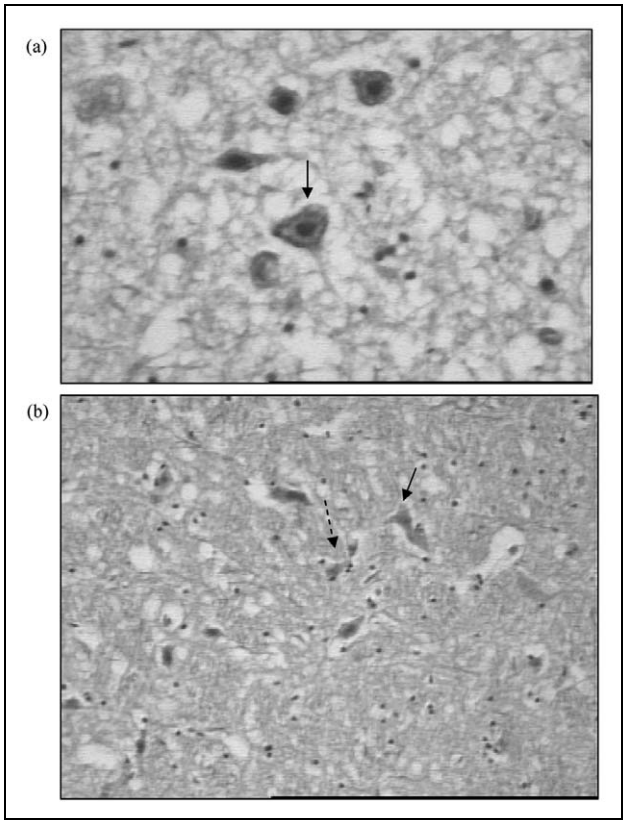

Figure 6. Histological sections of brain from cats experimentally intoxicated with sodium fluoroacetate (SFAC), presenting (a) cromatolysis central (→) HE 40 × 1.6, (b) satellitosis (⇢) e neuronophagia (→), suggesting ischemia HE ×320.

moderate liver degeneration (42.5%) and congestion (49%), gastroenteritis (43%), congestion and renal cortical-spinal degeneration (57% and 87%, respectively), bladder ecchymosis and suffusions (43%), cerebral edema, and congestion (43%).

At histopathology, the presence of edema (100%), congestion, hemorrhage (57%), and multifocal necrosis were observed in the myocardium (86%) and edema (86%), marked congestion, and hemorrhage in the lungs (71.5%). In the liver was observed hydropic degeneration and congestion (86%), fat degeneration (71.5%), and mononuclear infiltrate (71.5%); splenic shrinkage (100%) with predominant decrease at red pulp (71.5%). Renal tubular degeneration (100%), and hyaline (86%) with tubular necrosis (86%), diffuse congestion and hemorrhage (57%), and mononuclear infiltrate (86%) were also present. Already in the brain were observed congestion of the gray matter (86%) and white matter (71.5%), gliosis, satellitosis, neuronophagia and cell swelling (57%), and hemorrhagic spots cromatolysis diffuse (57%) (Figures 6 to 11).

Discussion

The hematological profile of cats with experimentally intoxicated SFAC did not show significant changes in the erythrogram, although there was a transient decrease in the concentration of hemoglobin and hematocrit after the convulsions. All the animals was treated with intravenous saline solution during the experiment, for maintenance of venous access and diuresis before and after convulsions. The intravenous fluid may have caused a transient hemodilution, which would justify the decrease in the concentration of hemoglobin and hematocrit in the erythrogram.[13,14,15]

The importance of leucopenia with neutropenia, lymphopenia, and eosinopenia absolute as well as transient thrombocytopenia, observed in animals of this study, are not described in the literature on intoxication by SFAC. The SFAC also has been studied as an experimental model of cytotoxicity, together with other cytotoxic agents such as radiation and certain chemotherapeutic inducers of leucopenia with neutropenia.[16-18] Thus, the

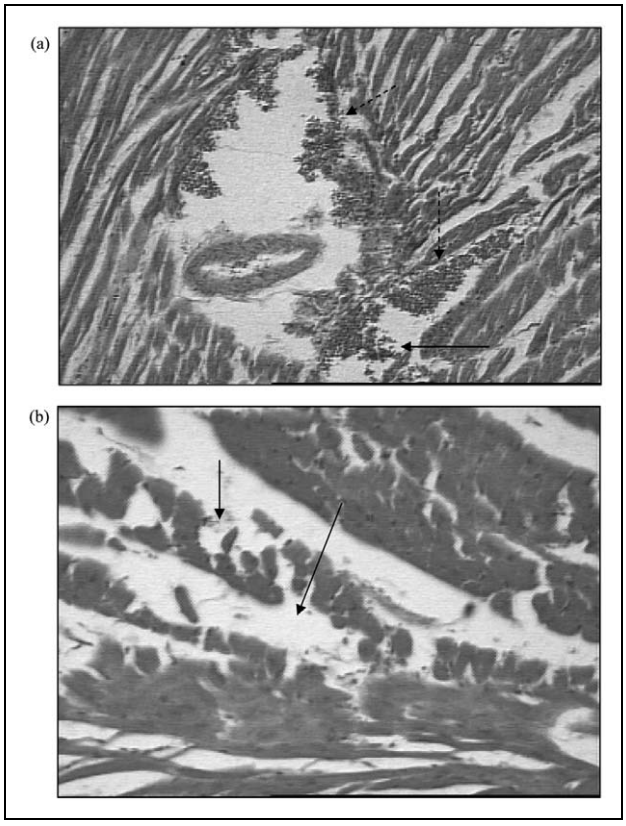

Figure 7. Histological section of myocardium from cats experimentally intoxicated with sodium fluoroacetate (SFAC) showing (a) areas of hemorrhage (→) and vascular endothelial cells adhered on (⇢) and (b) areas of acute ischemic degeneration and necrosis (→). HE ×200.

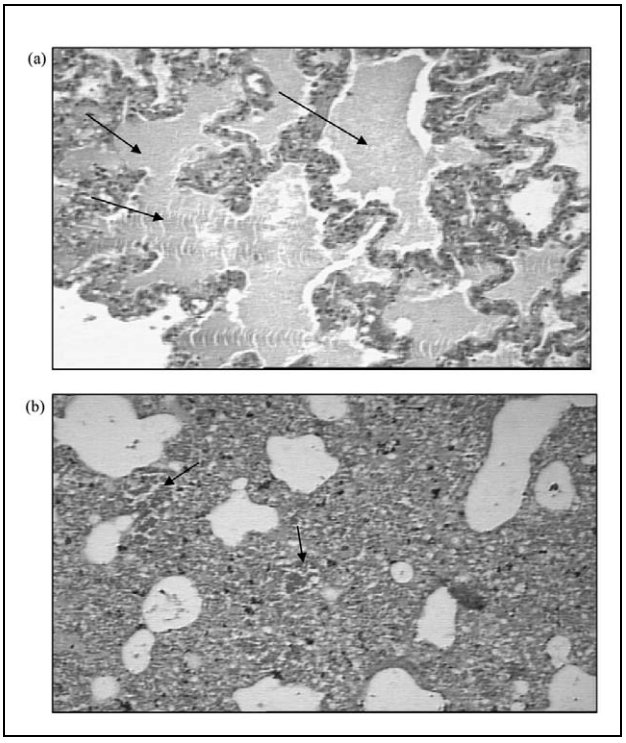

Figure 8. Histological section of the lungs of cats experimentally intoxicated with sodium fluoroacetate (SFAC) showing (a) hemorrhage and (b) diffuse edema pulmonary (arrows), beyond the presence of vascular endothelial cells adhered on (ICD). HE ×200.

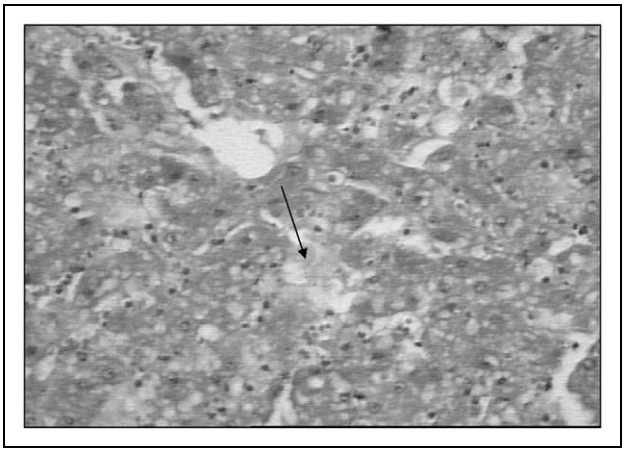

Figure 9. Area of hepatic necrosis in histological section of liver from cats experimentally intoxicated with sodium fluoroacetate (SFAC; arrow). HE 40 × 1.6.

cytotoxicity of SFAC may be one of the causes of leukopenia and thrombocytopenia observed in this study.

The SFAC also can be responsible for the decrease of energy supply to the proliferation of leukocytes and platelets during intoxication because the blast cells have high activity of the enzyme aconitase, which has hampered this action during the intoxication, thereby decreasing the granulocytosis.[14.15,18,19] In addition, the migration of leukocytes to inflammatory foci during intoxication may explain the leucopenia in this study, as well as the occurrence of inflammatory infiltrates in the involved tissues, and were also observed in histopathology, which will be discussed later.

The main clinical significance of transient leukopenia would be the susceptibility to contamination and secondary infections during the clinical recovery of the intoxication or even the first 96 hours after the intoxication. Furthermore, the marked thrombocytopenia can predispose the animals to bleeding during peripheral intoxication.[13,14] A further explanation for the thrombocytopenia will be described later in conjunction with the histopathological changes and vascular splenic.

The poisoned animals in this study did not show significant changes in values of serum urea and creatinine within the evaluated period. However, in intoxication by SFAC, animals with metabolic acidosis and

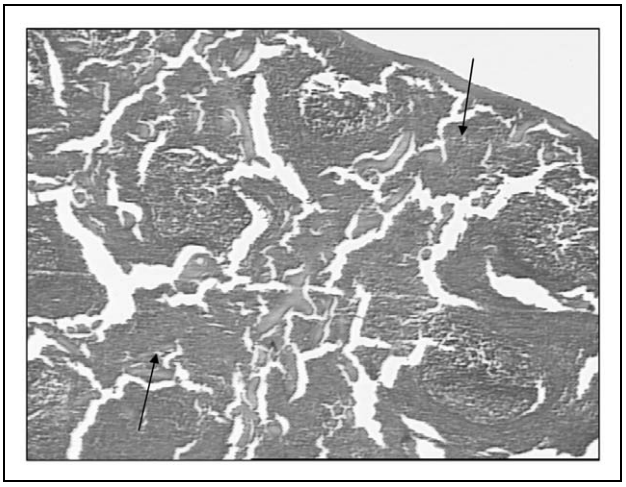

Figure 10. Retraction with decreased splenic red pulp in histological section of spleen of cats experimentally intoxicated with sodium fluoroacetate (SFAC; arrows). HE ×50.

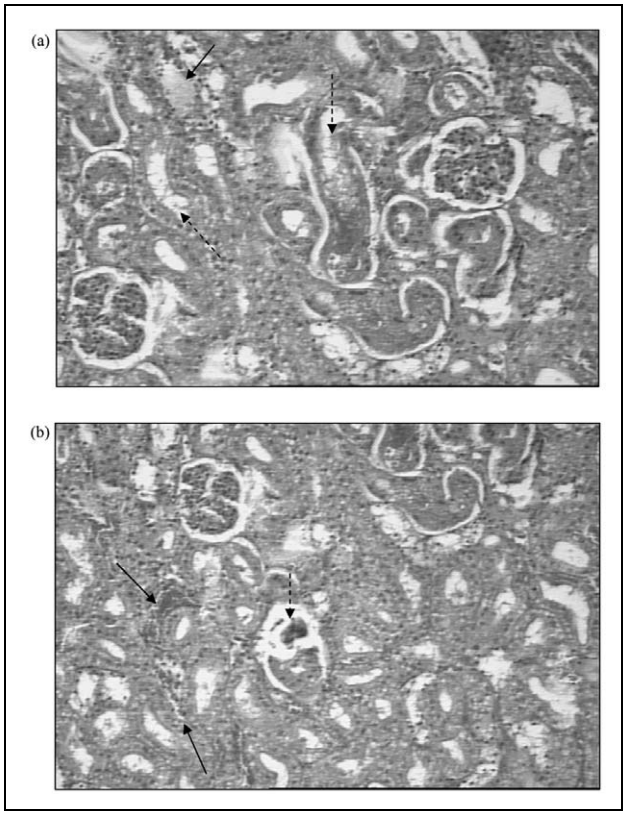

Figure 11. Corte histologico de rim de gato intoxicado experimentalmente com sodium fluoroacetate (SFAC) apresentando (a) areas de necrose tubular (⇢) degeneracao hialina (→); (b) necrose glomerular aguda (⇢), com areas de hemorragias difusas e congestao (→). HE 20 × 1.5.

prolonged increase of serum creatinine could indicate poor prognosis.[20,21]

In this study, the gradual increase of ALT, which was most evident 30 hours after intoxication (M4), can justify changes in the liver, kidney, skeletal muscles and cardiac metabolism.[22] The changes in the permeability of cell membrane the myocardium and CNS during intoxication by SFAC, are caused by the release of phospholipases, enzymes lysosomes and releases of free radicals during hipoxia, wich can result in irreversible injury and cell death.[23] Thus, in assessing the likely injury during liver intoxication by SFAC, an increase of alanine aminotransferase (ALT) in some species, such as primates, dogs, cats, rabbits and rats, is estimated.[24] In cats, the muscle degeneration is a rare cause of increased activity of ALT.[23,24] Moreover, many drugs may promote the increased activity of ALT, such as barbiturates,[23-25] which were also used to anesthetize animals experimentally intoxicated. The peak activity of this enzyme, which is reached within 3 to 4 days after tissue injury, should be considered.[23] As the animals of this study were evaluated for biochemical profile, until a period of 30 hours after the intoxication, there was no increase in activity of ALT.

The activities of the enzymes CK and LDH and especially its cardiac CK-MB isoenzyme also showed gradual increase, more evident from the convulsive episode. The increase in these enzymes may also be related to muscle injury, especially heart, which occur during the cardiotoxicity of SFAC intoxication. An increase of CK and LDH can be seen in situations such as instances of convulsions and other injuries and muscle tissue nonspecific as myocardium, brain, and intestine.[13,23,26] In dogs, the plasma activity of CK-MB isoenzyme is 30% to 45% of the total activity of CK.[26] In this study, the behavior of these enzymes was similar, with significant increase of CK and CK-MB. During a significant muscle or tissue injury, the LDH enzyme will only achieve high levels after several days, returning to normal only after several weeks. The enzymes CK and CK-MB, in turn, can reach high values in a few hours after the occurrence of myocardial injury during intoxication, returning to normal after 48 hours.[13,14] In this study, serum biochemical measurements were performed until 30 hours after injury, showing even higher values of these enzymes, during acute intoxication by the SFAC.

The CK-MB elevation can be present in 6 hours, reaching a peak within 24 hours after cardiac injury,

ensuring early diagnosis compared to the elevations of LDH and CK.[27] The elevations in the enzymes CK and CK-MB above suggest a cardiotoxicity with hypoxia or myocardial necrosis caused by SFAC.[13,27,28] In the present study, the increases of the enzymes CK and CK-MB above are probably related to the existing degree of cardiac injury in animals, which could be demonstrated histologically in the animals that came to death.

In this study, the animals showed an increase in total serum calcium, but within normal values for the feline species.[13] However, the chelating effect of citrate accumulated during intoxication by SFAC is better observed when the measured values of serum ionized calcium, which become reduced in this situation.[4,29,30] The levels of total serum calcium can be inversely proportional to serum levels of citrate, thereby explaining the effect on the chelation of calcium citrate, during intoxication.[29]

There was a gradual and transient hyperglycemia confirming the data reported in the literature.[7,9,10] The SFAC also increases the levels of serum glucose and glycogen, as well as the ammonia concentration, and brain convulsions occur by the decrease in cerebral energy supply.[7,9] The hyperglycemia can be a consistent finding in intoxication by SFAC,[9,10] due to increased levels of endogenous cortisol, which has hampered in their metabolism during intoxication.[9]

Moreover, the animals of this study showed hypokalemia, hypophosphatemia, and hypomagnesemia, not described in literature. Cats poisoned by SFAC invariably have episodes of vomiting among initial clinical signs of intoxication.[4] In this case, the gradual decrease in serum potassium levels may be justified, with the continued loss of electrolyte by vomiting in these animals. The decrease of serum phosphorus may be related to the increase in glycogenolysis, which occurs in intoxication by SFAC.[10,14] The glycogenolysis promotes greater demand for phosphate for activation of adenil cyclase in cell membranes. This enzyme sequentially activates many enzyme systems for energy production in the body.[13,14] The occurrence of convulsions in animals of this study may explain the decrease in magnesium, this may be the consumption of this ion in these situations, as in cases of acute diarrhea.[13,14]

During the intoxication by SFAC, as well as neurotoxicity and cardiotoxicity very much discussed, there are other tissues subject to the action of cellular hypoxia, resulting from the decrease in cellular oxidative metabolism, such as kidney, liver, and lungs.[31] In this study, mainly edema and hemorrhage in the myocardial were observed, with multifocal necrosis in more than 80% of the animals that came to death, confirming the findings of previous studies,[31-34] which affirmed the existence of these lesions, especially by myocardial hypoxia. The microscopic lesions include myocardial degeneration and necrosis of myocardial cells. There were no cases of myocarditis in this study, as reported by other authors,[32] and the ischemic lesion with multifocal necrosis of the occurrence of greater importance in the intoxication by histopathological SFAC. Degeneration and necrosis of the ischemic myocardium are also described in intoxications by SFAC.[32]

The histopathology of lungs, confirmed the presence of mononuclear inflammatory infiltrate. Venous congestion, pulmonary edema and hydropericardium, hemorrhages in the epicardium and endocardium and myocardial pallor with edema, hemorrhage, degeneration, and multifocal necrosis were also found by autopsy in another experiment with sheep intoxicated by SFAC.[33]

The heart failure may occur, together with the inhibition of glycolysis and decreased energy, leading to ischemic tissue injury,[32] which was also observed in this study. The myocardial necrosis and degeneration characterized the damage caused by ischemic of SFAC action, which was confirmed by histopathological examination, the absence of cellular inflammation in tissue affected.[22,35] In a study in ruminants, there was cardiac necrosis and liver with areas of hydropic degeneration and hepatic steatosis.[34] In horses, there was kidney and liver degeneration, myocardial necrosis with a predominance of polymorphonuclear gastroenteritis and swelling, vacuolization, and necrosis of the parietal cells.[36] A case report of sub-acute intoxication in human SFAC showed focal interstitial myocarditis and pulmonary congestion, hepatic and renal,[32] confirming the susceptibility of these tissues to the effects of SFAC and that was also observed in this study.

In this study, the hepatic lesions were characterized as processes of hydropic and fatty degeneration, congestion, and the presence of abundant mononuclear infiltrate. Concerning kidney injuries were observed significant diffuse congestion with hyaline degeneration and marked tubular necrosis, besides the presence of mononuclear infiltrate.

The neurotoxicity is characterized by predominance of cerebral congestion, areas of bleeding and occurrence of gliosis, satellitosis, and neuronophagia.

The neurons are highly susceptible to situations of anoxia, even if temporary. This can be a frequent cause of neuronal death.[36] These neurons are surrounded by macrophages derived from microglia and monocytes in the blood, also called neuronophagus. Then, the neuronal debris is phagocytized and this process is called as neuronophagia, which occurred in this study, showing the death of neurons. The satellitosis can be justified by the increase in the number of oligodendroglial cells, which are regarded as satellite cells in the central nervous system, (CNS) and in conditions of hypoxia, proliferate around neurons for the supply of nutrients to these cells.[37-39] Endothelial injury in the microcirculation was observed in histological sections of the brain, myocardium, and lungs of animals intoxicated, with the presence of red blood cells adhering to the vascular endothelium. The occurrence of this fact can mean the presence of endothelial injury with activation of the coagulation cascade and subsequent platelet aggregation, also known as disseminated intravascular coagulation.[22] This may also have contributed to the consumption of platelets, with consequent thrombocytopenia, which was observed in study of hematological profile. The lesions in the CNS were reported in a human, which showed diffuse brain atrophy, dilatation of the basal cistern, lateral ventricles and third ventricle.[38]

The changes found in the spleen, in animals intoxicated in this study, should also be considered. There were congestion and splenic retraction in all animals necropsied. There are no previous reports of changes in the spleen by SFAC intoxication. The splenic retraction may be related to the framework of transitional leukopenia and thrombocytopenia, seen in this study of the hematological profile. In adult animals, the spleen, especially the white pulp, is responsible for the production and maturation of certain types of white blood cells such as lymphocytes T and B.[39] The red pulp is responsible for the destruction of old red blood cells, bacteria, and any inert particle that is brought to it by the blood. In cases of immune cytopenia, as in some neutropenia, the neutrophils are phagocytized by macrophages in red pulp, which is also a reservoir for blood elements such as white blood cells and platelets.[17,39]

Another important finding in this study was the occurrence of catarrhal gastroenteritis observed in 50% of animals evaluated, demonstrating the important toxic action of SFAC on the gastrointestinal mucosa, which is also described in the literature.[37] The clinical signs of gastroenteritis with vomiting and diarrhea are frequently observed in cats intoxicated by SFAC.[4]

Conclusion

Cats experimentally intoxicated with 0.45 mg/kg oral sodium fluoracetate (SFAC) showed transitory leukopenia with neutropenia, lymphopenia and thrombocytopenia and eosinopenia absolute. Hyperglycemia and increased activities of the enzymes LDH, CK, and its CK-MB were observed between the biochemical changes in intoxication. Moreover, hypokalemia, hypophosphatemia and hypomagnesemia were also transient. Therefore, this study suggests like as laboratory protocol for the diagnosis of acute intoxication by sodium fluoroacetate in cats the implementation of hemogram with platelet count, dosage of blood glucose levels, serum enzymes CK, CK-MB and serum dosage potassium, phosphorus and magnesium.

The histopathological assessment revealed changes suggestive of ischemic and degenerative processes, especially in the brain, myocardium, lungs, liver, and kidneys.

All these changes are not pathognomonic but may be auxiliary to the diagnosis of intoxication by SFAC in cats, when associated with clinical signs described for the species.

Acknowledgements

Foundation for the Development of UNESP, Sao Paulo, Brazil (FUNDUNESP) and Coordination for the Improvement of People's Education (CAPES) for essential financial support. Laboratory of Clinical Analysis of Faculty of Medicine and Department of Pathology of Faculty of Veterinary Medicine and Animal Science, São Paulo State University, Unesp – Botucatu, Brazil, for the technical support.

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