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Successful management of ibuprofen induced acute kidney injury (AKI) with intra venous lipid emulsion in a dog

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Abstract
A pet parent presented an Eight years old, intact, male, cross breed dog to the Critical Care unit, Department of Veterinary Clinical Medicine, MVC, Chennai with the history of self medication with Ibuprofen oral tablet (200 mg, daily twice) for three days. After that, the pet was showing progressive weakness, vomiting, melena. At the time of presentation, the pet was recumbent and decreased mental status. Based on the history, clinical signs, hemato- biochemical and urine analysis and ultrasonographic examination, the case was diagnosed as "Ibuprofen induced Acute Kidney Injury". Treatment was initiated with intravenous fluid therapy (Inj. Ringer's lactate @ 20 ml/kg), Inj. Ondansetron @ 0.2 mg/kg IV, Inj. Pantoprazole @ 1mg/kg IV, Inj. Amoxicillin potassium clavulanate @ 7.5 mg/ kg and Intravenous lipid emulsion. IV lipid emulsion was administered as a bolus @ 1.5 ml/kg followed by constant rate of infusion @ 0.5 ml/kg/min. The pet's mental status was improved approximately 3 hrs after initiation of IV lipid emulsion. Activated charcoal was administered orally as a slurry form @ 1g/kg. The pet was recovered uneventfully after 5 days of treatment.

Keywords: AKI, dog, ibuprofen toxicity, IV lipid emulsion

Introduction
Ibuprofen is a commonly used non steroidal anti-inflammatory drug in human patients as an analgesic, antipyretic and anti-inflammatory. It inhibits the conversion of arachidonic acid into various prostaglandins by blocking the action of both COX 1 and COX 2 enzymes. It has highly protein bound nature (90 to 99%). After hepatic biotransformation, the inactive metabolites are excreted in the urine. Unlike human, ibuprofen has a narrow margin of safety in dogs and cats. The recommended dosage in dog is 5 mg/kg/day. However, the signs of toxicosis were noted in as low as 3 mg/kg every other day. According to ASPCA Animal poison Control Center (APCA), ibuprofen was the most common generic drug involved in frequent toxicosis in dogs (Khan and McLean, 2012) [3].

Case Description
Eight years old, intact, male, cross breed dog was brought to the Critical Care unit, MVC, Chennai with the history of anorexia, vomiting, melena and progressive weakness. The owner reported that self medicated the dog for limping with ibuprofen oral tablet (200 mg, daily twice) for three days. On physical examination, the dog had decreased mental status (Fig.1), congested conjunctival mucus membrane, tachycardia (178 beats/min), tachypenia (58 breaths/min) and decreased papillary light reflex.

Diagnosis and Treatment
Hemato- biochemical analysis revealed leukocytosis, azotemia and hyperphosphatemia (Table.1). Hypersthenuria (1.035) was observed on urine analysis. Ultrasonography of abdomen revealed hyperechoic renal cortex which is isoechoic to spleen and hyperechoic renal crest (Fig.3). Based on the above findings, the case was diagnosed as ibuprofen induced acute kidney injury.
The dog was treated with Inj. Ringer's lactate @ 20 ml/kg B.wt IV, Inj. Ondanstron @ 0.2 mg/kg. B.wt IV, Inj. Pantoprazole @ 1 mg/kg. B.wt IV, Inj. Furosemide @ 2mg /kg. B.wt IV, Inj. Amoxicillin potassium clavulanate @ 7.5 mg/kg. B.wt IV.
Intra venous lipid emulsion was administer as a bolus @ 1.5 ml/kg. B. wt over a period of

15 mins, followed by constant rate of infusion @ 0.5 ml/kg/min. The dog's mental status was improved approximately 3 hrs after initiation of IV lipid emulsion. Activated charcoal was administered orally as a slurry form @ 1g/kg. The fluid therapy and supportive treatment was continued for next five days. The dog was recovered uneventfully after 5 days of treatment (Fig.2).

Table I: Hemato- Biochemical values

Hb (g/dL)	9.8	Glucose (mg/dL)	95
PCV (%)	30.2	ALT (U/L)	53
RBC (m/cmm)	4.9	ALP (U/L)	220
WBC (/cmm)	38,000	Total protein (g/dL)	5.3
Platelet (/cmm)	1,90,000	Albumin (g/dL)	1.6
Neutrophil (%)	90	BUN (mg/dL)	105.6
Lymphocyte (%)	8	Creatinine (mg/dL)	5.4
Monocyte (%)	2	Calcium (mg/dL)	8.6
Eosinophil (%)	0	Phosphorus (mg/dL)	9.4
Basophil (%)	0	Cholesterol (mg/dL)	228

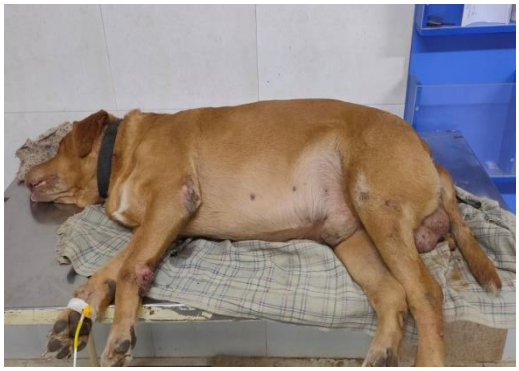

Fig 1: Comatose at the time of presentation

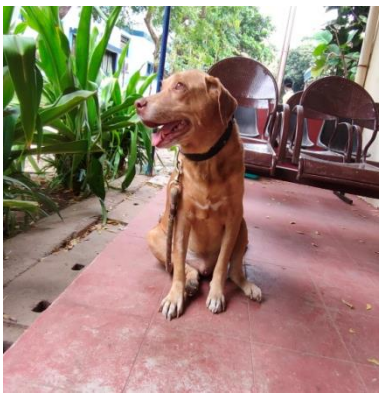

Fig 2: After treatment

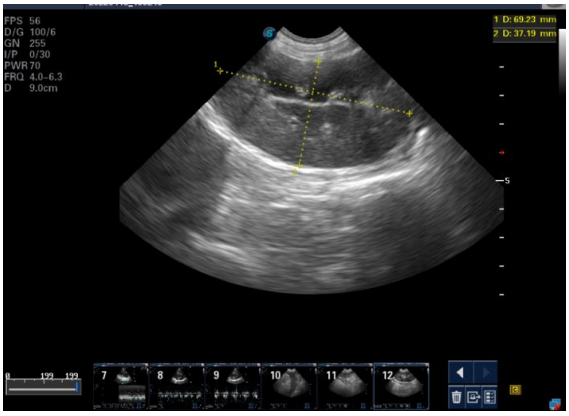

Fig 3: Ultrasound findings

Discussion

Dogs were poisoned with ibuprofen mainly by accidental ingestion of sweet coated numerous ibuprofen tablets by dog or self medicated by pet parents. Acute overdose of ibuprofen in dogs were associated with the signs of gastrointestinal, renal and central nervous system.

Dose as low as 25 mg/kg can cause GI signs like vomiting, gastric ulcers, hematemesis and abdominal pain within 24 hrs. Mechanisms behind this GI signs were thought to be inhibition of COX 1 enzymes and loss of natural gastric protective mechanism (Wallace *et al.*, 1990) [6]. At doses greater than 175 mg/kg can cause acute interstitial nephritis, renal tubular necrosis and acute renal injury. Vasoconstriction and reduced renal medullary circulation are responsible for the acute renal injury (Surdyk *et al.*, 2011) [4]. At the doses greater than 400 mg/kg can cause CNS signs like seizure and coma (Easley and Altemeier, 2000) [2]. Overdose around 600 mg/kg can cause acute mortality.

There is no specific antidote for ibuprofen toxicity. Treatment should be directed towards preventing or treating possible complications. Aggressive gastric decontamination by inducting vomiting or gastric lavage is required in acute cases (within 2 hrs). Induction of vomiting is contraindicated in comatose and recumbent animals.

GI signs were managed by individual or combination of therapy with H2 blockers (Ranitidine) or proton pump inhibitors (pantoprazole), sucralfate and misoprostol. Renal injury was treated with intravenous fluid therapy and diuretics. Seizure dogs were managed with diazepam or barbiturates.

Stabilized patients were treated with oral activated charcoal therapy because ibuprofen has marked enterohepatic recirculation (Tauk and Foster, 2016) [5].

The administration of intravenous lipid emulsion was thought to be bind with ibuprofen (Highly lipophilic in nature) (lipid sink theory). Recommended dosage of IV lipid emulsion was a bolus of 1.5 to 4 ml/kg followed by CRI @ the dose of 0.25 to 0.5 ml/kg/hr (Bolfer *et al.*, 2014) [1].

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