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Short Communication

Clinical management of paracetamol poisoning in cat

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A B S T R A C T

A six-month-old female cat and a four-month-old kitten were admitted to the hospital with the record of paracetamol administration and symptoms of facial and paw edema, cyanotic mucous membrane, dullness and depression, dehydration and loss of appetite. Based on history and clinical examinations, it was diagnosed to be a case of paracetamol poisoning and treated with acetylcysteine tablets at 150mg/kg body weight orally for the first time followed by 75mg/kg body weight orally for every 6-hours interval for seventeen times in the cat and ten times in the kitten. As a supportive treatment, two cats were given ascorbic acid at 30mg/kg body weight for three times a day for subsequent three days, as well as intravenous fluid therapy depending on severity. After careful treatment, both two cats were recovered successfully.

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1. INTRODUCTION

Paracetamol (acetaminophen) chemically is a phenol and the world's most extensively used non-prescribed inexpensive medication (Graham et al., 2013). Its antipyretic and analgesic properties make it popular in human medicine but as a consequence of this drug's insufficient glucuronidation *in vivo*, cats are highly sensitive to acetaminophen (Court and Greenblatt, 1997). It inhibits the action of the cyclooxygenase enzyme that functions as an inhibitor of prostaglandin synthesis where it is highly selective for cyclooxygenase-2 (COX-2) inhibitor (Graham and Scott, 2005). Acetaminophen is primarily bio-transformed into nontoxic products in the liver through conjugation with glucuronic acid and then eliminated by the kidneys in most of the mammals. N-acetyl-para-benzoquinoneimine (NAPQI) is produced from a small portion of acetaminophen metabolism through the cytochrome P-450 enzyme pathway and it is the major reason for paracetamol poisoning although toxic effects of NAPQI are limited by conjugation with glutathione.

Cats are especially vulnerable to the harmful effects of acetaminophen for a number of reasons. Cats create glucuronides with numerous chemicals slowly or not at all because they have fewer isoforms of the enzymes that facilitate the conjugation of glucuronyl transferase. Additionally, cats, in particular lack

a unique high-affinity acetaminophen glucuronoyl transferase, which conjugates acetaminophen with glucuronic acid. Because of the relative insufficiency of the glucuronide conjugation route, more medicine is conjugated to sulfates. Nevertheless, the sulfation process has a finite capacity, which is similarly smaller in cats than in other species. Once the sulfation route is exhausted, acetaminophen is permitted to stay in the circulation to be converted to NAPQI by cytochrome P-450 enzymes. Glutathione production is inhibited by the high dosages of acetaminophen, and the presence of NAPQI which quickly depletes glutathione reserves since the absence of specific affinity of acetaminophen to glucuronyl transferase conjugates acetaminophen with glucuronic acid (Allen, 2003).

Cats are typically exposed to hazardous quantities of acetaminophen when their owners medicate them without consulting a veterinarian (Avizeh et al., 2009). The toxicity of paracetamol in cat is not widely known, which explains why cats with paracetamol poisoning continue to appear in veterinary clinics. Although paracetamol poisoning has the potential to be lethal, it is clear that prompt treatment with proper drugs may save their lives. Hence, cat owners should be more aware of the dangers of giving conventional analgesics to their cats (Ilkiw and Ratcliffe, 2006). The cat owner orally provides paracetamol in the house to their pets to relieve pain and fever. However, the owner's negligence and a lack of understanding about the dangers of medications to the pets, the paracetamol poisoning of cat is a common incidence in Bangladesh.

2. CASE HISTORY

A six months old female non-descriptive cat weighing 2.0 kg was admitted to the S.A. Quaderi Teaching Veterinary Hospital, Chattogram Veterinary and Animal Sciences University (CVASU), Chattogram, Bangladesh. The owner reported that he administered 250mg (half tablet, Tab. NAPA Extra® 500mg,Beximco Pharmaceuticals Ltd., Bangladesh) paracetamol twice in the morning and evening with the intention of relieving pain for accidentally putting a heavy weight on his cat two days back. Clinical examination of the cat revealed a rectal temperature of 100^0F, facial and paws edema (Figure 1.A), bluish discoloration of tongue and gum mucous membrane (cyanosis) (Figure 1.B), severe dehydration, and loss of appetite.

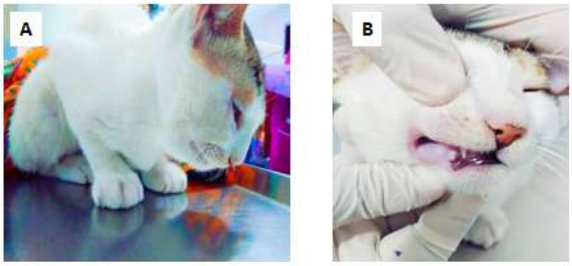

Figure 1. (A) Facial and paw oedema, sunken eye; (B) Bluish discolouration of gum (Cyanosis)

Similarly, on that day, a four months old non-descriptive kitten weighing 2.0 kg was admitted to the S. A. Quaderi Teaching Veterinary Hospital, CVASU. The owner reported that she administered 60mg paracetamol (Half tea spoon, Syp. ACE® 60ml, Square Pharmaceuticals Ltd., Bangladesh) twice daily for two days due to the common cold and fever of her cat. Clinical examination revealed a rectal temperature of 99^0F, light bluish discoloration of tongue and gum mucous membrane (cyanosis), pale conjunctival mucous membrane, sunken eyes, severe dehydration, dull and depressed appearance, off fed and lateral recumbency (Fig. 2). Based on history and clinical findings, both cases were diagnosed as paracetamol poisoning. Accordingly, paracetamol toxicity in cats was diagnosed and treated (Ilkiw and Ratcliffe, 2006; Pothiappan et al., 2018; Sangamitra et al., 2021).

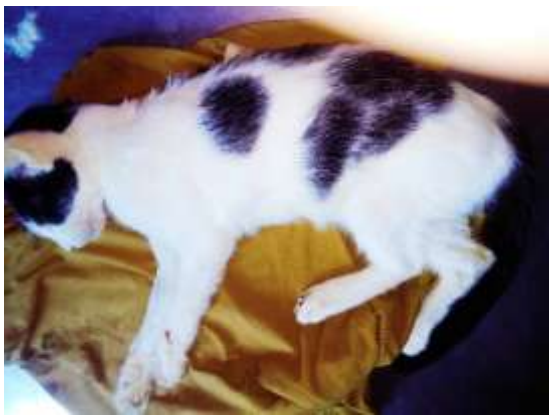

Figure 2. Lateral recumbency of kitten

3. TREATMENT AND FOLLOW UP

Each cat was treated with acetylcysteine 150mg/kg (Half tablet, Tab. Mucomist DT® 600mg, Beximco Pharmaceuticals Ltd., Bangladesh) orally first time. Then at every 6-hours interval, orally administered 75mg/kg acetylcysteine ($^1/_4$ tablet) seventeen times in the cat and ten times in the kitten. Both cats were also given ascorbic acid 30mg/kg body weight, thrice daily for subsequent three days (Syp. Vasco® 100ml, Opsonin Pharma Ltd., Bangladesh). A 60ml of 0.9% NaCl solution (Inj. NS 500ml, OPSO Saline Ltd., Bangladesh) was given to the patient intravenously to dilute the paracetamol from the blood and rehydration for subsequent three days in the cat. In the kitten, 25ml of 5% dextrose (Inj. DNS 5%, ACME Laboratories Ltd., Bangladesh) was given intravenously for energy supply, paracetamol dilution, and rehydration. Both owners were urged to provide the medications exactly as prescribed, to keep the animal in a comfortable environment to feed the animal a regular food and never to administer paracetamol again. In the case of cat, on the next day the owner reported the improvement of health as slightly reducing the bluish discoloration without diminishing the facial and paw edema. The day after that the owner reported gradual regression of facial and paw edema and taking a normal diet. In the case of kitten, the owner reported it was able to stand and slightly diminished the light bluish discoloration of tongue and gum mucous membrane and not taking diet that much. The next day, it was able to walk, bluish discoloration of tongue and gum mucous membrane disappeared and started taking normal diet.

4. DISCUSSION

Paracetamol poisoning in cats is very common through oral administration by educated and ignorant owners because of its easy availability in the market as well as in houses. For cats, any dosage of acetaminophen is unsafe and 50-100mg/kg body weight (BW) is reported as toxic but a small dosage like 10mg/kg body weight may cause toxicity and death (Allen, 2003). In the observed study, the owner orally administered 125mg/kg body weight and 30mg/kg body weight to a 6-month cat and a 4 month kitten several times to create poisoning and detect clinical indications. Avizeh et al. (2009) reported that a single dosage of acetaminophen (150 mg/kg) was harmful for cat, as evidenced by the appearance of clinical symptoms and an increase in blood concentrations of diagnostic liver enzyme, total and conjugated bilirubin. Clinical signs of paracetamol toxicity in cats include edema of the face and paws, bluish discoloration of the tongue and gum mucous membrane (cyanosis), severe dehydration, and loss of appetite. In kittens, the clinical signs include light bluish discoloration of the tongue and gum mucous membrane (cyanosis), pale conjunctival mucous membrane, sunken eyes, severe dehydration, dull and depressed look, off fed and lateral recumbency (Allen, 2003; Hanson and Jill, 2008; Pothiappan et al., 2018; Sangamitra et al., 2021). Induced vomiting and treatment with activated charcoal at a dosage of 2gm/kg body weight if ingestion happened were practiced within the last two hours (Anvik, 1984). In another research, two patients were admitted to the hospital after receiving paracetamol for two days and had already absorbed the paracetamol, as well as developed clinical symptoms that made it useless to induce vomiting and were treated with activated charcoal. For paracetamol poisoning, N-acetylcysteine is a specific antidote administered intravenously with a dosage of 140mg/kg body weight and then 6-hour interval orally or intravenously at 70 mg/kg body weight for 36 hours or until further clinical improvement (Anvik, 1984; Pothiappan et al., 2018). However, because N-acetylcysteine injection is not accessible in the region, the cat and kitten were given 150 mg/kg body weight orally at the initial dosage, followed by 75 mg/kg body weight orally every 6-hours until further improve. To form a substrate for glutathione and as the precursor of glutathione, acetylcysteine is metabolized in the liver and red blood cells and oxidized to form sulfate by increasing sulphation pathway capacity. In fact, it directly acts on NAPQI to form a conjugate that can be excreted. If acetylcysteine is administered in cats, it reduces paracetamol half-life by half (Bates, 2013).

The use of a specific antidote to treat poisoning is beneficial in reversing clinical symptoms and

preventing liver failure (Sidhu, et al., 2021). In this study, we have also prescribed ascorbic acid at 30 mg/kg body weight, three times a day for three days, which is similar with the study of Anvik (2004) where ascorbic acid was given in addition to acetylcysteine in paracetamol poisoning of cat. The conversion of methemoglobin to oxyhemoglobin may be aided by ascorbic acid (Steenbergen, 2003). Hepato toxicity may be averted with the use of ascorbic acid (Lake, et al., 1981). It is also conceivable that it interacts with NAPQI before binds to proteins, converting it to paracetamol (Bates, 2013). Reduced glutathione's innate protective potential to minimize hazardous metabolite covalent binding and consequent cellular harmful effects may be ameliorated by supplementing the ascorbic acid (Anvik, 2004). Sidhu et al. (2021) suggested intravenous 0.9% NaCl solution at 30ml/kg body weight and intravenous giving 12.5ml/kg body weight Inj. DNS 5% as supportive therapy for severe renal impairment in cats and kittens. In the presence of the glucuronyl transferase enzyme, paracetamol is biotransformed into a non-toxic compound that is excreted throughthe kidney (Sangamitra et al., 2021). The enzyme glucuronyl transferase converts acetaminophen to glucuronic acid for excretion in cats.In case of acute kidney damage, the patient needs supportive fluid treatment (Sidhu et al., 2021). However, because acetylcysteine injection is not accessible without emergency situation in Bangladesh, the acetylcysteine tablet is usually used orally at 6-hours interval.

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