Case Report

ACETAMINOPHEN TOXICITY AND ITS SUCCESSFUL MANAGEMENT IN A PUG DOG - A CASE REPORT

G. R. Baranidharan*[1], B.R. Baby Roshini [2], C. Jayanthy[3], A. Gopalakrishnan[4], Arjun V Thampi[5] and G.Vijayakumar[6]

Department of Clinics

Madras Veterinary College

Tamil Nadu Veterinary and Animal Sciences University, Chennai – 600 007

ABSTARCT

A pug dog was presented to Small Animal Outpatient Unit of Madras Veterinary College with the history of oral administration of 2.5 tablets of 500 mg acetaminophen. Physical examination of animal revealed a dull and depressed with pale mucous membrane. Haematological values were within normal range and biochemistry report revealed elevated Alanine amino transferase enzyme which indicated the hepatotoxic adverse effect of acetaminophen. Normal saline was administered intravenously. N-acetyl Cystine was administered @140 mg/kg intravenously after diluting in 5% dextrose. The owner was advised to give oral N-Acetyl cystine tablets at a dose rate of 70 mg/kg after 6 hrs and to repeat as such seven times. Oral liver supplements containing S-Adenosyl methionine and silybin was prescribed and advised to give at the dose rate of 5 ml/10 kg body weight. Hematinics was prescribed and advised to give orally at a dose rate of 2.5 ml/5 kg body weight twice daily.

Keywords: Acetaminophen, hepatotoxic, N-Acetyl cystine.

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INTRODUCTION

Acetaminophen (paracetamol), a commonly used antipyretic drug (Over the counter medication) is a para aminophenol derivative (N-acetyl-p-aminophenol) that possess antipyretic and analgesic effects and high doses may cause severe liver and methaemoglobinemia. In dogs, only a small portion of a dose is converted to reactive metabolites by the cytochrome P- 450 -dependent mixed function oxidase (MFO) system (Savides *et al.,* 1984). Likewise, a free radical may form through the MFO system and

[1]Assistant Professor, Corresponding author Email id: grbvet@gmail.com

[2]PG student

[3]Assistant Professor

[4]Assistant Professor

[5]PG student

[6] Professor and Head

cause oxidative damage to cellular molecules, such as haemoglobin, forming methemoglobin (Nash and Oehme, 1984). The antipyretic effects are mediated at hypothalamus due to inhibition of prostaglandin synthesis. Part of the drug is metabolized by glucuronidation and sulfation pathways to nontoxic conjugates, while some is excreted in urine unchanged or metabolized to toxic metabolite, N-acetyl-para-benzoquinoneimine via cytochrome P- 450 enzyme pathway leading to oxidative injury. The clinical signs are related to methemoglobinemia hepatic toxicity and death.

CASE REPORT

A male pug dog weighing 10 kgs (Fig 1) was presented to Madras Veterinary College Teaching Hospital with the history of oral administration of 2.5 tablets of 500 mg acetaminophen 24 hrs before presentation since the owner suspected pyrexia. On physical examination, the animal was dull and depressed, rectal temperature was 101°F), pale conjunctival mucous membrane, CRT(2s), mild dehydration, normal lymph nodes on palpation and chronic skin lesions. Abdominal palpation revealed no abnormalities. On auscultation arrhythmia was detected with a heart rate of 120 beats per minute and the respiratory rate was 28 breaths per minute. On hematological, CBC showed a mild stress leukogram, the haemoglobin concentration was 9.4 g/dl, red blood cell count was 5.05 million per cubic mm, packed cell volume was 24.5 per cent, platelet count was 193000 per cubic mm and the biochemistry evaluation revealed elevated Liver function values (SGPT- 450 IU) and serum bilirubin concentration of 1.6 mg/dl. Ultrasound of the liver and infectious disease screening revealed no pre-existing liver diseases. ECG of the patient revealed mild sinus arrhythmia and occasional VPC complex (Fig 2). The pug dog was maintained with isotonic fluid (Normal saline) at 10 ml/kg bodyweight. The antidote N-Acetyl cystine (availability 200 mg/ml) was administered intravenously at a loading dose of 140 mg/kg body weight (Nash and Oehme, 1984) diluted in 5% dextrose along with Pantoprazole @ 1 mg/kg was administered. The owner was advised to give oral N-Acetyl cystine tablets at a dose rate of 70 mg/kg after 6 hrs (availability 600 mg tablet) and to continue for 7 treatments. Oral supplementation of hematinics (Fecofol) @ 2.5 ml/5 kg body weight and oral liver supplements containing S-Adenosyl methionine (Silybin) @ dose rate of 5 ml/10 kg body weight were advised twice daily for 10 days.

Fig. 1. Pug with acetaminophen toxicity

Fig. 2. Occasional VPC complex

DISCUSSION

Usually, acetaminophen toxicity in dogs is preceded by facial edema, depression, hyper salivation and severe signs when presented with doses in excess of 200 mg/kg BW (Vilar and Buck, 1998) and (Khayyat *et al.*, 2016). In this case, mild clinical signs of acetaminophen toxicity were evidenced on presentation. N-Acetyl cystine, the antidote is used to prevent hepatic necrosis and is most effective when given within 8 hours of exposure and along with N Acetyl cystine, ascorbic acid can be given to reduce methemoglobin to haemoglobin (Nash and Oheme, 1984). Severe methemoglobinemia can be treated with methylene blue as it increase the reduction of methemoglobin. N Acetyl cystine is a mucolytic compound that contain high number of sulphydryl groups which counters acetaminophen toxicity by increasing serum sulphate and supplies of glutathione. Activated charcoal can inactivate acetyl cysteine, so the concurrent administration is not recommended (Schlesinger, 1995). A 200 mg/kg dose produced an increased echo density in kidney parenchyma that matched with renal damage in dogs (Fadel *et al*., 2021). Acetaminophen is rapidly absorbed from GI tract and clinical signs can occur even as early as 4 hrs after administration. The effect of the drug can range from progressive yanosis, dyspnea, depending on the amount of formation of methemoglobin (MacNaughton, 2003). Later effects can include hemoglobinuria, icterus and elevated hepatic values.

The antidote, N-Acetyl cysteine, works primarily to restore the levels of GSH by hydrolysis to cysteine, which is a substrate in GSH synthesis. It also provides sulfhydryl groups for the reactive metabolites to bind to, for excretion in the urine (Nash and Oheme, 1984). In dogs, the liver is typically the primary target of damage; however, no clinical evidence of hepatic damage (abdominal pain, vomiting, or icterus with elevated levels of ALT, ALP, and total bililrubin) was observed in this dog. Dogs exhibit the early effects of acetaminophen toxicosis within 4 to 12 hrs, progressive cyanosis, tachypnea and dyspnea, depending on the degree of methemoglobinemia. Signs attributable to hepatic necrosis usually occur approximately 36 hrs after the ingestion of acetaminophen to have occurred (Villar and Buck, 1998) whereas in this case only mild clinical signs occurred after 24 hrs post aceataminophen ingestion and hepatic necrosis was not evident even after 36 hrs. This pug dog case documented the milder clinical signs that might after ingesting large doses of acetaminophen and the possible reversal effect of early and aggressive treatment. Other atypical cases have been reported, in which dogs displayed

abnormal blood parameters including methemoglobinemia and heinz bodies with only minimal hepatic damage (Harvey *et al*., 1986). These variations may be due to a multitude of interrelated physiological factors and therapies.

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