

Hematobiochemical Alterations and Therapeutic Management of Meloxicam Toxicity in Deoni Bull

S. G. Chavhan¹ and R. K. Jadhav^{2*}

¹Department of Veterinary Pathology, College of Veterinary and Animal Sciences, Udgir. Maharashtra Animal and Fishery Sciences University, Nagpur, INDIA

²Department of Veterinary Clinical Medicine, Ethics and Jurisprudence, College of Veterinary and Animal Sciences, Udgir. Maharashtra Animal and Fishery Sciences University, Nagpur., INDIA

*Corresponding Author: jadhavrkl1@gmail.com

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Abstract

A three-year-old Deoni bull was admitted to the clinics with a history of prior treatment at a native place for mild fever and inappetence. After treatment at the native place, the affected animal started to show clinical signs such as marked anorexia and loose blackish feces with straining. Careful interrogation of the animal owner revealed prior treatment at a native place with parenteral antihistaminics, vitamin B complex, fluid therapy, oxytetracycline, meloxicam (75 mg) plus additional administration of four boluses (400 mg) of meloxicam orally in a single day. Clinical examination of the affected bull revealed normal body temperature, heart rate, respiration rate, pink pale conjunctivae, and frequent passing of loose blackish feces with straining and voiding of straw-coloured urine. Hematobiochemical analysis of the affected bull revealed a decrease in the concentration of hemoglobin and hematocrit along with a marked increase in blood urea nitrogen, creatinine, total protein, calcium, and phosphorus levels. A blood smear examination was found negative for haemoprotozoan infections. Based on the confirmed history of overdosing of meloxicam orally and parenterally along with characteristic clinical signs and hematobiochemical changes such as melena, voiding of straw-coloured urine, and marked elevation of renal biochemical parameters, the case was diagnosed for meloxicam toxicity. The affected bull was treated with fluid therapy, vitamin B complex, antihistaminics, antacids, and haematinics. Gradual clinical recovery was observed in the ailing bull with improvement in feed and water intake as well as restoration of fecal consistency and colour by the 10th day of treatment (Fig. 2). Laboratory evaluations on the 10th and 30th day revealed gradual restoration of hematological and biochemical parameters within normal reference ranges. In conclusion, accidental meloxicam overdoses in cattle can also lead to toxicity similar to one observed in pet animals characterized by loose black-coloured feces, straining while defecating, voiding of straw-coloured urine and elevated values of BUN and creatinine. Fluid therapy, supportive medications, and monitoring of kidney function and erythrogram may prove helpful in managing meloxicam toxicity in cattle.

Keywords: Bull, Clinical Signs, Hematobiochemical Alterations, Meloxicam Toxicity, Treatment.

Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) produce anti-inflammatory and analgesic effects with additional anti-pyretic, anti-endotoxemic, and antineoplastic effects and it is one of the fastest growing classes of drugs in Veterinary Medicine (Clark-Price, 2014). Although they are having potential to reduce fever, inflammation and pain, overdoses or prolonged therapy may cause deleterious effects on the body of patients. Use of various medicines (Jadhav *et al.*, 2017; Bhikane *et al.*, 2017; Jadhav and Bhikane, 2020) including meloxicam (Walton *et al.*, 2017; Kannan *et al.*, 2019; Flood and Stewart, 2022) without prescription may lead to overdosage and deadly toxicity in animals. The present case report highlights the clinical and hemato-biochemical alterations due to meloxicam toxicity in Deoni bull and its therapeutic management.

Case History and Clinical Findings

A 3-year Deoni bull weighing 265 kg with history of mild fever and inappetence was treated locally on the day of illness using antihistaminics, vitamin B complex, fluid therapy, oxytetracycline, meloxicam followed by onset of anorexia, absence of rumination, passing of black tarry loose feces and straining while defecation from second day of illness when bull was admitted to the clinics. The careful interrogation revealed parenteral administration of 75 mg dose of meloxicam along with additional feeding of 4 boli of Meloxicam (100 mg each) on the same day accidentally thereby approximating total dose of 475 mg meloxicam which was about 3.16-time higher dose rate than the prescribed dose over 24 hours' period. Detailed clinical examination revealed vital parameters within normal range, dullness, passing of black loose feces with straining (Fig. 1) and ruminal atony.

Diagnosis

Fecal sample and blood samples were collected for diagnostic investigations. Flootation of fecal sample revealed no any significant parasitic infestation. Hematological and biochemical analysis (Table 1) as well as blood smear examination was carried out from the collected blood and serum sample. Significant decline in hemoglobin and hematocrit was observed in the ailing bull. Similarly, biochemical profile revealed mild increase in liver enzymes while severe increase in values of blood urea nitrogen and creatinine indicative of severe kidney injury. Blood smear examination showed absence of any hemoprotozoan or rickettsial infections. The detailed history from animal owner and attending person confirming dosing of 475 mg of Meloxicam followed by onset of passing loose, blackish feces with straining, anemia, kidney and liver injury assisted in the confirmation of meloxicam toxicity in bull. The case was subjected to treatment and monitored over a period of 30 days clinically and hemato-biochemically.

Treatment

The bull was treated symptomatically with antibiotics (Amoxicillin+cloxacillin @ 10 mg/kg IV, fluid therapy (D5% @ 2 liters IV and RL @ 2 liters IV), vitamin B complex @ 10 ml IV, antihistaminic (Chlorpheniramine maleate) @ 0.2 mg/kg, carbazochrome salicylate @ 10 ml IM and antacid ranitidine @ 1 mg/kg IM. The bull showed clinical improvement with resumption of slight food and water intake on 3rd day of treatment along with mild improvement in fecal consistency with black colour similar to pre-treatment colour. The treatment was continued on the same line for 7 days except antibiotics. The improvement in fecal consistency and restoration of fecal colour to normal was observed on 10th day of treatment (Fig. 2) while feed and water intake was not completely restored. Biochemical analysis on day 10 revealed significant reduction in the values of BUN and creatinine to the extent of around 50% compared to initial values, although very high compared to those in normal animals along with hypoproteinemia and hypoalbuminemia. Hematology showed anemia. After second assessment the bull was further treated with fluid therapy (D5% @ 2 liters IV and Hydroxyethyl Starch 6% @ 500 ml IV), vitamin B complex for 3 days while haematinics were advised for 10 days. The treated bullock showed gradual improvement in feed and water intake during second treatment and complete resumption of feed and water intake was observed in the bull on day 5 after start of second treatment. Hematobiochemical analysis on day 30 showed significant improvement in the parameters and restoration to the normal physiological range.

Discussion

Collins and Tyler (1984) reported phenylbutazone toxicity in horses characterized by anorexia, depression, abdominal pain, diarrhea, melena, weight loss, ventral edema, petechial hemorrhages on mucous membranes,

hypoproteinemia with oral and gastrointestinal ulceration and renal papillary necrosis in horses died of toxicity. The toxicity was reported in only those horses who received phenylbutazone at the dose of > 8.8 mg/kg per day. Kannan *et al.* (2019) reported vomiting along with passing of black tarry feces in a 6-year-old Labrador dog accidentally overdosed with meloxicam for 2 days due to wrong dispensing of medicine by pharmacist. There is no literature about Meloxicam toxicity in cattle, but the straining while defecation, passing of black loose feces could indicate abomasal hemorrhages attributed to meloxicam toxicity in the bull.



Fig. 1: Deoni bull suffering from Meloxicam toxicity passing blackish-colored loose feces with straining.



Fig. 2: Improved fecal consistency and colour in Deoni bull suffering from Meloxicam toxicity on the 10th day of treatment

Non-steroidal anti-inflammatory drugs cause gastrointestinal damage, renal and hepatic injury, coagulation, and neurological disorders in animals depending up on the dose of medicine (Borchers, 2019). Non-steroidal anti-inflammatory drug toxicity has been frequently reported in dogs and cats compared to farm animals. The most common side effects attributed to NSAID use include vomiting, diarrhea, anorexia, lethargy, and melena with occasional signs of blood in feces, colitis, abdominal pain, aggressiveness, behavioral changes, hypersalivation, polydipsia, polyuria, adipsia, constipation, icterus, skin reactions, and weight loss. Excess dosing with NSAID have caused gastrointestinal perforations in dogs (Borchers, 2019; Monterio-Steagall *et al.*, 2013). In general, low toxic doses produce GI toxicity while moderate doses lead to both GI and renal injury while very high doses may produce acute neurological signs (Borchers, 2019).

Experimental induction of meloxicam toxicity in Wistar rats revealed weakness, lethargy, distended abdomen, dose dependent reduction in Hb, PCV, TEC, MCH and MCHC and dose dependent increase in value of serum alkaline phosphatase, decrease in total protein, albumin and globulins. Histopathology showed varying degree of hemorrhages, degeneration, necrosis and ulcers in stomach, intestine, liver and kidneys (Jadav *et al.*, 2014). Kannan *et al.* (2019) reported mild changes in corticomedullary junction of the left kidney with elevated values of BUN (192 mg/dl) and creatinine (4.73 mg/dl) in a dog which was accidentally dosed with 20 time more than the standard dose of meloxicam. The elevated values of BUN and creatinine in the bull suffering from Meloxicam toxicity in the present case are in accordance with the findings of Jadav *et al.* (2014) and Kannan *et al.* (2019) indicative of severe

renal injury.

As there is no specific antidote for treatment of meloxicam overdose different therapeutic regimens are used in dogs and cats as per the severity of toxicity. Walton *et al.* (2017) successfully used therapeutic plasma exchange along with supportive medication in management of meloxicam overdose in dog. Kannan *et al.* (2019) treated meloxicam toxicity in dog using synthetic analogue of prostaglandin E1, misoprostol along with supportive therapy. As there is no literature on therapeutic management of NSAID toxicity in bovines, the present case was treated with fluids, stypitics, antacids, vitamin B complex, antihistaminics and colloids which has shown gradual clinical recovery in the bull with long convalescence period. Hemato-biochemical assessment, clinical assessment along with supportive medications might be helpful in therapeutic management of meloxicam overdose in cattle which are very rarely predisposed to NSAID toxicity.

Table 1: Hemato-biochemical parameters in Meloxicam toxicity affected Deoni bull

Parameter	Day 0	Day 10	Day 30	Reference Range
Body temperature ($^{\circ}$ F)	100.9	101.2	100.6	100.50-102.50
Heart Rate (bpm)	52	54	50	40-80
Respiration Rate (bpm)	16	18	16	12-36
RBC ($\times 10^6/\mu$ l)	5.41	5.43	5.12	5-10
Hb (g/dL)	6.70	8.80	9.70	8-15
HCT (%)	24.60	27.01	28.89	24-46
WBC ($\times 10^3/\mu$ l)	9.33	9.40	9.17	4-12
Granulocytes (%)	18.80	46.20	44.40	15-65
Monocytes (%)	13.80	8.10	6.20	2-7
Lymphocytes (%)	67.40	45.70	49.40	45-75
Platelets ($\times 10^3/\mu$ l)	369	302	358	100-800
Alkaline Phosphatase (U/L)	392.00	311.00	212.10	0-488
ALT (U/L)	22.69	24.09	24.43	11-40
AST (U/L)	89.00	84.86	85.51	78-132
Total bilirubin (mg/dl)	0.12	0.22	0.26	0.01-0.50
Direct bilirubin (mg/dl)	0.09	0.11	0.15	0.04-0.44
Indirect bilirubin (mg/dl)	0.03	0.11	0.11	0-0.30
Total protein (gm/dl)	8.50	4.66	6.72	6.7-7.5
Albumin (gm/dl)	2.72	2.42	3.40	3.0-3.6
Globulin (gm/dl)	5.78	2.24	3.32	3.0-3.48
Blood urea nitrogen (mg/dl)	283.66	124.4	28.29	20-30
Creatinine (mg/dl)	20.54	9.87	1.28	1.0-2.0
Calcium (mg/dL)	13.00	9.76	9.83	9.7-12.4
Phosphorous (mg/dl)	9.24	7.84	5.89	5.6-6.5

Conclusion

Accidental meloxicam overdoses in cattle can also lead to toxicity similar to one observed in pet animals characterized by loose black-coloured feces, straining while defecating, voiding of straw coloured urine, and elevated values of BUN and creatinine. Fluid therapy, supportive medications, and monitoring of kidney function and erythrogram may prove helpful in managing meloxicam toxicity in cattle.

Contribution by Authors

Each co-author contributes equally.

Conflict of Interests

There is no conflict of interest.

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