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Case Report

Oxyclozanide Poisoning in Deoni Bulls and its Therapeutic Management

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Abstract

Three Deoni bulls were admitted to clinics with a history of anorexia, abdominal pain, and diarrhea with straining due to accidental overdosing of a combination comprising Oxyclozanide and Fenbendazole. Clinical examination revealed tachycardia, normal body temperature, and respiration rate along with slight salivation, loose foul-smelling feces, suspended rumination, absence of ruminal motility and signs of abdominal colic. Hematological analysis before treatment showed all parameters within normal reference intervals except a mild increase in monocyte count. Serum biochemical analysis revealed elevated levels of hepatic enzymes, blood urea nitrogen, and creatinine. As no specific antidote is available, the cases were treated symptomatically using fluid therapy, antihistaminics, vitamin B complex, and prebiotics- probiotics for 3 days. All three bulls recovered successfully after 3 days of treatment with restoration of food and water intake and rumination. In conclusion, oxyclozanide + fenbendazole poisoning may be observed in cattle due to accidental overdosing characterized by anorexia, salivation, abdominal pain and diarrhea with straining along with elevated levels of hepatic and renal biochemical markers. The extent of overdose and severity of clinical signs may decide the outcome of treatment as there is no specific antidote for oxyclozanide + fenbendazole toxicity in cattle.

Keywords: Cattle, Clinical Signs, Hemato-biochemical changes, Oxyclozanide Toxicity, Treatment.

Introduction

Various anthelmintic drugs are frequently used for prophylactic and therapeutic purposes in livestock farming for parasitic diseases. Formulations that are being used by farmers may have proneness for underdosing or overdosing. Overdosing with drugs which have narrow margin of safety may lead to toxicity. The common drugs that are responsible for causing poisoning in animals include antibiotics, anthelmintics and non-steroidal anti-inflammatory drugs (Xavier *et al.*, 2002; Muntener *et al.*, 2010). Anthelmintics are an category of drug used in livestock farming to get rid of different types of endoparasites in farm animals to prevent negative effects of worm infestations.

Few studies already have been published reporting poisoning with different anthelmintics in farm animals includes the combination of anthelmintics like Fenbendazole+Levamisole and Oxyclozanide+Levamisole (Jadhav *et al.*, 2017; Rather *et al.*, 2020). However, currently no literature is available regarding oxyclozanide + fenbendazole poisoning in livestock. The present communication reports the clinical signs, hemato-biochemical alterations and therapeutic management of accidental overdosing of a combination comprising Oxyclozanide and Fenbendazole in three Deoni bulls.

Case History and Clinical Findings

Three Deoni bulls of age 1 year, 2 years and 3 years having body weights 153 kg, 197 kg and 200 kg respectively belonging to the same owner were admitted to the Veterinary Clinical Complex with history of abdominal pain, anorexia and diarrhea with straining. History collected from the animal owner revealed the drenching of all three bulls with dewormer combination comprising Oxyclozanide (7.5% W/V) and Fenbendazole (2.5% W/V) leading to accidental overdosing (approximately 2.5 times the prescribed dose). The bottle of anthelmintic used for deworming was found to be a combination Oxyclozanide (7.5% W/V) and Fenbendazole (2.5% W/V). The symptoms of illness started few hours after drenching the bulls with dewormer in apparently healthy bulls before feeding.

Clinical examination revealed tachycardia, normal body temperature and respiration rate along with slight salivation, passing loose foul-smelling greenish black feces with straining, suspended rumination, absence of ruminal motility and signs of abdominal colic.

Hemato-biochemical Changes

Hematological analysis before treatment showed all the parameters within normal reference interval except mild increase in monocyte count. Serum biochemical analysis revealed elevated levels serum of hepatic enzymes (ALT, AST and Alkaline Phosphatase), blood urea nitrogen and creatinine (Table 1). Based on the confirm case history of overdosing of the dewormer followed by the onset of illness and elevated levels of various hepatic and renal serum biochemical parameters, the cases were diagnosed for oxyclozanide poisoning.

Therapeutic Management

All three bulls were treated symptomatically as there is no specific antidote for oxyclozanide poisoning. Treatment comprising of Dextrose 5% @ 2 liters IV twice daily, Inj. Vitamin B complex @ 5 ml IV once daily, Inj. Chlorpheniramine maleate @ 0.25 mg/kg IM once daily and orally pre-biotic, probiotic bolus @ 1 bolus twice daily for 3 days. Subsidence in abdominal pain was observed in all the bulls on the first day of treatment only. Resumption of rumination and feed intake was observed from the second day of treatment while restoration of fecal consistency and heart rate was observed from third day of treatment and onwards.

Discussion

A flukicidal drug oxyclozanide a salicylanilide anthelmintic developed in 1966 acts selectively on parasites through uncoupling of oxidative phosphorylation. Oxyclozanide is effective in the treatment of fasciolosis in ruminants (Broome and Jones, 1966; Walley, 1966; Swan and Schroder, 1981). The recommended dose rate of oxyclozanide in cattle is 10-15 mg/kg orally once. Salicylanilide compounds are considered as moderately safe with safety factor of around 3-6 times recommended dose level (Swan and Schroder, 1981). Similar clinical signs of oxyclozanide poisoning have been reported in rats as well as sheep and cattle. The clinical signs like diarrhea, anorexia, depression and weight loss have been reported at the dose rate of 30 mg/kg or higher both in sheep and cattle. Dramatic weight loss and death has been observed at dose rate of 60 mg/kg in the same species (Walley, 1966). Fenbendazole is also a commonly used broad spectrum anthelmintic with very high safety factor. The dosages of up to 2 gm/kg revealed no adverse effects in animals (Muser and Paul, 1984).

In the present study the dewormer combination used was oxyclozanide and fenbendazole among which fenbendazole has wide margin of safety. Hence the toxicity signs are attributed to oxyclozanide which is having narrow margin of safety. The prominent clinical signs recorded in oxyclozanide poisoning affected bulls were salivation, abdominal colic, diarrhea with foul smelling feces, depression and anorexia. Jadhav *et al.* (2017) reported salivation, hyperesthesia, straining, high temperature, tachycardia and tachypnea in bullocks suffering from oxyclozanide and levamisole combined dewormer poisoning. More or less similar signs like depression, anorexia and diarrhea was reported in sheep and cattle administered with higher dose (25 mg/kg) of oxyclozanide (Wally, 1966). No literature is available for only oxyclozanide poisoning in animals. But Fenbendazole being safest dewormer, the clinical signs observed in the ailing bulls could be attributed to overdosing with oxyclozanide. Acute oxyclozanide studies in mice showed mental depression, lying and motionless, slightly closed eyes, disordered hairs, anorexia and death at 3.5 hours after administration of dewormer with LD_{50} of 1.674 mg/kg (Jili *et al.*, 2016). Wang *et al.* (2019) subjected Wistar rats to acute oxyclozanide toxicity and reported depression, rough hairs, inappetence, cyanosis of limbs, tail and lips in severely affected rats which succumbed to death with LD_{50} of 3,700 mg/kg body weight per day.

Table 1: Vital Parameters and Hemato-biochemical Parameters in Oxyclozanide Toxicity affected Bulls

Parameter	Bull-1	Bull-2	Bull-3	Average	Reference Range
Body Temperature (^{0}F)	101	101.7	100.7	101.13	100.50-102.50
Heart Rate (bpm)	94	92	94	**93.33**	60-80
Respiration Rate (bpm)	24	24	24	24	10-30
RBC (x 10^6/µl)	6.88	7.92	6.76	7.18	5-10
Hb (gm/dl)	9.1	9.8	8.3	9.06	8-15
HCT (%)	33.6	35.2	29.4	32.73	24-46
WBC (x 10^3/µl)	10.58	8.26	7.38	8.74	4-12
Neutrophils (x 10^3/µl)	7.16	0.46	2.91	3.51	0.6-6.7
Monocytes (x 10^3/µl)	0.28	0.94	1.53	**0.91**	0-0.84
Lymphocytes (x 10^3/µl)	3.14	6.86	2.94	4.31	2.5-7.5
Platelets (x 10^3/µl)	527	333	631	497	100-800
Alkaline Phosphatase (U/L)	418.0	771.10	317.10	**502.06**	0-488
ALT (U/L)	65.42	49.50	61.88	**58.93**	11-40
AST (U/L)	219.2	284.6	304.1	**269.30**	78-132
Total bilirubin (mg/dl)	0.42	0.18	0.28	0.29	0.01-0.50
Direct bilirubin (mg/dl)	0.25	0.11	0.15	0.17	0.04-0.44
Indirect bilirubin (mg/dl)	0.17	0.07	0.13	0.12	0-0.30
Total protein (gm/dl)	11.14	5.74	6.62	**7.83**	**6.74-7.46**
Albumin (gm/dl)	2.15	2.87	1.95	**2.32**	**3.03–3.55**
Globulin (gm/dl)	8.99	2.87	4.67	**5.51**	**3.0-3.48**
Blood urea nitrogen (mg/dl)	62.33	43.15	39.38	**48.28**	20-30
Creatinine (mg/dl)	6.97	3.77	3.97	**4.90**	1.0-2.0

No significant deviations were reported in hematological parameters of the bulls suffering from oxyclozanide poisoning in the present study except mild increase in monocyte count. On the contrary Swan (1999) reported neutrophilia and lymphopenia in animals with oxyclozanide poisoning. Biochemical analysis revealed elevated values of alkaline phosphatase, ALT and AST along with blood urea nitrogen and creatinine indicative of hepatic and renal injury due to oxyclozanide overdosing. Similar findings of elevated values of ALP, AST, BUN along with other enzymes was observed in Wistar rats subjected to experimental oxyclozanide toxicity (Wang *et al.*, 2019).

As there is no specific antidote for oxyclozanide poisoning, symptomatic and supportive therapy helps in relieving the clinical signs and hastens the clinical recovery of the ailing animals. Previously Jadhav *et al.*, (2017) treated case of acute levamisole+oxyclozanide toxicity in Red Kandhari bullock using Atropine sulfate, fluid therapy, vitamin B complex, antihistaminics, corticosteroids and antibiotics. The present cases showing mild to moderate clinical signs and toxicity being attributed only to oxyclozanide they were treated with only fluid therapy, vitamin B complex, anti-histaminic and prebiotics-probiotics and showed good clinical recovery within 2-3 days of treatment with restoration of fecal consistency, food intake, rumination after 3 days' treatment.

Conclusion

Oxyclozanide overdosing in cattle can lead to poisoning characterized by salivation, abdominal pain, loose foul-smelling diarrhea with straining, hepatic and renal injury. The fluid therapy along with supportive medications and proper monitoring of these cases may prove helpful in the successful recovery.

Contribution by Authors

Equal contribution. All authors declared that 'written informed' consent was obtained from the approved parties for the publication of this article and accompanying images.

Conflict of Interests

There is no conflict of interest.

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