Research Article

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Incidence of adverse drug reaction (ADR) in ruminants in various parts of Maharashtra

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Abstract

For better understanding the drug safety program, reporting of the adverse drug reaction and adverse drug events are quite well organized in the human pharmacovigillance in India. Many aspects of the ADR/ADE are even unknown to the users of Veterinary medicinal products. Smallest to smallest as well as biggest ADR is to be reported to respective branches of government agency. Sudden exposure to complicated guidelines may leads to confusion and work intolerance in personals that are handling / using the various veterinary medicinal products for the treatment and betterment of animal health. A step by step understanding is a need of time for the field of veterinary pharmacovigillance (PV), as most of the users of VMP are staying in rural parts of India and may not be that much educated. Hence through interviews from 500 Field Veterinarians, data of last 5 years was analyzed and presented for this paper. Based on the severity on the health of the animals, ADR/ADEs were classified as Minimal, moderate, severe and accidental. Most of the time severe ADR/ADEs leads to death in ruminants.

Keywords: Adverse Drug Reaction (Adr), Adverse Drug Events (Ade), Pharmacovigillance (Pv), Reporting, Ruminants, Minimal, Moderate, Severe.

Introduction

Indian livestock industry plays very crucial role in the Indian economy; most of the livestock business is situated in the rural areas and rural economy almost completely depending on the agriculture and livestock production. Cattle, buffalo, sheep goats are the ruminants, which are reared by variety of economic classes, like- organized farmers, unorganized farmers, tribal, shepherd etc. many times these animals are undergone variety of disease conditions that includes, infectious and non- infectious conditions. For the treatment of these various disease conditions Veterinarians need to use various types of Veterinary Medicinal Products. Many times some of the Veterinary Medicinal Product (VMPs) are showing adverse drug reaction or adverse drug events (ADR/ ADE) in the animals, during or after use of VMP. These adverse effects are ranges from minimal, moderate, severe to life threatening and some are accidental adverse events recorded due to forceful drenching of oral VMPs, some times.

Materials and methods

The field data of various adverse drug reactions has been collected from 500 field veterinarians and classified in to minimal, moderate , severe and life threatening depending on the severity of the incidence. Details of routes administration of veterinary medicinal products were recorded. Detailed clinical signs, production losses and detailed postmortem examinations of the representative dead ruminants were carried out and recorded.

Observations and Results

Self-experience of 22 years in the field of Veterinary Research and treatment of animals and data collected from 500 Veterinary doctors of last five years, ADR is classified in different categories for better understanding of of ADR/ ADE of VMP for the persons who are involved in use of various VMP and following observations were noticed.

1. Minimal adverse drug reaction: minimal ADR is termed as a ADR having short and transient ADR and get subsides in due course of time without altering much in the normal physiology and productive losses of ruminants. These ADR/ ADE can be usred by the nominal symptomatic treatments. The details of cases and observations are mentioned vide Table no 1.

2. Moderate: this type of ADR is having noticeable alterations in the productive losses and normal physiology of ruminants and showing remarkable clinical signs of ADR of VMP. If

not managed by treatment it may convert to severe or life threatening or permanent disability. The details of cases and observations are mentioned vide Table no 2.

3. Severe: in this type of ADR of VMPs, animals showed severe clinical signs, permanent disabilities and having very less response to the curative managemental therapy. In many conditions this was found to be life threatening and no cure was observed. Animals those were died and if animal owners given permission to do postmortems; in such cases post mortem examinations were carried out. The details of numbers of cases has been given vide Table no 3. Out of 125 dead cases of Intramuscular penicillin injections 21 cases were examined for the detailed post mortem examinations and out of 54 cases of Intrammamary penicillin ointment 10 cases were examined for the detailed postmortem examinations. Post mortem findings were found similar in both the types of cases; that includes- severe congestion of mucous membranes and sub cutaneous tissues, tracheas were severely congested and showed pin point hemorrhages, scanty of froth in primary bronchi, lungs were severely congested, edematous and emphysematous. Pin point hemorrhages on the pleura, epicardium, endocardium and serosa and mucosa of tubular organs. Liver, kidneys were severely congested and engorged with blood. Body cavities showed small quantity of serous fluids. Lymph nodes were congested and edematous.
4. Accidental ADR due to faulty drenching of VMPs: this type of ADR may cause sudden death in ruminants when animals are resisting drinking dispensed VMPs. And forceful drenching leads to sudden death due to asphyxia. Details about numbers of cases has been given vide table no 4. In case of oral medications of purgatives, out of total 12 cases, 4 cases were died; in case of oral administrations of calcium gels total 23 cases were noticed and out of them 6 cases were died. In case of oral administration of bolus total 25 cases were recorded and out that 5 cases were died. Detailed post mortem examination was carried on all the dead animals. Post mortem an examination includes severe congestion of trachea, bronchi and bronchi were blocked with drenching medicinal products. Severe emphysema of lung and hemorrhages on heart muscles, thoracic muscles and serosae of organs. The masses were occludes complete deeper respiratory tree.
5. Accidental and faulty choice of routes of administrations: in this category regular strict routes of administration may be intramuscular, Intravenous, Subcutaneous, intradermal, intra - conjunctival, intrauterine, intra – peritoneal etc. Many times animals showed excitement and fear of strange persons, who are handling the animals at the time of treatment. Besides this sometimes lack of knowledge of administration routs of various VMP, are accidently altered the advised routes which leads to ADR. The incidences of this type of ADR are given in table no 5.

Table 1: VMP causing Minimal ADR.

VMP	Clinical signs observed	Period required to be restore the normal condition
Deworming agents Niclosamide, albendazole (2560)	Intermittent diarrhea , transient anorexia , less milk production	2 to 3 days
Oral amoxicillin bolus (256 cases)	Anorexia, diarrhea, constipation in some animals	4-5 days
Oral glucogenic precursors (110 cases)	Diarrhea	2-3 days
Oral liver tonics with liver fractions (59 cases)	Diarrhea	3-4 days
Subcutaneous administration of vaccines (1085)	Swelling at site of injections, sometimes hard swelling at site of injections	15 to 20 days 80 to 90 % of swellings get subsides but 10 to 20 % swelling remains for longer period up to 1 year.
Subcutaneous administration of ivermectins , doramectins (447 cases)	Swelling at site of injections, sometimes hard swelling at site of injections	Subsides after 20 to 30 days
Subcutaneous administration of ivermectins , doramectins (217 cases)	Besides swelling, local irritation, shaking of head, salivation, restlessness evident	Subsides after symptomatic treatment
Intramuscular administration of oil based long antibiotics – Oxytetracyclin, Amoxycillin (658 cases)	Swelling at site of injections, sometimes hard swelling at site of injections	4-7 days
Intramuscular administration of aqueous based VMPS e.g. NSAID (785 cases)	Pain and warmness at the site of injections	1-2 days
Intravenous administration of isotonic physiological saline (257 cases)	Swelling at site of injection	Immediately after completion of IV fluid therapy

Intravenous administration of calcium preparations (88 cases)	Shivering, restless ness	Subsides within in 30 min to 1 hour
Intravenous administration of calcium preparations (95 cases)	Sudden drop in milk production	5-6 days required to restore normal physiological functions
Intrauterine therapy for uterine infections (113 cases)	Restlessness , colic, twitching of tails , hyperpnoea	4-5 hours

Table 2: VMP causing moderate ADR

	Clinical signs observed	**Period required to be restore the normal condition**
Closantel (690 cases)	Blindness in sheep and goats	Remains as permanent disability
Dexamethasone (311 cases)	Abortion and loss of milk production	Animals may not give milk for that particular lactation
Intramuscular multi minerals injections (58 cases)	Weakness, nervous signs and downers cow like symptoms and paralysis.	Weakness and downers syndrome can be subsides after curative treatment after 10-15 days. Paralytic animals didn't recovered remains paralytic for more than 15 to 20 days and died due to inanition
Intra-muscular diamezine aceturate (128 cases)	Hypersensitivity , Salivation , respiratory distress , shivering, falling down , sweating and colic in some of the animals	If not treated immediately, death may be occurred in 15 to 20 minutes
Intramuscular injections of buparvaquone (21 cases)	Hypersensitivity , Salivation , respiratory distress , shivering, swelling and cyanosis of udder	Death may observe if not treated by curative treatment. But Temporary loss of milk production for 15 to 20 days
Oral or parenteral (fluoroquinolone) enrofloxacin in growing young animals below 2 months (23 cases)	Lameness, shortening of legs , stiffness of joints, increased decumbency intervals	Permanent lameness and bone deformities remained

Table 3: VMP causing severe ADR.

VMP	**Clinical signs observed**	**Period required to be restore the normal condition**
Intramuscular penicillin (125 cases) Intrammamry penicillin ointment. (24 cases)	Hypersensitivity , ocular, nasal discharge , salivation, collapsed suddenly	Most of the cases not respond to treatment, death is ensured.
Intravenous calcium preparations (52 cases)	Respiratory distress and sudden collapsed	Most of the cases of visible ADR are died immediately after completion of calcium saline
Intravenous oxytetracyclins (10 cases)	Respiratory distress, salivation, nasal discharge, and sudden collapsed	Most of the oxytetracyclin sensitive cases are died immediately.

Table 4: Accidental ADR due to faulty drenching of VMPs.

VMP	Clinical signs observed	Period required to be restore the normal condition
1. Oral medications of purgatives (12 cases) 2. Oral administrations of calcium gels (23 cases) 3. Oral administration of bolus (25 cases)	Severe coughing, shivering, abdominal respiration, violent coughing reflex, sudden collapsed, lateral recumbency and death in some of the animals.	Most of the cases not respond to treatment, death is ensured. The intensity of clinical signs and incidence of deaths were based on quantity of VMP enter into trachea. Immediate treatment was found to be helpful in some of the cases where drenching material was less in quantity.

Table 5: Accidental ADR due to change in the parenteral routes of administration of VMPs.

VMP	Clinical signs observed	Period required to be restore the normal condition
Intravenous solutions (Antibiotics, Calcium preparations, hypertonic saline etc.) accidently enter to sub cutaneously	Swelling, pain around blood vessels, restless ness and respiratory distress	Local treatment with gel/ ointment and symptomatic treatment will reduce intensity of clinical signs immediately.
Subcutaneous injections went to intramuscular (Vaccines and Ivermectin)	Swelling, pain around blood vessels, fever , salivations, restless ness and respiratory distress	Local treatment with gel/ ointment, cold fomentation and symptomatic treatment will reduce intensity of clinical signs immediately.
Intramuscular injections went to subcutaneous (NSAIDS, antibiotics, supportive tonics with liver fractions, iron preparations, hormones, etc)	Swelling, pain around blood vessels, fever , salivations, shaking of head, restless ness and respiratory distress	Local treatment with gel/ ointment, cold fomentation and symptomatic treatment will reduce intensity of clinical signs immediately.
Intramuscular injections went to Intravenous (antibiotics, Oily long acting antibiotics, vaccines,)	Sudden anaphylactic reactions, respiratory distress, salivation and sometime sudden death can occur.	Generally found to be life threatening if volume of drugs is more.

Discussion

Minimal, moderate, severe adverse drug events ADEs were detected by many of the field Veterinarians and these ADR/ ADE were not found life threatening in minimal ADR/ ADE and immediately after symptomatic treatments these ADR/ADE get subsides. Where as moderate ADR/ ADEs leads to some permanent disability in animals, and severe DR/ ADEs were found to be life threatening and deaths of animals observed. Literature of the Similar types of findings is scared to observed, because in India reporting of ADR/ ADEs of VMP has been not considered seriously [1]. Pharmacolvigillance survey study of some of the antibiotics, antipyretics, anthelmentics and other miscellaneous VMPs were carried out by Ghadevaru et al for period of one year in the state of Tamil Nadu and total 102 cases of animals reported [2].

Conclusions

After classifications of various ADR caused by various VMPs, for better understanding of the ADR in ruminants. It could be concluded that in the primary phase of drug regulatory system and reporting of ADR/ ADE, system step by step implementations of different international guidelines and laws will be possible at the Indian conditions. Many of the Veterinarians, and personals involved in the business of Ruminants VPM and their use, sale and post marketing surveillances will be benefited with these classifications. No doubt many multinational veterinary pharmaceutical companies are following the regulations as per their country of origin; these countries are following well-set guidelines in their country but in India its implementations remains limited to only employees of these companies.

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Conflicts of Interest

No any conflicts of interest

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