

Full Length Research Paper

A pharmaco-epidemiological survey of commonly used veterinary drugs in Southern Nigeria

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A pharmaco-epidemiological survey was carried out on the commonly used veterinary drugs in Nigeria. This study was necessitated by the dearth of information regarding the side effects of the commonly used veterinary drugs in Nigeria. It has been noticed that most of the drugs used in the country were imported from developed countries. Though the drugs have been tested for side effects, it has not taken into cognizance that different effects may be observed when used in the tropics because of pharmacogenetics. The survey was done via the means of a structured questionnaire. Results of the survey showed that various drugs used by practitioners caused different drug reactions and in some instances have led to the death of the animal.

Key words: Pharmacological, epidemiological, veterinary drugs, side effects.

INTRODUCTION

An adverse drug reaction (ADR) could either be the drug exaggerated pharmacologic effects or its aberrant/idiosyncratic reactions. Drug exaggerated pharmacologic effects are common, dose related, predictable and less serious. The aberrant reactions on the other hand are uncommon, not dose related, unpredictable and less serious (Strom, 2000).

Veterinarians have often encountered unexpected, undesirable or adverse effects associated with the use of drugs (Dogana, 2011). Knowledge of such adverse effects usually is committed to memory where it forms part of the practitioner's clinical experience (Stowe, 1980). However, such unsystematic dissemination of information is inadequate in view of the present day demands for safe, as well as effective drugs.

Pharmaco-epidemiology is the study of the use and effects of drugs in animal or human populations. It is a comparatively new applied field, bridging between clinical pharmacology and epidemiology. From clinical pharmacology, it borrows its forms of inquiry and from epidemiology, it borrows its method of inquiry. A pharmaco-epidemiological survey involves making a regulatory decision about approving a drug for

marketing or the clinical decision on when to prescribe a drug. It also involves sourcing for information about the effects of drug use, which includes post-marketing assessment and drug surveillance, benefit-to-risk drug profiles beneficial and adverse drug reactions and methodologies to study the outcomes of drug therapy (Strom, 2000).

Other benefits of pharmaco-epidemiological study include effects of drug use, which may have been missed by the manufacturer during clinical trials, which may also be desirable in some other context.

Justification

The lack of documented information regarding the side effects of commonly used veterinary drugs in Nigeria necessitated this study. The objectives are:

- (i) To discover if drug reactions other than those reported by the manufacturer have been noticed by practicing veterinarians;
- (ii) If the drug reactions noticed have been harmful or beneficial in some other aspects not pertaining to that condition;
- (iii) To also gather information about the efficacy of drugs used in the country; and

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Table 1. Number of veterinary doctors on call in veterinary clinics.

Number of veterinary doctors on call	Percentage of veterinary clinics
0	2.0
1	33.0
2	42.0
3	12.5
7	10.5

(iv) To gather information about the preferred drugs used by practicing veterinarians in some parts of the country.

METHODOLOGY

Study areas

The study areas were spread around Oyo, Edo and Rivers States in Southern Nigeria.

Sources of data collection

Data collected for this study was done via the means of a structured questionnaire. The questionnaire was designed with the objectives of the project in mind.

The questionnaire

The questionnaires were originally designed for veterinarians and veterinary establishments. The veterinary establishments visited include veterinary clinics, farms and consultancy service units. The questionnaires were sent to the veterinarians in Government parastatals especially those in agricultural agencies. The designed questionnaire was divided into 3 parts: The first part was designed to collect general information about the veterinary establishment. The second component of the questionnaire sought to know the common drugs used by the veterinarians in treating the various disease conditions. The third component sought information on the various drug reactions, which included the adverse effects of the drugs and other interactions, which may have occurred if any of the drugs were combined or a different route of administration was used.

Statistical analysis

The statistical analysis used for this survey was the SPSS package.

RESULTS

Twenty-seven questionnaires were eventually returned and they were analyzed quantitatively and qualitatively. The quantitative analysis was done by means of a computer package (SPSS) and was used mainly for the first part of the questionnaire to answer questions surrounding the distribution of the veterinary clinics that were visited, the number of practicing veterinarians in

that establishment and also the average number of cases seen every week. The second part of the questionnaire was also analyzed with the use of the SPSS programme and showed the drugs, which the veterinarians preferred using.

The third part of the questionnaire was opened ended and it was also given a bit of analysis.

Information about the veterinary clinics visited

(a) It was observed that most of the veterinary clinics visited had one or two veterinary doctors on call. Table 1 provides information about the number of veterinary doctors on call.

(b) The survey showed that most of the veterinary clinics had been in existence for about 1 to 4 years with some clinics been about 8 to 12 years of age, the oldest veterinary establishments were that of the government with some as old as 30 years or more. Table 2 gives an insight to how long the veterinary clinics have been in existence.

Information regarding drug use

Table 3 shows the use of Penicillins. The most frequently used drug among the Penicillins was Procaine Penicillin and it was reported to be used by 41.5% of the respondents. This was followed by Ampicillin, and Cloxacillin. Penicillin G was not used by any of the respondents.

The use of Tetracyclines is shown in Table 4. The most frequently used drug among the tetracyclines was oxytetracycline and it was used by 74.1% of the respondents. Only 3.7% of the respondents used deoxycycline, while 22.2% of the respondents reported the use of both drugs.

Table 5 shows the use of Antimycotics. The most frequently used Antimycotic was Griseofulvin; It was used by 32.3% of the respondents.

Table 6 shows the use of Anthelmintics. The most frequently used anthelmintic was Levamisole with 40.4% of the respondents using the drug. Mebendazole was next with 31.3% of the respondents using the drug.

Table 7 shows the use of Antiprotozoals. Berenil

Table 2. Year of existence of veterinary clinics.

Age of clinics (Years)	Number of respondents (%)
1-4	30.0
4-8	25.0
8-12	25.0
12-16	10.0
20 years and above	10.0

Table 3. Use of penicillins.

Drug	Number of respondents (%)
Penicillin G	0.0
Procaine penicillin	41.5
Ampillin	29.3
Cloxacillin	24.4
Others	4.8

Table 4. Use of tetracyclines.

Drug	Number of respondents (%)
Oxytetracycline	74.1
Deoxycycline	3.7
Both drugs	22.2

Table 5. Use of antimycotics.

Drug	Number of respondents (%)
Amphotericin	9.7
Nystatin	19.4
Griseofulvin	32.3
Crystal violet	25.8
Copper sulphate	12.8

Table 6. Use of anthelmintics.

Drug	Number of respondents (%)
Thiabendazole	15.8
Mebendazole	31.3
Thiophanate	0.0
Febendazole	12.5
Levamisole	40.4

(Diaminazene aceturate) was the drug most frequently used by 62.5% of the respondents. Other drugs used include quinapyramine, imizol and quinuronium sulphate. Diampron was not used by any of the respondents.

Table 8 shows the use of Ectoparasiticides. Diazuntol was the most frequently used ectoparasiticide with 51.2% of the respondents using it. Malathion was the least frequently used drug with 17.1% of the respondents using it.

Table 9 shows the use of anti-tumour agents. Vincristine was the most frequently used drug by 56.2% of the respondents, while Methoxerate, Flurouracil and Vinblastine were the least frequently used drugs.

Table 10 shows the use of premedicants. Atropine and Xylazine were the two premedicants, which were most frequently used by 35.2 and 28.2% of the respondents, respectively.

Table 11 illustrates the use of sedative/anaesthetic agents. Ketamine was the most preferred for inducing anaesthesia by 42.8% of the respondents. Pentobarbitone was next in line by 28.6% of the respondents. Other drugs used by the respondents include Thiopentone and Methohexitone. None of the respondents used Propofol.

Information on the side effects reported

Anthelmintics

Levamisol was reported by about 69% of the respondents to cause deleterious effects to the central nervous system with clinical manifestations of vomiting and convulsions. Some cardiovascular effects were also reported by about five of the respondents and they included tachycardia.

Antiprotozoan

Diaminazene aceturate (Berenil) was the common antiprotozoan drug that was reported by 14% of the respondents to elicit central nervous signs, such as staggering gait and coma. Death was reported in 4% of the questionnaires with the use of the drug. It was also reported to cause paralysis of the hind limbs. The drug was also reported to cause lumps at the site of injection by three of the respondents. The effects observed were at therapeutic doses.

Antibacterials

Long acting oxytetracycline was reported to cause death at greater than therapeutic dose by 10% of the respondents. Short acting tetracycline caused death in one instance with intravenous administration. Procaine penicillin caused reddening and rashes on the under belly and this was reported by 11% of the respondents.

Ectoparasiticides

Asuntol was reported by 30% of the respondents to

Table 7. Use of antiprotozoal.

Drug	Number of respondents (%)
Berenil	62.5
Quinapyramine	6.25
Diampron	0.0
Imizol	25.0
Quinuronium sulphate	6.25

Table 8. Use of ectoparasiticides.

Drug	Number of respondents (%)
Asuntol	31.7
Diazuntol	51.2
Malathion	17.1

Table 9. Use of anti-tumour agents.

Drug	Number of respondents (%)
Methotrexate	6.5
Flurouracil	6.5
Cyclophosphamide	24.3
Vincristine	56.2
Vinblastine	6.5

Table 10. Use of premedicants.

Drug	Number of respondents (%)
Atropine	35.2
Acepromazine	14.1
Diazepam	21.1
Xylazine	28.2
Buprenorphine	1.4

Table 11. Use of sedative/anaesthetic agents.

Drug	Number of respondents (%)
Thiopentone	22.9
Methohexitone	5.7
Pentobarbitone	28.6
Propofol	0.0
Ketamine	42.8

cause central nervous signs such as convulsion, hypersalivation and muscle spasms. It was also shown to cause respiratory collapse in three of the questionnaires. 6% of the respondents reported the drug to cause

defecation and vomiting. Effects of this drug were commonly observed at therapeutic doses and when the animal licked the solution off its skin. Malathion was reported to cause twisting of the facial muscles by one of the respondents.

Anti-tumor agents

Vincristine was reported by 6% of the respondents to cause damaging effects to the cardiovascular system which led to bleeding and it also caused a low packed cell volume (PCV) and death. It was also reported to cause hair loss by one of the respondents.

Vaccines

Attenuated live vaccines of the anti-rabies and Distemper, Hepatitis, Leptospirosis, Parvoviral and Parainfluenza (DHLPP) were reported to cause abortion and still birth when administered at the third trimester of pregnancy by three of the respondents. DHLPP was also reported to cause disturbances to the digestive and excretory system by one of the respondents.

Anaesthetics

Xylazine was reported by about 50% of the respondents to elicit central nervous signs, which include ataxia, convulsive seizures and death at greater than therapeutic doses. Ketamine caused respiratory system depression in one instance.

Vitamins

Vitamin B complex administration was reported to cause swelling of the skin and face and also restlessness and vomiting. In one instance, vitamin B complex led to shock.

DISCUSSION

This study has given us a lot of information about the various effects of the drugs, which were used by veterinarians in Nigeria. Some of these effects agree with the findings already reported in literature about their toxicities.

In this study, Levamisol, which was the mostly used anthelmintics was also the most toxic anthelmintic. The mode of action of this drug involves stimulation of the parasympathetic and sympathetic ganglia in susceptible worms (Plumb, 1999). The adverse effect of the drug reported from literature includes hypersalivation,

excitement and head shaking usually at greater than therapeutic doses. Reports from this survey showed that these effects may also occur at sub-therapeutic and therapeutic doses.

Berenil (Diaminazene aceturate) is the most commonly used by respondents in this study and is the least toxic trypanocide (Arowolo and Eyre, 1984). The adverse effects reported for berenil in this study agrees with the information from the literature. These include local reactions from site of injection and central nervous system signs like staggering gait, coma and death in few instances.

Oxytetracycline is the most commonly used by respondents in this study. This is a tetracycline derivative obtained from *Streptomyces rimosus*. Their mode of action involved bacteriostatic action. The adverse effects of the drug from literature include discoloration of bones and teeth. Oxytetracycline is also known from literature to be well tolerated after acute overdoses. The survey in contrast reported death in some instances due to Oxytetracycline use (Plumb, 1999).

In this study, Procaine Penicillin is the most commonly used penicillin. The effects, which were reported by the survey, were concurrent with that obtained from literature. Asuntol and Malathion are the most frequently used ectoparasites by respondents in this study. These are both organophosphates and they act by principally binding to and inhibiting acetylcholinesterases (Kaur and Dhanju, 2004). Toxicosis results primarily from the inhibition of Acetylcholine and the toxicity reported from the survey are similar to what was seen in literature.

The most commonly used antitumour agent in this study is Vincristine. This is a vinca alkaloid isolated from a plant *Cantharanthus roseus*. The pharmacology of vincristine involves binding to microtubular proteins (Tubulin) in the mitotic spindle thereby preventing cell division during metaphase. The adverse effects of vincristine reported from literature include myelosuppression and neuropathic symptoms. The survey also shows vincristine to cause low packed cell volume (PCV) and also alopecia.

The adverse reactions reported with the use of Anti-rabies vaccine were numerous and they included local reactions at the injection site and systemic reactions, which include headaches and abdominal pain. It was however reported to be safe for use during pregnancy (Bartholomew, 2001). The survey on the other hand, reported the vaccine to cause abortion at the third trimester. The effects of xylazine and ketamine reported by the survey, were concurrent with what obtained from literature.

Risks of the survey

One of the risks of conducting the survey is the possibility that it could identify an adverse drug reaction, which was not caused by the drug in question. Also, it should be

noted that some of the drug reactions, which were reported might perhaps have been due to idiosyncratic reactions, which may have taken place in only isolated cases. Another important point is that the information acquired from the survey could provide a false security of a drug, which was reported to show no adverse reactions.

Conclusion

From the survey, it can be inferred that some of the drugs used by veterinarians in the country show adverse reactions and these should be investigated with an aim to improve of the drugs, as well as increase in awareness by practicing veterinarians.

RECOMMENDATIONS

1. In the best interest of animal welfare, veterinarians should make the adverse drug reaction experiences known to other practitioners in order to forewarn them of potential problems.
2. The pharmaceutical industries should also be informed about these adverse drug reactions, as they are usually co-operative in investigating the problems related to adverse drug reactions.
3. Consistent adverse reactions with a particular drug should necessitate changes in labelling, warning and package inserts.
4. A regular reporting system should also be developed so that those drugs that continually elicit adverse reactions should be brought to notice.
5. The Veterinary arm of the National Agency for Food, Drug Administration and Control (NAFDAC) should effectively commence operations to evacuate such drugs from the market.

Limitations of the study

The following challenges were encountered during the survey.

- (i) Delay in completing the questionnaire that led to repeated visits and in some instances involved traveling to remind the respondents to fill the forms.
- (ii) Unclear/illegible handwriting, which led to difficult interpretation.
- (iii). Careless handling of the questionnaire, which meant a fresh questionnaire had to be sent and completed again by the respondents.
- (iv) Insufficient records of the effects noticed, which led to the questionnaires been completed from memory and lacking inadequate detail.

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