Ann. Ist. Super. Sanità
Vol. 28, N. 4 (1992), pp. 421-424

VETERINARY DRUG SURVEILLANCE

Agostino MACRI' *(a)* and Romano MARABELLI *(b)*

(a) Laboratorio di Medicina Veterinaria, Istituto Superiore di Sanità, Rome, Italy
(b) Ministero della Sanità, Direzione Generale dei Servizi Veterinari, Rome, Italy

Summary.- *The possible adverse effects of the application of veterinary drugs are considered with special reference to their illegal use or misuse in the different categories of animals (pet, sporting, food-producing). The risks of unacceptable drug residues in animals and their products, the environment and man are taken into consideration. The need is stressed for proper veterinary surveillance by previous assessment of priorities such as animals' health status, economic aspects, quality of food of animal origin, safeguard of the environment.*

KEY WORDS: veterinary drugs, animal health, human health, surveillance.

Riassunto (Farmacovigilanza veterinaria). - *Vengono presi in esame i possibili effetti negativi dell'uso dei farmaci veterinari con particolare riguardo all'impiego illegale o errato degli stessi nelle diverse categorie di animali (da affezione, sportivi, da reddito). Sono presi in considerazione i rischi connessi con la presenza di livelli inaccettabili di residui farmacologici negli animali e nei loro prodotti, nell'ambiente e nell'uomo. Si sottolinea la necessità di istituire un'adeguata farmacovigilanza veterinaria previa individuazione delle priorità da rispettare, quali lo stato di salute degli animali, gli aspetti economici, la qualità degli alimenti di origine animale, la salvaguardia dell'ambiente.*

PAROLE CHIAVE: farmaci veterinari, sanità animale, sanità umana, vigilanza.

Introduction

Drug regulations state that drug surveillance should be exerted over all therapeutical and prophylactic products and that responsibility for such a service should be entrusted to:

1) pharmaceutical industries manufacturing individual drugs;

2) primary health care physicians and veterinarians who shall report all possible adverse drug reactions (ADRs);

3) national health authorities forming a system for collection of data to be subsequently transmitted to EEC competent authorities.

Accumulating information may be used to modify the modes of application of those drugs showing detrimental side-effects or even to revoke authorization in especially serious cases.

Drug surveillance, therefore, is committed to uncover the possible appearance of ADRs. Schemes have been defined including all possible pathological effects deriving from the administration of drugs and such schemes have been internationally recognized [1].

The EEC regulations concerning human drugs apply also for a large part to veterinary ones and, as already mentioned, the same measures are foreseen as for the recording of drug-associated conditions and for notification to national and EEC authorities.

Application of drug surveillance to veterinary medicine

First of all, a distinction should be made in the application of drugs to food-producing animals (meat, milk and/or eggs), to pets (dogs, cats), and finally to such animals as sporting or simply saddle horses whose meats may however be used for human consumption.

Therefore, the possibilities of a practical, proper application of a drug surveillance system should consider the ways drugs are used according to the function the animal is intended for.

Use of drugs in pet animals

The use of drugs in pet animals is in a certain way similar to that followed in humans. Usually, people using drugs in dogs and cats are strongly interested in their

animals' health and are generally very cautious in administering drugs in cases of actual need and under veterinary supervision.

Under such circumstances, the application of drug surveillance is comparatively "easy" since both the veterinarian and the pharmacist are usually involved and possible adverse side-effects can be detected by a good medical follow-up.

Use of drugs in sporting animals

Owners of sporting animals are interested in their animals' health in view of their performances in contests. As a consequence, besides the drugs given to prevent or treat the different conditions, a variety of anabolizing and stimulating substances are employed capable of enhancing the animals' performances. Sometimes the different drugs are illegally used through distribution and application sources which do not consider the need for veterinary prescription and for distribution by the pharmacist.

The illegal use of drugs during contests is so frequent that horse-racing organizations have established a control system for the detection of illegal substances in the biological fluids of horses after contests. The situation is even more complicated in the "palio" contests taking place in different cities where no controls exist and abuses are much more frequent.

Use of drugs in farm animals

The employment of drugs in food-producing farm animals has a prevailingly economic relevance since the primary objective is the safeguard of animal health in order to increase productivity.

Actually, the correct use of drugs in farming activity brings farmers certain advantages since any healthy animal yields optimal zootechnical production which, in addition, is of better hygienic-sanitary quality.

No doubt that the misuse of drugs or even their illegal use may be economically advantageous for farmers, as in the case of growth-promoting (anabolizing) hormones, antithyroid and beta-agonist substances, yet with adverse effects on animals' health and on the hygienic-sanitary quality of produced foods.

Present legislation foresees the possibility of using only registered drugs, i. e. drugs previously evaluated as to their efficacy and safety. Of course, these products have costs adequate to their quality. A parallel, or clandestine market is however known to exist which offers the same drugs, non-authorized products or even active principles in the form of unprocessed chemical substances at very low costs.

This situation is certainly favourable to farmers who make a cost-benefit analysis when purchasing drugs and, in most cases, such an analysis suggests to choose illicit sources of drug supply. On the other hand, this practice exerts very adverse effects on animals health, hygienic-sanitary quality of foodstuffs produced and on the environment.

Objectives of veterinary drug surveillance

As already said, the objective of drug surveillance is to detect possible adverse effects of the drug in order to be able to take the measures required to undo the resulting risks.

The possibilities of exercising veterinary drug surveillance depends upon the different target animals and their rearing purposes.

With regard to companion animals, in the drug surveillance, the same basic criteria can be applied as those followed in human drug surveillance, and the ADRs established for human drugs can be to some extent adapted to those intended for pets. Possible adverse effects, in fact, involve almost exclusively the health of animals which can be affected by the administration of a drug: essentially careful clinical observations are required in such a case.

As far as "sporting" animals are concerned, besides the detriment to their health, also a possible deterioration of their competitive performances should be considered.

Lastly, it should be borne in mind that the meat from sporting horses may be used for human consumption and that, although to a minor extent, it is necessary to check the possible persistence of drug residues. EEC regulations should be applied to maximum residue levels (MRLs), and controls are even more complicated when illicit use of drugs is suspected.

The situation becomes much more complex and hard to solve in food-producing farm animals because the aspect of animals' health is not sufficient alone to define an adequate drug surveillance programme.

It is necessary, in fact, that the following side-effects be duly considered:

1) changes in the health status of animals;
2) possibility of inducing drug-resistance;
3) persistence of residues in produced foodstuffs;
4) effects on the environment.

Health status of animals

Most of drugs used in animal production have been tested for long and seldom produce ill effects. However abuses are frequent and drugs may be employed in the form of raw materials to be directly added to feeds or drinking water; in such cases incorrect dosing is possible or, worst still, scarcely pure drug may be administered with resulting detriment to animal health.

Another aspect to consider is the incompatibility between some drugs or the fact that a number of products are not tolerated by some animal species. For example, it is known that tiamuline is incompatible with ionophorous antibiotics and that the latter are toxic to equine animals.

Improper drug administration is also to be considered (e.g. beta-agonists, anabolic hormones, antithyroid substances) which, right thanks to the pathological effects they induce in animals, provide relevant zootechnical advantages essentially resulting in increased body weight.

Of particular interest is the appearance of undesirable effects in animals following vaccination. In most cases allergic reactions or other biological reaction are produced that compromise the health status and productivity of animals.

Of greater concern is the possibility that insufficiently inactivated live vaccines might spread the disease which should conversely be prevented. Vaccination accidents of this type are dangerous both for animal health and because of the serious economic losses which may follow systematic vaccination.

Induction of drug-resistance

One of the most serious risks run in intensive farming is the extreme spreading capability of infectious diseases, hence the need to put animals under a "protective pharmacological umbrella" of different antibacterial drugs. Low doses favour the occurrence of drug-resistant bacterial strains and parasites. As a result, drugs must be continuously substituted and be active and capable of controlling developing drug-resistant strains.

The presence of drug-resistant strains may pose problems also to the hygienic-sanitary quality of food of animal origin, especially if involved organisms are enterobacteria in general and salmonellae in particular.

Persistence of residues

The regulations on drug residues establish the allowed MRLs for the different active pharmacological principles. As a result, the modes of use should be indicated of each medicinal preparation so as to comply with accepted MRLs.

The situation is extremely complicated due to the large variety of preparations and also owing to the complexity of the analytical procedures required, which often call for the application of very sophisticated techniques and instrumentation. It is apparent, however, that the presence of residues exceeding allowed MRLs may depend not only on the medicinal product, but also on the mode of its application and finally, on the interindividual variations which occur in field conditions.

Adverse impact on the environment

The drugs administered to animals are released in the excreta either unchanged or in the form of metabolites which are then transferred to the environment with zootechnical slurries.

The presence of drugs in slurries may pose the following problems:

1) to affect the functionality of sewage treatment plants by inhibiting the activity of the purifying bacterial flora;

2) to exert a toxic action on aquatic and/or terrestrial flora and fauna;

3) to accumulate in vegetable and/or animal organisms and to subsequently enter the human and/or animal food chain.

Modes of application of veterinary drug surveillance

Veterinary drug surveillance in pet animals should be exercised using methodologies derived from those employed in human drug surveillance, i. e. by observations and identification of possible adverse effects in treated animals. However, specific ADRs of easy clinical recognition should be established in order to enable the veterinarian to readily collect information and to pass it to competent authorities as well as therapeutic knowledge.

Veterinary drug surveillance in sporting horses may be applied by resorting to the same principles as in pet animals, but giving due consideration to the athletic performances of the animals. ADRs should therefore include also possible behavioural changes during training and contests.

Similar considerations may apply to some animal species with peculiar productive features such as carrier pigeons, canaries, race dogs, minks, etc., and these productive features should be kept in check during drug surveillance.

Another particular case is breeding animals (bulls, boars, cocks and hens) having great economic interest and whose dosing should receive special care. In these animals, therefore, it is necessary to verify whether drugs are likely to affect reproductive processes and, as a result, an evaluation should be made of fertility rates, embryo toxicity, teratogenesis, offspring weight, etc.

The application of drug surveillance in food-producing animals is exceedingly more complex in that it requires the control of a number of parameters completely alien to human drug surveillance. In fact, besides the control of the animals' health status, other factors should be considered such as the possibility of economic losses connected with decreased production, possible changes in the hygienic-sanitary qualities of produced foods, the appearance of drug-resistance and, finally, the possibility of adverse effects on the environment.

Conclusions

The following points should be considered in exercising proper veterinary drug surveillance:

1) distribution channels and modes of application of drugs are different from those employed in human medicine;

2) besides ethical reasons associated with the safeguard of animals' health, very important economic interests exist in the field of veterinary drugs, and these have become an essential production factor in livestock industry;

3) possible ADRs do not involve only animal health, but may also concern the quality of foods of animal origin, the health of the consumer and even of the environment.

However, the most important aspect is the necessity to make a basic choice by identifying the priorities of ADRs to consider, i.e. to establish whether the control of animals' health status should receive priority or greater attention should be given to economic-productive aspects, to the hygienic-sanitary quality of produced foods or to the environment.

Once such basic choices have been made, drugs deserving greater attention and animal species to keep under control will be identified.

These are the questions which have to be adequately solved before starting a veterinary drug surveillance programme.

Submitted on invitation.
Accepted on 10 July 1992.

REFERENCES

1. WOOD, A.J. & OATES, J.A. 1987. Adverse reaction to drugs. In: *Harrison's principles of internal medicine*. 10th ed. R. Peterson *et al.* (Eds). New York, McGraw. pp. 402-409.