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REVIEW ARTICLE

A Rational Pharmacotherapeutic Approach for Veterinary Practitioners

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ABSTRACT

Owing to the multiplicity of patients, rational prescribing has been made a relatively challenging task for veterinary practitioners. However this intricate task can be executed through the acquisition of comprehensive knowledge concerning the pathophysiology of respective disease and the pharmacological aspects of drug(s) to be prescribed for a particular ailment. Moreover the implementation of optimal diagnostic aptitude, excellent communication skills and risk-benefit analysis are imperative to confront this challenge. Adoption of a pharmacotherapeutic technique provokes the evasion of empherical and symptomatic therapeutics. A precise diagnosis on the basis of history, clinical findings and diagnostic tests (if applicable) enables the veterinarian to determine the inevitability of therapeutic intervention. Selection of any therapeutic option should be performed only if the potential benefits outweigh the side-effects. Factors related to the drug(s), patient and illness must be taken into consideration for the selection of an adequate dosage regimen. Caution needs to be undertaken to circumvent any stress during handling of animals for therapeutic purpose. Pertinent directions concerning the feeding practices should be provided to the owner, wherever needed. Proper follow-up is required to validate the projected outcome of treatment. Appraisal of the treatment plan is recommended in case of failure to attain the desirable therapeutic goal.

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Veterinary profession stipulates the provision of health care facilities to a variety of patients including companion, food-producing, draught, competitive, zoo and laboratory animals. Therefore rational prescribing and appropriate medication has been a fairly challenging task for veterinary practitioners. Pharmacotherapeutics is the practical execution of pharmacological concepts for the treatment of pathological conditions. It encompasses the pharmacological basis of therapy as well as the pathophysiological aspects of disease process. Adoption of a pharmacotherapeutic technique provokes the evasion of empherical and symptomatic therapeutics. Rational prescribing can be accomplished through the possession of comprehensive knowledge pertaining to the pathophysiology of respective disease and the pharmacological aspects of drug(s) to be prescribed for a particular ailment. Furthermore, the implementation of optimal diagnostic aptitude, excellent communication skills and risk-benefit analysis also play a pivotal role in augmenting the expertise of the prescribers. This manuscript aims to devise a pharmacotherapeutic protocol for efficient execution by the veterinary practitioners.

History taking (anamnesis)

Anamnesis, being the elementary source of information, is considered as a gateway towards diagnosis. However the validity and relevance of such information depends upon the vigilance and observational proficiency of the owner. For example the evidence of previous oral medication and topical insecticide administration can reflect a possible case of drenching pneumonia and organophosphate poisoning respectively. Careful and logical questioning of the owner is vital for precise diagnosis and therefore it should accentuate to the following aspects.

Signalment of the patient

It comprises of the identification number, breed, age, sex, colour and production class of animal (Jackson and Cockcroft, 2002). Gathering of such information can help

to identify and subsequently control the diseases that affect a specific group of animals.

Owner's complaint

The nature or type of complaint should be properly recorded as it provides a basis for imminent findings and reveal the exigency of problem. Owners usually perceive abrupt changes in the behavior of animals which can be incredibly prolific from the diagnostic standpoint.

Disease information

Information regarding the onset and course of illness as well as the signs and symptoms observed by the owner must be suitably inquired. Vaccination, deworming or any other medication (if provided) should also be taken into consideration. This will help to preclude any inadvertent drug interaction or therapeutic failure.

History of the farm

Inquisition about recently performed managemental practices (such as castration, shearing, tagging, dehorning and hoof trimming) may be found quite useful from diagnostic point of view. Shearing and hoof trimming in sheep have been reported to enhance the prevalence of caseous lymphadenitis and lameness respectively (Jackson and Cockcroft, 2002).

Climate and weather

Certain diseases such as fly-strike and endoparasitic infestation are closely correlated with the season. Therefore climatic condition must be taken into account while probing the risk factors for a definite malady.

Clinical examination

Adoption of a topographical approach is requisite to carry out clinical examination. Temperament of the animal should be warily observed as it can signify the degree of morbidity. Deformities of posture, gait and conformation must also be noticed. Visual inspection is critical for the detection of grossly observable lesions (such as abscess, wound, abrasion, fracture, hematoma, tumor, hernia and cyst) or ectoparasitic infestation. Signs and symptoms manifested by the animal should be essentially taken into consideration. The body temperature, pulse rate, respiratory rate, capillary refill time and mucosal colour should be recorded.

Sampling and laboratory tests

Whenever required, the collection of samples (such as blood, milk, pus, sputum, urine or cerebro-spinal fluid sample or skin scrapping) and subsequent laboratory examination should be aptly conducted. Diagnostic tests if considered necessary must be carried out to intensify the apparent diagnosis.

Diagnosis

It should be cautiously carried out on the basis of history, clinical findings and diagnostic tests (if applicable). The precise diagnosis of an ailment enables a veterinarian to determine the necessity for therapeutic intervention. Selection of any therapeutic option should be performed only if the benefits outweigh the side-effects.

Selection of appropriate dosage regimen

Dosage regimen consists of dose rate, route of administration, dosing interval, frequency of administration and duration of therapy. Drug(s) with best suited and specific action against the particular disease must be selected. Selection of appropriate drug(s) and route of administration depends upon the following factors.

Patient-related factors

Following factors regarding the patient must be taken into account for determining an optimal dosage regimen.

Species

Certain drugs are having a narrow margin of safety in particular animal species but not in others. For instance cats, being deficient in glucoronide conjugatory mechanism are unable to properly clear acetylsalicylic acid, acetaminophen and other phenolic drugs (Court, 2007). Oral administration of certain drugs (such as broad spectrum antibiotics) can instigate dysbiosis, superinfection, digestive disturbance and diminution or failure of the drug response in case of animals with a fermenting digestive tract.

Sex

From a physiological and reproductive standpoint a male animal holds a relative uniformity throughout the entire life span. But the lifetime of a female animal consists of gestation, lactation and dry period, each of which is characterized by typical physiological and pharmacological attributes. A significant disparity has been reported between male and female dogs in terms of their response to centrally administered angiotensin II (Doursout *et al*., 1990).

Breed

Breed has been particularly implicated in modulating the drug pharmacodynamics and pharmacokinetics (Fleischer *et* al., 2008). The delayed absorption pattern and associated low bioavailability of moxidectin in Aberdeen Angus compared with holstein calves (Sallovitz *et al*., 2002) provides an excellent example of such variation. Moreover the volume of distribution of amikacin was found to be considerably lower in greyhound dogs as compared to beagles (KuKanich and Coetzee, 2008).

Age

New born animals are characterized by an assorted pattern of pharmacodynamics and pharmacokinetics (Eberini, 2008). Underdevelopment of hepatic and renal systems in immature animals (Baggot and Short, 1984) and greater percentage of body water account for the prolonged drug half life (Nouws, 1992). In consequence of their smaller muscular mass and less prominent veins, neonatal and young animals should not be medicated either through intramuscular or intravenous routes. Accordingly oral administration is generally used in such patients. Factors like diminished gastrointestinal motility (Hilmer *et al*., 2007), reduced plasma protein binding, and impaired hepatic and renal functions (Modric and Martinez, 2010) are implicated to yield a modulated drug response in geriatric animals.

Physiological status

Consideration of this element is attributable to substantial physiological diversity among dry, pregnant and lactating animals. From a pharmacokinetic standpoint, pregnancy-induced hypo-albuminemia can influence the distribution pattern of drugs having high plasma protein binding capacity (Beierle *et al*., 1999). Increased cardiac output and glomerular filtration rate while delayed gastric emptying occur during gestation (Cono *et al*., 2006). Many drugs are contraindicated during pregnancy due to their ability to cross placental barrier and cause fetal malformations. Escalation in drug clearance and volume of distribution but diminution in its half life was observed in lactating cows (Shem-Tov *et al*., 1998). Parentrally administered weak basic drugs are trapped in the milk through the mechanism of ion trapping as basic drugs are more readily ionized when they enter into acidic fluids and vice versa, and as the ionized forms of drug molecules are unable to undergo diffusion therefore they are retained inside the fluids.

Type of animal

The therapeutic management of animals meant for sporting and food purposes require particular attention. Failure to provide a legitimate therapy can lead to disqualification of a competitive animal. Similarly the acts of prescribing and medication for food-producing animals should also be subjected to regulatory considerations.

Number of target animals

While treating an individual animal, the veterinarian is liable to employ the most suitable route of administration. But collective medication at flock or herd level is often required for vaccination and deworming and such practices are costly, time consuming and labour intensive. Consequently, oral administration of drugs (in drinking water or as medicated feed) is considered as the preferred method that enables the veterinarian to treat all animals in a convenient manner with minimal cost and labour.

Temperament

Therapeutic handling of pets and other docile animals carries very little or no risk of injury to the animal or veterinarian. Hence any optimal route of administration can be benefited for the sake of medication. A route of administration that requires minimum handling of the animal (such as intramuscular route) can be used for aggressive and wild animals. Moreover the administration of drugs in drinking water or as medicated feed is also applicable for such patients.

Condition of patient

Oral route is not feasible for the medication of unconscious animals and those suffering from emesis. Similarly intra-rectal drug administration is ineffective for diarrheic patients.

Circadian rhythm

Many significant physiological aspects of mammals undergo alteration with change in circadian rhythm. Hence the impact of circadian rhythm on drug response is not unforeseen (Beauchamp and Labrecque, 2007). A remarkable variation was observed in the volume of distribution and half life of pentazocine administered to dogs in the morning and during the dark cycle (Ritschel *et al*., 1980). Therefore wherever applicable this factor should be taken into consideration while deciding the dosage regimen.

Drug-related factors

The following factors relevant to drug, can also influence the clinician's decision regarding the selection of a dosage regimen.

Dosage form

The type of dosage form can be regarded as an indicator of suitable route to be employed for the administration of a drug. For instance capsules are meant for oral whereas ointments are intended for topical administration. Emulsions and oil-based preparations are not suitable for intravenous administration. Oral sustained-release dosage forms are less efficacious in monogastric species due to a shorter gastro-intestinal transit time.

Physico-chemical properties of the drug

Physico-chemical properties comprise of molecular weight, lipophilicity, hydrophilicity, polarity and degree of ionization of the drug. These factors govern the extent of absorption and distribution of drugs and thus can provide direction for selecting an adequate route of administration. Drugs with tremendous lipid solubility, smaller molecular weight and poor ionization capacity possess high tendency to undergo diffusion and after being given through any suitable route, such drugs can gain access to the blood stream, extracellular fluid and cellular compartments. In contrast, hydrophilic, polar and ionized drugs are effectively absorbed only after being given through a parenteral route.

Nature of the drug

Acid labile drugs and drugs having significant first pass effect (such as nitroglycerine) and those susceptible to enzymatic or microbial degradation become ineffective if given orally. Drugs that are unable to cross blood brain barrier must be given through intrathecal route for the treatment of meningitis.

Spectrum of activity

This is mainly pertinent in case of antimicrobial agents. A narrow spectrum antimicrobial agent should be selected when the target organism is properly identified and its sensitivity is determined. Broad spectrum antimicrobial agents must be reserved for the treatment of mixed type or serious life threatening infections

Type of activity

When attempting the treatment of a bacterial infection, it is also momentous to consider the type of activity possessed by the drug. If optimal drug delivery is uncertain due to inaccessibility of the target infection site or when the host animal is suffering from immuno-suppression then the clinician should opt for a bactericidal drug. But a bacteriostatic drug should be preferably used to combat against an infection associated with toxin producing bacteria.

Adverse effects

Different drugs with analogous clinical indication can substantially vary in terms of their safety margin. Therefore drug with minimal toxicity profile may be chosen.

Drug incompatibilities

Lack of physical or chemical harmony between two (or more than two) drugs indicates that their mixing and simultaneous administration should be strictly avoided. Mixing of incompatible drugs can cause drug inactivation, precipitation or formation of toxic product (Papich, 2007).

Drug interactions

Drugs that are presumed to interfere with the action or pharmacokinetic processing of each other should neither be co-administered nor given in quick succession.

Contraindications

Acquisition of proper awareness concerning the absolute contraindications for all routinely prescribed drugs is an obligation for every clinician. Of particular interest are gestation, lactation, concurrent disease and immaturity in which certain drugs are normally not recommended as their side effects overshadow the advantages.

Drug residues

Drugs that are linked with residual effect should either be avoided in case of animals meant for eggs, milk or meat production or alternatively their recommended withdrawal periods should be strictly followed.

Cost-effectiveness

Unlike human patients and pets whose life and wellbeing are always considered precious, it is the value and productive capacity of a food-producing animal that determines the maximum cost of therapy (Langston and Clarke, 2002). Therefore highly cost-effective drug products must be chosen and unethical pharmaceutical endorsements should be evaded.

Availability

Sometimes veterinarians are required to offer health care services at remote areas where the supply of medicines and other pharmaceutical commodities are limited. Therefore, prior to prescribing a particular drug product it is always recommended to ascertain its availability in the local market.

Disease-related factors

Following aspects relatable to disease should also be taken into consideration while choosing a specific dosage regimen.

Nature of disease

Topical route can be used to alleviate a localized pathological condition. But a systemic disease entails the administration of proposed drug through oral or parentral route to ensure its widespread disposition across the body.

Severity of disease

The rapid onset of drug action after intravenous administration implies its applicability in fulfilling the therapeutic urgency associated with acute conditions whereas the most convenient, cost-effective and patient-oriented route of drug administration should be preferred for chronic diseases.

Desired effect

Certain drugs are linked with diverse responses after their use through various routes. For instance magnesium sulphate exerts purgation after oral administration whereas intravenous injection using a saturated magnesium sulphate solution is used to induce euthanasia. When dealing with such a drug the selection of route should be based upon the desirable outcome.

Medication/drug administration

Medication errors should be always avoided as these can lead to iatrogenic diseases. Provision of adequate training, instructions and ancillary handling aids needs to be ensured if the medication is to be performed by the owner. In such cases, the success of medication depends upon the level of owner's compliance. Poor compliance can enhance the likelihood of recurrent diseases and withdrawal symptoms (Maddison, 2011).

Avoidance of stress

Caution needs to be undertaken to circumvent any stress during handling of animals for therapeutic purpose since some animals may exhibit fright or aggressiveness if improperly handled. On account of altering the release of several hormones, stress can induce physiological modification which in turn influences the usual pharmacological response (Martinez and Modric, 2009). Delayed gastric emptying attributable to stress (Watanabe *et al*., 2002) can remarkably reduce the absorption of drugs administered through oral route. Likewise stress-induced impairment of blood-brain barrier can predispose patients to the neurotoxic action of administered drugs (Friedman *et al*., 1996).

Dietary restrictions

Pertinent directions concerning the feeding practices should be provided wherever required. Certain dietary components can influence the pharmacokinetic pattern of drugs through the induction or inhibition of drug metabolizing enzymes. Moreover drugs that are having interactions with feed should be either given before feeding or alternatively these should be given through a route other than oral.

Follow-up

Proper follow-up is required to validate the projected outcome of treatment. Appraisal of treatment plan is recommended in case of failure to attain the desirable therapeutic goal. Veterinarians are also liable to report the adverse drug reactions to manufacturer and concerned drug regulating authorities.

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