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Veterinary antimicrobial stewardship program: An Indian perspective

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Abstract

Antimicrobial resistance has threatened the public health worldwide and measures have been taken to tackle it, one of the important measures that can effectively reduce the impact of the development of antimicrobial resistance is the implementation of antimicrobial stewardship programs (ASPs). The ASPs used effectively in human medicine in many countries, its application in veterinary practice is still in infancy especially in countries like India. This paper focuses on the need for implementing ASPs in veterinary practice to avert the antimicrobial crisis and outlines the modus operandi of its implementation and execution. Further constraints in its implementation are also discussed.

Keywords: Antimicrobial resistance, antimicrobial stewardship, veterinary, India

Introduction

Antimicrobial resistance among pathogenic and commensal microorganisms emerged globally and lack of development of newer antimicrobials in recent years is becoming a serious public health threat [1-4]. The report of UN *Ad hoc* Interagency Coordinating Group on Antimicrobial Resistance warned that drug-resistant diseases could cause 10 million deaths each year by 2050 [5]. Misuse and/or overuse of antimicrobial agents is suggested as an important cause behind the rise of antimicrobial resistance. This is more commonly attributed to overuse of antimicrobials in food animal veterinary practice and is more common in countries like India, where the ease availability and inappropriate use is higher [6]. There are 27 different classes of antimicrobials are used in animals and many of their counterparts are also used in human medicine, the common antimicrobials used in veterinary practice are penicillin in the form of procaine and benzathine salts, streptomycin, bacitracin, tetracyclines, aminoglycosides, cephalosporins, macrolides, polymyxins and fluoroquinolones [7]. The global average annual consumption of antimicrobials per kilogram of animal produced was estimated to be 45 mg/kg, 148 mg/kg, and 172 mg/kg for cattle, chicken, and pigs, respectively and this was estimated to increase by 67% between 2010 and 2030 [8]. This is very common to observe that many infections and diseases are caused by several multiple drug resistant organism are on the rise in both human and veterinary medicine like those caused by methicillin-resistant *Staphylococcus aureus* (MRSA), MDR *Salmonella*, MDR and XDR *Mycobacterium tuberculosis*, vancomycin-resistant enterococci (VRE), extended spectrum beta-lactamase-producing Gram-negative bacilli (ESBL), carbapenemase producing Gram-negative bacilli (CRE), erythromycin resistant campylobacters, carbapenemase-resistant *Klebsiella pneumoniae* and *Clostridium difficile* infections [4, 9-11]. Hence, there is an urgent need to use these nonrenewable resources responsibly by implementing antimicrobial stewardship programs (ASPs) [12].

Antimicrobial stewardship programs and its status

Antimicrobial stewardship is defined as “A coherent set of actions which promote using antimicrobials responsibly” [12]. The Infectious Disease Society of America (IDSA) has defined it as a “rational, systematic approach to the use of antimicrobial agents in order to achieve optimal outcomes” [13]. Antimicrobial stewardship therefore involves proper selection of antimicrobials, its duration, dose and route of administration for the given patient so that gives maximal effect and also preserves it for future use [12]. The application of ASPs in human medicine, worldwide has shown to improve clinical outcome and has also reduced the emergence and spread of resistant organisms [3, 14].

The goals of ASPs as given by Doron and Davidson [15] are (i) selecting appropriate antimicrobials and administering at right dose, for right duration of time (ii) to prevent unnecessary, misuse or overuse of antimicrobials (iii) to prevent development of antimicrobial resistant organisms.

While selecting the antimicrobial agent the prescribers must keep in mind two aspects one is to give optimal therapy to the patient and second to preserve its effect for the future patient by avoiding its overuse and development of resistance [16]. It is noted that more than fifty percent of the antibiotic prescription are unjustified due to unnecessary prescription and inappropriate use [16-18]. The prescription behavior of many physician / veterinarian is influenced by fellow colleagues and senior physician, empirical knowledge and based on the access and availability to the particular antimicrobials.

The WHO as well as OIE has classified the antimicrobial agents as critically important, highly important, and important groups and certain newly developed antimicrobials were designated not to be used for animal use, while others are to be used exclusively for food animal practice [18]. Creating awareness on antimicrobial stewardship to veterinary graduates, field veterinarians is important as veterinarians are also prescribing huge quantum of antimicrobial agents as part of practice. Thus, the contribution of veterinary practice to evolution and spread of antimicrobial resistant organism cannot be underestimated and is particularly true for dairy farming and poultry sector, where the non-therapeutic use and inappropriate dosing of antimicrobials is common [19]. This misuse of antimicrobials is more common in case of developing countries like ours where, the animal farming practices are higher than other countries due to increased demand for animal protein [18].

The WHO has developed global action plan (GAP) in 2015 to address the issue of antimicrobial resistance and ASPs is identifies as one of the intervention under GAP [3]. In India, ICMR has launched the Anti-Microbial Resistance Surveillance and Research Network (AMRSN) in 2013 for rationalizing ASPs across the country [20]. The ICAR in collaboration with FAO has formed Indian network for fishery and animal antimicrobial resistance (INFAAR) in 2017, at national level with a network of 21 veterinary laboratories to generate data on antimicrobial resistance data for animal and fisheries this will be coordinated by National Institute of Veterinary Epidemiology and Disease Informatics (NIVEDI) and National Bureau of Fish Genetic Research [21]. Therefore, there is a need to widen such network across the country through which a database of antimicrobial susceptibility pattern for different pathogens as well as commensal organisms (indicator pathogens) encountered in veterinary practice can be created and constantly updated. This kind of effort will promote evidence based use of specific antimicrobial agents against specific pathogens rather than use of broad spectrum antimicrobial agents, as it was noted that higher the use of broad spectrum antibiotics greater is the prevalence of resistant organisms [16].

Role of diagnostics stewardship in antimicrobial stewardship

When we discuss about ASPs, the role of rapid and accurate diagnosis cannot be overemphasized and the diagnostic labs plays crucial role in the implementation of ASPs [13]. Rapid disease diagnostics are inevitable for diagnostic stewardship

which in turn ensures prudent use of antimicrobials. On the contrary, in India there are very limited laboratory diagnostic facilities especially for veterinary cases. Therefore, diagnostic stewardship need to be implemented with rapid diagnostics for the clinical cases in field settings.

Implementing ASPs in veterinary practice

The core principles of implementing an antimicrobial stewardship program in veterinary practice given by American Veterinary Medical Association [22] should be considered. Using these principles and based on literature available for implementing ASPs in human medicine [3, 20, 23-26]. The steps can be initiated at every veterinary colleges or university level with functional collaboration among the faculties of clinics, Veterinary Microbiology, Veterinary Public Health and Epidemiology and most importantly Veterinary Pharmacology and Toxicology. The collaborative partnership among the team will ensure effective communication of information by active read back of results by para-clinicians and decision support to the clinicians for prudent use of antibiotics. The team should be given the following responsibilities:

- Preparing treatment guidelines/ antimicrobial use policy for common infectious diseases and conditions affecting organ systems and formulate prescription guidelines. This should also include classifying available antimicrobial agents into first choice drugs, restricted drugs and reserve drugs based on international guidelines of OIE and WHO.
- Development of electronic or online decision support system.
- Regular auditing of the prescriptions the team and mechanism for obtaining feedback from the clinicians must be in place.
- Preparing guidelines for infection control measures that can be adopted in dispensaries, hospitals and in farms.
- Monitoring the antimicrobial agent usage / consumption pattern.
- Active surveillance by carrying out antimicrobial susceptibility testing in a harmonized manner and the drugs to be tested for each pathogen must be defined.
- Should periodically review and analyze the AMR data and suggest modifications in the treatment guidelines, if necessary antimicrobial cycling/ rotation policy may also be adopted.
- Education and training of veterinary graduates and field veterinarians by conducting hands on training and seminars on real world opportunities and blended learning periodically.
- Monitor the ASPs based on the following '5R' parameters right indication, right drug, right dose, right duration and right frequency and publish the findings at regular intervals.

Thus an effective antimicrobial stewardship program can use pre-prescription or post prescription approach or a combination of both for effective implementation and functioning [15].

Challenges to be addressed in implementing ASPs in veterinary practice

With regard to implementation of ASPs in human medicine in India certain barriers were reported these include lack

funding, lack of human resources, lack of information technology, higher priorities, lack of awareness among administrators and prescriber opposition [3, 27]. These barriers are applicable to veterinary practice as well but in addition there are other challenges specific to veterinary practice which is discussed below.

- **Cost benefit:** Implementation of ASPs may not give any added economic benefits in the short course of time to the veterinary institution. But it will certainly preserve the efficacy of antimicrobials thereby; it will reduce the additional loss induced by resistant organisms or the cost involved in their treatment.
- **Inadequate rapid and accurate diagnostic facilities/expertise:** This is an important challenge to be addressed as it directly influences the selection and prudent use of antimicrobials. But its effect can be reduced by investing on creation of state of the art laboratories and increasing the training of students and staff. Conducting blended learning courses on samples collection for specific diseases may be organized.
- **Knowledge gaps in antimicrobial resistance and testing methods:** Relevant data on antimicrobial susceptibility pattern for the region may not be available in veterinary practice, this results in use of broad spectrum or selection of inappropriate antimicrobials. This issue can be resolved by literature search and conducting specific need based research. The veterinary students and field veterinarians may be given periodical training on the issue of antimicrobial resistance and the testing methods.
- **Poor cooperation of farmers in follow up:** This is one of the major issue in veterinary practice as many times the animal owner never returns to clinics after one or two visit or when the animal is apparently normal, citing practical difficulties therefore, most of the time the antimicrobial course could not be completed.
- **Over the counter sale of antimicrobial agents to farmers & para vets:** This is common in India and measures to curb the over the counter sale of antimicrobials must be implemented by enforcing suitable law to monitor the drug supply and sale. Irrational use of antibiotics are aggravated due to over the counter sale of antibiotics either without prescription/reuse of old prescription or informal consent of the farmer/ paravet should be prevented
- **Lack of availability of the certain antimicrobials:** When we wish to implement ASPs specific and narrow spectrum antimicrobials must be available, this is often a constraint in small animal practice wherein, it results in prescription of broad spectrum antimicrobials or newer generation antimicrobials meant for human use.

Conclusion

The issue of antimicrobials resistance is really a threat of public health and it's high time to preserve the efficacy of the 'magic bullets' to the win war against infectious diseases. Implementation of antimicrobial stewardship program in veterinary practice is one of the important measures that can reduce the rate of development of resistance and also reduce the morbidity and mortality associated with infections caused by resistant organism. In addition, we should also employ alternative infection control or prevention measures like improving general hygiene, sanitation, proper waste

management and disposal, vaccination, harnessing the advantages of ethno veterinary practices, implementation of biosecurity measures, etc. to address the issue of antimicrobial resistance. With increasing incidence of antimicrobial resistance and its complexity, the stake holders *viz.*, policy makers, veterinary universities and veterinary practitioners should play pro-active role in making theory into practice of through antimicrobial stewardship programs. Also looking ahead we need to collaborate with medical, fishery and agriculture experts to address the issue under the one health umbrella.

Conflict of interest

None to be declared

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