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Vikash Kumar
Ph.D. Scholar, Division of Dairy Extension, ICAR-NDRI, Karnal, Haryana, India

Jancy Gupta
Ph.D. Scholar, Division of Dairy Extension, ICAR-NDRI, Karnal, Haryana, India

Correspondence
Vikash Kumar
Ph.D. Scholar, Division of Dairy Extension, ICAR-NDRI, Karnal, Haryana, India

Synthesis of policies among stakeholders to combat antimicrobial resistance in livestock animals: Indian perspective

Vikash Kumar and Jancy Gupta

Abstract
Objective: Synthesise the policies to Combat Antimicrobial Resistance among Stakeholders in livestock animals with sharp focus on Indian perspective.
Result and Discussion: The rapid rise in use of antimicrobial seeks the judicious extension approaches and outreach to track the decision-making among the stakeholders. Absence of synthesis and approach focussed on behavioural science resulted weak stress on practices related to judicious use of antimicrobials among stakeholders. The active participation of all stakeholders in decision making, valid veterinary-client relationship, meta-ethnography on antimicrobial themes, insight in to perceived behavioural control, addressing the descriptive norms and adequate consideration resulting wider costs and benefits (and knock-on effects) of related behaviour change can be alternative extension approaches which need insight to address the antimicrobial resistance and increase the field outreach.
Implication: Antimicrobial stewardship and social capital framework can be corpus of the grass-root research to incorporate a clear understanding of the social and economic contexts of antimicrobial usage practice and behaviours ensuring its effectiveness for policy formulations. These aspects can establish effective surveillance and feasible policies at the grass-root level for the control of antimicrobial resistance.

Keywords: antimicrobial stewardship, veterinary-client relationship, surveillance, decision-making, sub-optimal use

Introduction

Antimicrobial resistance is spreading rapidly irrespective of geographical, legal as well economic difference and boundary between the countries in which it is present and can be transmitted to other countries (Harbarth and Samore, 2005) [17]. This issue is gaining pace in developing countries like India which is guided by International human welfare bodies as well as developed countries to take the necessary action and impede the severity of issue by taking the corrective and precautionary measures to fight against it. This issue has linkage with antimicrobial use and resistance among livestock as well as humans, mediated by use of common antimicrobials among them as well as reducing the effectiveness of antimicrobials to cure the antimicrobial diseases and preventing the healing power of antimicrobials to the surgical treatments. Antimicrobial resistance issue calls for surveillance, antimicrobial stewardship and policy formulation aimed at synchronization of efforts by integrating all the stakeholders. The antimicrobial conservation practices demands the strategies which should be consistent with scientific and professional agenda to ensure its sustainability. Collaboration between social scientists and policymakers in designing and evaluating any attempts to introduce behavioural change strategies is lacking the co-ordination and holistic approach in the present time. Adequate consideration is needed which is having the wider costs and benefits (and knock-on effects) of any behaviour change. These different approaches are likely to be acceptable to a varying degree by different stakeholders and also likely to be differentially effective. Considering the seriousness of the issue, United Nations General Assembly High-Level Meeting, held in September 2016, addressed the consequences and situation (World Health Organization, 2016) [44]. The over-use of antimicrobials for dairy animal increased the burden of antimicrobial resistance that is detrimental to human health is now under consideration which requires thorough cross-disciplinary research to incorporate a clear understanding of the social and economic contexts of antimicrobial usage practice and behaviours (Munro *et al.* 2007) [26].

Stakeholders addressing the global catastrophe of antimicrobial resistance

Antimicrobials are prescribed by veterinarians, sold through over-the-counter sales and paravets to the dairy farmers. Antimicrobial use is influenced by farmer's demand for antimicrobials, ineffective or less effective treatment by veterinarians or paravets, the farmer's expectation from the veterinarians and farmer's confidence in veterinarian's diagnosis (Gibbons *et al.* 2013) [14]. Interesting enough, in the antimicrobials resistance discussion, the educative approach has hardly been used in the past. The most important factor in changing behaviour of farmers is social pressure witnessed by the proper guidance of field level veterinary professionals and thus aimed at eliminating the orthodox nature of farmers against this issue. The contribution of farmers as key stakeholder in active participation was hindered because they belong to farm and were end users so they were always under the questioning and as well as social pressure (Lam *et al.* 2016) [22].

Awareness and understanding about the issue

Strategic objective should aim at to improve understanding of the issue through effective communication, training and education *(*World Health Organization, 2015*)* [42, 43]. Several fronts should be considered. Public communication programmes should encourage behaviour change in stakeholders and incorporate antimicrobial resistance as a core component in the professional education of professionals. The financial incentives encourage the prescription of antibiotics in India, which should be addressed through additional legislative support (Kakkar *et al*. 2017) [19].

Policy formulations vis-à-vis Indian perspective

The Indian Council of Medical Research has established a surveillance network for India, targeting medically important microbes as identified by WHO (Laxminarayan and Chaudhury, 2016) [23]. The Red Line Campaign was launched in February 2016 (Travasso, 2016) [40] to control 'over-the-counter sales' of antibiotics and inappropriate prescriptions. The Planning Commission recommended surveillance initiatives for antimicrobial use, development and implementation of National Infection Control and treatment Guidelines, operational research on use of antimicrobials, utilization of antibiotic sensitivity testing facilities and creating awareness about rational use of antibiotics (Planning Commission Working Group 3, 2010.) [29].

Policies to be focussed on alternatives

Cadila approach of developing the antibiotic resistance breakers (ARBs) to restore effectiveness of older classes of antibiotics is an innovative way against issue of resistance (Brown, D. 2015) [8]. Open Source Drug Discovery (OSDD launched by the Council of Scientific and Industrial Research (CSIR) in 2008, to identify new treatment regimens bacterial diseases. It reorganized the bringing of newer drugs in market by sharing of resources, risks and rewards by crowdsourcing with the help of online network and wet-lab collaborators, through web-based wiki portal with Infosys support *(*So AD *et al*. 2014*)* [36]. Nano-antibiotics can improve the scheme of dosage schemes based targeted therapy. The nanoparticles has found its greatest application towards drug delivery systems which are able to deliver higher doses of available antibiotics aim to overcome the problem of drug-resistant bacteria in future (Ramesh *et al.* 2017) [31].

Surveillance

The National Programme on the Containment of Antimicrobial Resistance was launched in the Twelfth Five-Year Plan. The objectives were to establish a laboratory based AMR surveillance system, collect quality data on antimicrobial resistance, strengthen infection control guidelines, promote rational use of antibiotics; and generate awareness about judicious use of antimicrobials in the community *(*National Centre for Disease Control, 2012*)* [27]. The data sources in tertiary medical centres, the surveillance process (especially with respect to diagnostic tests) are limited. Data collection, storage, transmission and analysis also have several limitations. Linking of IPC programmes to antimicrobial resistance surveillance can be identified as key policy integrations to promote more successful such programmes in India (Kakkar *et al.* 2017) [19].

One-health perspective

One health perspective complies the multifaceted and comprehensive measures which are imperative to combat infectious diseases, curb the development and impede the spread of antimicrobial resistance and preserve the future efficacy of antibiotics (Founou *et al*. 2016) [12]. The One Health assessment includes societal costs of missing labour, health-seeking behaviour, animal health impacts, costs of animal-origin food production, and reduced consumer confidence in safety and international trade of such food. Remunerations of surveillance may take years to comprehend which are dependent on effective and accepted interventions (Queenan *et al*. 2016) [30].

Traces of antimicrobial resistance in India

A survey conducted by the National Dairy Research Institute identified tetracycline, gentamicin, ampicillin, amoxicillin, and penicillin due to their lower costs as common antibiotics used in India *(*Grover *et al.* 2013*)* [16]. In India, the most common disease for which antibiotics used is mastitis, against which beta-lactams and streptomycin are commonly used *(*Unnikrishnan *et al.* 2005*)* [41]. Methylene resistant *Streptococcus aureus* resistance has also been isolated from milk samples of cows suffering from mastitis *(31)*. Beta-lactam antibiotics were detected from 11% of milk samples in Delhi *(*National Dairy Research Institute, 2011 [28]. In the same city, 40% of the samples witnessed one or more antibiotics the residues in the meat *(*Bandyopadhyay *et al.* 2015*)* [6]. A high level of resistance was reported from Shiga toxin-producing *E. coli* among calves from Gujarat and the Kashmir suffering from diarrhoea *(*Kawoosa *et al.* 2007; Arya *et al.* 2008*)* [20, 4]. Resistance was abundant for kanamycin and cephalexin antibiotics which were above 50% for seven of the antibiotics tested *(*Arya *et al.* 2008*)* [4]. *Salmonella* isolated from poultry eggs, has also shown to be resistant to many antibiotics groups *(*Suresh *et al.* 2006; Kumar *et al*. 2012,*)* [38, 21].

Severity and losses due to resistance

There is a serious lack of surveillance initiatives in resource-constrained settings where the burden of infections requiring effective antimicrobials continues to become higher (Ashley *et al.* 2011; Cars *et al.* 2008) [5, 9]. Although the majority of antimicrobial use occurs in agricultural settings, relatively little attention has been paid to how antimicrobial use in farm animals contributes to the overall problem of antimicrobial resistance. There is insufficient information about the conditions and factors that lead to the mobilization, selection

and movement of resistant bacteria or resistant genes into and between animal and human populations (Alvan *et al.* 2011) [3]. Failure of initial antimicrobial therapy leads to prescribing of more costly and many times more toxic alternatives, encouraging the experiential prescribing of broad-spectrum of antimicrobials in future diagnosis (Boucher *et al.* 2009) [7]. The global health security risks and losses of GDP due to antibiotic resistance ranges from 0.4 to 1.6% *(*Smith *et al.* 2005*)* [35]. The annual cost of antibiotic-resistant infections accounts to approximately between US$21 million and US$34 million in the present time *(*Spellberg *et al.* 2011*)* [37].

Approaches to fight the catastrophe of antimicrobial resistance

Highlighting the roles of different stakeholders from prescription to usage of antimicrobials in light of socio-economic factors which affect the decision making ability and choice of farmers to adopt the antimicrobials should be highlighted. The practices among the dairy farmers can be corrected and marked by exploring the role of social science in the biological phenomena of antimicrobials resistance which will be helpful in further policy formulation. Social science therefore has a key role to play in measuring, modelling, understanding the changing the social environment in relation to antimicrobial resistance. It is evident that lack of synthesis and approach regarding existing behavioural science research relevant to antimicrobial resistance and also weak focus on behaviour change strategies can dump global prosperity. Different approaches are likely to be acceptable to a varying degree by stakeholders which are differentially effective. Assessing the general awareness, behavioural aspects, animal husbandry practices of dairy farmers with respect to environmental impacts and spread of antimicrobial resistance through human- animal linkage can be assessed further provided by exploratory study at grass root level. Ascertaining perceptions of these stakeholders about antimicrobial use and highlight some of the ethical issues and challenges in changing practice can be helpful in preparing appropriate strategies and strengthening the policies regarding the judicious use of antimicrobials.

Awareness about antimicrobial resistance and antimicrobial usage pattern

Evidence from the literature suggests that inappropriate use of antimicrobials in dairy cows continues to occur on farms resulting in negative consequences for animal and human health (Sawant *et al.* 2005; Raymond *et al.* 2006) [34, 32]. Antimicrobials available for treatment of bacterial disease vary in their availability (prescription by veterinarians vs. over-the-counter purchase by the farmers), generation and class of antimicrobials used, route and ease of administration, spectrum of activity, labelled uses of antimicrobials, and consideration of withdrawal periods before selling the milk in to the market (Hill *et al.* 2009) [18]. The need to focus on awareness should be focussed, both for farmers and antibiotics providers, which was highlighted by awareness survey conducted by WHO (World Health Organization, 2015) [42, 43]. Also, the approaches should be considered to assess the antimicrobial conservation practices and the perceived severity of the issue from farmers felt perspectives. The uses of sub-therapeutic doses of antibiotics are considered as driver for the aggravating resistance issue in countries where the use of antibiotics for growth promotion is not prohibited legally (Laxminarayan and Chaudhury, 2016.) [23].

Policies and strategies against antimicrobial resistance vis-à-vis Indian perspective

Over- the-counter sales of antibiotics should be prohibited. The consumption of expensive classes of antibiotics like carbapenems has incresed in India, mostly due to over-the-counter sales and inappropriate prescriptions (Laxminarayan *et al.* 2013) [24]. One Health approach to surveillance is lacking in India. Another weakness of the existing surveillance systems for antimicrobial resistance in India is that they do not account for the use of antibiotics (Ganguly *et al.* 2011) [13].

Alternative approaches to extend the extension outreach against the issue

Seeking a novel approach, there is need to crumb together decision-making process so that availability of still medicines could be ensured even in next 100 years. One alternative approach to prudent use of antimicrobials involves boosting the cattle's own ability to defend itself (Del-Rio-Navarro *et al.* 2012) [10]. It incorporates electing the judicious dosage regimens for traditional antimicrobials based on pharmacodynamics principles and emerging new antimicrobials to target new bacterial targets. Thus preserving effective antimicrobials as long as possible should be encouraged. This approach should be used by extension researchers to track the present level of awareness, knowledge and inculcate the 'ought to be' information in it. Good communication skills and participation in continuing education programmes could increase veterinarian's self-reliance in clinical and diagnostic practices because they would be able to convince the farmer's demand and able to escape the biasness. In order to have the conversation with farmers when they are unsatisfied, they should be provided counselling in animal husbandry and management, training them to engage in shared decision-making could ensure valid veterinary-client relationship. The meta-ethnography can be conducted to identify themes on perceptions of antimicrobial prescribing decisions to reduce inappropriate antimicrobial use mediated by over-the-counter sales and paravets (Tonkin-Crine *et al.* 2011) [39]. Descriptive norm that 'veterinarians prescribe antimicrobials' and injunctive norms that include 'moral consideration' can be used to assess the issue of increasing resistance could impart significant importance in designing normative interventions by the change agents (Goldstein *et al.* 2008) [15]. Behavioural intentions of farmers regarding antimicrobial usage can be modelled by measurement of attitude, subjective norm, and perceived behavioural control (PBC). Thus, it evaluates performance of behaviour, perceived normative views, and their perceived control regarding the antimicrobial usage among the stakeholders (Ajzen, 1991) [2].

The 'Social dilemma' due to inconsistency among appropriate decisions as suggested by veterinarians, made by neighbours and personal choice could be addressed by considering proximity and scalogram and Venn-diagram analysis. 'Tragedy of commons' is the area of thought can be useful to deal with major societal and global problems. (Hardin, 1968). The judicious use of antimicrobials from farmer's community view point is not always consistent with optimal use from the perspective of the individual farmers (Metlay *et al.* 2002) [25]. This demands the intervention of social scientists to be addressed by the anthropologist seeks extension outreach. The need for antimicrobial stewardship to deal with the factors underlying the behaviour norms and attitude to target the behaviour change interventions can be a better extension

approach to address the issue. Social capital framework can be alternative approach in psychological context to determine the impact of trust and reciprocity on farmer's preparedness to delay in using antimicrobials or its overuse under the particular circumstances (Ronnerstrand and Sundell, 2015) [33].

Limitations to assess the issue and track its outreach

The information collected to establish surveillance are mostly based on the expressed responses and perception of the respondents to the issue, their ability to recall and on the opinion expressed by them after being approached by the surveyor. Farmers might not maintain record books or update various records regarding antimicrobial usage. Therefore accuracy of data might depend on the memory of the respondents. However every possible effort to make sure that the data collected might be the best of the knowledge of the respondents and bear minimal distortion could be made. Hence, complete freedom from individual bias and prejudices of the surveyor cannot be claimed under normal conditions. The policy to be formulated on the basis of the outcome of the survey may not confirm to the international policy specifications because perceived need is different between a developing and developed country. Care should be taken to include all the relevant variables for the study, still missing of some of the variables cannot be ruled out easily because very few researches in India had conducted extension research at grass-root level. Nevertheless, it can be hoped for a better insight to understand awareness of dairy farmers (small, medium and large) as well as assessing the usage pattern of antimicrobials with respect to the level of decision making at the farm level could be well recognized by the efforts of social scientists and serve as hub to integrate all stakeholders in their decision-making regarding judicious use of antimicrobials.

Conclusion

The contribution of social science to combat the antimicrobial resistance has not been well recognised at present because of the resistance being a biological issue. In this condition, if extension agents and policy makers conduct significant package of practices aimed at publishing a corpus of research could be insufficient and ineffective in the absence of ground level surveillance. Yet, the issue of research outside of the discipline of biological science and integration with social science that draws on psychological and extension outreach concepts and theories, and visualise the involvement of all the stakeholders from antimicrobial prescription to antimicrobial usage could be identified. Concepts and theories like antimicrobial stewardship, prudent use of antimicrobials and one-health approach have already borne fruit thus forming the basis for the sought interventions. The mounting call for behavioural and social science integrated research is unavoidably going to bring more attention of the extension researchers and policy makers into the field of antimicrobial research which is the demand of the scenario. In addition to veterinarians, it should also include pharmacist and farmers in modelling decision making which has the carry-over effect on each other's decision regarding the antimicrobial usage. Interventions in Policy making regarding the practices in veterinary hospitals followed by diagnostic approach and clinical practices influenced by farmer's demand and economic condition of farmers seek a valid veterinary-client relationship. Veterinary ethics guiding the involvement of veterinarians in continuing education awareness programmes will have a role to play examining the foundations could act as pillar to tackle issues of antimicrobial resistance. The substantial increase in resources invested in antimicrobial resistance research by the research councils along with extension scientist's potential, it is predictable that the future contribution of the extension discipline will far beat up the contractions and lack of insight in order to pave the way for addressing the issue that had become catastrophe in the present date.

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