ejpmr, 2018,5(5), 252-258

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

IMPROVING KNOWLEDGE OF ANTIMICROBIAL RESISTANCE AMONG MEDICAL UNDERGRADUATES

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Article Received on 22/02/2018 **Article Revised on 14/03/2018** **Article Accepted on 05/04/2018**

ABSTRACT

Background: Globally, resistance to antimicrobial agents (AMA) has been recognized as a major health concern. The main objective of this study is to evaluate the impact of an educational intervention on the knowledge of antimicrobials and antimicrobial resistance (AMR) among medical undergraduates. This will not only boost their understanding but also act as a guide in the development of effective interventions for containment of AMR. **Methods:** We administered a 16 point questionnaire, before and after a 1 hour interactive educational lecture on rational use of AMA, development of AMR and measures to curb it. Individual question changes and overall student changes were analysed. All hypothesis tests were two tailed with a significance level of 0.05. **Results:** Of the 450 participants, 357 (79.3%) took the pre-test and post-test and were present for the interactive educational lecture. Most of them (89%) were aware that an AMA should be taken for a required duration to ensure complete therapy. However, many believed that AMA speed up the recovery of common cold and cough (51.3%). Significant improvements ($p < 0.001$) were seen with the largest improvement seen with those questions that discussed that administration of newer AMA and fixed dose combinations translate into higher cure rates. **Conclusion:** This AMR awareness initiative resulted in significant improvement in medical undergraduates' knowledge of rational use of AMA. Promoting AMR awareness, if replicated across populations could lead to positive health outcomes.

KEYWORDS: Antimicrobial Resistance, Antimicrobial Agents, Multidrug Resistance, Antibiotics, Knowledge Awareness, Educational Intervention.

INTRODUCTION

Antimicrobial agents (AMA) are one of the most commonly prescribed drugs across the globe.[1,2] But substantial increase in the consumption of AMA withstands their phenomenal success.[3] AMA are widely prescribed for upper respiratory tract infections which are caused by viruses in nearly 80-90% cases.[4,5] This indiscriminate use of AMAs produces a selection pressure for the emergence of resistant strains of bacteria. Although development of resistance is a natural process, it is the irrational and indiscriminate use of AMA in humans and animals that is hastening the process. These resistant strains of bacteria and resultant AMR are difficult to treat and demand more extensive therapy.

Over the past several years, antibiotic resistance especially multidrug resistance to both gram positive and negative pathogens has become a worldwide problem.[6] Rapidly increasing rates of infection due to methicillin-resistant S. aureus (MRSA),[7] vancomycin-resistant E. faecium (VRE), and fluoroquinolone-resistant P. aeruginosa have been reported from the Centers for Disease Control and Prevention (CDC).[8] Experts now suggest that stringent measures are required urgently to curb the menace of AMR.[9,10] One of the most important measure to minimise the development and spread of AMR is rational use of antibiotics.[11,12]

Apart from targeting prescribing physicians, young medical students also need to be a focus for group interventions. Medical students are an integral part of future health related progress of the community in development of health educational programs and policies. It is important to understand their motivation, knowledge and attitudes towards rational use of AMA before development and implementation of safe AMA promotional programs. Gaining a baseline understanding of current AMA related knowledge must be a first step in program development. Thus, this study is an attempt to sensitize and educate medical undergraduates about rational use of AMA and steps to curb AMR.

METHODS AND MATERIALS

Study set up

The present study was conducted among the second year MBBS undergraduate students in the Department of Pharmacology, Vardhaman Mahavir Medical College (VMMC) and Safdarjung Hospital, New Delhi, India.

Study design

A cross-sectional, voluntary, self-administered questionnaire survey was administered that consisted of 16 questions assessing subjects' knowledge and attitude regarding AMA usage and AMR. A pre-test and post-test experimental design was used. All the questions with similar ideas were grouped together either as knowledge items or attitude items (Table1) and a 5-point Likert scale, where responses ranged from 'strongly agree' to 'strongly disagree' was used in the study. Questionnaire was filled anonymously by the medical undergraduates.

The questionnaire was pilot tested in a small group of ten subjects to assess its reproducibility and suitability. Feedback was taken from these participants regarding their understanding with respect to the questionnaire. The Cronbach alpha was estimated to be 0.7, suggesting good internal consistency and an overall reliability. After completion of the pre-test, all the participants were educated in a one hour interactive educational lecture about rational use of AMAs, appropriate prescribing, AMR, its importance, and preventive measures to curb their indiscriminate use. The post test was undertaken after two weeks of the educational lecture. The same group of students were used in the pre-test and post-test.

Ethical approval: The study was conducted after approval by the Institutional Ethics Committee of Vardhaman Mahavir Medical College & Safdarjung Hospital, New Delhi, India.

Statistical analysis

Responses to questions were calculated as absolute numbers and percentages. Changes in pre-test and post-test scores were analysed using paired t test. All hypothesis tests were two tailed with a significance level of 0.05. Analyses were performed using SPSS.

RESULTS

A total of 450 students were administered the questionnaire in the study. Among them, 357 (79.3%) students participated voluntarily and completed the pre-test and post-test. In order to simplify the analysis, we reduced the five point response options of the Likert scale into three, such that agree includes strongly agree and agree, disagree includes strongly disagree and disagree and the third option was neither agree nor disagree. Table 1 describes dimension-wise overview of the items on knowledge and attitude included in the questionnaire. Table 2 shows statement-wise responses to knowledge and attitude questionnaire of undergraduate medical professionals on a pre-test and post-test expressed as absolute numbers (%).

Table. 1: Dimension-wise overview of the items included in the questionnaire.

Knowledge related items
Antibiotic designates synthetic & naturally obtained drugs that attenuate microorganisms.
AMA speeds up the recovery of common self-limiting ailments like common cold and cough.
AMA can cure certain infections due to viruses.
AMR is a significant problem in our hospital.
Amoxicillin-clavulanic acid is safe in pregnancy.
Hospital antibiotic policy based on evidence based guidelines and local sensitivity pattern determines empirical/presumptive antimicrobial prescribing.
In non emergency conditions bacterial culture and sensitivity should be done before initiating therapy.
AMA should be available only on a prescription by a registered medical practitioner to curb AMR.
Attitude related items
AMA are commonly overused due to increasing self-medication by patients.
AMA should be taken for atleast 2 days before stopping it.
AMA are indicated in all cases of diarrhea with severe dehydration.
AMA are indicated in all cases of common cold and cough to prevent secondary bacterial infections.
AMA should be stopped after the completion of requisite prescribed duration of therapy.
Strict adherence to AMA in chronic diseases could minimize resistance and ensure complete recovery.
AMA should be preferably taken in fixed dose combinations.
Newer AMA should be used as they offer higher cure rates with less chances of resistance.

Table. 2: Statement-wise responses to knowledge and attitude questionnaire of undergraduate medical professionals on a pre-test and post-test expressed as absolute numbers (%).

Statement	Pre-Test			Post-Test			P value#
	Agree	NA/ND*	Disagree	Agree	NA/ND*	Disagree	
Antibiotics are both synthetic & naturally obtained	284 (79.6)	16 (4.5)	57 (15.9)	334 (93.6)	8 (2.2)	15 (4.2)	<0.001
AMA speed up recovery of common cold and cough	183 (51.3)	36 (10.1)	138 (38.6)	53 (14.8)	12 (34)	292 (81.8)	<0.001
Overuse of AMA is due to self-medication	325 (91)	16 (4.5)	16 (4.5)	341 (95.5)	6 (1.7)	10 (2.8)	<0.001
AMA are taken for at least 2 days before stopping	185 (51.8)	102 (28.6)	70 (19.6)	77 (21.6)	32 (9)	248 (69.5)	<0.001
AMA are indicated in diarrhoea with severe dehydration	91 (25.5)	67 (18.8)	199 (55.7)	27 (7.6)	11 (3.1)	319 (89.4)	<0.001
AMA prevent secondary bacterial infections in viral diseases	166 (46.5)	37 (10.4)	154 (43.1)	73 (20.4)	21 (5.9)	263 (73.7)	<0.001
AMA can cure viral infections	137 (38.4)	38 (10.6)	182 (51)	34 (9.5)	16 (4.5)	307 (86)	<0.001
AMA should be stopped after prescribed duration	319 (89.4)	14 (3.9)	24 (6.7)	337 (94.4)	9 (2.5)	11 (3.1)	<0.001
Bacterial culture & sensitivity should be done routinely	289 (80.9)	32 (9)	36 (10.1)	329 (92.2)	12 (3.4)	16 (4.5)	<0.001
AMR is a significant problem in our hospital	274 (76.8)	68 (19)	15 (4.2)	338 (94.7)	7 (2)	12 (3.4)	<0.001
Hospital antibiotic policy determines empirical treatment	277 (77.6)	63 (17.6)	17 (4.8)	321 (89.9)	26 (7.3)	10 (2.8)	<0.001
Amoxicillin-clavulanic acid is safe in pregnancy	165 (46.2)	124 (34.8)	68 (19)	271 (75.9)	62 (17.4)	24 (6.7)	<0.001
Strict adherence to AMA could minimize resistance	199 (55.7)	62 (17.4)	96 (26.9)	274 (76.8)	46 (12.9)	37 (10.4)	<0.001
AMA sold only on prescription	309 (86.6)	28 (7.8)	20 (5.6)	336 (94.1)	13 (3.6)	8 (2.2)	<0.001
AMA should be preferred in fixed dose combinations	267 (74.8)	57 (16)	33 (9.2)	132 (37)	28 (7.8)	197 (55.2)	<0.001
Newer AMA offer higher cure rates	224 (62.7)	67 (18.8)	66 (18.5)	126 (35.3)	32 (9)	199 (55.7)	<0.001

*NA/ND=neither agree nor disagree, #P value for paired t test

Knowledge on AMA and its rational use

In baseline assessment, majority of the participants (n=284, 79.6%) were aware that antibiotics are naturally obtained from microorganisms and their analogues can be synthesized in the laboratory. More than three quarter (n=274, 76.8%) of the respondents correctly identified that AMR is an important and serious problem. However, there was a notable lack of knowledge about AMAs and its usage. In particular, only 38.6% (n=138) of the respondents agreed that AMA do not speed up the recovery of common cold and cough and 49% (n=175) were not aware that AMA do not cure infections due to viruses. Approximately 55.7% (n=199) of the participating students were aware that AMA are not required in cases of diarrhoea with dehydration unless it is associated with bacteriological infection that is confirmed on stool culture. There was statistically significant improvement in knowledge regarding the role of AMA in viral infections (p<0.001) and self-limiting illness like diarrhoea (p<0.001).

Selection of an AMA

Majority of the participants (n=289, 80.9%) agreed that bacterial culture and sensitivity testing should be done before initiating antimicrobial therapy. Our participants (n=277, 77.6%) were aware that empirical/presumptive therapy could be initiated in certain cases in accordance with the hospital antibiotic policy based on evidence based guidelines and local sensitivity patterns.

AMA selection and therapy varies in children, adults, elderly and pregnancy. While assessing respondent's knowledge regarding AMA usage, only 46.2% (n=165) of the participants were aware that amoxicillin clavulanic acid is safe in pregnancy at baseline. Most of them (n=267, 74.8%) were unaware that certain fixed dose combinations like norfloxacin-tinidazole, ofloxacin-tinidazole offer no added advantage in disease management. These irrational combinations increase the chances of resistance and adverse drug reactions. Significant improvement were identified for the selection of AMA in pregnancy and fixed dose combinations (p<0.001).

Awareness about development of AMR

Indiscriminate and widespread use of AMAs has led to the development of AMR. At baseline, among the factors favouring development of AMR, self-medication was recognised as an important contributor (n=325, 91%). As for strict adherence to AMA in chronic diseases that could minimize resistance and ensure complete recovery, only 55.7% (n=199) of the respondents were aware of it. On the other hand, 89.4% (n=319) of the respondents agreed that AMA should be stopped only after completion of requisite prescribed duration of the therapy and not after symptomatic improvement (n=70, 19.6%).

Measures to curb AMR

When it comes to the practices towards AMA usage, purchase of AMA only on prescription by a registered medical practitioner was recognised as an important step to curb AMR by 86.6% (n=309) of the participants. However, majority of them (n=224, 62.7%) incorrectly associated newer AMA as a replacement to existing therapy to achieve higher cure rates and decreased resistance. There was significant improvement for all the participants regarding the status of newer AMA and measures to curb AMR ($p<0.001$).

DISCUSSION

We aimed to assess the knowledge of medical undergraduates about AMA and AMR. We observed that majority of the medical students need sensitization about AMA, their usage and AMR. Traditionally, antibiotics were defined as compounds naturally produced by a microbe that kills or inhibits the growth of another microbe. In modern terms, an antibiotic has broadly come to mean any synthetic or naturally occurring low molecular weight molecule that inhibits or attenuate the growth of other microorganisms.[13] About 80% of our participants were aware of this distinction between antibiotic and AMA. It is known that AMA if used appropriately can cure common bacterial infections. However, there are conditions wherein they do not provide symptomatic relief or hasten recovery of infections like common cold, cough and uncomplicated diarrhoea. These self-limiting viral infections mostly require only supportive therapy in the form of anti-histaminics in cold and cough and fluid replacement in diarrhoea. Antibiotics are indicated in cases of bloody diarrhoea or if bacterial infection is confirmed on stool microscopy and culture.[14] More than half of the students answered correctly that AMAs are not required for watery diarrhoeas due to viral etiology. These findings are in line with Garcia et al who evaluated AMR and antimicrobial prescribing among medical doctors in two large hospitals in Lima and Peru and demonstrated that almost 90% of them were aware that antibiotics have no role in acute diarrhoea.[15]

However, only about a quarter of the participants were aware that administration of an antibiotic do not speed up the recovery of upper respiratory tract infections like common cold and cough. Similar results have been reported by Khan et al and Godycki-Cwirko et al.[16,17] In these cases, antibiotics are indicated only in superimposed secondary bacterial infections based on susceptibility testing. Majority of the students understood the importance of culture and sensitivity testing before initiating antimicrobial therapy. In certain emergency conditions, empirical therapy may be initiated and modified based on local sensitivity patterns. Thriemer et al reported similar findings among a survey with final year medical students and residents in the University Hospital of Kisangani, Congo where 89.7% of the participants agreed that knowledge of local antibiotic resistance pattern was essential for good prescribing.[18]

In certain populations like children, elderly and pregnant women AMA cannot be prescribed as in general population. Therapeutic efficacy and safety is an important concern in these groups. For example, drug exposure during pregnancy poses a risk to the growing fetus. Many AMA such as tetracycline, doxycycline, and streptomycin are contraindicated during pregnancy because of teratogenicity. Only a few AMA like penicillins, macrolides, cephalosporins have been used relatively safely during pregnancy.[19] Most of our participants were aware that certain AMA groups like penicillins, amoxicillin- clavulinate are safe during pregnancy.

Fixed dose drug combinations (FDCs), are combinations of two or more active drugs in a single dosage form. FDCs are acceptable only when the dosage of each ingredient meets the requirement of a defined population group and when the combination has a proven advantage over single compounds administered separately in therapeutic efficacy, safety or compliance.[20] Some rational FDCs included in the 19th model list of essential medicines prepared by the World health organisation (April 2015) are sulfamethoxazole plus trimethoprim, levodopa plus carbidopa, lamivudine + zidovudine + nevirapine and antitubercular drug combinations. However certain FDCs, for instance, combination of ciprofloxacin + tinidazole, ofloxacin + ornidazole and nimesulide + paracetamol do not offer any advantage in the terms of clinical cure or decreased duration of therapy.[21,22] This fact needs to be emphasized as only few students understood the hazard posed by irrational FDC in terms of increasing exposure and risk of adverse drug reactions.

Developing countries may have limited access to antimicrobials, particularly to new drug classes, hence AMA play a pivotal role in limiting the morbidity and mortality.[1,23,24] However, widespread inappropriate and indiscriminate use of AMA has led to increased exposure risk at the patient level and AMR at the community level.[25,26] WHO defines AMR as the "resistance of a microorganism to an antimicrobial drug that was initially effective for treatment of infections caused by it".[27] A multifaceted strategy is required to control the

emergence of development of AMR and to improve the health care outcomes.[28] It is recognized that high prevalence of AMR requires action at the level of the patients, physicians and regulatory authorities to curb it. Education of both physicians and patients would form the cornerstone of the strategy. Patient's expectations, health care professionals and patient's lack of education and availability of over the counter medication in our country are some important determinants that can increase the chances of development of resistance.[29] Rational prescribing by the medical professionals is of paramount importance in the battle against AMR. They should be aware of evidence based guidelines and local sensitivity patterns to ensure prescribing in compliance with the hospital antibiotic policy. To maximize the benefit-to-risk ratio of AMA therapy, it is essential to ensure that the most appropriate drug should be chosen for the patient. It has been recommended that selection of the drug should be based on its efficacy, safety, cost and suitability for that patient.[30] In addition, it is crucial to be vigilant for potential risk factors that may increase the possibility of a patient experiencing adverse events or failure of treatment. For example, concomitant use of antitubercular drug with oral contraceptives may result in contraceptive failure, or combination of two hepatotoxic drugs or nephrotoxic drugs should preferably be avoided.[31]

Self-medication is an important contributor to increasing prevalence of AMR.[32,33] Patients need to be educated about the importance of appropriate dose timing and duration of therapy. This assumes even greater importance/significance in chronic diseases like tuberculosis, leprosy etc. They should be encouraged about the appropriate and rational use of antibiotics.[11,12] Our participants were cognizant of this fact. At the regulatory level, implement strict regulations on the sale and purchase of AMAs, their availability only on a valid prescription by a registered medical practitioner should be enforced. More than three quarter of the respondents agreed with this notion.

In recent years, the discovery and approval of new classes of antimicrobials for human use has been declined. Despite some encouraging new discoveries, pharmaceutical industry has not kept pace with the ever-evolving antimicrobial resistance. Most of the newer drugs are modifications of the known antibiotic drug classes and approaches.[34] These newer AMAs address some of the current problem of antimicrobial resistance. However, their usage must be reserved for severe life threatening conditions caused by multi drug resistant bacteria and not as a routine replacement for infections cured with existing drugs. Majority of the students need to be sensitized that newer AMA will not lead to higher cure rates for common infections. They should not be routinely prescribed on an outpatient basis and their use restricted under strict monitoring and supervision in a hospital setting.

Our results demonstrate that the medical students though aware of AMA and its uses; their knowledge on AMR should be strengthened. Recent studies also focusing on public education aim at highlighting the problem of irrational and unjustified use of antibiotics and the need to curtail the development of resistance and adverse drug effects.[6, 12, 35] Our study enlightens the importance of outcome based education, to ensure that the medical graduates are fit for practice.[36] This can be utilized for educating the students about rational use of AMA, so that as prescribers, they maximise their effective and efficient use and minimize the development of resistance.[16,37]

CONCLUSION

We conclude the awareness of antimicrobial resistance as being a serious public health concern. Our study provides an insight into the importance of principles of protocol development for AMA use in health care system, apart from teaching about AMA. The medical education strategies should aim to change the behaviour of health care professionals, not only increase the knowledge. The students should be made aware and a sense of responsibility should be nurtured; that as future doctors, they are not only responsible for the benefit and the welfare of their patients but also for the society at large. A good knowledge of antimicrobial agents and positive attitude towards rational prescribing at health care levels would assist in better implementation of policies to curtail AMR.

ACKNOWLEDGEMENT

None.

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