Brief Original Article

Poor compliance with the antibiotic policy in the intensive care unit (ICU) of a tertiary care hospital in India

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Abstract

Introduction: Most developing countries are adopting antibiotic policies to contain the acute problem of drug resistance; however, several obstacles prevent their fulfillment. This study was undertaken to prospectively determine the compliance with the antibiotic policy in the intensive care unit (ICU) of a tertiary care hospital and possible reasons for non-compliance.

Methodology: Compliance with the newly introduced antibiotic policy was studied for a period of six months. A total of 170 cases from the ICU were included. Relevant information regarding patient characteristics, treatment details, infection control, and antibiotic prescribing practices in the ICU with reference to the antibiotic policy was collected. Reasons for non-compliance were studied.

Results: The rate of compliance with the antibiotic policy was 21.18%. Heavy use of antibiotics prior to the time of admission in the ICU was the major cause of non-compliance. Microbiological investigation had been sent in only 51.17% of the cases and change in treatment protocol based on culture report was done in 53.3%. The rate of use of third-generation cephalosporins was 76.78%.

Conclusions: We found non-compliance with the antibiotic policy in the ICU mainly due to improper and inappropriate antibiotic usage in other indoor units of the hospital. In our case, a policy covering the entire hospital is required to meet the goals of antibiotic usage restriction. An effective surveillance, review, and evaluation process should be an integral part of the policy, even in developing countries, to measure the effects of such policies.

Introduction

With the emergence of drug resistance and multidrug-resistant organisms (MDRO) as a major threat to public health, more nations are adopting antibiotic policies to contain excessive usage of antibiotics. Developed nations have provided substantial evidence showing that guidelines to control antimicrobial resistance can be effective, but these pertain to resistance trends and antibiotic usage suited to their conditions only [1].Requirements in developing countries are quite different. Though data are insufficient to create trends for specific organisms and antibiotics, there is clear-cut evidence of growing resistance that is affecting patient and therapeutic outcomes directly and affecting the economy of the country indirectly [2]. Realizing the immediate need for antibiotic usage guidelines, the Global Antibiotic Resistance Partnership (GARP) was launched in order to develop actionable policy recommendations specially suited to low-income countries. Even though many developing countries have implemented some guidelines, they are far from strictly adhering to those [3]; hence, there are no sufficient studies to prove the guidelines' effects.

The intensive care unit is conducive to the development of antimicrobial resistance primarily because of the considerable use of antibiotics prophylactically, thus reducing risk of specific infections at the cost of emergence of MDRO. There have been a good number of studies about compliance with the antibiotic guidelines and assessment of antibiotic usage in various units of the hospital [4,5], but very few of these have tried to focus on the causes of non-compliance.

The present study was undertaken to determine compliance rates with the antibiotic policy and the shortcomings that might have prevented its proper implementation in the ICU. To the best of our knowledge, this is the first report of its kind from the subcontinent.

Methodology

An antimicrobial usage guideline was devised for the 20-bed multidisciplinary adult ICU in a tertiary level 1,200-bed healthcare center in Varanasi, north India. The guidelines consisted of antimicrobial use protocol based on prevalence of pathogens according to sites of isolation and their corresponding antibiograms. Patient risk stratification was determined based on previous history of antibiotic intake, days of hospitalization, and clinical condition of the patient. Guidelines for managing specific situations such as ventilator-associated pneumonia, bacteraemia, and urinary tract infections were provided. Proper instructions regarding appropriate sample collection prior to presumptive therapy were provided in the guidelines along with several options for escalation (change or addition of antibiotics following culture sensitivity report), de-escalation (withdrawal of antibiotics), or continuing with the presumptive therapy, based on the microbiology report. Standard drug dosages of the antibiotics were also provided in the guidelines, based on a consensus from all the clinicians of the hospital, specifying correct doses to be given based on body weight/age, preferred route of administration, and proposed duration of therapy. Use of third-generation cephalosporins was assessed and considered inappropriate when it failed to follow the guidelines based on the type of therapy (prophylactic or empirical), combinations of antibiotics, and course of therapy. Data were analysed statistically using odds ratio (95% CI). Clinical staff was motivated to adhere to the antibiotic policy; their compliance was observed for a period of six months prospectively. Data about patient characteristics including demographic factors, clinical features, and diagnosis, along with daily prescribing of drugs in doses as noted in the treatment sheets were collected and assessed using a standardized data collection form. Whenever non-compliance was observed, the attending physician was asked for an explanation. Finally, each case was evaluated on these aspects against the guidelines for compliance based on the collected data.

Along with this, the effectiveness of infection control practices was also studied through regular detection of nasal methicillin-resistant *Staphylococcus aureus* (MRSA) carriage rate and vancomycin resistant enterococci (VRE) carriage rate in stool among the ICU patients. Briefly, nasal swabs from anterior nares were collected weekly from all the patients admitted to the ICU and were inoculated onto mannitol salt agar media. Following 48 hours incubation at 35°C, all the mannitol fermenting colonies presumptive of *S. aureus* were further plated on 5% sheep blood agar and confirmed by Gram staining, catalase, and tube coagulase testing. MRSA screening was performed with a 30 µg cefoxitin disc (Hi Media Labs, Mumbai, India) as per standard protocol [6]. For screening of VRE carriage in stool, stool samples/rectal swabs from the patients were taken weekly and plated on bile esculin azide agar (BEAA) with 6 µg/mL vancomycin (Hi Media Labs, Mumbai, India). Colonies suggestive of enterococci (colonies with a dark brown halo) were subcultured on brain heart infusion agar (BHI) and further confirmed by Gram staining, catalase test, growth in 6.5% NaCl, and PYR test (pyrrolidonyl amidase).

Results

A total of 170 cases were studied, comprised of 98 male and 72 female patients. Of these, 35.29% (n = 60) were diagnosed with respiratory infections, 28.24% (n = 48) with traumatic injuries, and 22.94% (n = 39) with postoperative complications. The compliance rate with the antibiotic policy was 21.18% (36/170), implying that in only 21.18% of cases the policy was followed.

Microbiological investigation had been sent for only in 51.17% (87/170) of the patients following admission to the ICU. The majority (71.26%, 62/87) were endotracheal tube cultures, of which only 3.4% (3/87) were sent for investigation prior to the initiation of the empirical therapy. A change in treatment protocol based on culture report was done in 53.3% (32 of the 60 culture-positive patients) of the cases, whereas de-escalation was done in 33.3% cases (16 out of 48). However, the drug dosages for the antibiotics were correctly used with respect to age or body weight of the patients in compliance with the guidelines in 87.05% (148/170) of the cases. None of the treatment sheets mentioned a stop date for the antibiotic prescribed, but treatment was reviewed daily. Vancomycin and/or teicoplanin had been used empirically in 20% of the cases (8 out of 40) and linezolid in 3.7% (1 of 27 cases). The usage rate of third-generation cephalosporins was 76.78% (132/170). Ceftriaxone was the most commonly used antibiotic. Third-generation cephalosporins were significantly associated with inappropriate use as prophylactic therapy (p < 0.05), mostly when used in combination with other antibiotics (p < 0.05), as shown in Table 1.

Table 1: Factors associated with third-generation cephalosporin use

	Appropriate usage (n = 40)	Inappropriate usage (n = 92)	Odds ratio (95% CI)	P-value
Therapy				
Prophylactic	13	63		
Empiric	27	29	0.22(0.10-0.49)	<0.001*
Multiple therapy				
Single antibiotic	9	8		
Antibiotics in combination	31	84	3.05(1.11-8.38)	<0.045*

*p-value significant

Table 2: Reasons for non-compliance to the antibiotic policy

Reasons	No. of cases (%) (n = 95)
Patient transferred to ICU already on antibiotics	62 (65.26)
Culture report sterile	16 (16.84)
Unavailability of blood culture bottles	5 (5.2)
Diagnosis could not be made	10 (10.52)
Unaware of existence of such a policy	2 (2.1)

The nasal MRSA carriage rate was found to be 36.3% among patients admitted to the ICU; their fecal VRE carriage rate was 55.5%.

The prevalence of commonly isolated pathogens and their susceptibility profiles did not vary notably in the pre- and post-assessment periods. However, sample contamination rate due to improper collection was markedly decreased, from 21% to 2%.

The major reasons for non-compliance with the policy, as shown in Table 2, was the fact that most of the patients had prolonged hospitalization in other indoor units (65.26%; 62 of the 95 non-compliant cases) and were subsequently transferred to the ICU while on several antibiotics. The physicians in the ICU, therefore, had not much choice other than continuing treatment. Following prior antibiotic use, 16.84% (16/95) had sterile blood culture, as no causative organism could be isolated.

Discussion

The ICU is an ideal location for resistance in today's hospitals due to the interplay between poor infection control and the tremendous selective pressure of antimicrobial agents [7].

In most situations, initial antimicrobial therapy is decided based on the clinical features of the patient. Situations become worse when, due to prior antibiotic use, repeated microbiological cultures fail to confirm the pathogenic cause, as seen in this study. Moreover, extensive surveys of ICUs have shown that in most situations, decisions regarding treatment initiation and termination and choice of antibiotics are made by the clinicians alone without the involvement of a microbiologist in nearly 95% situations [8].Under such circumstances, treatment becomes host directed instead of being pathogen directed [9] and consequently follows a broad spectrum approach, thus requiring the use of more and more antibiotics. Host-directed treatment also limits the scope for de-escalation in the quest for providing full protection to the patient irrespective of the susceptibility pattern of the causative pathogen.

Although it is well known that restricting antibiotic use can reduce antimicrobial resistance, there are very few studies that show a direct association. Among the few, the association is most evident between reduced use of third-generation cephalosporins and the prevalence of multidrug-resistant Gram-negative bacilli [10]. Developing countries lack evidence of third-generation cephalosporin use in hospitals, though higher ESBL prevalence indirectly suggests their overuse [11]. In our setting, the prevalence of ESBL among the *Klebsiella pneumoniae* isolates has been reported to be 46% [12], which is quite high. Moreover, the study showed significant inappropriate prophylactic use of third-generation cephalosporins, mostly as combination therapy. Limiting the use of third-generation cephalosporins by substituting with other drugs should be a priority.

Another indicator of the indiscriminate use of third-generation cephalosporins was the high fecal carriage rate of VRE (55.5%). This is not only indicative of tremendous selective pressure on the gut flora by antimicrobial agents with potent antianaerobic

activities [13], but also warns against the probabilities of the transfer of drug resistance leading to outbreaks of MDROs in the ICU.

Though vancomycin has been used as first-line therapy in 20% of situations in the ICU, earlier studies have justified this practice based on a higher prevalence of MRSA [8]. Our study showed considerable nasal MRSA carriage rate (36.3%). The prevalence of infections caused by MRSA in our setting was 40.61% [14]; empirical glycopeptides use, therefore, can be regarded as a correct approach. At the same time, it should be noted that infection control practices must be equally valued to contain the emergence and spread of MRSA.

The major cause of non-compliance as detected in this study supports the established fact that many of the resistant pathogens in the ICU are actually brought from elsewhere in the hospital [7]; therefore, monitoring antibiotic usage only in the ICU might not be very effective. This study also revealed that ensuring regular microbiological culture facilities and proper dissemination of guidelines can possibly further increase compliance. In this study, though a proper audit based on electronic data and their retrospective assessment was not done, feedback from the physicians helped to determine the major problems with the stewardship program. Studies have shown that audit and feedback strategies can be significantly effective in increasing adherence to antibiotic usage guidelines [15]. The provision of a written explanation for any deviation from the hospital policy, which was not done in this study, could have accounted for a higher compliance rate and a better assessment of the major hindrances against compliance.

Another important factor in this context is the non-participation of the pharmacy in the implementation of the guidelines. It has been shown that proper medicine management by the pharmacy helps to ensure medicine is appropriately administered [16]. Antibiotic cycling programs can then be applied to minimize antibiotic selection pressures.

Implementation of the antibiotic policy may seem very relevant in ICU settings, but in our situation, a policy covering the entire hospital would be required to meet the goals of antibiotic usage containment. Therefore, we recommend the implementation of such guidelines in every hospital unit based on continuous surveillance of antibiograms. Active involvement of the pharmacy by keeping records and monitoring broad-spectrum antibiotic use along with prompt, judicious, and tactful decisions regarding the use of antimicrobials by infectious disease specialists, and

physicians' willingness to abide by the decision based on their clinical acumen is imperative for the effective implementation of antibiotic policies in low-resource settings.

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