Original Article

Impact of antibiotic restriction on broad spectrum antibiotic usage in the ICU of a developing country

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Abstract

Objective: To reduce rates of nosocomial pneumonia and cost of antibiotic therapy.

Methods: By means of a policy implementation the following broad spectrum antibiotics were restricted to usage in the ICU for 72 hours: Cefepime, Meropenem, Imipenem, Tazocin, Polymixin B and Vancomycin, after an institutional based pharmacy and therapeutic committee approval. The ICU pharmacist would alert the ICU residents or consultants after 48 hours of the computer based antibiotic entry that the order would expire within hours. Telephone approval was obtained followed by a formal consultation if deemed necessary by the ID specialist or primary team. Antibiotic usage was standardized by defined daily doses (DDDs) per 1000/patient-days.

Results: A cumulative 34% reduction was seen in the use of all broad spectrum antibiotics in our ICU after the enforcement of the antibiotic restriction policy. The largest reduction was seen in the use of Tazocin (190 DDDs) and Meropenem (60 DDDs). The policy resulted in a reduction by 40% of overall broad spectrum antibiotic pharmacy costs. The number of multidrug resistant organisms has remained static but the ventilator associated pneumonia rates have declined.

Conclusion: Streamlining the formulary to control antibiotic choices and the creation of a restriction program using the expertise of infectious disease physicians resulted in significant reductions in the use of and expenditure for broad spectrum antibiotics (JPMA 57:484:2007).

Introduction

Resistance of common hospital-acquired bacteria to antibiotics is a worldwide problem. It can lead to increased morbidity, mortality, length of hospital stay, and healthcare expenditures.[1] In the setting of an intensive care unit (ICU) of a developing country where health costs are borne by the patients and to some extent the hospitals, it is causing a huge economic burden.[2] Our patients are getting sicker due to the rampant usage of broad spectrum antibiotics leading to resistance and nosocomial infections with more and more virulent organisms.[3] Acute increases in antibiotic resistance may be due to antibiotic selection pressures, over-crowding and other environmental changes, all of which are present in our setting. The most resistant organisms are found in units where patients are immuno-compromised, are subject to invasive procedures or remain for long periods.[4] Institutions elsewhere in the world have enhanced patient care through therapeutic optimization of the use of antimicrobial agents through the use of antibiotic restriction policies implemented widely throughout the hospital.[5]

Patients suffering from nosocomially acquired sepsis have a high mortality rate and spend a prolonged time in the ICU, leading to high direct and indirect costs[6], [AKUH ICU Quality Indictors 2004-5]. Particularly productivity losses due to premature death represent a considerable burden to the society and entire families are destroyed economically. Irrational use of antibiotics is a direct cause of emergence of such resistant nosocomial infections and a national healthcare issue with no targeted interventions present in Pakistan. Studies in the West have indicated that restriction of usage of some antibacterial agents is a successful method to decrease antibiotic consumption and a way to bring cost savings and help prevent emergence of resistant microorganisms in hospitals.[7] However, no such policies have thus far been tried in centers here.

International rates for resistant organisms such as MRSA (methicillin resistant staphylococcus aureus) and ventilator associated pneumonias (VAP) have been on the rise. Studies have quoted a rate of 40% with a mortality of close to 16%.[8,9] These are reflected in our Hospital acquired Infection (HAI) per 1000 patient days rate in the last quarter prior to the antibiotic restriction policy of 3.89 per 1000 patient days (PD), which has increased from 1.0 /1000 PD. Similarly our ventilator associated pneumonia rates had increased in the time period prior to the policy from 1.2 per 1000 PD to 5.3/ 1000 PD. This was above the 50th percentile of NNIS (National nosocomial infection surveillance) USA data.[10]

Implementation of antibiotic restriction policies

have helped in controlling rates of resistant organisms spread and contain costs in intensive care units across the world. However it has never been reported in a developing country such as Pakistan, where resistance trends are on the rise.

The present study had an objective to show that restricting the use of broad spectrum antibiotics reduces rates of usage and cost of antibiotics, as well as shows reduction in the rates of nosocomial pneumonia.

Materials and Methods

The study was conducted for 6 months from October 2005 till March 2006, in the intensive care unit of a tertiary care hospital in an urban center of the country, serving a population of over ten million. It is a multidisciplinary 12 bedded adult ICU. All drug and antibiotic entries are made centrally by means of a computer based service, linked from all units of the hospital to the pharmacy.

After formulating an antibiotic restriction policy by a team comprising of intensivists, infectious disease specialists, microbiologist and a surgeon, the following broad spectrum antibiotics[11] were restricted to usage in the ICU for 72 hours: Cefepime, Meropenem, Imipenem, Tazocin, Polymixin B and Vancomycin. This was implemented after an institutional based pharmacy and therapeutic committee approval was obtained. Appropriate cultures were to be obtained prior to therapy. The ICU pharmacist would alert the ICU residents or consultants after 48 hours of the computer based antibiotic entry that the order would expire within hours. This was done by means of a stamp on the chart and verbal indication. At this point the residents were to obtain 'ID (infectious disease) approval' from a team of designated ID specialists identified earlier. Telephone approval was obtained followed by a formal consultation if deemed necessary by the ID specialist or primary team. No cost was incurred to the patient if only an approval was sought. In case of approval being denied or not obtained the antibiotic would auto- discontinue (auto-d/c).

Although antibiotic control programs have been successful in other countries, this represents the first attempt at successful antibiotic control in a large Pakistani teaching hospital.[12] The Antibiotic restriction policy was enforced from January 1st 2006. Therefore, we looked at data 3 months before and 3 months after the policy implementation (two quarters).

Antibiotic usage was standardized by defined daily doses (DDDs) per 1000/patient-days.[13] It is an international unit for drug utilization measurement and is defined as "the average maintenance dose per day for a drug used for its main indication" This has been assigned by the WHO (World Health Organization) Collaborating center for drug statistics methodology.[14-19] It enables the researcher to access trends in drug consumption based on inventory/distribution data and is a technical measurement unit that allows comparison.

DDD = No. of Units used x no. of grams per unit / DDD of antibiotic in grams.

'Patient days' were defined as occupied bed - days or :

No. of beds x occupancy x no. of days[17]

All data were entered into SPSS version 14 and analyzed. Data analysis was done by unpaired t-testing with a confidence interval of 95% and a p of < 0.05 significant.

Cost data were expressed in rupees and percentage of prior use. Changes in antibiotic usage was determined by comparing the total usage in two blocks of October - December 2005 and January - March 2006 when the streamlined formulary and restricted group of antibiotics, controlled by the Infectious Disease (ID) and ICU teams were initiated.

Results

Our compliance of antibiotic restriction policy was 89%, whereby 89% of the time the policy was adhered to and on other occasions either no approval was obtained or the primary team deferred continuation of the drug. Figure 1 shows comparative data of the two time periods being reviewed and the impact on various antibiotics and their number of daily defined doses (DDD) per 1000 patient days. Apart from Vancomycin and Amikacin, the use of which went up by 45 points and points respectively all other antibiotics showed a reduction in the DDD. A cumulative 34% reduction was seen in the use of all broad spectrum antibiotics in our ICU after the enforcement of the antibiotic restriction policy. The largest reduction was seen in the use of Tazocin (190 points) and Meropenem (60 points).

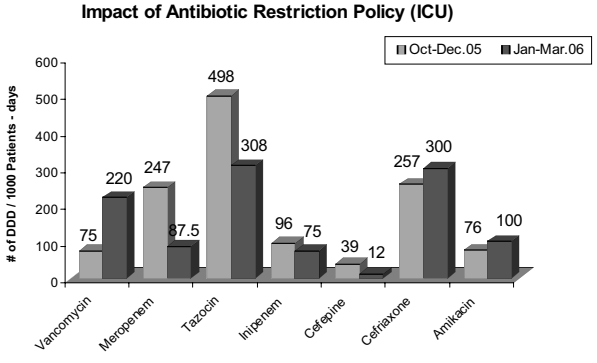

Figure 1. Impact of antibiotic restriction policy (ICU) on DDD /1000 patient days.

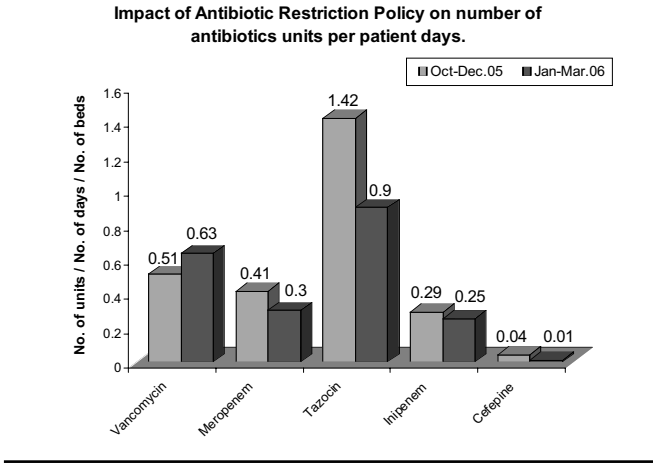

Figure 2. Impact of antibiotic restriction policy (ICU) on No. of units of antibiotics.

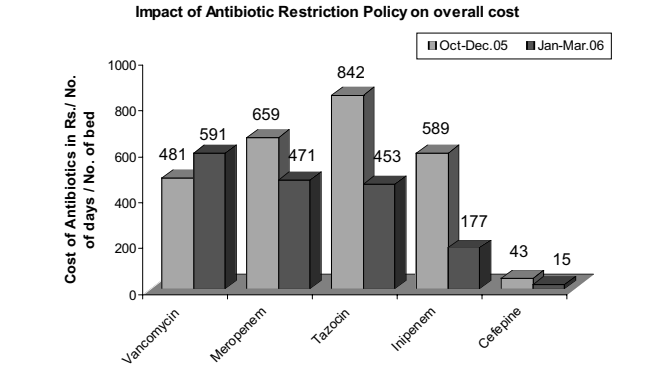

Figure 3. Impact of antibiotic restriction policy (ICU) on cost of antibiotics in Rupees.

Figure 2 shows the impact on number of units of antibiotics per patient days. Again there is an overall reduction of 33% in the usage with the exception of vancomycin. Taking a Confidence interval of 95% and 0.05 as the significant value of p, this proved significant (p value of 0.04) by Student's t-test analysis.

The successful implementation of the model resulted in a reduction by 40% of overall pharmacy broad spectrum antibiotic costs, as shown in Figure 3. The cost of vancomycin went up by a modest 22%, however Tazocin and Meropenem showed a decline of 46% and 29% respectively.

We also monitored the growth of multidrug resistant organisms such as MRSA, VRE (vancomycin resistant enterococcus), Acinetobacter, Enterobacter, Pseudomonas and Klebsiella. The incidence has remained static however the cumulative VAP rates, defined as a positive culture by tracheal aspirate or broncho-alveolar lavage (BAL) with chest X-ray findings or clinical correlation on a patient who is being mechanically ventilated has gone down from 5.3 to 2.3 HAI /1000 PD in the quarter following the policy implementation.

Discussion

An antibiotic restriction program constituted an effective and cost-saving strategy to optimize antibiotic use in a tertiary care center ICU, improving cost and emergence of multi drug resistant organisms as well as ventilator associated pneumonia rates and significantly reduced the usage of broad spectrum antibiotics. In a developing country where resources are limited antibiotic prescription patterns limiting the use of different antimicrobials should be promoted to reduce the selection pressure that aids the development of resistance.[20] This in turn would reduce length of stay and severity of illness amongst the critically ill patients and also the cost incurred.[21] Surprisingly the use of Vancomycin, a glycopeptide antibiotic particularly used for MRSA, went up increasing the cost as well during the study period, however this may correlate to the slight reduction seen in MRSA and VAP rates in the ICU. Although the trends are favourable, a review of simply one quarter is insufficient to reach a definitive conclusion, however, it is a step in the right direction.

Streamlining the formulary to control antibiotic choices and the creation of a restriction program using the expertise of infectious disease physicians resulted in significant reductions in the use of and expenditure for broad spectrum antibiotics. Problems faced were delay in drug order processing and drug delivery by pharmacy if continuation was decided. There was often confusion about who will take the ID approval whether it would be the ICU team or the primary team. Ours is an open ICU where patients are admitted by primary teams and managed conjointly by the intensivist and an ICU team as well as looked over by the primary team. The therapeutic use of 2nd line agents increased and the compliance rate is also on the incline. Despite these problems this program proved successful and there was an overall reduction in the pharmacy costs which make up a large part of the patient bill.

Acknowledgements

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