



USE OF CARBAPENEMS AND THIRD GENERATION CEPHALOSPORINS IN ICU AND THE EFFECT OF AN EDUCATIONAL MODULE IN RATIONALIZING USE

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ABSTRACT

OBJECTIVE: The global increase in antibiotic resistance is promoted by the widespread and indiscriminate use of broad spectrum antibiotics. The future looks bleak regarding availability of new antibiotics particularly against gram negative organisms. Rational use of antibiotics is vital in establishing a successful strategy to control and prevent both the clinical impact and the development of further resistance. The objective of the study is to determine the current practice of carbapenems/third generation cephalosporins usage in ICU of Government Medical College Amritsar and to estimate the proportion of appropriate usage in the form of rationality in therapy after educational intervention. **METHODS:** The present study was conducted for a period of one year. The pre and post intervention studies were carried out for four months each with one month of educational intervention between them. Educational intervention was done in the form of interactive sessions regarding rational use of antibiotics based on accepted international guidelines. The rationality of usage of carbapenems/third generation cephalosporins was assessed based on antibiograms and clinical condition of the patients. The total use of the antibiotics was calculated as Defined Daily Dose for 76 patients. **RESULTS:** Educational intervention did not lead to decrease in the overall usage of antibiotics in the ICU as DDD in pre and post intervention phase was 1773 and 1762 respectively but 14% improvement towards rationality in prescribing carbapenems/third generation cephalosporins was observed with 12% reduction in the duration of treatment. **CONCLUSION:** Educational intervention, sensitization of health personnel and formulation of an institutional antibiotic policy can be effective tools in promoting rational use of antibiotics. Institution based antibiotic policy is a need of the hour. A Drug and Therapeutic Committee is required to implement the institutional antibiotic policy which can help in reducing antibiotic resistance in the long run.

KEYWORDS : Carbapenems, Daily Defined Dose, Antibiotic Resistance, ICU

INTRODUCTION

The global increase in antibiotic resistance is promoted by the widespread use of broad-spectrum antibiotics, creating a continuous selective pressure on bacteria. This resistance is depleting the number of effective antimicrobial agents and most of the drugs currently in the clinical pipeline are modifications of existing groups of antibiotics and are only short-term solutions.(1) Since there have been few new agents active against Gram-negative bacteria in particular developed over the last two decades, it is important to make the best of existing antibiotics. Therefore, rational use of antimicrobial agents is vital in establishing a successful strategy to control and prevent both the clinical impact and the development of further resistance. Careful selection of the appropriate antimicrobial agent combined with correct dosing, duration of treatment and route of administration are all important to the success of this strategy and need to be coupled with antimicrobial resistance surveillance. (2) Progress against the treatment strategy approach for optimising clinical outcomes whilst preventing antibacterial resistance based on antibiotic de-escalation will be reviewed with particular emphasis on the role of the carbapenems. This approach attempts to balance the need to provide appropriate initial treatment whilst limiting the emergence of antibacterial resistance.

METHODOLOGY:

This was a Prospective interventional study conducted for a period of one year in the ICU of a tertiary care hospital. Sample Size estimation by Two proportion hypothesis testing – to achieve a difference of 25% improvement in appropriate usage of carbapenems and 3rd generation cephalosporins after the learning module intervention, with a power of 80% and alpha error of 0.05, a sample size of 59 is needed in each arm. We aim to achieve a number of 75 before and 75 after intervention.

Pre-existing data from case files of patients admitted was recorded which included demographic profile of the patients, and timing along with the frequency of the carbapenems and 3rd generation cephalosporins administered. The pre and post intervention studies were carried out for four months each with one month of educational intervention between them. Educational intervention was done in the form of interactive sessions regarding rational use of antibiotics based on accepted international guidelines. The rationality of usage of carbapenems/third generation cephalosporins was assessed based on antibiograms and clinical condition of the patients. The total use of the antibiotics was calculated as Defined Daily Dose per 100 patients for 76 cases and compared to post intervention phase to determine whether

there is a reduction in antibiotic use.

Educational intervention: Educational intervention by conducting Lecture sessions within the hospital using Powerpoint slides (1 hour). Topics covered were:

- Audit of the prescription practice for antibiotics in ICU
- Antimicrobial susceptibility pattern for infections from ICU
- Pharmacological issues of carbapenems and 3rd generation cephalosporins
- Advice on appropriate use of antibiotics for important conditions in the ICU
- Provide feedback of results obtained during preintervention

Eligibility criteria: All consecutive seventy six adult patients admitted to ICU except those who were already on carbapenems and third generation cephalosporins at the time of admission . Even the terminally ill (e.g. malignancy) were excluded from the study.

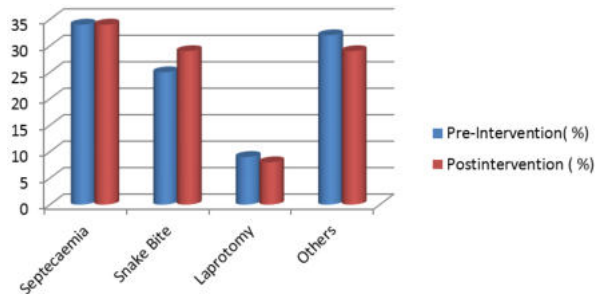
Primary Outcome Parameters:

1. Pattern of carbapenem or 3rd generation cephalosporin usage in the ICU
2. Rationality of above antibiotics used with relation to choice, dose, route, frequency, and duration
3. Percentage of patients on carbapenems or 3rd generation cephalosporins with proper indication in compliance with existing or literature based guidelines.
4. Overall consumption of above antibiotics as DDD per 100 patients
5. Improvement of percentage with proper indication and decrease in overall consumption after educational intervention

RESULTS & DISCUSSION :

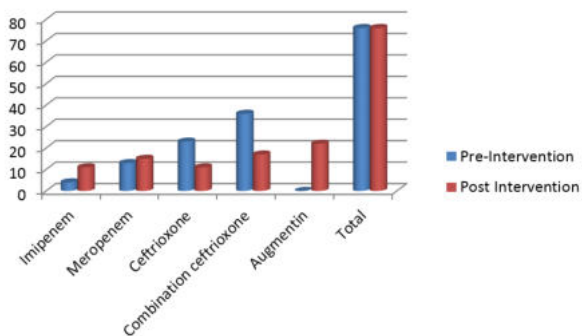
Global increase in antibiotic resistance is promoted by widespread & indiscriminate use of broad spectrum antibiotics. No new antibiotics are in the pipeline as drug research in this field is not considered profitable by pharmaceutical companies. Hospitals are ideal reservoirs for the acquisition of resistance due to high concentration of organisms, many of which are extremely pathogenic, inhabitants with compromised health and large amounts of different antibiotics constantly in use. Nosocomial infections are mostly due to resistant pathogens and are difficult to treat so for adequate initial treatment of serious infections we start empirical therapy. Empiric therapy is based on the site and severity of infection, and physician assessment of the likelihood for deterioration and mortality. Therapy chosen should cover the likely infecting pathogens and for that awareness of predominant causative pathogens is obligatory from up to date specific antibiogram that helps in selection of empirical antibiotics

Data for 76 consecutive adult patients meeting the eligibility criteria in each phase of pre and post intervention admitted to ICU was analyzed for the study. In the pre intervention group majority (34%) of the analyzed cases were of septicemia, 25 % were snake bite cases, 9% were post laprotomy cases shifted with endotracheal tube to ICU and others (32%) were the patients with head injury, pneumonitis, meningitis, poisoning, CVA, LVF and drug reactions. Comparison of type of case admission in ICU in both the phases is shown in graph 1.



Graph 1: Comparison of types of cases in pre and post intervention phase

The most commonly prescribed antibiotic in pre intervention phase was combination of ceftriaxone with betalactamase inhibitors sulbactam (47%). Single antibiotic ceftriaxone, imipenem and meropenem was given to 31%, 17% and 6% respectively. Antibiotic prescription comparison in pre and post intervention phase is described in graph 2.



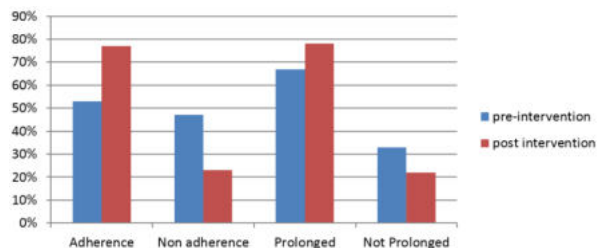
Graph 2: Comparison of antibiotic prescription in pre and post intervention phase

Recommended empirical antibiotic therapy for patients with snake bite, peritonitis, septicemia and pneumonia are Augmentin, Piperacillin+Tazobactam, carbapenem/Cefepime and Augmentin/ Piperacillin+Tazobactum where as prescribed antibiotics in pre-interventional phase were only ceftriaxone or its combination with sulbactam. Adherence to the guidelines regarding indication, antibiotic choice and dose pattern improved in the post intervention period. Overall improvement in adherence for use of cephalosporins and carbapenems in post intervention period was 75%. Prescription of cephalosporins and carbapenems was analyzed and compared with the recommended guidelines in different conditions. It was observed that with the intervention there was 100% improvement in the prescribing pattern for snake bite and 92% septicaemia cases whereas pattern remained the same even after intervention for peritonitis and pneumonia cases as described in table 1

Table 1: Recommended and prescribed antibiotics for different clinical conditions

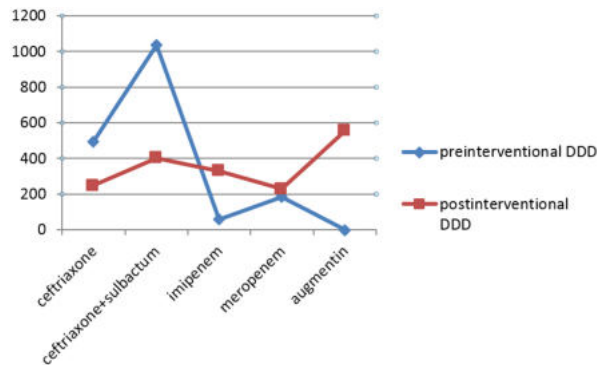
Diagnosis	Recommendation	Pre-intervention prescription	Post-intervention Adherence
Snake bite	Amoxycillin + clavulanic acid	Ceftriaxone+ Sulbactum	100%
Peritonitis	Piperacillin+Tazobactum	Ceftriaxone+ Sulbactum/ Ceftriaxone	0%
Septicaemia	carbapenem/Cefepime	Ceftriaxone	92%
Pneumonia	Amoxycillin + clavulanic acid / Piperacillin+Tazobactum	Ceftriaxone+ Sulbactum/ Ceftriaxone	0%

Adherence to the treatment guidelines improved from 53% to 77% but overall duration of treatment was prolonged in post- intervention phase from 67% to 78% as shown in graph 3



Graph 3: Adherence to prescription and treatment duration guidelines in pre and post intervention phase

This non-adherence was mainly because of the lack of awareness among the treating physicians posted in ICU and there was a remarkable improvement after educational intervention especially for the prescription of patients of snake bite and peritonitis where adherence was 100% and 93 % respectively.



Graph 4: DDD of the intravenous drugs used in preintervention phase and post intervention phase

This interventional study mainly focused on the impact of interventions on the use of third generation cephalosporin and carbapenems in patients of ICU. The results shown in our study had a wide deviation from the standard international and national guidelines regarding use of antibiotics in different clinical situations in ICU. There was not much decrease in the overall consumption of antibiotics as the DDD in the pre and post intervention period was 1773 and 1762 respectively but from the results shown in graph 4 divulge a positive effect of educational intervention. The adherence to guidelines for use of antimicrobials improved which is reflected by increased utilization of amoxicillin and clavulanic acid combination where as the use of ceftriaxone and sulbactam dwindled dramatically. Educational intervention, sensitization of health personnel and formulation of an institutional antibiotic policy can be effective tools in promoting rational use of antibiotics. Institution based antibiotic policy is a need of the hour. Ours is the under resourced institution so proper implementation and periodic evaluation of this policy is essential to achieve results. A Drug and Therapeutic Committee is required to implement the institutional antibiotic policy and continued search for new methods of intervention is the need of the hour. This can help in reducing antibiotic resistance in the long run.

CONCLUSION:

Administering the adequate empirical therapy with broadest-spectrum antibiotic therapy at the time of admission to improve outcomes (decrease mortality, prevent organ dysfunction, and decrease length of stay) using ICU specific antibiograms. Once patient is settled then focusing on de-escalating the antibiotics to avoid long course of empiric therapy as a means to minimize resistance and improve cost-effectiveness.

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