RESEARCH PAPER

Antimicrobial Justification form for Restricting Antibiotic Use in a Pediatric Intensive Care Unit

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Objective: To study whether introduction of an 'antimicrobial justification form' deters clinicians from prescribing restricted antimicrobials and results in de-escalation of these antimicrobials.

Methods: Clinicians were asked to fill a justification form if prescribing an antimicrobial from the pre-identified restricted group. Antimicrobial usage pattern over next year was compared with that in the one year preceding the introduction of justification form.

Results: Significant overall decrease in antimicrobial usage (40.5% *vs* 34.6%) was noted in the post-intervention group along with a significant increase in the de-escalation of antibiotics.

Conclusion: Introduction of a justification form before prescribing antimicrobials or at the time of deferring de-escalation can be useful in restricting usage of antimicrobials

Keywords: *Antimicrobial agents, Antimicrobial resistance, Nosocomial infections.*

Nosocomial infections are very common in intensive care unit (ICU) settings, leading to prolonged morbidity, escalation of treatment costs, and mortality [1-5]. Antibiotic resistance increases due to inappropriate empiric antimicrobial treatment [6].

There is evidence that early and adequate administration of antibiotics ("Hit Hard - Hit Fast" approach) improves survival in severe sepsis and septic shock patients [7]. Thus it becomes difficult for a physician to balance the approach of early and aggressive treatment against conservative approach. The antibiotic stewardship can be done by different means – either by restraining the prescription or switching to a narrower spectrum, or stopping antibiotics when not needed [8, 9]. All these methods of restricting the use of antimicrobials carry potential of creating conflict between the treating physician and the infection control team. In this study, we evaluated efficacy of an intervention wherein physicians were made to fill a justification form before using selected spectrum antimicrobials.

METHODS

The study was conducted in a 14-bedded pediatric intensive care unit (PICU). All children admitted to PICU from 1st June 2013 to 31st March 2014 (post-intervention group) were enrolled in the study, and those admitted at the same time previous year (1st June 2012 to 31st March 2013) were taken as historical (pre-intervention) controls. The study was approved by the Institutional ethical committee.

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Piperacillin-tazobactum, meropenem, linezolid, vancomycin, colistin, tigecycline, teicoplanin, daptomycin, aztreonam, ticarcillin, amphotericin B, fluconazole, voriconazole, and caspofungin were classified as restricted group antimicrobials. Records of patients admitted in PICU during pre-intervention period were retrieved and patients who received antimicrobials from "restricted group" were labeled as group A. The 'Restricted antimicrobial use justification form' was introduced in PICU on 1st May 2013 and the staff was educated about it for a month, and the study started from 1st June 2013. Admissions to PICU during this period (post-intervention group) were prospectively analyzed and those patients who received antimicrobials from the restricted group were labeled as group B.

The justification form had to be filled within 24 hours of starting a restricted antimicrobial. The treating consultant was notified of the culture report within 48-72 hours by the infection control nurse. The treating consultant was asked for a justification form if the

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antibiotic was decided to be continued. This was again reviewed on day seven, and any decision to continue the antibiotic had to be followed by filling another justification form. Any change of antibiotic within the restricted group also warranted filling a justification form. Monthly review of the forms was done by the hospital infection control committee. A sample size of 288 cases and 288 controls was calculated to be sufficient to document a reduction in use of restricted antimicrobials from estimated 40% to 25% with a power of 0.9 and type I error of 0.01. Student t-test and chi-square test were used for statistical analyses.

RESULTS

There were 872 patients in the pre-intervention period out of which 353 (40.5%) received one of the restricted antimicrobials (Group A). There were 821 patients in the post-intervention cohort, of which 284 (34.6%) received one of the restricted antimicrobials (Group B) (P=0.01). The population of children in both study periods was comparable in terms of mortality and the average duration of PICU stay (***Table* I**). Children in group B were significantly sicker with higher number of ventilated patients (112 *vs* 83, P<0.001) and higher mean PRISM scores (6.9 vs 5.2, P=0.001) in comparison to Group A. There was also a reduction in the number and average duration of use of most antimicrobials with significant de-escalation in group B (***Table* II**).

TABLE I DEMOGRAPHIC AND MORBIDITY PROFILE BEFORE AND AFTER INTRODUCTION OF THE JUSTIFICATION FORM

Parameter	*Before (n=353)*	*After (n=284)*
Male gender, *n* (%)	229 (64.9)	192 (67.6)
Age (y), mean (SD)	3.39 (4)	3.36 (3.8)
Infants, *n* (%)	151 (42.8)	113 (39.8)
Ventilated* *n* (%)	83 (23.5)	112 (39.4)
PRISM Score,# Mean(SD)	5.2 (6.3)	6.9 (5.1)
Morbidity pattern, *n*		
Respiratory	116	101
Neurology	33	25
GIT and Hepatobiliary	14	17
Oncology	6	4
Sepsis	100	78
Post surgical and trauma	18	17
Infections (Viral,protozoal,etc.)	54	30
Miscellaneous (metabolic, nephro)	12	12

**P=<0.001; #P=0.001; PRISM= Pediatric risk of mortality*

DISCUSSION

In this study, we observed that introduction of 'antimicrobial justification form' in a PICU has the potential of restricting use, and de-escalation of selected antimicrobial agents. As both the groups were comparable in terms of demographic profile, and disease spectrum and severity, the reduction in the initial usage and later de-escalation of these antimicrobials can be attributed to the awareness created by the justification form.

Few other studies also have shown similar impact. An earlier study from Pakistan documented reduction in use of carbapenems and antifungals with the introduction of a 'reserve antibiotic indent form' [10]. A study by Ozkurt, *et al*. [11] concluded that enforcement of restriction policy decreased consumption of restricted antibiotics by 40%. Himmelberg, *et al*. [12] found that removal of antimicrobial restriction policy resulted in increased use and higher expenditures for previously restricted agents, along with an inappropriate usage of at least one agent.

The main limitation of this study is a historical control rather than a randomized controlled design. Also, we did not compare overall use of antibiotics as our study aimed to evaluate the impact of justification form on selected antimicrobials. Other factors potentially affecting antimicrobial usage were also not adjusted for in the statistical analysis.

TABLE II ANTIBIOTIC USAGE BEFORE AND AFTER INTRODUCTION OF ANTIBIOTIC JUSTIFICATION FORM

Antibiotic	*Initial No. (%)*			*De- escalation Mean (SD)*			*Duration of antibiotic (days)No. (%)*		
	Group A	*Group B*	*P value*	*Group A*	*Group B*	*P value*	*GroupA*	*Group B*	*P value*
Piperacillin-Tazobactum	220 (62.3)	193 (68)	0.2	58 (26.4)	89 (46.1)	<0.001	5.4 (3.2)	4.8 (2.9)	0.04
Meropenem	123 (34.8)	108 (38)	0.45	14 (11.4)	30 (27.8)	0.002	7.4 (3.4)	6 (3.7)	0.003
Linezolid	82 (23.2)	122 (43)	0.001	12 (14.6)	51(41.8)	<0.001	7.4 (3.9)	5.5 (3.7)	0.001
Vancomycin	60 (17)	11 (3.8)	<0.001	24 (40)	5 (45.5)	0.75	6.1 (4.9)	6.3 (5.8)	0.8

Group A: Pre-intervention; Group B: Post-intervention.

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WHAT THIS STUDY ADDS?

- Introduction of a justification form before prescribing antimicrobials or at the time of deferring de-escalation can be useful in antibiotic stewardship.

We conclude that introduction of 'antimicrobial justification form' has the potential of restricting the use of selected antimicrobials in a PICU. Well-designed cluster-randomized trials evaluating similar policies need to be conducted in various settings where antibiotic abuse may be a problem.

Contributors: HSB: study design, collection of data, data entry, drafting of article; FARS: designing the study, data analysis, drafting of article; PKP: designing the study, data analysis, statistical analysis, revision of article; DR: data collection, data analysis, drafting of article; DC: designing the study, data analysis, drafting of article. All authors approved the final version.

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