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Impact of pharmacist-led antibiotic stewardship program in a PICU of low/middle-income country

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INTRODUCTION

The use of antibiotics in paediatric intensive care units (PICU) is very high (ranging from 67% to 97%) due to several reasons including high incidence of community-acquired sepsis, healthcare-associated infections or as a postoperative prophylaxis.[1] This high antibiotic use leads to several problems including development of antibiotic resistance, drug toxicity and drug interactions.[2] The Infectious Diseases Society of America and Society for Healthcare Epidemiology of America has initiated antibiotic stewardship programme (ASP) for better delivery of antibiotics in hospitalised patients in 2007 and updated in April 2016, was also advocated by other paediatric healthcare agencies.[3] The cornerstone for ASP is appropriate selection, dose and duration of antibiotics. The advantages of ASP include decrease in antimicrobial resistance and cost of care.[4] Reports published on ASP in intensive care units have demonstrated significant improvement in consumptions of antibiotics.[5] There are limited published reports on paediatric ASP especially related to PICU.[6 7] We implemented pharmacist-led ASP in our PICU and compared it with the historical data on the usage of antibiotics in terms of days of therapy (DOT) per 1000 patient days as well as cost of therapy (COT).

OBJECTIVE

To assess the effect of implementation of pharmacist-led customised ASP and to compare with historical control on usage of antibiotics as well as COT in our PICU.

METHODS

We conducted a multidisciplinary-team pilot project of pharmacist-led prospective-audit-with-feedback ASP from April to June 2016 in our closed multidisciplinary-cardiothoracic PICU. The team members of ASP were paediatric intensivist, critical care pharmacist (KH) specially trained in ASP and paediatric infectious disease physician. The four main components of this programme were[1]: selection of appropriate agent, based on the patient characteristics' like where the patient came from (community or another hospital/ward), previous antibiotics received in current illness, nature of disease/infection and microbiological details available if any before the PICU admission[2] appropriate dose,[3] de-escalation/discontinuation (stop or change to narrow spectrum antibiotic based on definitive diagnosis after 48 hours) and[4] recommendation regarding interactions or monitoring of therapy. During the morning rounds, pharmacist discussed these four components on each patients. DOT was defined as the number of antibiotics patient received in a day.[8] Basic demographic (age, gender) characteristics, Paediatric Risk of Mortality III score for severity assessment, admitting diagnostic categories, indications of antibiotics, details of ASP, COT (only cost of drug unit) and outcome as alive/dead were recorded. The COT was taken from the pharmacy bill. The same data were also collected from January to March before the start of ASP. DOT per 1000 patient's days for overall antibiotic and specific antibiotics (most commonly used antibiotics in PICU like ceftriaxone, vancomycin, meropenem and colistin, etc) were calculated. Data were entered into SPSS V.20 and appropriate statistical tests were used to compare DOT/1000 patient's days as well as COT before (from historical control data) and after implementation of ASP.

RESULTS

During ASP period, 127 patients were enrolled and 135 patients were enrolled from historical control for same period. Patients' characteristics were same for both periods (table 1).

Table 1 Patients' characteristics and antibiotics data during the pre-ASP and ASP periods

Variable	ASP−n (%)	ASP+n (%)	P value
Median age in months (IQR)	26 (93)	24 (65)	0.485
Gender male	150 (62.5)	86 (63)	
PRISM-III	5.68 ± 5.14	7.4 ± 6.3	
Diagnosis			
Respiratory system diseases	27 (20)	31 (24.4)	> 0.05
Cardiovascular system diseases	12 (9)	13 (10.2)	
Neurological diseases	25 (18.5)	16 (12.6)	
Surgical disease	58 (43)	41 (32.3)	
Miscellaneous	13 (9.5)	26 (20.5)	
Empirical	57 (42)	60 (47.4)	
Prophylaxis	58 (43)	55 (43.2)	
Therapeutic	20 (15)	12 (9.4)	
Intervention	None	29 (22.6)	
Dose	None	11 (8.5)	
Choice	None	15 (11.7)	
Duration/stop	15 %	6 (4.6)	
Monitor/interaction	None	6 (4.6)	
DOT	1937	651	
<2 days	8 (6)	57 (45)	
>5 days	87 (64)	8 (6)	
Patient's days (PtD)	557	492	
DOT/1000 PtD	1937/0.557=**3477**	651/0.492=**1323**	<0.0001
DOT-vanco	346	174	0.002
DOT-mero	323	154	0.001
DOT-colis	115	100	0.70
DOT-ceftri	532	186	0.00
Cost in PKR	2 212 468	929 568	0.00
Mortality (%)	22 (16.2)	20 (15.7)	

ASP, antibiotic stewardship programme; CVS, cerebrovascular disease; DOT, days of therapy; PKR, Pakistani Rupee; Pt D, patient days; PRISM, Paediatric Risk of Mortality.

Median age was 26 months (range 1 months–16 years.) and male was >60% in both periods. Total DOT was 651 in ASP period and 1937 in the pre-ASP period (P<0.0001). DOT/1000 patient days was 3447 and 1323 in the pre-ASP and ASP periods, respectively (P<0.0001). There was a 64% reduction in antibiotics utilisation in ASP period. The appropriate use of empirical antibiotic therapy for culture-negative infection-like symptoms (duration ≤2 days) increased from 6% (8/135) to 45% (57/127) (P<0.0001). The DOT of colistin remained same during both the periods (DOT=115 vs 100, P=0.70). COT decreased from US$22 125 in the pre-ASP period to US$9296 in the ASP period (P<0.0001) with cost reduction of 58%. Pharmacist interventions during the ASP period were 29 (22.6%) and included: dose adjustment (n=11), selection of antibiotic (n=15), de-escalation (n=5), monitoring and interactions recommendation (n=6). Mortality was 16.2% and 15.7% during the pre-ASP and ASP period, respectively.

DISCUSSIONS

We showed a significant and robust impact of ASP on antibiotic utilisation in our PICU. There was 64% reduction in antibiotics use and 58% cost reduction during this customised ASP. Antibiotics, being the most commonly prescribed medications in critical care setting, are epicentre of antimicrobial resistance. Published ASP reports from adult critical care had demonstrated significant positive impact on utilisation of antibiotics with no associated increase in healthcare-associated infection rates, length of stay or mortality like our report.[5] There are two main forms of ASP either prior authorisation/restriction policy or prospective-audit-with-feedback

interventions. We followed the latter approach and found it effective like few other clinical reports.[9 10] Stocker *et al* reported from their PICU that there was an improvement on empirical use of antibiotics (<3 days) from 18% to 35%, similarly our empiric antibiotic usage improved from 6% to 45%.[7] Like previous reports, we also observed that the most common pharmacist interventions were selection and dosing of antibiotics. Pentima *et al* reported that about 61% of ASP intervention was dose related.[11] Lee *et al* successfully implemented ASP in intensive care units of a tertiary care paediatric hospital and found 62% cost reduction.[6] With this customised ASP, we can potentially save about US$51 000 (PKR 5 million) annually which being in a low/middle-income country is very significant. This is only cost saving from drug-unit cost excluding pharmacy charges, nurse's time and other associated expenses of hospital pharmacy which becomes very relevant from limited human resource perspective.

This is the first report from PICU of a low/middle-income country showing highly successful implementation of quality improvement project with a high potential of cost saving. The limitations include a single centre, private sector hospital project implemented over a limited period of time, so its generalisability has limitation. We did not use defined daily dose as recommended by WHO. It is difficult to use in paediatrics because of weight-based dosing. Furthermore, we were unable to report length of therapy (course) along with DOT.

Contributors AH: conceived the idea, did literature search, designed the study, wrote and proofread the manuscript. KH: did the literature search, collected data, helped writing manuscript and proofread it. RI: data management, entry, analysis, writing manuscript and proofread it. QA: led the ASP, did literature search and summarised it, designed data collection tool, collected data, analysed data, wrote manuscripts, proofread it and is the final guarantor of the manuscript. SAA: data collection, entry, analysis, manuscript writing and proofreading. HJ: data gathering, manuscript writing, proof reading. SAA: idea, study design, data collection tool design, manuscript writing and proofreading.

Competing interests None declared.

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