



ORIGINAL ARTICLE

Antibiotic prophylaxis in organophosphorus poisoning: A study of health and economic outcomes



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Received 12 December 2015; accepted 25 July 2016

Available online 30 July 2016

KEYWORDS

Organophosphorous poisoning;
Antibiotic prophylaxis;
Intensive care;
Antibiotic resistance;
Direct costs

Abstract *Objective:* Organophosphorus poisoning (OPP) is a major concern for developing countries. There are no guidelines for the prophylactic use of antibiotics in the management of OPP which in such critical cases might add to the economic burden of the patients as well as antibiotic resistance. We compared the health and economic outcomes in patients prescribed with prophylactic antibiotics with respect to the patients not prescribed with any antibiotics. *Methods:* A retrospective observational study was carried out for two years for patients admitted to ICU with OPP. Patients were graded for severity of OPP, and divided into two groups based on prophylactic prescription and no prescription of antibiotics. The length of stay (LOS), hospitalization cost and outcomes were measured and compared between the two groups using statistical tests. *Results:* Out of the 254 patients observed, 108 were prescribed with prophylactic antibiotics and 94 were not prescribed with any antibiotic. There was a significant difference between LOS, cost of treatment and outcomes in the two groups ($p < 0.001$). When antibiotics were not prescribed, the odds of improvement was 1.854 times higher compared to those who received prophylactic antibiotics although after adjusting for severity of poisoning, significance was lost. On an average, 2–3 antibiotics were prescribed to every patient in the first group. *Conclusion:* OPP is an important health concern where issues of antibiotic misuse and overuse are practiced. Our study suggested that

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Peer review under responsibility of King Saud University.



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systemic antibiotic prophylaxis did not offer any advantage over non-use of any antibiotics in patients with OPP.

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1. Introduction

Organophosphorus (OP) compounds are popularly used as insecticides and pesticides in agriculture in the developing countries. OP compounds are toxic when consumed and cause severe poisoning via inhibition of acetyl cholinesterase enzymes and sustained cholinergic neurotoxic effect. OP poisoning (OPP) as either accidental occupational hazard, or intentional suicidal consumption is a common reason for admissions to intensive care units (ICU) in India. OPP management guidelines stress on the quick administration of anticholinergic antidote after gastric decontamination and gastric lavage along with management of respiratory distress by mechanical ventilation (Eddleston et al., 2008, 2004, 2002; Roberts and Aaron, 2007). However, there is no evidence to support beneficial role of prophylactic antibiotics in such patients. On the contrary, prophylactic antibiotics add to the burden of antimicrobial resistance and carry risk of *Clostridium difficile* diarrhea (Riddle and Dubberke, 2009). Heightened concern about the impact of antimicrobial resistance on health and economic outcomes has prompted health-care personnel to establish guidelines on appropriate use of antimicrobial agents through antimicrobial stewardship programs. Economic burden of illness associated with OP poisoning in developing nations is further compounded by additional and probably unnecessary antimicrobial therapy. Thus it is essential to study the antibiotic prescription practices in the management of OP poisoning to provide scientific basis for antibiotic usage guidelines. We sought to assess the antibiotic utilization, health and economic burden of prophylactic antibiotics among patients admitted to ICU with OP poisoning in a large tertiary care center (see Fig. 1 and Table 1).

2. Methodology

We carried out a retrospective review of all the cases of OP poisoning admitted to ICUs of Kasturba hospital, Manipal, from January 2013 to December 2014. The patients were classified into mild, moderate and severe poisoning cases according to the clinical presentation of OPP referring to Namba's criteria (Namba et al., 1971). Medical records of patients were screened for antibiotics prescribed during their hospital stay. Patients who were transferred from other hospitals or with prior antibiotic exposure were excluded from the study. Patients who received antibiotics at any instance during their hospital stay were later categorized into three sub-categories according to the type of antibiotic therapies such as prophylactic, empirical and definitive. Antibiotic prescription was categorized as prophylactic when the antibiotic was prescribed from the first day of admission to the ICU without a clinical or microbiological evidence of infection, empirical when the antibiotic was prescribed during the ICU stay based on the clinical manifestations of the patient without a conclusive microbiological evidence of infection and definitive when the

antibiotic was prescribed based on the results of a microbial culture and sensitivity test.

For the purpose of analysis, patients were grouped into two categories A and B. Group A comprised of all the patients prescribed with prophylactic antibiotics on the first day of their hospitalization and Group B consisted of the patients admitted with OP poisoning but were not prescribed any antibiotic throughout their hospital stay.

The outcome of the patients with OPP was also noted at the time of discharge.

2.1. Statistical analysis

The statistical analysis was performed by using the Statistical Package for Social Sciences (SPSS) version 15.0. A univariate test of association was used to study the association of the two groups and the different factors such as gender, severity of poisoning and the outcome. A Mann-Whitney U test was used to test for the difference in Length of stay as well as total hospitalization cost across both groups of patients. To study the impact of the significant factors, we performed multiple logistic regression analysis, with Improvement status as a dichotomous outcome, and antibiotic use and severity of poisoning as independent variables. A p -value < 0.05 was considered significant.

3. Results

A total of 254 patients were admitted to the ICU with OP poisoning over a period of two years. Out of these patients, we analyzed 202 patients distributed under Group A (108, 42.5%) and Group B (93, 37%). Fifty-two (20.5%) patients were treated with either empirical or definitive antibiotic therapy and were excluded from analysis. The patient population comprised predominantly of males (66.8%) and the average age was 30 years. Out of the 202 patients, 58 (28.7%) had mild, 81 (40.1%) moderate and 59 (29.2%) severe grades of poisoning. The distribution of moderately poisoned patients was almost similar in both the groups. Severely poisoned patients were more in the Group-A than in Group-B.

The median length of stay of a patient in group-A was 9 days and was found to be significantly higher ($p < 0.001$) in Group A compared to patients in Group B. The hospitalization costs and the total medicine costs were also significantly higher in the Group-A patients compared to Group-B patients.

There was a significant variation among the outcomes in the Group-B patients as compared to Group-A patients as shown in Table 2. Patients with favorable outcomes were significantly more in Group-B whereas patients with unimproved or deceased status were more in the Group-A patients. The results also showed that when antibiotics were not prescribed, the odds of improvement was 1.854 times higher compared to those who received prophylactic antibiotics although after adjusting for severity of poisoning, significance was lost.

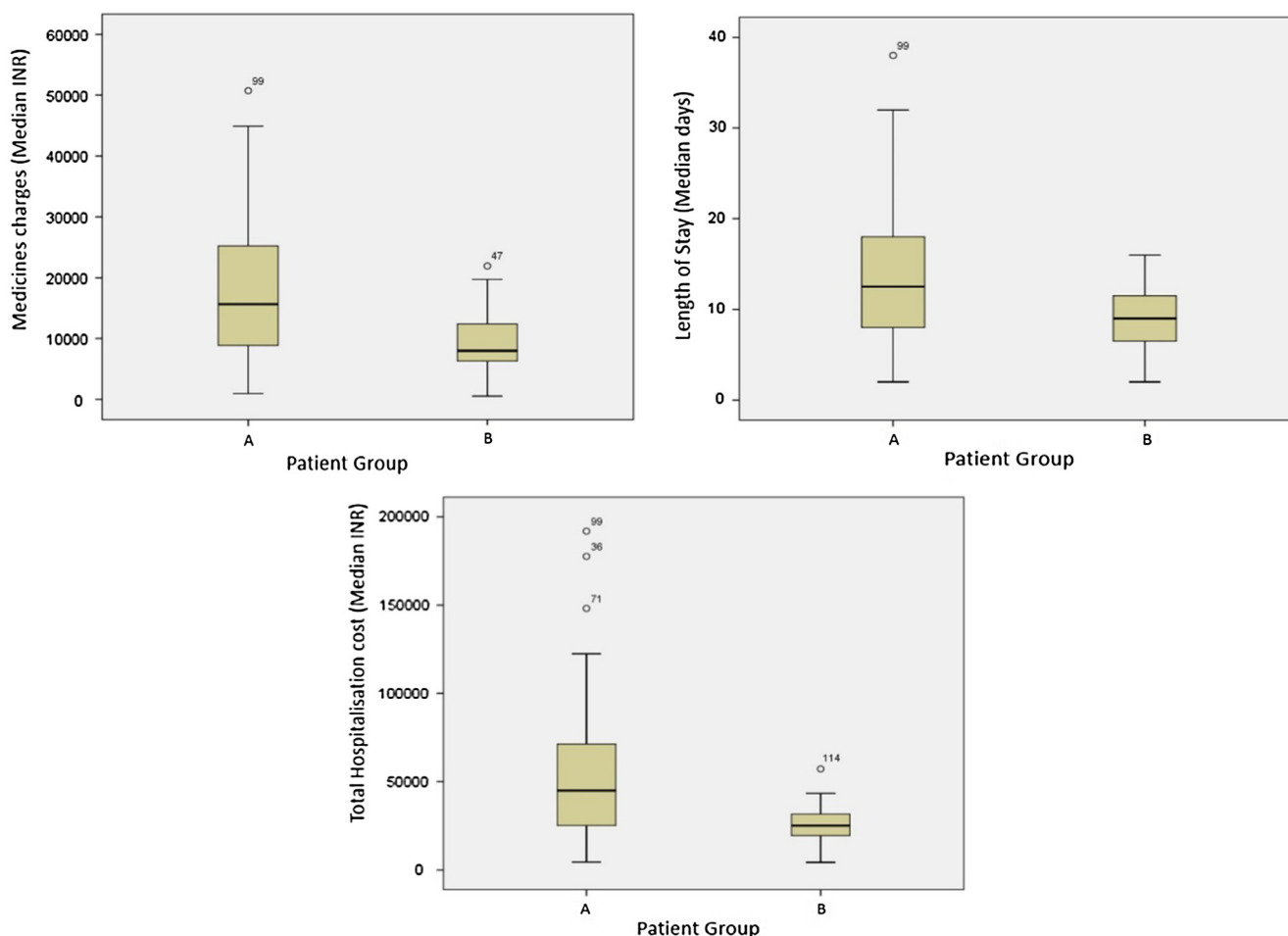


Figure 1 Comparison of LOS, Medicine costs and total hospitalization cost in the two study groups.

Microbiological culture was requested for 125 (49.21%) patients of whom only 58 (53.7%) belonged to Group-A. There were a total of 250 antibiotic prescriptions among the patients in Group-A. The majority of patients (47, 43.5%) were prescribed single antibiotic, while 24 (22.2%) were prescribed two and 37 (34.3%) three or more antibiotics respectively. Common antibiotics prescribed were beta lactam-beta lactamase inhibitors (33.6%) followed by third generation cephalosporins (30%), metronidazole (8.0%), linezolid (5.6%), carbapenem (4.0%), colistin (4.0%) and others (14%). On an average each patient received 2–3 antibiotics.

4. Discussion

Our study addresses one of the common but important clinical problems in developing nations and the lacunae in management guidelines. Organophosphorus compound poisoning either in the form of self-poisoning or accidental consumption requiring intensive care in the hospital is an important concern in developing nations. OPP is a major contributor to the cause of death by intentional self-harm which features in the top-ten causes of death in India (Country statistics and global health estimates by WHO and UN partners, 2015). The majority of the patients who are affected by OPP are from the lower socioeconomic strata and usually are not supported by health insurance (Banerjee et al., 2012). In a developing nation like

India, where health insurance still remains an unfulfilled dream, OPP is detrimental for both the nation's economy and the individual. The irrational use of antibiotics may lead to increased cost burden on patients and growth of antibiotic resistance (Schultz et al., 2014). In this study, we tried to address issues of rationality of prophylactic antibiotic prescription, and its influence on outcome of patients with OPP.

We found that the systemic prophylactic antibiotic was used in nearly half of patients with OPP. While there is lack of substantial evidence to recommend the use of prophylactic antibiotics in these patients, we propose the urgent need to study the prescription practices among intensivists in resource limited nations. Antimicrobial prophylaxis can be used effectively to prevent infection, but its use should be limited to specific, well-accepted indications to avoid excess cost, toxicity, and antimicrobial resistance. In OPP, respiratory failure needing mechanical ventilation, possible aspiration events and the presence of other indwelling devices prompt the intensivist to use prophylactic antibiotics. Among several approaches to prevent development of ventilator associated pneumonia, most favorable are selective digestive decontamination and adherence to VAP bundles; however, there is lack of evidence to support the use of systemic antibiotic prophylaxis (Bonten, 2011). Further, early antibiotic prophylaxis carries risk of development of superinfections by more resistant organisms (Rotstein et al., 2008). Our results show that the prophylactic

Table 1 Basic characteristics of patients with OPP and cost analysis of antibiotic prescriptions.

Variables	Total (Group-A + Group-B)	Patients receiving prophylactic antibiotics (Group-A)	Patients without any antibiotics (Group-B)	<i>p</i> -value
No. of patients, <i>n</i> (%)	202	108 (53.5)	94 (46.5)	
Age (Median years)		35	28	
Gender <i>n</i> (%)				<i>p</i> < 0.001
Male	135	85 (63.0)	50 (37.0)	
Female	67	23 (34.3)	44 (65.7)	
Severity of poisoning				<i>p</i> = 0.001
Mild	58	22 (37.9)	36 (62.1)	
Moderate	85	44 (51.8)	41 (48.2)	
Severe	59	42 (71.2)	17 (28.8)	
LOS (median days)		12.5	9	<i>p</i> < 0.001
Mortality	16	12 (75.0)	4 (25.0)	<i>P</i> < 0.001
Outcomes, <i>n</i> (%)				<i>p</i> = 0.007
Favorable	157	76 (48.4)	81 (51.6)	
Unfavorable	45	32 (71.1)	13 (28.9)	
Costs (Median INR)				
Hospitalization cost		47205.5	25157.0	<i>p</i> < 0.001
Total medicine cost		17235.0	7982.0	<i>p</i> < 0.001
Antibiotic cost		2432.0	NA	

Table 2 Association of prophylactic antibiotics and outcome after adjusting for severity of poisoning: binomial logistic regression analysis (for a favorable clinical outcome).

Variables		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Antibiotic prescription ^a	Not prescribed	2.623 (1.281, 5.371)	1.854 (0.860, 3.995)
Severity of poisoning ^a	Moderate	3.129 (2.138, 10.212)	4.262 (1.931, 9.409)
	Mild	8.944 (3.129, 25.565)	7.529 (2.582, 21.949)

^a Reference category: Prophylactic antibiotics prescribed and Severe poisoning.

prescription of an antibiotic in case of OPP is likely to be a burden on the patient in terms of morbidity and cost. Also, we are at a stage in time where the threat of antibiotic resistance has grown to the proportions of epidemics and is a matter of serious concern for the world. The facilities of microbiology and pharmacy are underutilized while making the prescription decision. Our study indicates that OPP cases might constitute a major chunk of the events of indiscriminate use of antibiotics.

The prophylactic use of antibiotics in case of critically ill patients originates from the effort of the physician to provide all the available provisions to the patient for his betterment. However, prophylactic prescription of antibiotics leads to increased cost and morbidity burden on the patients in ICU (Namiyas et al., 1999). The irrational prescription of antibiotics in such cases would aggravate the growing antibiotic resistance and morbidity of the patients. Our study shows that prophylactic antibiotics did not contribute significantly to the favorable outcome in our patients while we observed that those who received antibiotic prophylaxis showed significantly higher adverse outcome. Although severity of poisoning is a major determinant of outcome, this factor alone may not support the use of unnecessary antibiotics. These practices can be

curbed by the efficient use of the microbiology and pharmacy facilities in a healthcare team (MacKenzie et al., 2007). The effect on hospital-cost reduction and overall cost-reduction with the use of a multidisciplinary team is huge as found in the literature (Gums et al., 1999). The implementation of a hospital antibiotic management team can lead to a reduction in such instances of irrational prescription of antibiotics thus checking on antibiotic resistance and lowering the cost and morbidity burden on patients (Knox and Holmes, 2002).

The practice of evidence-based medicine should be followed in the critical care units where the life-threatening conditions of the patients are addressed. The prophylactic prescription of antibiotics without consultation of an Infectious disease specialist or the culture and sensitivity report is reported to be more inappropriate (Erbay et al.).

Our study had few limitations as well. Due to retrospective nature of the study, we could not retrieve the detailed information on definitive evidence on the exact time of development of infection in individual patients. Hence we could not arrive at more conclusive information to develop guidelines on antibiotic prophylaxis in these patients. It was a single-centered study having a narrow regional focus. Ideally, a multi-centric study including various geographical regions would provide

more concrete evidence in this area. Further research with larger sample size should be taken up in this field to help establish guidelines regarding the use of antibiotics in OPP cases.

5. Conclusion

OPP is an important health concern where issues of antibiotic misuse and overuse are practiced. Our study suggests that systemic antibiotic prophylaxis did not offer any advantage over non-use of any antibiotics in patients with OPP. Improved adherence to infection control practices, optimum utilization of laboratory tests and antimicrobial stewardship programs are very essential to curb resistance and improve health benefits in OPP.

Acknowledgement

We acknowledge the support of Kasturba hospital, Manipal, for permitting us to carry out this study and providing access to patient records. We also acknowledge the support of Manipal College of pharmaceutical sciences for providing support in the form of computer laboratory access.

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