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Research Article

Prevalence of Ventilator Acquired Pneumonia in Organophosphorus Poisoning Patients in Tertiary Care Hospital

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Abstract

Background: Ventilator associated pneumonia (VAP) is a major cause of poor outcome among patients in the intensive care units (ICU) world-wide. OP poisoning patients are very susceptible to respiratory associated problems especially respiratory muscle paralysis. Such patients generally need ventilation support which has high chances of getting VAP.

Objective: To find out the Prevalence, causative organisms and treatment pattern of VAP in OP poisoning patients in tertiary care hospital in South India.

Methods: A retrospective study was conducted in a tertiary care teaching hospital of South India from 2008 to 2013, total of 500 patients were enrolled for the study and data was collected from the medical records in a suitable designed case record form. Information regarding demographical details, severity assessment, type of pneumonia acquired, causative organisms for VAP, complications, treatment and outcome measures of patients was recorded. Data was entered in SPSS 20.0 and analyzed for the results.

Results and Conclusion: The mean age of the Patients admitted was 33.31 ± 14.5 years and majority of them were found to be males (69.4%) and (30.6%) were females. Among the study population, 54 (10.8%) patients acquired VAP. The most common organisms found to have caused pneumonia were gram negative organisms such as Pseudomonas aeruginosa (1.2%), Klebsiella pneumoniae (1.0%) and Acinobacter (0.6%). The most commonly used antibiotics in the treatment of VAP were beta-lactam antibiotics like Cephalosporins (56.1%), Penicillins (31.9%). Respiratory problems are common in OP poisoning patients and hence are very susceptible to VAP. Proper screening and identification of organisms in the early stage with appropriate antibiotics will help in better outcome.

Keywords: Pneumonia; Ventilator; Organophosphorus; Pralidoxime

Introduction

Development of pneumonia after 48 h in patients with mechanical ventilation is known as ventilator associated pneumonia (VAP) [1]. It is responsible for greater than 80% of mortality rate among the hospital acquired pneumonia [2,3]. According to a study by Chawla, the Incidence of VAP in Asian countries were found to be 3.5 to 46 per 1000 ventilator days. In an Indian study with 51 critical care unit patients, the incidence of VAP was found to be 46 per 1000 ventilator days [4,5]. According to World Health Organization (WHO), every year 3 million cases of pesticide (mainly OP compounds) poisoning occurs, resulting in 2,50,000 deaths, of these, about 2 million are suicidal poisonings and about 1 million are accidental [6]. Acute self-poisoning is one of the risk factor commonly associated with VAP due to its admission in intensive care units (ICU). Among them organophosphorus poisoning, contribute majority of the ICU admission due to self-poisoning. Risk factors includes males, geriatrics, APACHE II score of 15, multiple organ system failure, use of antibiotics for more than 2 weeks, diabetes mellitus, immunosuppression, dialysis, pre-existing pulmonary disease, presence of intubation or enteral feeding, mechanical ventilation, and supine position. Additional risk factors are re-intubation, use of paralytic sedative and length of ICU stay [7].

The outcome of VAP is mostly associated with initial antibiotic management with proper identification of susceptible strains. In India, incidence of VAP varies from 9-29% according to reported studies by Trivedi et al. and Chandrakanth et al. [8,9]. Also, In India the fifth leading cause of death is pneumonia [10].

However, proper implementation of simple, effective and preventive measures such as, non-invasive ventilation, precaution during emergency intubation, minimizing the occurrence of re-intubation, avoidance of tracheostomy as far as possible and minimization of sedation may help reduce the morbidity [11].

In many Asian countries, clinicians have to rely on local data as the national surveillance data on the epidemiology of VAP are not available. Organophosphate (OP) insecticides inhibit both acetyl cholinesterase and pseudo cholinesterase activities. The inhibition, leads to accumulation of acetylcholine at synapses which causes overstimulation and disruption of neurotransmission in both central and peripheral nervous systems causing exaggerated manifestations of nicotinic and muscarinic receptors. It is a serious condition that requires rapid diagnosis and treatment. The clinical course of OP poisoning may be quite severe and may need intensive care management. The major reason for mortality is respiratory failure, hence careful monitoring, appropriate management and early recognition of this complication is required [12,13]. In organophosphorus (OP) poisoning there is an inhibition of acetylcholineterase enzyme due to OP compound as a result of this acetylcholine concentration build up which is associated with overstimulation of cholinergic receptors throughout the central and peripheral nervous systems [14]. This usually associated with main features include muscle fasciculations, muscle cramps, muscle twitching and muscle weakness. Cholinergic circuits are also integral part of the central control of respiration [15]. Thus OP poisoning patients are very susceptible to respiratory associated problems especially respiratory muscle paralysis. Such patient generally needs ventilation support which generally has high chances of getting VAP. Proper screening and

identification of organisms in early stage with proper antibiotics will help in better outcome [16].

The main objective of our study is to find out the Prevalence, causative organisms and treatment pattern of VAP in OP poisoning patients in tertiary care hospital in South India.

Methodology

A retrospective study was conducted in a tertiary care teaching hospital of South India. Data was collected retrospectively from medical record section from 2008 to 2013 in a suitable designed case record form. All the patient related data were collected from medical records which includes demographical details of the patients such as age, gender, social habits, comorbidities, type of compound consumed, previous treatments patients received outside the hospital before being admitted in this tertiary care. The severity of the patients poisoning was assessed using different scales such as Apache-II, Glasgow coma, and Poison Severity. All the information regarding treatment given, type of complication developed along with outcome measures of patients such as recovery, discharge against medical advice, death, hospitalization period and ventilation period also recorded. Among the patients who developed pneumonia as complication information such as type of pneumonia that they acquired (ventilator acquired pneumonia or aspiration pneumonia), the different organisms involved in causing the pneumonia and the different antibiotics used in the treatment of the patients pneumonia were recorded. Data was entered in SPSS 20.0 and analyzed for the results.

Results

A total of 500 patients from the year 2009 to 2013, admitted for management of OP poisoning, were enrolled for the study.

The demographical characteristic of the patients are given in the (Table 1). The mean age of the study population was found to be 33.31 ± 14.5 years. Gender wise distribution showed that majority of them were males who constituted 69.4% of the study population. Majority of poisonings were intentional (95%). Amongst the population 12.4% (n=62) patients were smokers and 32.2% (n=161) patients were alcoholic. The quantity of OP compound consumed was found to be (mean ± SD) 95.18 ± 87.32 ml. The average pre-hospitalization period was found to be (mean ± SD) 1.40 ± 1.68 days.

Among the study population, 2.2% (n=11) of the patients were hypertensive, followed by 1.8% (n=9) of the patients had mental illness, followed by 1.4% (n=7) who had diabetes and 1% (n=5) of the patients had seizures and finally 0.8% (n=4) had both hypertension and diabetes.

Among the study population majority of them were farmers [n=115 (23.8%)] followed by household [n= 111 (23%)] (Table 1).

Among the different OP compounds consumed, methyl parathion contributes to 22.1% of the total OP admissions during the study period (Table 2).

Among the study population majority of them received atropine (64.4%) from an outside hospital before getting admitted in our tertiary center (Table 3).

Among the population studied almost the entire population (n (%), 495 (98.8%)) received atropine in their treatment. Whereas 345 (68.9%) patients received pralidoxime and 122 (32.6%) received glycopyrrolate (Table 4).

Among the study population the average plasma cholinesterase level was found to be 1834.49 ± 2602.41 (mean ± SD). The average apache II score was 8.54 ± 6.97(mean ± SD), and GCS score 11.54 ± 3.43 (mean ± SD) (Table 5).

Patient Demographics	
Male n, (%)	347, (69.4%)
Female n, (%)	153, (30.6%)
Mean age ± SD in years	33.31 ± 14.5
Smoker n, (%)	62, (12.4%)
Alcoholic n, (%)	161, (32.2%)
Details of OP exposure	
Suicidal n, (%)	475, (95%)
Mean Quantity of OP Consumed ± SD	95.18 ± 87.32
Co-Morbid illness	
Hypertension	11, (2.2%)
Diabetes	7, (1.4%)
Diabetes+Hypertension	4, (0.8%)
Seizures	5, (1%)
Mental illness	9, (1.8%)
Pre-hospitalisation period ± SD	1.40 ± 1.68
Occupation	
Farmer n, (%)	115, (23.8%)
Household n, (%)	111, (23%)
Student n, (%)	54, (11.2%)
Labour n, (%)	52, (10.8%)

Table 1: Demographics of the OP poisoning patients.

OP Compound	Frequency (%)
Unknown	101 (22.6%)
Dimethoate	24 (5.4%)
Methyl-Parathion	99 (22.1%)
Chlorpyrifos	74 (16.6%)
Quinolphos	17 (3.8%)
Monocrotophos	32 (7.2%)

Table 2: Different OP compounds consumed.

Previous Treatment	n, (%)
Atropine	322, (64.4%)
Pralidoxime	206, (43.5%)

Table 3: Previous treatment received.

Type of OP poisoning Treatment	n, (%)
Atropine	495, (98.8%)
Pralidoxime	345, (68.9%)
Glycopyrolate	122, (32.6%)
Atropine+Pralidoxime	345, (68.9%)
Atropine+Glycopyrolate	122, (32.6%)

Table 4: Treatment given during the course of hospital stay.

Amongst the study population 75.4% (n=377) had a recovery, and 11.6% (n=58) died. Out of the entire study population 13% (n=65) were discharged against medical advice, 24.4% (n=122) developed intermediate syndrome, 46.9% (235) received ventilation. The average hospitilization period in days was found to be 12.6 ± 9.67 (mean ± SD) and average duration of stay in ICU in days was found to be 8.44 ± 7.77 (mean ± SD) (Table 6).

Among the study population 10.8% (n=54) developed pneumonia. Ventilation acquired pneumonia was seen in 8.4% (n=42) of the study population. The most frequent causing organism seen in the study population were found to be *Pseudomonas aeruginosa* seen in 1.2% (n=6) patients, *Klebsiella pneumoniae* seen in 1.0% (n=5), and *Acinobacter* seen in 0.6% (n=3) (Table 7).

Severity Assessment of OP poisoning	Mean ± SD
Plasma cholinesterase	1834.49 ± 2602.41
ApacheII_Score	8.54 ± 6.97
GCS_Score	11.54 ± 3.43

Table 5: Severity assessment.

Outcomes	n, (%)
Recovery n, (%)	377, (75.4%)
Discharge against medical advice n, (%)	65, (13%)
Death n, (%)	58, (11.6%)
Intermediate syndrome present	122, (24.4%)
Ventilation received	235, (46.9%)
Mean Hospitalization period ± SD	12.6 ± 9.67
Duration in ICU ± SD	8.44 ± 7.77

Table 6: Outcomes.

Pneumonia	n, (%)
Pneumonia [Yes]	54, (10.8%)
Ventilation Acquired Pneumonia [Yes]	42, (8.4%)
Aspiration Pneumonia [Yes]	12, (2.4%)
Organisms:	**n, (%)**
Pseudomonas aeruginosa	6, (1.2%)
Klebsiella pneumoniae	5, (1.0%)
Acinobacter	3, (0.6%)

Table 7: Development of pneumonia among the OP poisoning patients and susceptible organisms.

In this study the antibiotics that were most commonly used in the patients were found to be Cephalosporins 56.1% (n=281), Penicillins 31.9% (n=160), Aminoglycosides 4.8% (n=24), Quinolones 4.2% (n=21), Oxazolidindiones 2.6% (n=13). In this study different regimens of antibiotics were used, 1 drug regimen contains a single class of antibiotic, seen in 49.9% (n=250) of patients, 2 drug regimen contains a combination of two different classes of antibiotics, seen in 22.4% (n=112) of patients, 3 drug regimen contains a combination of three different classes of antibiotics, seen in 0.4% (n=2) of patients and 4 drug regimen contains a combination of four different classes of antibiotics, seen in 0.2% (n=1) of patients. The average duration of antibiotic administration in days was found to be 7.54 ± 3.8 (mean ± SD) (Table 8).

Discussion

Patients admitted in our study were belonging to productive age (mean age 33.31 ± 14.5 years) group and majority of them were males (69.4%). An Indian study by Nilamadhab showed similar results with the mean age of 31.5 ± 12.37 years and majority of poising was observed in males [17]. Another study by Rao et al. showed that about two- third of the patients, admitted in Warangal due to acute exposure of OP poisoning were less than 30 years and males predominated over females [18,19].

Our study showed that majority of admissions was due to consumption of methyl parathion which belongs to WHO Ia category. In a similar study in South India by Rao et al. showed that majority of the cases were admitted due to ingestion of WHO class Ib pesticides and monocrotophos contributed to major portion among them [18]. A study in Srilanka by Hoek and Flemming revealed that majority of cases admitted were due to WHO II type of pesticides [20]. In this study, majority of patients admitted due to OP poisoning were agriculturists. A similar result was found in a study by De Alwis LB in Sri Lanka which showed that 75% of total poisonings occurred in agriculturists [21]. Another study by Gannur et al. [22] showed that 37.8% of the total OP poisoning occurred among agricultural workers.

Antibiotics	n, (%)
Cephalosporins	281, (56.1%)
Penicillins	160, (31.9%)
Aminoglycosides	24, (4.8%)
Quinolones	21, (4.2%)
Oxazolidindiones	13, (2.6%)
Regimens	
Drug Regimen	250, (49.9%)
Drug Regimen	112, (22.4%)
Drug Regimen	2, (0.4%)
Drug Regimen	1, (0.2%)
Duration of Antibiotic, Mean ± SD	7.54 ± 3.8

Table 8: Drug treatment given during the course of hospital stay.

Among the severity indices GCS and APACHE-II were found to be the most predictable and precise in assessing the initial severity and prognosis in OP poisoning. Moreover GCS is easy to perform, and does not require complex physiologic parameters and laboratory methods.

Our study showed that 54 (10.8%) patient out of the entire study population acquired pneumonia of which 42 (8.4%) acquired ventilator acquired pneumonia and 12 (2.4%) acquired aspiration pneumonia. In a similar study in south India by Kavitha et al. it showed that 17 (32.7%) patients who acquired VAP had organophosporus poisoning and 8 (15.7%) patients who acquired non VAP had oraganophosphorus poisoning [1].

Our study showed that the most common organisms found to have caused pneumonia were gram negative organisms, *Pseudomonas aeruginosa* found in 6 (1.2%) patients, *Klebsiella* pneumonia found in 5 (1.0%) patients, and *Acinobacter* found in 3 (0.6%) patients. In a similar study by Vijayanarayana et al. it showed that the most common isolates causing pneumonia were found to be *Klebsiella* pneumonia (30.9%), *Acinobacter* species (29.4%), *Pseudomonas aeruginosa* (16.7%), *Escherichia coli* (9.1%) and methicillin resistant *Staphylococcus aureus* (MRSA; 3.7%, 73%) [23].

Our results show that beta-lactam antibiotics were most commonly used in the treatment of pneumonia, such as cephalosporin's which was used in 281 (56.1%) patients and penicillin's used in 160 (31.9%) patients. In a similar study by Vijayanarayana et al. it showed that the most highly used antibiotic in the treatment of hospital acquired pneumonia was pipericillin/tazobactum, followed by ceftriaxone [24].

Conclusion

From our study it is seen that hospital acquired pneumonia (HAP) like ventilator acquired pneumonia (VAP) and aspiration pneumonia are very susceptible in patients suffering from organophosphorus poisoning. In the treatment of the HAP the most commonly seen organisms are found to be gram negative bacteria such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Acinobacter*. Proper screening and identification of the organism is very important in helping to determine the right course of treatment with the appropriate antibiotics. From our study the antibiotics seen to be most commonly used in the treatment of VAP were beta-lactam antibiotics such as penicillins and cephalosporins. Management with specific antibiotic at the optimal dose will help in eradication of organisms at a shorter period of time and results in better outcome.

References

1. Saravu K, Preethi V, Kumar R, Guddattu V, Shastry AB, et al. (2013) Determinants of ventilator associated pneumonia and its impact on prognosis: A tertiary care experience. Indian J Crit Care Med 17: 337-342.

2. Raghavendran K, Jean Nemzek DVM, Napolitano LM, Knight PR (2011) Aspiration-Induced lung injury. Crit Care Med 39: 818-826.

3. Jaoude PA, Knight PR, Ohtake P, Ali A El-Solh (2010) Biomarkers in the diagnosis of aspiration syndromes. Expert Rev Mol Diagn 10: 309-319.

4. Rakshit P, Nagar VS, Deshpande AK (2005) Incidence, clinical outcome and risk stratification of ventilator-associated pneumonia: a prospective cohort study. Indian J Crit Care Med 9: 211-216.

5. George DL (1995) Epidemiology of nosocomial pneumonia in MICU. Med Clin Chest Med 16: 29-44.

6. World Health Organization (2015) The impact of pesticides on health.

7. Chawla R (2008) Epidemiology, etiology and diagnosis of hospital-acquired pneumonia and ventilator-associated pneumonia in Asian countries. American journal of infection control 36: 93-100.

8. Anushre CC, Vinod A (2010) Incidence of ventilator associated pneumonia. Journal of Medical and Clinical Research 1: 11-13.

9. Trivedi, T, Shejale S, Yeolekar M (2000) Nosocomial pneumonia in medical intensive care unit. The Journal of the Association of Physicians of India 48: 1070-1073.

10. Ramanakumar AV (2005) Respiratory Disease Burden In Rural India A Review From Multiple Data Sources. Internet Journal of Epidemiology 2: 2.

11. Joseph NM, Sistla S, Dutta TK, Badhe AS, Rasitha D, et al. (2010) Ventilator-associated pneumonia in a tertiary care hospital in India: role of multi-drug resistant pathogens. The Journal of Infection in Developing Countries 4: 218-225.

12. Sungur M, Güven M (2001) Intensive care management of organophosphate insecticide poisoning. Critical Care 5: 211-215.

13. Bardin PG, van Eeden SF, Moolman JA, Foden AP, Joubert JR (1994) Organophosphate and carbamate poisoning. Archives of internal medicine 154: 1433-1441.

14. Eddleston M (2008) The pathophysiology of organophosphorus pesticide self-poisoning is not so simple. Netherlands Journal of Medicine (NJM) 66: 146-148.

15. Carey JL, Dunn C, Gaspari RJ (2013) Central respiratory failure during acute organophosphate poisoning. Respiratory Physiology & Neurobiology 189: 403-410.

16. Hunter JD (2006) Ventilator associated pneumonia. Postgrad Med J 82: 172-178.

17. Nilamadhab K (2006) Lethality of suicidal organophosphorus poisoning in an Indian population: exploring preventability. Annals of General Psychiatry 5: 17.

18. Rao S, Venkateswarlu CH, Eddleston M (2005) Pesticide poisoning in south India: opportunities for prevention and improved medical management. Tropical Medicine and International Health 10: 581-588.

19. Batra AK, Keoliya AN, Jadhav GU (2003) Poisoning: an unnatural cause of morbidity and mortality in rural India. Journal-Association of Physicians of India 51: 955-959.

20. Hoek W, Flemming K (2006) Analysis of 8000 Hospital Admissions for Acute Poisoning in a Rural Area of Sri Lanka. Clinical Toxicology 44: 225-231.

21. De Alwis LB (1988) Agrochemical poisoning in Sri Lanka. Forensic Science International 36: 81-89.

22. Gannur DG, Maka P, Reddy N (2008) Organophosphorus compound poisoning in Gulbarga region - A five year study. Indian J Forensic Med Toxicol 5: 3-11.

23. Vijayanarayana K, Rau NR, Anantha Naik N, Bhavani Y, Girish T, et al. (2014) An Appraisal of Sensitivity and Resistance Pattern of Organisms Isolated from Hospital Acquired Pneumonia Patients. RJPBCS 5: 384-398.

24. Vijayanarayana K, Rau NR, Anantha Naik N, Bhavani Y, Thunga G, et al. (2014) Analysis of antibiotic utilization and cost of treatment in hospital acquired pneumonia. AJPHS 4: 944-947.