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Research

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The Impact of VAP Staff Education on VAP Morbidity and Mortality in Alexandria University

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ABSTRACT

Background: Staff education had several success stories in reducing Ventilator-associated Pneumonia (VAP) rate. However, the stability of supplies and the top management support were not addressed in most of these studies. In addition, both were considered essential in several reviews.
Aim: To determine the efficiency (VAP rate) and efficacy (mechanical ventilation morbidity and mortality) of VAP staff education with deficient supplies and lack of top management support.
Methods: Quasi-experimental study with before and after prospective cohort in two medical/surgical ICUs of Alexandria university affiliated hospitals during the period from September 2007 till May 2013. The intervention phase included the provision of supplementary supplies, interactive education for physicians and nurses followed by a VAP campaign. All VAP episodes not only the first one was included.
Results: A total of 598 patients were enrolled in the study. The adherence to expanded VAP bundle significantly increased in the post-intervention phase as follows; head of bed elevation (from mean of 40 to 100% with p=0.001), oral care (from mean of 20 to 100% with p=0.001), daily sedation vacation (from mean of 56.5 to 91% with p=0.001), daily assessment of weaning (from mean of 9 to 25% with p=0. 03), peptic ulcer prophylaxis (from mean of 83 to 100% with p=0.001), DVT prophylaxis (from mean of 82 to 100% and p=0.001), cuff pressure measurement (from mean of 9 to 60% with p=0.001), and hand hygiene (from mean of 8 to 28.5% with p=0.001).The VAP rate decreased significantly by 35% (from 66.5 to 43 per 1000 MV days) with p= 0.002 and CI 9.73-37.15 in spite of significant increase of the ventilator utilization ratio (p <0.001) in the post-intervention phase. The MV, antibiotic and ICU days did not change significantly in the post-intervention phase. The distribution of organisms did not differ significantly between both groups (p=0. 465). The sensitivity of most of carbapenems and β-lactam/β-lactamase inhibitors to Acinetobacter, Klebsiella andPseudomonas decreased significantly in the post intervention phase whereas the sensitivity of vancomyicin to Staphylococcus aureus remained the same.
Conclusions: In spite of the lack of top management support and fluctuating supplies, VAP staff education was still efficient in reducing VAP without affecting mortality or MV days or ICU length of stay.

ABBREVIATIONS: VAP: Ventilator-associated Pneumonia; MDRP: Multidrug Resistant Pathogens.

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INTRODUCTION

Ventilator-associated Pneumonia (VAP) is peculiar from other Hospital Acquired Infections (HAIs) in several aspects. VAP has the highest prevalence, complex pathogenesis (and therefore multiple preventive procedures) and controversies in diagnosis and treatment which hindered accurate diagnosis and optimal therapy.[1-2] In addition, the high prevalence of Multidrug Resistant Pathogens(MDRP) further complicates the VAP management and magnifies the morbidity and mortality impact of VAP. Therefore prevention is the most effective treatment.[1]

Several evidence based interventions proved to reduce VAP which have been incorporated into guidelines by several organizations.[3-7] Implementing evidence-based guidelines into consistent delivered care at bedside still remains a challenge.[8] Staff education programs for single procedures[9-11] or selected bundle of several interventions significantly reduced VAP rate in several studies.[12-24] Furthermore, staff education and involvement was recommended in several guidelines.[3,5,25]

The top management support and availability of supplies were considered crucial for a successful VAP program.[2,26,27,28] After the initial failure of VAP reduction in two ICUs of Alexandria Main university hospital which was attributed to deficient supplies, lack of top management support and passive education.[29] In addition to repeated failure to obtain funding or top management support for the VAP program, we conducted a study with the purpose to assess the efficiency (VAP rate) and efficacy (Mechanical ventilation morbidity and mortality) of VAP staff education without top management support and full availability of supplies.

METHODS

Prior to the initiation of the study, the approval of the Alexandria University Ethical Committee on the general plan of the study, and the detailed patient management plan was taken. An informed consent was obtained before enrolment in the study (before completing the 48 hour period of mechanical ventilation).

Study location: This study was carried out in ICU1 and ICU3 of Critical Care Medicine department in Alexandria University affiliated Hospital, which is a major adult urban teaching, primary and tertiary care facility with 1900 beds, serving 3 governorates. Both ICU1 and ICU3 are 15 beds; medical/surgical with approximately 1269 and 610 admissions per year respectively.

Through FOCUS PDSA cycle (which is considered the primary engine of this study), we first found an opportunity in the failure of previous study to reduce VAP rate. Second, we organized a multidisciplinary team from critical care medicine, internal medicine, pulmonology, microbiology infection control and nursing. Third, we clarified the current process through reviewing outcomes and limitation of the previous study. Fourth, we understood the causes of process variation through reviewing local VAP studies with bacterial investigation of VAP pathogenesis, and the proposed solutions in sampling, suctioning, oral hygiene, draining circuit condensate, hand hygiene and patient transport according to available resources. Fifth, we Selected the process improve mentusing quasi-experimental study using before and after prospective cohorts with process and outcome indicators and cost-effectiveness data to evaluate the efficiency and efficacy of the VAP staff education and to be re-modelled with Plan Do Study Act cycle.(Study design)

This study was performed after initial failure of passive education from September 2007 till June 2009[29] (involving four lectures 20 minutes each in physician lounge room, scientific meetings and limited bedside teaching for the residents) without availability of enough supplies to reduce VAP rate. The current intervention program was designed to overcome the limitations of the previous study followed by post-intervention phase which was compared to the pre-intervention phase of the previous study with collection of more patient data retrospectively for VAP risk stratification.

Study period: The conceptual framework of study consisted of pre-intervention phase: from September 2007 till May 2008, intervention phase from July 2009 till August 2012 and post-intervention phase from September 2012 till May 2013.

The intervention phase was optimized by avoiding certain limitations from the previous study *via*[1] providing supplementary supplies donated to the hospital to decrease the gap between the required and the available (such as alcohol and suction catheters, beds for semi-seating position, and cuff pressure manometers)[2], providing lectures for nurses, together with bedside teaching[3], implementing regular end tracheal cuff pressure adjustment and blind mini BAL (bronchoalveolar lavage)[4], utilizing interactive lectures to physicians[5], carrying out a hand hygiene then a VAP campaign which included two days workshop, skill stations, group discussions, VAP folder for self education, and a concentrated bedside teaching.

Study population: This study was conducted on all patients requiring continuous Mechanical Ventilation (MV) for more than 48 hours who were admitted to both units during the study period. Patients with VAP which was not acquired in our units or those whom were transferred to other units before weaning from the ventilator were excluded. The screening for potential participants were performed at least every 48 hours as well follows up of participants for the development of VAP and final outcome.

All patients in the pre and post-intervention phases were evaluated for baseline and VAP risk stratification data (age, gender, primary diagnosis, severity of illness by Acute Physi-

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ological and Chronic Health Evaluation II "APACHE II", history of chronic respiratory illness and Glasgow Coma Scale "GCS").They were followed up for the development of VAP by modified American College of Chest Physicians (ACCP) criteria for diagnosis of VAP: "New and persistent (≤72 h) radiological infiltrate with two or more of the following; Fever (increase in core temperature of > 1°C and a core temperature >38.3°C or <35.5°C), leucocytosis (25% increase in circulating leukocytes from baseline and a value >10,000 cells/ml.), purulent tracheal aspirate or sputum"[30] until death, discharge out of ICU or transfer to another ICU.

VAP rate per 1000 ventilator days (primary outcome),[31] ventilator/Device utilization ratio (DU),[31] adherence to VAP preventive practices (expressed as percentage of positive observation during the scheduled ICU visits), culture results of VAP samples obtained by Bronchoscopic Broncho-Alveolar Lavage (BAL)[32] or modified blind mini-BAL (by using saline filled catheter instead of protected catheter and guiding it into desired bronchus through neck positioning then performing a lavage),[33] MV days and ICU Length of Stay (LoS), and outcome (secondary outcomes) were collected in the pre and post-intervention phases.[34-35] VAP rate was tracked through control charts (U chart).[36]

STATISTICAL ANALYSIS OF THE DATA[37]

Data was fed to the computer and analyzed using IBM SPSS software package version 20[38] Qualitative data was described using number and percent. Quantitative data was described using mean and standard deviation for normally distributed data while abnormally distributed data was expressed using median, minimum and maximum. Comparison between different groups regarding categorical variables was tested using Chi-square test. The distributions of quantitative variables were tested for normality using Kolmogorov-Smirnov test, Shapiro-Wilk test and D'Agstino test, also Histogram and QQ plot were used for vision test. If it revealed normal data distribution, parametric tests were applied. If the data was abnormally distributed, non-parametric tests were used. For normally distributed data, comparison between two independent populations was done using independent t-test. For abnormally distributed data, comparison between two independent populations was done using Mann Whitney test. Significance test results were quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.

RESULTS

A total of 2560 patients were screened in both ICU1 and ICU3 (Figure1). After exclusion of non-MV patients, MV for =48 hours, and patients with VAP acquired in other units, 598 patients were enrolled in the pre and post-intervention phases. One patient in the ICU3 stayed on MV for 276 days till the end of the study who was excluded as an extreme value. The rates of loss to follow up were 4.4 and 4.3% in the pre and post-intervention phases respectively. The number and qualification of physicians caring for patients (5-6/unit/shift) did not differ between both groups. Similarly, the number of non-registered nurses in the morning and evening shifts did not differ between both groups (4-5/unit in the morning and 1-2 in the evening and night shift). Whereas, the number of registered nurses dropped to the half in the post-intervention phase in the evening and night shift (0-1). The residents who were involved in the formal teaching (lectures or workshop) represented 80-87% of all residents, whereas the nursing staff who was involved in workshops represented 90-95% of all nursing staff (registered and non-registered nurses) in both units.

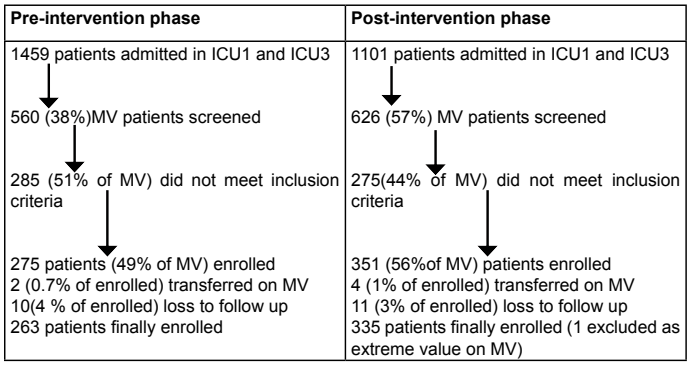

Figure 1: Study population of the pre and post-intervention study group.

The demographic characteristics and VAP risk stratification data were similar between the pre and post-intervention groups except for the admission diagnosis which differed significantly in the post-intervention phase (decreased cardiac cases and increased surgical cases) (Table 1).

Primary outcome: Among the 263 patients constituting the study sample in the pre-intervention phase, 132 patients fulfilled the criteria of clinically defined VAP using ACCP clinical criteria with an incidence of 50.2%. Out of the 132 clinically defined VAP cases, there were 116 laboratory (lab) confirmed VAP (4 were not sampled, 4 sterile samples, and 8 contaminated). The incidence of lab confirmed VAP was 44.1% (Table 1). The sensitivity of the lab to verify clinical diagnosis was 87.9%.

APACHE II: Acute Physiological and Chronic Health Evaluation II GCS: Glasgow Coma Scale Lab: Laboratory#: Chi square test $: Mann Whitney test &: Student t-test*: Statistically significant at $p \leq 0.05$

Among the 335 patients constituting the study sample in the post intervention phase, 138 patients fulfilled the criteria of clinically defined VAP using ACCP clinical criteria with an incidence of 41.2%. Out of the 138 clinically defined VAP, 116 were lab confirmed VAP (4 were not sampled, 9 sterile

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	Pre-intervention (n= 263)	**Post-intervention (n= 335)**	**p**
Sex	141 (53.6%)	154 (46.0%)	
Male	122 (46.4%)	181 (54.0%)	#0.064
Female	48.0 (1.0 – 86.0)	52.0 (1.0 – 91.0)	$0.099
Age			
Diagnosis type	42 (16.0%)		
Trauma	44 (16.7%)	53 (18.5%)	#0.961
Cardiac	57 (21.7%)	20 (6.0%)	#<0.001*
Respiratory	7 (2.7%)	58 (17.3%)	#0.179
Surgical	31 (11.8%)	27 (8.1%)	#0.005*
Neurological	0 (19.0%)	52 (15.5%)	#0.190
Medical	32 (12.2%)	91 (27.2%)	#0.055
Toxicological	19.0 (4.0 – 42.0)	34 (10.1%)	#0.434
APACHE score	50 (19.0%)	19.0 (7.0 – 38.0)	$0.752
History of chronic respiratory illness	9.24 ± 2.94	63 (18.8%)	#0.949
GCS	132 (50.2%)	9.41 ± 2.40	&0.467
Clinically defined VAP	34 (25.8%)	138 (41.2%)	#0.028*
Early onset	98 (74.2)	21 (15.2%)	#0.005*
Late onset	116 (44.1%)	117 (84.8)	#0.554
Lab confirmed VAP		116 (34.6%)	#0.018*
Number of VAP attack of MV pts	100 (75.8%)		
Single (1 attack)	32 (24.2%)	107 (77.5%)	#0.121
Multiple (≥2 attacks)	6.0 (2.0 – 67.0)	31 (22.5%)	#0.249
MV days	9.0 (2.0 – 110.0)	6.0 (2.0 – 76.0)	$0.119
ICU stay	8.0 (0.0 – 96.0)	9.0 (2.0 – 147.0)	$0.185
AB days		8.0 (0.0 – 99.0)	$0.089
Outcome	160 (60.8%)		
Death	103 (39.2%)	183 (54.6%)	
Discharge	**(n= 208)**	152 (45.4%)	#0.127
Distribution of organisms	47 (22.6%)	**(n= 272)**	
Gram positive	*27 (13%)*	54 (19.9%)	
staphylococcus aureus	161 (77.4%)	*40 (15%)*	#0.465
Gram negative	*54 (26%)*	218 (80.1%)	
Klebsiellapneumonia	*49 (23.6%)*	*47 (17%)*	
Pseudomonasaeroginosa	*11 (2.9%)*	*55 (20%)*	
Acinetobacter	**(n= 132)**	*74 (27%)*	
Mono versus poly-microbial	97 (73.5%)		
VAP	35 (26.5%)	**(n= 151)**	
Mono-microbial		63 (41.7%)	
Poly-microbial		88 (58.3%)	#<0.001*

Table 1: Comparison between pre and post-intervention groups according to demographic characteristics, VAP risk stratification, primary and secondary outcomes

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samples, 9 contaminated) with an incidence of 34.6% and a sensitivity of lab verification for clinical diagnosis was 84.1% (Table 1). Therefore, there was statistically significant decrease in the incidence of clinically defined VAP by 17.9 % (p = 0.028) and lab confirmed VAP by 21.5% (p= 0.018) in the post-intervention phase (Table 1). The incidence of early onset VAP decreased significantly (from 25.8 to 15.2% with p = 0.005), on the other hand the incidence of late onset, single and multiple VAP decreased insignificantly (p = 0.554, 0.121, and 0.249 respectively) in the post-intervention study group (Table 1).

During the 9 month of the pre-intervention phase, a total of 179 VAP episodes occurred during a total of 2740 ventilator days, with a VAP rate of 66.5 per 1000 ventilator days. Following the intervention, a total of 200 VAP episodes occurred during a total of 4619 ventilator days, and VAP rate dropped significantly to 43 with a decrease of 35.3% and p value of 0.002(mean difference of 23.4 and confidence interval of 9.7-37.1),although the DU ratio increased significantly by 51.3% and p =0.001 (Figure 2 and Table 2).

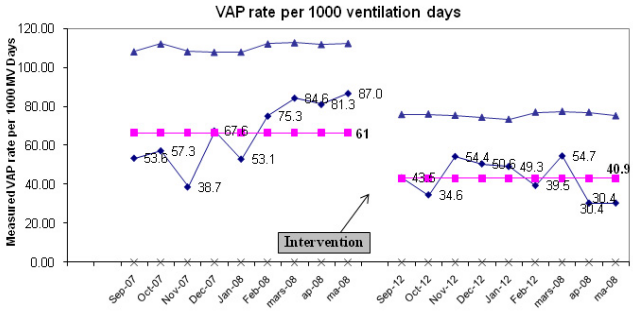

Figure 2: Control chart of VAP Rate per 1000 ventilation days in the pre and post-intervention phases in ICU1 and 3

	Pre-intervention (n= 9 months)	Post-intervention (n= 9 months)	p
VAP rate pre 1000 ventilator days	66.49 ± 16.75	43.05 ± 9.79	0.002*
Ventilation utilization ratio	0.39 ± 0.04	0.59 ± 0.03	<0.001*

Data was expressed as Mean ± SD. for normally distributed data

	Mean difference	95% Confidence interval of the difference
VAP rate pre 1000 ventilator days	23.44	9.73 – 37.15

Table 2: Comparison between the pre and post-intervention groups according to VAP rate and ventilation utilization ratio

Short term outcome: There was a highly significant increase in the compliance or adherence to VAP preventive practices in the post-intervention study group as follows: head of bed elevation (from mean of 40 to 100%, p < 0.001), oral care (from mean of 20 to 100% , p < 0.001), daily sedation vacation (from mean of 56.5 to 91%, p <0.001), daily assessment of weaning (from mean of 9 to 25%, p =0.03), peptic ulcer prophylaxis (from mean of 83 to 100%, p < 0.001), DVT prophylaxis (from mean of 82 to 100%, p < 0.001), cuff pressure measurement (from mean of 9 to 60%, p <0.001), and hand hygiene (from mean of 8 to 28.5%, p =0.001) (Figure 3).

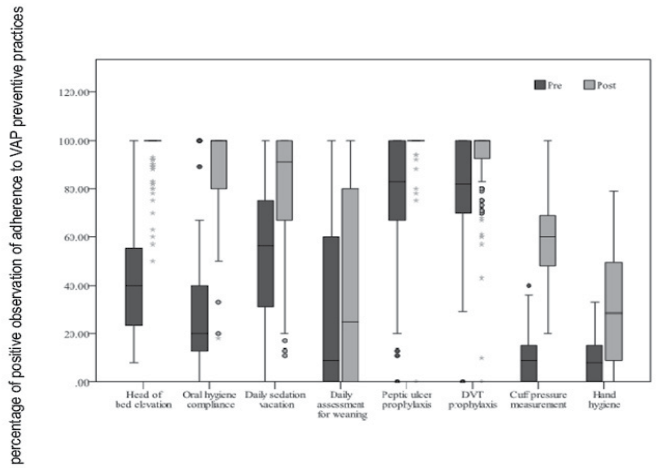

Figure 3: Comparison between the pre and post intervention phases according to compliance to VAP preventive practices (expressed as percentage of positive observation) in both ICUs

Secondary Outcome: There was insignificant difference between the pre and post-intervention groups as regards duration of mechanical ventilation, ICU length of stay, antibiotic days, and mortality with p=0.119, 0.185, 0.089 and 0.127 respectively (Table 1).

MICROBIOLOGY AND SENSITIVITY PATTERN

The distribution of organisms did not differ significantly between the pre and post-intervention groups with p value of 0.465, on the other hand the incidence of poly-microbial VAP increased significantly in the post-intervention phase with p value <0.001 (Table 1). The most common organisms in the pre-intervention phase were Klebsiella, Pseudomonas followed by Staphylococcus aureus, while in the post-intervention phase were Acinetobacter, Pseudomonas, Klebsiella followed by Staphylococcus aureus (Table 1).

The antibiotic sensitivity pattern of Klebsiella decreased significantly to impinem, piperacillin-tazobactam, cefoperazone-sulbactam, and amikacinin the post-intervention phase. Similarly, the sensitivity of Pseudomonas decreased significantly to carbapenems, β-lactam β-lactamase inhibitor combinations, third and fourth generation cephalosporins and aminoglycosides in the post-intervention phase. The Acinetobacter sensitivity decreased significantly to carbapenems, piperacillin-tazobactam and trimethoprim sulfamethoxazole in the post-intervention phase. On the other hand the Staphylococcus aureus sensitivity to vancomycin still remained the same (100%).

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DISCUSSION

Several effective interventions are not always adopted despite evidence supporting their use,[39-40] and this is not different when it comes to VAP prevention.[41-44] Although guidelines have been used to promote consistency and reduce variation in clinical practice, the successful implementation of any guideline is by no means assured and is dependent upon many factors, including implementation strategies that need to be tailored to the local situation.[8] Educational program has been utilized in VAP prevention in different aspects, mainly education for single procedures as hand hygiene,[9] oral hygiene,[10] sedation protocol[11] or staff education for either Institute for Healthcare Improvement (IHI) bundle[45] or its modification[46-47] or other selected ventilator bundle which includes several interventions for VAP prevention.[48-50]

The baseline characteristics and VAP risk stratification data (age, sex, APACHE II score, GCS, and history of chronic respiratory illness) were homogeneous between the pre and the post-intervention groups except for the admission diagnosis which differed significantly with a marked decrease of cardiac cases and increase of post-surgical cases in the post-intervention group. This was directly attributed to the diversion of most of acute coronary syndrome cases to new cardiac ICU during the intervention phase. The long lag between the pre and the post-intervention phases in the present study during which the circumstances related to admission in both units had changed, might contributed to these discrepancies in diagnosis type. However, neither the diagnosis type nor the place from which the patient was transferred (medical ward, scheduled surgical or emergency surgery) did increase risk of VAP in three studies.[51,52,53]

The DU ratio (a measure of invasive practices in a unit which constitutes an extrinsic risk factor for VAP[54] and a marker for severity of illness of patients[31] was highly significantly increased in the post-intervention group by 51%.This might be explained by the increased number of ventilators in the post-intervention phase. In addition, the registered nurse/patient ratio dropped by 50% in the evening and night shifts in the post-intervention phase which might have reduced patient care. This might have contributed to the increased risk of VAP in the post-intervention group as a result of shortage of competent nursing staff[55-56] and the highly significantly increased DU ratio. In spite of this, the VAP rate was decreased significantly by 35% as well as the clinically and laboratory confirmed VAP and the early onset VAP. On the other hand, the incidence of late onset, single and multiple VAP showed an insignificantly decrease.

Several educational program have reduced VAP rate such as Zack et al by 57%,[17] Babcock et al by 38-61%,[18] Apisarnthanarak et al by 59%,[16] Salahuddin et al by 51%,[57] Leblebicioglu et al by 46%,[20] Bouadma et al by 43%,[58] Blamoun et al by 100%,[59] Berriel-Cass et al by 60%[60] Lansford et al by 59.4%,[61] and International Nosocomial Infection Control Consortium (INICC) multimodal program by 30.7-79% in several studies.[21,23,62-64] The discrepancy between the adherence rate to VAP preventive practices and VAP rate reduction in those studies precluded any relation between the adherence to our VAP bundle and VAP rate reduction in this study. Similarly Zilberberg et al[65] revealed that the major methodological flaws in the design, reporting, and results of the published studies precluded any conclusive statements about bundle compliance and VAP reduction. Similarly, Beattie et al[66] failed to preclude any link between bundle compliance and development of VAP which they attributed to retrospective nature and small sample size of their study.

VAP bundle adherence, especially the overall adherence, is not the only determinants of the magnitude of VAP reductions. Other factors are important like working policy and procedures, nursing staffing, and equipment supply[67] which might explain different effect in these studies. Another explanation is that these VAP prevention programs utilized different educational (and sometime quality tools) to implement different combination of VAP preventive practices, this might have explained the different effects between studies. This was also illustrated by Marra et al[68] who tested the effects of different bundles introduced sequentially and had different results.

As in our earlier study that failed to reduce VAP rate, some educational studies also did not reduce VAP rate as Abbot et al[14] and Bloos et al[15] in spite of utilizing a variety of educational tools. Similarly Bingham et al,[13] did not reduce VAP which they attributed to frequent changes in personnel and leadership in the organization. In addition Hawe et al,[8] Papadimos et al,[69] Bigham et al,[70] and Cocanour et al,[71] after failure of passive education to improve bundle compliance and VAP rate, active education significantly improved bundle compliance and VAP rate. This suggests that addition of procedural or quality tool to interactive education significantly improved program efficiency.[69]

Morris et al[72] reduced clinically defined and laboratory confirmed VAP, while Rosenthal et al,[64] Bouadma et al[58] and Bigham et al[70] reported a significantly decreased clinically defined VAP only. Babcock et al[18] and Apisarnthanarak et al[16] did not affect time of onset of VAP. It might be suggested that the high incidence of early onset of VAP in the pre-intervention phase (known to be caused by intubation related aspiration) was more feasible to correction by educational program which was higher than those studies. The success stories of VAP reduction are often reported from hospitals with high baseline VAP.[73] On the other hand, Omrane et al[74] found that early onset VAP significantly decreased and late onset VAP significantly increased by educational program but through incidence density (per 1000 ventilation days). To the best of our knowledge, only Bouadma et al[58] reported decreased incidence of single and multiple VAP

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without statistical processing.

In this study, the secondary outcomes (ICU, MV and AB days and MV mortality) did not change significantly with staff education. Leblebicioglu et al,[20] Rosenthal et al,[62] Omrane et al[74] Morris et al,[72] and Bigham et al[70] did not find significant difference in total MV days or hospital stay. Apisarnthanarak et al,[16] Rosenthal et al,[64] and Youngquist et al[75] reported a significant decrease of hospital stay in the post-intervention phase. While, Abbot et al[14] and Bloos et al[15] reported a significant decrease of MV days despite unaffected ICU stay. Bouadma et al[58] did not find difference in MV days inspite of significantly reduced ICU stay. Apisarnthanarak et al[16] and Rosenthal et al[64] Bouadma et al[58] Bigham et al[70] Marra et al[68] reported no significant difference of mortality rate with educational program. Several educational programs did not evaluate outcomes other than VAP rate.[17-18,20] Hawe et al[8] and Morris et al[72] found a trend to reduced unit and MV mortality. Morris et al[72] found that antibiotic days did not change in all MV patients with VAP education.

The educational program did not affect the microbiology of organisms causing VAP (gram positive or negative) inspite of increased incidence of poly-microbial VAP. Similarly, educational program by leblebicioglu et al,[20] Rosenthal et al,[64] and Babcock et al did not affect the microbiology of infections, suggesting that intervention improved ventilator management and care rather than eliminating a particular nosocomial reservoir of infection.[18] While Apisarnthanarak et al,[16] Morris et al,[72] and Bouadma et al[58] reported only an outbreak of acinetobacter, decreased rates of methicillin-resistant Staphylococcus aureus acquisitions,and higher trend of staphylococcus aureus in the post-intervention study group respectively. Although the antibiotic sensitivity of most common organisms decreased to most relevant antibiotics in this study, Leblebicioglu et al[20] Rosenthal et al[64] reported non-significant change of antibiotic resistance to Acinetobacter, Pseudomonas and Staphylococcus aureus between the pre and post-intervention groups. This might be explained by the high rates of antibiotic abuse in our units. It might also be suggested that the reducing effect of VAP educational program on MV days and ICU stay might have been reversed by the highly significant increase of MDRP. However we did not evaluate other factors affecting MV days, ICU stay as other hospital acquired infections, ICU performance, and iatrogenic ICU complications (Table 3).

Antibiotics	Klebsiella		p	Pseudomonas		p	Acinetobacter		p
	Pre (n= 54)	Post (n= 47)		Pre (n= 49)	Post (n= 55)		Pre (n= 3)	Post (n= 74)	
Meropenem	45 (83.3%)	35 (74.5%)	0.273	36 (73.5%)	14 (25.5%)	<0.001*	2 (66.7%)	5 (6.8%)	0.021*
Impinem	47 (87.0%)	28 (59.6%)	0.002*	37 (75.5%)	10 (18.2%)	<0.001*	3 (100.0%)	13 (17.6%)	0.008*
Tazobactam-piperacillin	48 (88.9%)	18 (38.3%)	<0.001*	39 (79.6%)	17 (30.9%)	<0.001*	1 (33.3%)	0 (0.0%)	0.039*
Cefoparazone-sulbactum	42 (77.8%)	7 (14.9%)	<0.001*	33 (67.3%)	2 (3.6%)	<0.001*	0 (0.0%)	0 (0.0%)	-
Cefotaxime	5 (9.3%)	2 (4.3%)	0.445	2 (4.1%)	0 (0.0%)	0.220	0 (0.0%)	0 (0.0%)	-
Ceftriaxone	4 (7.4%)	2 (4.3%)	0.683	3 (6.1%)	0 (0.0%)	0.101	0 (0.0%)	1 (1.4%)	1.000
Cefepim	17 (31.5%)	10 (21.3)	0.248	16 (32.7%)	6 (10.9%)	0.007*	0 (0.0%)	0 (0.0%)	-
Ceftazidim	7 (13.0%)	6 (12.8%)	0.976	10 (20.4%)	4 (7.3%)	0.049*	0 (0.0%)	1 (1.4%)	1.000
Amikacin	18 (33.3%)	27 (57.4%)	0.015*	20 (40.8%)	8 (14.5%)	0.003*	1 (33.3%)	2 (2.7%)	0.114
Gentamyicin	15 (27.8%)	19 (40.4%)	0.180	18 (36.7%)	6 (10.9%)	0.002*	1 (33.3%)	8 (10.8%)	0.315
TMP-SMX	8 (14.8%)	9 (19.1%)	0.561	0 (0.0%)	1 (1.8%)	1.000	2 (66.7%)	3 (4.1%)	0.010*
Levofloxacin	21 (38.9%)	21 (44.7%)	0.556	20 (40.8%)	4 (7.3%)	<0.001*	1 (33.3%)	5 (6.8%)	0.219
Ciprofloxcin	14 (25.9%)	13 (27.7%)	0.844	11 (22.4%)	4 (7.3%)	0.028*	0 (0.0%)	4 (5.4%)	1.000
Ampicillin-sulbactam	3 (5.6%)	3 (6.4%)	1.000	4 (8.2%)	0 (0.0%)	0.049*	0 (0.0%)	0 (0.0%)	-
Amoxacillin-clavuanate	6 (11.1%)	8 (17.0%)	0.391	4 (8.2%)	0 (0.0%)	0.049*	0 (0.0%)	0 (0.0%)	-

Patients may have more than one organism in single VAP episode, so sum of organisms exceed the total number of VAP episodes

TMP-SMX: trimetho primsulfamethoxazol

Table 3: Comparison of antibiotic sensitivity pattern of gram negative organisms implicated in VAP cases in the pre and post intervention groups in Critical Care Unit 1 and 3.

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The costs of educational program were estimated not to exceed 1000 $ (conference rooms renting, folder and booklet materials printing), and additional infection control supplies not exceeding 3000$. There were no additional salaries for personnel sharing in the education program. Assuming a continued infection rate of 66.5 (of the pre-intervention phase) during the post-intervention phase, 302 VAP episodes would be expected to occur in the 4619 ventilator days in both units. Several studies measured the cost of a single VAP episode as low as 4,947-5,800 and up to 40,000$.[76-78] As our educational program prevented 102 episodes in post-intervention study group. The cost saving of this educational program was estimated to be at least 0.5 million dollars. Using the same calculation; Babcock et al[18] prevented 98 episodes and consumed 592000$, and therefore had a cost-saving of 0.4 million dollars.

Similarly, Apisarnthanarak et al[16] reported a 37-45% reduction of mean hospital (466$ *vs*. 293$ with P =0.001) and monthly antibiotic costs (4769$ *vs*. 2622$ with p =0.001) with VAP prevention program. Zilberberg et al[79] concluded that the available data of VAP prevention program is still difficult for accurate cost-effectiveness studies because it relates to such important downstream outcomes of VAP prevention as the use of antibiotics and hospital length of stay.

Several reviews addressed the discrepancy between the results of VAP education as Jansson et al[12] who suggested that it might be due to the wide range of definitions of VAP applied, lack of a universal method of outcome evaluation, variations in the implementation strategies (i.e. in the execution and frequency of education), ventilator bundle and various complementary interventions (reminders, feedback etc.) Moreover, the effects of extraneous factors or other potential sources of bias on their findings were inadequately reported resulting in both practical and methodological difficulty.[12]

Klompas et al[80] attributed the paradox of VAP intervention (either a single procedure like oral hygiene,[81] semi-sitting position,[82] silver coated tubes,[83-92] continuous subglottic suction,[1,93,94,95,96] or multiple procedures) to VAP misclassification; as it dramatically reduce VAP whereas most of them have no impact on clinical outcome (MV days, hospital stay, or mortality). As the sensitivity and specificity of microbiological diagnosis are only 50%-70% and 40%-95% respectively,[97-99] This include non-infectious mimics of VAP with bacterial colonization which are easily affected by simple preventive measures.[90]

These reviews also concluded that active implementation strategies (i.e. educational programs) were linked to significant improvements in the overall adherence to ventilator bundles and a significant decrease in clinical outcomes: incidence of VAP, duration of mechanical ventilation and hospitalization costs.[12] The opportunities for decreasing VAP rates seem to be greatest when multi-module programs were applied with an average reduction of more than 40%.[73] Arabi et al[100] concluded that simple cost-effective measures reduced the incidence of VAP significantly in developing countries with limited healthcare resources. For this reasons, staff education and involvement was recommended in most VAP prevention guidelines as American Thoracic Society and Infectious Disease Society of America[5] (I), Center of Disease and Control[3] (IA), SHEA and Infectious Disease Society of America[25] (A-II)

The pre-intervention VAP rate was higher than that reported in multicenter surveillance networks. The mean rates were 61 per 1000 ventilator-days in both ICUs. As compared to National Healthcare Safety Network 2008 (NHSN; formerly National Nosocomial Infections Surveillance [NNIS]) system, the 50th percentile of major teaching medical-surgical ICUs was 2.3,[91] INICC 2008 mean VAP rate of medical/surgical ICU was 14.7,[92] German Krankenhaus Infektions Surveillance System (KISS) surveillance system was 8.0 cases in all ICUs,[93] and the French national surveillance system median rate in all ICUs was 16.4 cases per 1000 ventilator-days in 2008.[94]

In the post-intervention phase, the mean VAP rates were 41 per 1000 ventilator days in both ICUs. As compared to NHSN 2011, the 50th percentile of major teaching medical-surgical ICU was 1,[95] KISS mean VAP rate of 6.8.[96] The large differences between our VAP rates and international VAP rate can be explained by several factors.

First: The NNIS and INICC utilized the CDC definitions while we utilized ACCP criteria for diagnosis. Skrupky et al[97] when compared the CDC and ACCP definition in the same study group showed large discrepancy (1.2 *vs*. 8.5 per 1000 ventilator days). Similarly the difference between the NNIS, KISS rates and the rates in France might be attributed to the different criteria for defining VAP across networks.[58]

Second: Studies from limited-resource countries have shown that VAP rates were more than three-fold higher than those in developed countries,[35,92,98-99] where lower-middle income countries had higher VAP rates than upper-middle-income countries (9.0 vs. 0.5 per 1000 MV-days).[100] Thus this higher VAP rate might be related to limitations associated with socioeconomic factors: the ICU equipment is less advanced than in developed countries, medical resources are relatively insufficient, there are crowded wards, patient-nurse ratio is low, and there is low compliance with preventive measures.[23] In an Egyptian respiratory ICU (in Cairo) VAP rate were 73.4 per 1000 ventilation days by CDC definition.[101]

Third: There were higher device associated infection rates and higher device-utilization ratios in major teaching hospitals (those hospitals with an important role in teaching programs and with clinical clerkships) than from all other hospitals.[102] These

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differences may result from differences in case mix (including differences in numbers of patients with severe trauma or with organ transplantation), in staffing, or in procedures.[102] Fourth: most of the surveillance system record the first VAP episodes or utilize the more rigid CDC criteria for diagnosis of second VAP attack by complete resolution of initial infections.[103] Therefore, The high VAP rate per 1000 ventilator days in both the pre and the post-intervention phases showed the compelling need that initiated the present study and still demanding for further VAP intervention Campaigns.

The major limitation of this study was the long time lag between the pre- and post-intervention phase (51 months) which might contributed to the resistance pattern of organisms prevailing. Although, this might be partly attributed to the lack of resources for program implementation, this might have attenuated the effect of the educational program. The second limitation of this study was that the personnel collecting the compliance to VAP preventive practices were different in both phases. In addition the observation of VAP preventive practices was only done in the morning shift in both the pre and post-intervention phases of both units.

The third limitation that both pre and post-intervention phases were observational non-randomized study (ICU staff and patients were non-blinded to the intervention). This raised the possibility of factors that have occurred which accounted for these results. For these reasons, we evaluated confounding factors which are considered the risk factors for VAP and used it for risk stratification. However the double blinded randomized trial is not applicable for the educational program because of failure to segregate its effect from study and control groups and also randomization of patients to receive or not to receive good care that has been recognized by IHI and Joint Commission on Accreditation of Healthcare Organizations' (JCAHO) may be unethical. Therefore educational program can only be applied through pre and post-intervention observation study as in all previous studies. Other factors like seasonal variation has been excluded as pre and post-intervention phase has been performed in the same months (both from September till May)

The fourth limitation; that this was a single medical center study, so the results cannot be generalized to other hospitals. However the quite similar results from several studies, suggests that this intervention might be applicable for other resource limited facilities, especially in developing countries. For this reasons, we explained our setting in details so that it can be compared to other facilities.

The fifth limitation of our study was its susceptibility to a number of biases. The clinical diagnosis by the modified ACCP criteria had limited specificity [30,104-105] and the possibility of misclassification bias cannot be ruled out. However the same observer and diagnostic criteria were used in both the pre and post-intervention study groups which might have attenuated the effect of any misclassification bias. Also the same personnel performed all patients' data collection in the pre and post-intervention study group. Thus observer bias might have occurred, although discussion of all suspected VAP cases have been done with surveillance team. Similarly the health-care worker was informed of surveillance and might have haw-throne effect (observer effect).

In spite of the importance of top management support and full availability of supplies, VAP staff education was still effective in reducing VAP through tailoring of educational and procedural tools. As in relation to our initial failure to reduce VAP rate as with Hawe et al,[8] Papadimos et al,[69] Bigham et al,[70] and Cocanour et al[71] it is suggested that active implementation strategies and multi-module program increase the success of VAP prevention programs.

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