Nosocomial Tracheobronchitis in Mechanically Ventilated Patients: Frequency, Aetiology and Outcomes

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Abstract

Objective: The aim of this study was to determine the frequency, etiology, microbiological sen-sitivity and outcomes of nosocomial tracheobronchitis (NTB) in mechanically ventilated patients admitted in surgical intensive care unit.

Methodology: A prospective observational study was conducted in the Surgical Intensive Care Unit (ICU), Department of Anaesthesiology, Civil Hospital Karachi from April 2009 to April 2010. All the patients on mechanical ventilator for more than 48 hours in the ICU were evalu-ated according to the criteria for the diagnosis of nosocomial tracheobronchitis (NTB). Out-comes of the patients were measured in terms of development of nosocomial pneumonia after NTB, length of ICU stay, duration of mechanical ventilation and mortality in the ICU.

Results: Two hundred and eighteen patients were evaluated for this study. Nosocomial tracheobronchitis was diagnosed in 72 patients. The frequency of NTB was 33%. Sixteen types of or-ganisms were identified, 61.23% cases were poly-microbial, while in the remaining 39.7% cases single organism was isolated. The most common organism was gram negative Acinetobacter spp (51%), followed by Klebsiella spp (29%) and Pseudomonas aeruginosa (16.6%). Escherichia coli and other gram negative rods were 13.8 % and 11.4%, respectively. There were 4.16 % cases of MRSA isolated in patients who had positive cultures for gram negative organ-isms (poly-microbial). Ceftriaxone was given in 44% cases as empirical therapy and continued in 33% cases after microbial sensitivity and replaced in 11% cases after culture sensitivity to Cefiperazone + salbactum and in 14% cases cefiperazone was given in combination therapy. Imipenem was used in 28.5% of patients. Quinolones were used in 19% contaminated cases of gut surgeries. Nosocomial tracheobronchitis was significantly associated with increased length of ICU stay and longer duration of mechanical ventilation in our patients when compared to those patients who did not develop NTB ($p<0.001$). Moreover, out of 72 patients, 11 developed subsequent nosocomial pneumonia. There was no statistically significant difference noted in mortality rates among patients with NTB and without NTB (43% vs. 41%). The mortality was related to concomitant comorbitidies, primary cause and surgical outcomes.

Conclusion: Nosocomial tracheobronchitis is a common infection in mechanically ventilated patients that significantly affects the development of pneumonia and length of ICU stay for the patients. This study was an insight to the state of NTB in an ICU setup. The higher frequency of NTB demands such studies to set protocols in every intensive care unit.

Keywords: Intensive care unit, mechanical ventilation, nosocomial tracheobronchitis, endotra-cheal tube.

(ASH & KMDC 19(1):21;2014).

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Introduction

Patients on mechanical ventilation via an oro-tracheal or naso-tracheal tube have a substantially increased risk for developing nosocomial tracheobronchitis. These patients breathing through naso-tracheal or oro-tracheal tube bypass the normal host defense mechanisms. Tracheal intubation thwarts the cough reflex, compromises mucocilliary clearance, injures the tracheal epithelial surface, provides a direct conduit for rapid access of bacteria from upper into the lower respiratory tract and al-

lows the formation of biofilm on the surface of Endotracheal tube (ETT). As a consequence, the biofilm acts as reservoir of pathogens, dislodgement of dry biofilms fragments are carried further into the lungs by ventilators gas flow and the resulting infection are relatively resistant to the action of microbial therapy[1,2,3,5,8]. The combination of these factors puts the mechanically ventilated patient at great jeopardy of developing ventilator associated tracheobronchitis which can lead to development of nosocomial ventilator associated pneumonia. Nosocomial tracheobronchitis (NTB) and nosocomial pneumonia (NP) are the second most commonly occurring hospital acquired infections among patients who require mechanical ventilation[1-5]. The sequence of colonization to NTB and, in some patients, to NP is related to increasing bacterial load, multidrug-resistant bacteria, and defective host defenses[4].

Tracheobronchitis is defined as fever (>38^{0}C) with no other recognizable cause, increased sputum production and a positive tracheal aspirate culture without radiological evidence of pneumonia[1, 3,6]. Diagnostic criteria for NTB and NP overlap in terms of clinical signs and symptoms and share similar microbiologic criteria when endotracheal sputum aspirate (ETA) samples are used. Quantitative analysis showing bacterial loads of >1x10^{5}cfu/ml indicate NTB. However, diagnosis of NP requires a new and persistent infiltrate on a chest radiograph and bacterial load in quantitative analysis of ETA of >1x10^{6}cfu/ml is required for the diagnosis of NP. In addition, serial quantitative cultures to identify multidrug-resistant pathogens and their antibiotic sensitivities help earlier targeted antibiotic treatment of NTB and prevent consequent NP, decreases length of mechanical ventilation and Intensive Care Unit (ICU) stay.

In fact, many studies have been done to find out the frequency, etiology and outcomes of nosocomial pneumonia but little is known about nosocomial tracheobronchitis (NTB)[1,6]. Therefore, the aim of this clinical observational prospective study was to determine the frequency of NTB, aetiology and outcomes in our population.

Patients and Methods

After approval from ethics committee and departmental permission, this observational cross sectional study was conducted in the Surgical Intensive Care Unit, Department Of Anaesthesia, Civil Hospital Karachi from April 2009 to April 2010. Patients aged between 18-80 years, who were ASA status 1-4 on mechanical ventilation with oral endotracheal intubation for duration of ventilation more than 48 hours, had temperature >38^{0}C or <36^{0}C, new or increased production of respiratory tract secretions, were selected on the basis of non probability convenience sampling. The patients with history of pulmonary tuberculosis, COPD, community acquired pneumonia, infiltrates in the lungs on chest radiograph before development of ventilator associated NTB, tracheostomy and ventilatory support in any other ICU other than the study place Surgical Intensive Care Unit (SICU) were excluded from the study.

The mechanically ventilated patients who met the inclusion criteria were included in the study. Demographic data in terms of age, height, weight, American Society of Anaestheiologist (ASA) status, gender, co-morbids, diagnosis, and nosocomial tracheobronchitis were evaluated by prospective surveillance of nosocomial infections. Patient characteristics and demographic data were collected by anaesthesia residents and trained infection control staff nurses. All patients were assessed daily and at the time of discharge by the conductor of this study. Clinical examinations were carried out on all the patients. Adequate hand washing and wearing gloves between patients before examination were made possible to avoid cross contamination from patient to patient. Other strategies to reduce ventilator associated nosocomial infections included use of new breathing circuit in every case, exchange of a heat moisture exchanger placed between Y-piece and patient when soiled. Mouth cavity and teeth were cleaned with chlorohexidyl solution. All patients were intubated through oral route and kept in semi- recombinant position during most of the period of mechanical ventilation, if not

otherwise contraindicated. Moreover, H2 receptor blocker intravenous ranitidine was given to every patient for stress ulcer prophylaxis. Throughout the study, tracheal aspirates for quantitative bacterial analysis were obtained; first sample was taken on admission, after 48 hours, weekly thereafter and, whenever needed according to clinical assessment .In every patient body temperature was recorded with esophageal probe. Nosocomial tracheobronchitis was suspected when temperature found above 38ºC with no other recognized cause of fever or <36ºC, new or increased production of airway secretion and positive endotracheal aspirate culture (>1x10^5cfu/ml) with-out any radiological evidence of pulmonary infection including new development of infiltrates, consolidation, cavitations, plural effusion. Nosocomial pneumonia was labeled when bacterial load found > 1x10^6cfu/ml with occurrence of new infiltrates on chest radiograph. All samples for culture were collected using no touch technique avoiding contaminations to prevent false positive results. Bronchial brushing or lavage was not taken as criteria for the diagnosis of ven-tilator associated pneumonia. Throughout ICU stay blood sample, urine, central line and wound discharge were sent for culture and sensitivity according to clinical status. Outcome of the patients was measured in terms development of ventilator associated nosocomial pneumonia, length of mechanical ventilation and ICU stay in days and mortality

Statistical analysis was performed using SPSS version10. Quantitative data was presented as mean ± SD (range), while frequency and percentage were calculated for qualitative values. Frequencies of outcome variables were compared between patients with (cases) and without NTB (controls) by means of Chi-square test. Student t test was applied to compare the quantitative variables among cases and controls. Differences between patient characteristics were considered significant if p-value was found < 0.05.

Results

During the study period of one year, a total of 218 patients were ventilated postoperatively on mechanical ventilators in surgical intensive care unit for period of more than 48 hours. All the patients were evaluated according to the criteria for the diagnosis of nosocomial tracheobronchitis (NTB). Out of total 218 patients studied, 64 patients were excluded due to the early development of nosocomial pneumonia on the basis of radiological findings and clinical correlation. Whereas, out of the remaining 154 patients, 82 patients did not develop nosocomial tracheobronchitis and were considered as controls. Seventy two patients (33.0%) were diagnosed as nosocomial tracheobronchitis and were considered as cases. These cases of NTB were studied for frequency, etiology, microbiological sensitivity and outcomes Fig.1. Demographic data of age and weight were comparable between patients who developed or did not develop NTB, Table1. The mean time from admission to the initiation of NTB symptoms on ventilators were 7 ± 4.23 days. Out of 72 patients with NTB, 11 patients developed subsequent nosocomial pneumonia (NP). The frequency of the patients developing only NTB was 27.9% and patients who developed NP as the consequence after NTB was 5.04%. In endotracheal tube culture re-ports 16 types of organisms were identified, out of which 61.23% cases were polymicrobial, while in the remaining 39.7% cases single organism was isolated Table 2. The most frequently cultured organism was gram negative Acinetobacterspp 51% while the second most occurring organism was Klebsiella spp 29.1%, the next was pseudomonas aeruginosa 16.6%. Escherichia coli and other gram negative rods were 13.8% and 11.4%, respectively. There were 4.16% cases of MRSA isolated in patients who had positive culture for gram negative organisms (poly-microbial), Table 3.

Antimicrobial therapy was started in 98% empirically in patients with NTB and 97% patients without NTB on admission in hospital or before admission to SICU. In SICU antibiotics were selected according to the antibiogram made from the recorded data of ETT culture results of over last six months and in correlation with the clinical condition of the patients. Ceftriaxone was given in 44% cases as empirical therapy and continued in 33% cases

after microbial sensitivity and replaced in 11% cases after culture sensitivity to Cefiperazone and salbactum and in 14% cases cefiperizone was given in combination therapy. Imipenem was given in 28.5% of patients. Quinolone was used in 19% cases of contaminated gut surgeries, Table 3.

There was a statistically significant difference in terms of outcomes measured, subsequent pneumonia was developed in 11 patients after NTB ($p< 0.01$). It was significantly associated with increased length of ICU stay and longer duration of mechanical ventilation when com-pared to those patients who did not develop NTB ($p<0.001$). There was no significant difference found in terms of mortality rates among patients with NTB and without NTB. The mortality was related to concomitant comorbidities, primary cause and surgical outcomes, Table 4.

Discussion

Although much work has been done on detection and consequences of nosocomial pneumonia, but unfortunately little attention is paid towards aetiology and outcome of nosocomial tracheobronchitis (NTB) in surgical patients, who generally require mechanical ventilatory support for predictive period of time as compared to medical patients. Inadequate understanding and management can lead to development of ventilator associated pneumonia or worsening of nosocomial tracheobronchitis resulting in prolonged ICU stay due to difficult weaning from ventilators[1].

This study was conducted in the patients admitted in surgical intensive care unit requiring post operative ventilation for more than 48 hours, and at risk of developing infections. We found out that total frequency of ventilator associated NTB was 33.0%, the patients who developed NTB only was 27.9% whereas 5.04% case of NTB progressed to NP. However, 16 species of organ-isms were identified, 61.23% cases were polymicrobial while in the remaining 39.7% cases single organism was isolated. The most frequently cultured organism was gram negative Acinetobacterspp (51%), followed by Klebsiella spp (29%) and Pseudomonas aeruginosa (16.6%). Nosocomial tracheobronchitis was significantly associated with increased length of ICU stay, and longer duration of mechanical ventilation in our patients when compared to those patients who did not develop NTB ($p<0.001$) (Table 4). There was no significant difference noted in mortality rates among patients with NTB and without NTB (43% vs. 41%).

The prevalence of nosocomial tracheobronchitis is variable in different setups in different countries. Several clinical prevalence studies have been carried out in Europe and USA, showing nosocomial lower respiratory tract infections rate, other than ventilator associated pneumonia (VAP) ranges from 4.0-17.8%, but NTB was not specifically reported[1,11]. However, few large sample studies have specifically determined incidence of NTB in intensive care units. Kampf et al., in a multicentre study included 151 patients, and Rello et al. evaluated NTB in 161 ICU patients and reported a significant incidence in their surgical ICU[14,15].

Nseir and colleagues evaluated a large sample of 2,128 patients ventilated for >48 hours, including 283 surgical patients and 1,845 medical patients in ICU[1]. A total of 201 (10.6%) NTB cases were diagnosed in surgical ICU compared to 9.9% in medical ICU ($p=0.01$, OR 1.64). In our study NTB frequency is much higher than previously reported studies in Europe and USA. The higher rate in our study is more likely attributed to improper practice of infection control due to defective nursing care, contamination of breathing circuits, improper hygiene of mouth and gastric regurgitation which are the established causes of colonization of the lower respiratory tract by bacteria and NTB, such as pseudomonas aeruginosa, which is in turn associated with subsequent development of overt pneumonia[8,16,18].

Similarly, in our aetiological analysis the most frequently cultured organism were Acinetobacter (51%), Klebsiella spp (29.1%) and pseudomonas aeruginosa (16.6%), whereas Nseir and coworkers found pseudomonas aeruginosa the most common organism (31.8%) and Klebsiella spp was isolated

in only 4% cases in their culture results. Isolation of various organisms in different frequency supports the idea of generating individual antibiogram for every ICU setup for effective management after knowing the incidences, aetiology and antibiotic sensitivity[1,19,20].

To our knowledge very few studies have looked into the outcomes of NTB. The impact of NTB on length of ICU stay and duration of mechanical ventilation are less reported than that of nosocomial pneumonia. We found increased length of ICU stay and prolonged mean duration of mechanical ventilation in patients with NTB when compared to controls ($p<0.001$), Table 4. Likewise, Nseir et al. also found increased duration of ICU stay and length of mechanical ventilation in patients with NTB (35.2 ± 26days) compared to those patients without NTB (18.1 ± 15.1 days), $p<0.001$.Other studies also report the similar outcome of NTB that attributed to difficult weaning from ventilator[1,5,13].

However, we found an insignificant difference in terms of mortality in patients with NTB and without NTB. Moreover, fewer other studies also mentioned statistically insignificant difference in mortalities between cases and controls, which is consistent with our results. This shows that NTB prolongs only the length of stay and days on mechanical ventilation, but does not increase the mortality[1,5,6,13,15].

Previous studies based on ATS guidelines for nosocomial respiratory tract infection suggest that the initial antibiotic therapy should be based on specific risk factors that influence the spectrum of causative microorganism in the particular patients. Considering the importance of adequate initial antimicrobial, a de-escalating strategy i.e. starting with broad spectrum therapy followed by narrow spectrum specific therapy, according to the microbiological results is recommended. This deescalating strategy provides optimal benefit for the patients with severe infections, while switching to the specific antibiotic therapy according to the microbiological data may help to minimize the risk of emerging resistance[3,4,14,19].

In most circumstances, initial narrow spectrum antibiotic regime should not be used since they do not cover the most common microorganism and necessitate the modification of initial regimen due to poor clinical response or primary resistance. According to the American Thoracic Society guidelines (ATS) regarding initial treatment for gram negative bacteria, imipenem, ciprofloxacin and gentamicin display good cover, in contrast to broad spectrum penicillin and cephalosporins that were used in most of our patients during hospitalization before admission to SICU, and continuation of same regime resulted in growth of multi drug resistance bacteria which were later found sensitive to cefiperizone and salbactum (24%), imipenem (28.5%)[3,5,6,7,19,20].

The variability in the aetiology and antibiotic sensitivity explains the importance of local ICU protocol for determining the antibiogram according to the culture and sensitivity results and thus somehow ensures adequacy of the initial empiric therapy[19,20]. This study will definitely help in setting the proper antibiotic regime in our ICU. This study and other such studies which find the etiology and microbial sensitivity have some limitations. First, the results may not be applicable to patients of other ICU due to different incidence of microorganism and antimicrobial resistance. Next, patient's population may include patients with comorbids like COPD which needs further modification in the treatment. Further studies should be conducted in continuity to know the changing trends and impact of antibiotic treatment according to culture and sensitivity on outcome of nosocomial tracheobronchitis in future.

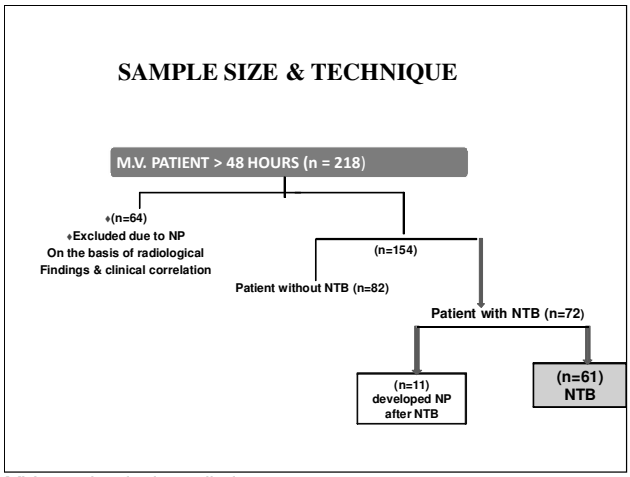
Conclusion

Nosocomial tracheobronchitis is a common infection in mechanically ventilated patients in surgical intensive care units, and it significantly affects the outcome of the patients. This study is an insight to the state of NTB in an ICU setup. Moreover, such studies should be carried out in every intensive care unit for prevention and management of NTB in future.

Acknowledgement

Authors thank Prof. Najeeb Ansari for his expert advices in the manuscript writing.

Fig 1. Shows the final sample size of the patients with NTB (Nasocomial tracheobronchitis included) in the study.



MV: mechanical ventilation

Table 1. Demographic characteristics of patients with and without nosocomial tracheobronchitis (NTB)

	NTB (n=72) Mean±SDorN(%)	Non NTB (n=82) Mean ±SD or N (%)	p-value
Age	41.05± 13.7	45.34±11.32	NS
Gender - male	33 (46)	35 (43)	NS
Weight	62.67± 9.6	59.24±11.65	NS
HOH (%)	79 (96.5)	80 (98)	NS
HOA (%)	71 (98)	79 (97)	NS
ASA I	50 (69.5)	56 (68)	NS
ASA II	9 (12.5)	11 (14)	0.01
ASA III	9 (12.5)	10 (12)	0.001
ASA IV	4 (5.5)	5 (6)	0.001

HOH=History of hospitalization, HOA=History of antibiotics;
NS: non-significant
ASA=American Society of Anesthesiologists Grading.

Table 2. Bacteria isolated from endotracheal tube culture of patients diagnosed as nosocomial tracheobronchitis .

Bacteria isolated from ETT cul-ture	%(N) of the patients
Acinetobacterspp	51(37)
Klebsiellaspp	29.1(21)
Pseudomonas aeruginosa	16.6(12)
Escherichia coli	13.8(10)
Other gram-ve rods	11.4(8)
Caogulase negative staph	4.16(3)
Staphylococcus aureus MRSA	4.16(3)
Enterobacter aerogenes	3.1(2)
Streptococcus spp	3.1(2)
Proteus mirabillus	3(2)

MRSA: methicillin-resistant Staphylococcus aureus; MSSA: methicillin-sensitive Staphylococcus aureus.

Table 3. Antimicrobial therapy and percentage (%) of patients which received therapy for nosocomial tracheobronchitis (NTB) in intensive care unit (ICU)

Antibiotics used in NTB	% (N) of NTB patients received
Metronidazole	67.5(48)
Ceftriaxone	44(31)
Gentamycin	32 (23)
Imipenum	28.5(21)
Cefiperazone+salbactum	24(17)
Ciprofloxacin	19 (14)
Augmentin	18(13)
Tazocin 9(7)	
Amikacin	7.5(5)
Vancomycin	6(4)
Benzyl penicillin	6(4)
Maxipime	1.5(2)

Table 4. Outcome of patients with and without ventilator associated nosocomial tra-cheobronchitis.

	NTB (n=72) Mean ±SD	Non-NTB (n=82) Mean ±SD	p-value
ICU LOS Days	6.51 ± 4.6	3.12 ± 1.0	0.001
Lenght of days on MV	5.47 ± 4.1	2.15 ± 1.0	0.001
Mortality %	43	41	0.067

NTB: nosocomial tracheobronchitis; LOS: length of stay;
MV: mechanical ventilation

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