doi • 10.5578/tt.57434
Tuberk Toraks 2018;66(1):52-56
Geliş Tarihi/Received: 07.12.2016 • Kabul Ediliş Tarihi/Accepted: 30.09.2017

KLİNİK ÇALIŞMA
RESEARCH ARTICLE

Characteristics of influenza pneumonia patients admitted to the ICU due to hypoxemic respiratory failure

Özlem EDİBOĞLU[1]
Sena ATAMAN[1]
Cenk KIRAKLI[1]

[1] Intensive Care Unit, Izmir Dr. Suat Seren Chest Diseases and Chest Surgery Training and Research Hospital, Izmir, Turkey
[1] *İzmir Dr. Suat Seren Göğüs Hastalıkları ve Göğüs Cerrahisi Eğitim ve Araştırma Hastanesi, Yoğun Bakım Ünitesi, İzmir, Türkiye*

SUMMARY

Characteristics of influenza pneumonia patients admitted to the ICU due to hypoxemic respiratory failure

Introduction: *Hypoxemic respiratory failure due to influenza pneumonia during epidemic seasons sometimes may require mechanical ventilation support and intensive care unit (ICU) stay. We aimed to evaluate the characteristics and risk factors of influenza pneumonia patients admitted to our ICU due to hypoxemic respiratory failure.*

Materials and Methods: *Patients admitted to our ICU between December 2015 and March 2016 who had hypoxemic respiratory failure due to clinically and radiologically suspected influenza pneumonia were enrolled.*

Results: *Twenty two patients (11 male) met the enrollment criteria. Median age and APACHE II score was 45 (36-63) years and 19 (13-25) respectively. Maximum set PEEP levels during mechanical ventilation was significantly lower in patients who survived [10 (8-10) vs 13 (10-16), p= 0.025)]. Deceased patients spent more time under a PaO_2/FiO_2 ratio below 100 [72 (24-90) vs. 0 (0-48) hours, p= 0.024]. Survival rate was 88% (7/8) in patients who had noninvasive ventilation (NIV) success while it was only 7% (1/14) in patients who had undergone invasive mechanical ventilation (p< 0.001). Overall mortality was 64%.*

Conclusion: *Viral pneumonia may result in severe hypoxemic respiratory failure and ARDS especially during epidemic seasons. NIV success, time spent under a PaO_2/FiO_2 ratio below 100 and low serum albumin levels at admission may be predictors of severity of the disease and mortality.*

Key words: *Pandemic influenza A (H1N1), intensive care, mechanical ventilation, mortality*

ÖZET

Hipoksemik solunum yetmezliği ile yoğun bakıma başvuran influenza pnömonili hastaların özellikleri

Giriş: *Epidemi mevsiminde influenza pnömonisi sebebiyle gelişen hipoksemik solunum yetmezliğinde yoğun bakım ve mekanik ventilasyon tedavisi gerekebilir. Bu hastalar genç olmasına rağmen mortalitesi yüksektir.*

Yazışma Adresi (Address for Correspondence)

Dr. Özlem EDİBOĞLU
İzmir Dr. Suat Seren Göğüs Hastalıkları ve Göğüs Cerrahisi Eğitim ve Araştırma Hastanesi, Yoğun Bakım Ünitesi,
İZMİR - TURKEY
e-mail: ozlemediboglu@gmail.com

Materyal ve Metod: *Aralık 2015 ile Mart 2016 tarihleri arasında, klinik ve radyolojik olarak viral pnömoni şüphesi olan hastalar çalışmaya alındı. Demografik özellikler, risk faktörleri, mekanik ventilasyon desteği ihtiyacı ve tipi, laboratuvar değerleri, pulmoner (ECMO) ve renal (CRRT) destek ihtiyacı ve mortalite oranı kaydedildi.*

Bulgular: *Yirmi iki hasta çalışmaya dahil edildi. Ortalama APACHE II skoru 19 (13-25) ve yaş 45 (36-63) idi. Semptomların başlama süresi 7 (6-9) gün idi. En sık görülen semptomlar öksürük, ateş, nefes darlığıydı. Sekiz (%36) hastada risk faktörü mevcuttu. Mekanik ventilasyon sırasında uygulanan maksimum PEEP değeri yaşayan hastalarda daha düşük idi [10 (8-10) vs. 13 (10-16), p= 0.025)]. PaO_2/FiO_2 oranı 100'ün altında geçirilen süre ölen hastalarda daha kısa idi [72 (24-90) vs. 0 (0-48) saat, p= 0.024]. Ölen hastalarda serum albumin düzeyi daha düşük bulundu [2.6 (2-3.1) vs. 3.5 (2.6-3.7) g/dL, p= 0.033]. İki hastaya ECMO ve 5 hastaya CRRT uygulandı. Survi oranı NIV başarısı olan hastalarda % 88 (7/8) iken, invaziv mekanik ventilasyon uygulandığında %7 (1/14) olarak bulundu (p< 0.001). Mortalite %64 olarak bulundu.*

Sonuç: *İnfluenza pnömonisi sırasında ARDS ve hipoksemik solunum yetmezliği görülebilmektedir. Tam destek uygulansa dahi bu hastalarda mortalite yüksek olabilmektedir. NIV başarısı, PaO_2/FiO_2 oranı 100'ün altında geçirilen süre ve serum albumin düşüklüğü hastalık şiddeti ve mortalite belirteci olarak bulunmuştur.*

Anahtar kelimeler: *Pandemik influenza A (H1N1);yoğun bakım;mekanik ventilasyon; mortalite*

INTRODUCTION

Viral infections can cause pandemic outbreaks with varying severity especially in winter. Since 2009 different types of influenza virus have been detected which led to pneumonia with hypoxemic respiratory failure (1). Many of these patients may require mechanical ventilation and intensive care unit (ICU) support (2). Although non-invasive ventilation (NIV) is increasingly used in hypoxemic respiratory failure many of these patients still may need intubation (3-5). Mortality rate is high and seems to be correlated with the severity of hypoxemia (6,7).

We aimed to evaluate the characteristics and risk factors of influenza pneumonia patients admitted to our ICU due to hypoxemic respiratory failure.

MATERIALS and METHODS

This was single center observational cohort study. Twenty two of 314 patients enrolled the patients admitted to the ICU between December 01, 2017 and March 31, 2017. We prospectively collected data on all patients with hypoxemic respiratory failure and bilateral infiltration on chest X-ray due to suspected influenza pneumonia during pandemic season. Nasopharyngeal swap specimens were obtained from all patients to identify viral infection on admission to the ICU. Severity of illness was assessed with Acute Physiology and Chronic Health Evaluation (APACHE II) instrument. Demographic characteristics (e.g. age, gender, smoking status, place of residence), risk factors, symptoms, PaO_2/FiO_2 on admission, need and type of mechanical ventilatory support, laboratory values, time spent as PaO_2/FiO_2 < 100 and < 200, need of extracorporeal pulmonary (ECMO) and renal support (CRRT) and mortality rate were evaluated. We also recorded time from the onset of symptoms to admission to the ICU, days of antiviral treatment, presence of viral confirmation or not, duration of ICU and hospital stay and mortality.

Statistical Analysis

Data are expressed as median (25^{th}-75^{th} percentile) or n (%) and compared using Mann Whitney U test or Fischer's exact test where appropriate.

RESULTS

Twenty two patients with hypoxemic respiratory failure included to the study. Overall mortality was 64%. Eleven (50%) patients were male. Median age was 45 (36-63) years and APACHE II score was 19 (13-25). Time from the onset of symptoms to admission to the ICU was 7 (6-9) days. All patients were treated with oseltamivir, 75 mg twice a day. Most common symptoms were shortness of breath (77%), cough (59%) and fever (41%) respectively. None of the patients was obese (body mass index < 20). Risk factors were present at 8 (36%) patients. Most common risk factor was diabetes mellitus. One (4%) patient was pregnant, and underwent Cesarean section (C/S) while in the ICU. Patients' demographics and clinical characteristics are shown in Table 1.

Viral confirmation was present only in three patients. influenza A, subtype H1N1 was positive in two patients and influenza B was positive in one patient. Although no viral confirmation in the other patients,

Table 1. Patients demographics and clinical characteristics

Age, years	45 (36-63)
APACHE II score	19 (13-25)
Male, n (%)	11(50)
Smoking history	13(59)
Cigarette, pack year	40 (23-80)
Risk factors, n (%)	8 (36)
Diabetes mellitus	4 (18)
COPD	1(4)
Congestive heart failure	2 (9)
Pregnancy	1(4)
Obesity	0 (0)
Duration of admission to ICU, days	7 (6-9)
White blood cells, cells/mm^3	6400 (4600-11600)
Hemoglobin, mg/dL	14 (12-15)
Hematocrit, %	42 (37-44)
Platelets, cells x10^3	179 (127-268)
C-reactive protein, mg/dL	19 (12-23)
Eosinophil count, cells/µL	00 (00-00)
Creatinine mg/dL	9 (7-1,4)
Lactate dehydrogenase, U/L	567(417-901)
Albumin, g/dL	2,8 (2,5-3,3)
pH	7.42 (7.36-7,48)
$PaCO_2$, mmHg	35 (29-45)
PaO_2/FiO_2	113 (62-150)
CRRT, n	5
ECMO, n	2
ICU stay, days	7 (4-10)
Hospital stay, days	10 (8-17)

APACHE II: Acute Physiology and Chronic Health Evaluation, COPD: Chronic Obstructive Pulmonary Disease, ICU: Intensive Care Unit, CRRT: Continuous Renal Replasman Therapy ECMO: Extracorporeal Membranous Oxygenation. Data are expressed as median (25th -75th percentile) or n (%) where appropriate.

the diagnosis of viral pneumonia was made clinically and radiologically in epidemic season.

Median PaO_2/FiO_2 ratio on admission was 113(62-150). There was no difference between survivors and nonsurvivors according to PaO_2/FiO_2 ratios. We applied NIV at admission to ICU in all patients. When the NIV failure had seen IMV applied immediately. Both NIV and IMV has been set up according to ARDS (Acute Respiratory Distress Syndrome) management strategy. Maximum set PEEP levels during mechanical ventilation and the time under PaO_2/FiO_2 ratio below 100 were significantly higher and serum albumin levels were significantly lower in nonsurvivors when compared to survivors (Table 2).

We performed ECMO (Novalung, Xenios AG, Germany) treatment via veno-venous cannulation in two patients. One patient died because of massive hemorrhage from the cannulation site during ECMO. We did not encounter any ECMO related complication in the other patient but he died because of septic shock. Five patients underwent CRRT due to acute renal failure.

DISCUSSION

The main finding of this study is the high mortality rate in influenza pneumonia patients admitted to the ICU due to hypoxemic respiratory failure. Severity of hypoxemia, serum albumin levels and NIV failure seems to be related with mortality in these patients.

Pandemic influenza infections generally occur below 60 years of age because of acquired immunity in older population. Nin et al. reported that only 7% patient were above 65 years (8). In several studies median age of the patients were reported between 27 to 44 (7,9,10). In this study median age was 45 years.

Table 2. Comparison between survivors and nonsurvivors

Patient data	Survivors	Nonsurvivors	p
PaO_2/FiO_2 on admission	113 (103-136)	113 (51-150)	ns
Time spent PaO_2/FiO_2 < 100, hours	0 (0-2)	3 (1-5)	0.033
NIV success, n (%)	7	1	ns
PEEPmax, cmH_2O	10 (8-10)	13 (10-16)	0.025
Albumin, g/dL	3.5 (2.6-3.7)	2.6 (2.0-3.1)	0.024
Need of mechanical ventilation, n (%)	1	14	ns

NIV: Noninvasive ventilation, PEEPmax: Maximum positive and expiratory pressure.

We found that 36% of patients had risk factors. Four of patients had diabetes mellitus, two had cardiac failure and one had COPD. Pregnancy was present in one patient and she was underwent C/S in the ICU. Obesity which has BMI > 30, pregnancy, and diabetes mellitus were the most frequently seen comorbid conditions (2,10-12). Contrary to the literature, obesity was not seen as a risk factor in this study.

In our study NIV was applied via full face mask with ICU ventilator which has a dedicated NIV mode. Although the beneficial effect of NIV therapy in hypoxemic respiratory failure is still debatable, some studies suggest that the most important factor in NIV success was the etiology of hypoxemia (5,12). Since 2009 NIV was widely used in influenza pneumonia cases who had hypoxemia) in an attempt to decrease rate of endotracheal intubation in about 40% of cases (3-5,13). NIV has been used as a first line ventilatory support in patients with clinical criteria of acute respiratory distress syndrome (ARDS) with a success rate of more than 50% (14). Intubation rate reported in acute hypoxemic respiratory failure was around 25-54% and 60% in noncardiogenic pulmonary edema patients in literature (4,15,16). NIV failure rate was correlated with ARDS stages and severity of hypoxemia. In mild ARDS patients (31%) intubation rate was reported close to in non ARDS patients (35%). Moderate and severe ARDS patients had higher intubation rates (64% and 84%). Among patients with moderate ARDS, those with $PaO_2/FiO_2 < 150$ had higher risk of intubation (4). Our patients PaO_2/FiO_2 rate on admission to ICU was 113, time spent under $PaO_2/FiO_2 < 100$ was longer in nonsurvivors and intubation rate was found 63%.

Mortality rates among these patients admitted to ICU were reported around 16-41% and most of these patients need invasive ventilatory support (2,17,10). In this study survival rate was found 78% at patients who had NIV success while Teke et al. reported this data as 92% (12).

We found that albumin levels were lower in nonsurvivors. Sanz et al. also found hypoalbuminemia in severe hypoxemic patients with Pneumonia Severity Index (PSI) I-III and $PaO_2/FiO_2 < 300$. Hypoalbuminemia is an indicator of the patients' nutritional status and also there are some studies suggesting that it can also be an independent risk factor for mortality in critically ill patients (6,18).

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