Original Article

Study of application of Non Invasive Ventilation in patients of severe pneumonia and acute respiratory failure caused by novel influenza A H1N1 virus

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ABSTRACT

Background: Respiratory system is the most common organ system affected in patients of H1N1influenza. Many patients requires mechanical ventilation for treatment as they develop ALI/ARDS due to primary viral or secondary bacterial pneumonia. In resource poor countries like us, providing ICU ventilator to all patients can produce a difficult task for health care system. Noninvasive ventilation can be an option provided appropriate patients are chooses at right stage of disease-probably in early stage of acute hypoxic respiratory failure.

Aim: (1) To identify the patients suitable for non-invasive ventilation in patients of swine flu with signs of respiratory failure (2) To study outcome of NIV in these patients with aim to identify factors for the so called "late failure of NIV".

Materials and Methods: This study is meant to analyze data from patients of Novel H1N1 influenza patients admitted to swine flu isolation ward during January to December 2015 at PDU Hospital, Rajkot. From 650 patients admitted as suspected case, 283 were confirmed by RTPCR. Among 84 patients who were offered NIV 43 died during course of treatment. It is a retrospective study to analyze the patients who remains stable on NIV for at least 24 hrs. There were 66 such patients.

Results: Out of 66 patients studied, 40 successfully treated with NIV. After initial 24 hrs factors which were statistically significantly associated with NIV late failure were-pregnancy (including postpartum period), tachycardia on admission and high total count during course of treatment (suggesting developing bacterial pneumonia).

Conclusion: NIV can be used in selected patients of viral pneumonia. In pregnant or postpartum patients NIV should be used with caution. Signs of developing of bacterial pneumonia and MODS herald the chances of NIV failure. Co morbidities are not a strong predictor for NIV failure. Avoiding intubation can decrease complications particularly in immunocompromised patients. Use of steroid does not have significant effect on respiratory function improvement.

Key words: H1N1 influenza A infection, severe pneumonia, NIV late failure

INTRODUCTION

On April 21, 2009 the center for disease control on prevention reported the detection of 2 cases of human infection with 2009 influenza A (H1N1) in California [1,2]. WHO declared global pandemic on June 11, 2009 [3,4]. The first case of 2009 pandemic influenza A H1N1 virus infection in India was reported in May, 2009 and in Saurashtra and Kutch region of Gujarat in August, 2009 [5].

Respiratory system was most common organ system to be involved in H1N1 patients and severe pneumonia and ALI/ARDS being common complication.

NIV has established role in management of COPD (acute hypercapnic respiratory failure) and in cardiogenic pulmonary edema but its use in acute hypoxic respiratory failure i.e. ALI/ARDS cases remains controversial [6-15].

From physiological point of view, the application of positive airway pressure opens alveolies in under-ventilated areas of lung and increases forced respiratory capacity thus decreases right to left shunt and improves oxygenation. [12]

Intubation increases chases of secondary bacterial pneumonia, so NIV is suitable option particularly in immunocompromised patients. [12]. On the other

hand in poorly selected patients or poor timed intubation results in very poor outcome in AHRF patients.

Our center was established for treatment of H1N1 influenza patients coming from Saurashtra and Kutch region of state of Gujarat in September 2009.In our study period of January to December 2015, there were total 650 patients admitted to isolation ward, among them 283 patients had confirmed novel influenza A infection. Among all critical patients 57 patients died (either offered NIV or intubated right on admission).

In comparison to other studies done for NIV in AHRF, we tried to correlate with primary clinical parameters which would be more helpful to centers where investigations like blood gas analysis, CT scan thorax and culture reports are not possible repeatedly.

MATERIAL AND METHODS

We retrospectively evaluated medical records of all patients admitted to H1N1 ward during the year 2015 at P.D.U. Govt. Medical College and hospital, Rajkot. We included only adult patients, all of them having confirm H1N1 influenza A infection detected by RTPCR test of nasal/throat swab or respiratory secretions. Out of 283patients, we studied patients who were offered NIV treatment (i.e. not having any contraindication for NIV).There were total 84 patients who were offered noninvasive ventilator. We isolated the patients who either remained stable or improved after first 24 hrs. of noninvasive ventilation. So we omitted the patients who were either too sick-needed intubation in less than 24 hrs. of NIV or who were too stable and required mechanical ventilation only for less than 24 hrs. which came to 66 patients from 84 patients and we tried to identify various clinical parameters which may be responsible for so called late failure of NIV.

Statistical Analysis
Mean comparison for continuous variables were done using t test. For categorical variables chi-square test was used. Statistically significance was set at p<0.05.

RESULTS

We analyzed the data from 66 study participants. The age of them varies from 15 to 82 years. There were more female patients than male. Patients from rural area predominate. Breathlessness, cough and fever were most common symptoms in more than 90% patients, other less common symptoms mentioned in table no.1.

Table 1: Characteristics in all patients remaining stable for 24 hours (n=66)

Parameter	Result
Age	
Mean	43.5
Range	(15-82 years)
SEX	
Female	39(59.1)
Male	27(40.9)
Inhabitance	
Rural	39(59.1)
Urban	27(40.9)
Symptoms	
Breathlessness	65(98.5)
Cough	66(100)
Fever	62(93.9)
Palpitation	10(15.15)
Hemoptysis	5(7.57)
Chest pain	5(7.57)
Nausea	2(3.03)
Vomiting	1(1.51)
Diarrhoea	1(1.51)
Addiction	
Smoking	6(9.09)
Alcohol	1(1.51)
Tobacco	3(4.54)
Lifestyle	
Hardworking	63(95)
Diet	
Vegetarian	60(90.91)
Mixed	6(9.09)
General Examination signs	
Pallor	6(9.09)
Jaundice	0
Cyanosis	0
Clubbing	0
Oedema feet	0

(Figures in parenthesis are percentages)

Among 39 female patients 4 were in per or postpartum period. Most common co morbid condition was diabetes (24.2%).Frequency of other co morbidities like hypertension.IHD, stroke, ESRD, COPD, PLWHA, asthma etc. are mentioned in table no.2.

Depression, psychiatric illness, hypothyroidism, silicotuburculosis, positive IgM for Dengue fever, tuberculosis were present in one patient each. Two patients noticed to have muscular dystrophy. Addiction, diet and life style pattern are noted in table no.1.Expect for pallor (9.1%), and no other significant general examination finding was noted. Tachycardia and tachypnea were common findings. Mean blood pressure ranges from 70 to 114 mm

Hg. As these were the patients of severe pneumonia, initial SpO2 with 4 lit O2 by mask ranged from 40% to 98% with mean of 81.71 %. (table no.3)

Table 2: Co morbidities in all patients remaining stable for 24 hours (n=66)

Co morbidity	Total no. (Frequency in %)
Diabetes	16(24.24)
Hypertension	10(15.15)
IHD	4(6.06)
Pregnancy*	4(6.06)
Stroke	2(3.03)
PLWHA	2(3.03)
ESRD	1(1.51)
COPD	2(3.03)
Other co morbidities †	8(12.12)
Valvular Heart diseases	0
Asthma	0

*Including postpartum period
†See text for detail

Hemoglobin concentration and platelet counts were normal in most patients. However total count on admission ranges from leucopenia (400/cumm) to leucocytosis (26000/cumm).Highest WBC count during entire course of treatment varies from 4400/cumm to 32800/cumm. In natural course of disease development secondary bacterial pneumonia over primary viral pneumonia in later phase of disease causes rise in WBC count. (Table no.3)

Table 3: Vital data and laboratory parameters in all patients remaining stable for 24 hours (n=66)

Parameter	Observed value
Pulse mean(range) per min.	101.82(74-138)
Mean blood pressure mean (range) mmhg	90.80(70-114)
Respiratory rate mean(range) per min	30.68(18-48)
SpO2 mean(range) %*	81.71(40-98)
Haemoglobin lowest mean(range) gm.%	10.56(6.20-14.20)
WBC count on admission mean(range)cells per cumm	7293.69(800-26000)
WBC count highest mean(range)cells per cumm	14434(4400-32800)
Platelet count mean(range) on admission lac/cumm	1.87(.29-5.70)
Platelet count mean(range) lowest lac/cumm	1.43(.02-4.60)
Platelet count mean(range) highest lac/cumm	3.34 (.80-8.80)
RBS† Mean (Range) mg%	167.64(72-428)
S.creatinine mean (range) mg%	1.26(.50-11.90)

*On 100% O2 by mask at admission
†Highest blood glucose noted during treatment

Patients' blood glucose level and serum creatinine levels vary according to underlying disease and course of the illness (e.g. MODS).

As shown in table no.4, variable clinical data were compared between 40 patients who were treated successfully and 26 patients who required intubation during course of disease, aiming to identify the factors for so called late failure of NIV after first 24 hours. There was no significant differences regards to age or sex distribution NIV success to late failure group. Rural inhabitance was associate slightly better outcome but it is not statistically significant.

Table 4: Comparison between NIV success and NIV late failure group

Parameter	NIV success (n=40)*	NIV late failure (n=26)*	P value†
Mean Age years	43.85	42.96	0.796
Female sex	24	15	0.852
Rural inhabitant	25	14	0.485
Pregnancy	0	4	0.029
Co morbidities None	20	10	
Co morbidities one	12	12	
Co morbidities two	8	3	0.283
Co morbidities three	1	0	
Smoking	3	3	0.577
Alcohol	1	0	0.417
Tobacco	2	1	0.826
Life style hard working	39	24	0.322
Diet mixed	2	4	0.152
Mean pulse rate/min	98.35	107.15	0.026
Average mean blood pressure mmhg	90.05	91.96	0.376
Mean respiratory rate per min	27.85	35.04	0.125
SpO2 %	82.95	79.81	0.339
HB lowest gm.%	10.51	10.64	0.761
WBC count on adm. cells/cumm	7289.75	7300	0.993
WBC count highest cells/cumm			
WBC count highest cells/cumm	12405.26	18290	0.002
Platelet count on adm.lac/cumm	1.75	2.06	0.154
Platelet count lowest lac/cumm	1.52	1.30	0.299
Platelet count highest lac/cumm	3.48	3.07	0.352
RBS mg%	174	156.85	0.456
S.creatinine mg%	1.02	1.62	0.089
Subcutaneous emphysema	2	0	0.247
Steroid use	14	12	0.365

The presence of one or up to three co morbidities seems to have no correlation to outcome in our study. Addictions, type of diet or life style pattern were not having significant impact either. Among other parameters mean blood pressure, respiratory rate and initial SpO2 do not have significant correlation to outcome, however tachycardia on admission was on higher side (mean pulse rate 107.25/min.) in NIV late failure group than NIV success group(mean pulse rate 98.35) which was significant with P value of 0.026(<0.05).

All 4 pregnant or postpartum female patients required intubation at some point of time, correlating significantly-P value 0.029.

Among laboratory parameters HB%, platelet counts, RBS were noted as almost same rate. Highest WBC count noted during entire course of treatment was significant higher in NIV late failure group withp value 0f 0.002.

One patient of known case of ESRD had creatinine of 11.9 mg%. Mean creatinine was 1.62 mg%(highest 3.2 mg%) in NIV failure group, which was slightly higher than mean level of 1.02 mg% in success group but not statistically significant.

Two patients developed subcutaneous emphysema but succeeded treatment on NIV and it did not lengthen the mechanical ventilation period (6 & 3 days) or total hospital stay (13 & 16 days).

Twenty six patients were given systemic steroid treatment in early part of admission when total WBC count and other features were in favor of viral and not the bacterial pneumonia. Use of steroid did not seem to improve outcome or increased the rate of intubation.

DISCUSSION

As we selected adult patients age distribution was likewise.Sex distribution was same as few studies done our country [5, 6, 7, and 8].Rajesh et al noted the fever, cough and breathlessness in most patients similar to our study [7].

In our study diabetes was most common co morbid condition with hypertension and IHD being next, while COPD, Asthma and HIV/AIDS were noted less compared to other studies [1-8].Perhaps because this study done in recent time in latter phase of swine flu pandemic when older patients with chronic diseases are more commonly effected than young patients with Asthma or PLWHA.

Hemodynamic changes and compromised respiratory system associate with pregnancy adds risk of severe pneumonia in H1N1 patients. All the 4 patients of this group in our study required intubation. Few studies done on our country also noted increase in adverse outcomes in pregnant females and postpartum period [16].In our study higher pulse rate at admission and higher WBC count during entire course of treatment was associated with increased chances of intubation. Few studies have compared these parameters in isolation but it can be assumed that tachycardia and bacterial pneumonia were associated with poor assessment scores (SOFA, APACHE II etc.) which resulted in poor outcome in most studies [1-4, 5-8, 11-13].

In few studies steroid use was associated with poor outcome but in our study its effect was neutral, perhaps because in our study it was used only in initial period of viral pneumonia, however there was no benefit as well.

Apart from sleep disturbance due to noise of NIV and initial discomfort with face mask, important side effect of NIV was subcutaneous emphysema in two patients however having no adverse outcome.

CONCLUSION

NIV can be useful in viral pneumonia with AHRF; its use decreases scarcity of ICU ventilators and avoids endotracheal tube related side effects. Pregnancy or postpartum period, developing bacterial pneumonia (high pulse rate, high WBC count) is associated with high failure rate. Routine use of steroid is not advocated. Adult vaccinations against influenza and Pneumoniae should be advocated in our country especially in patients with chronic diseases. Our experience with global pandemic will help in developing protocols in future.

Limitations of study

Being a retrospective study, the study is less accurate to lead any changes in guidelines or management protocol. Unavailability of any of scoring system (e.g. SOFA, APACHE etc.) causes difficulties in comparison with other studies in the field of critical care.

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