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Prone Position Combined with NIV in Non-intubated ICU/HDU Patients during the COVID-19 Pandemic

Sanullah Tareen¹, Mohammad Yasin² ✉, Aria Masoom³, Maqbool Ahmed Langove¹, Abdul Baqi Achakzai¹, Nasir Mahmood⁴

¹FJ Institute of Chest Diseases, Quetta - Pakistan ²Department of Pulmonology, Ayub Medical College, Abbottabad - Pakistan

³Department of ENT, Bolan Medical College, Quetta - Pakistan ⁴District Headquarters Hospital, Haripur - Pakistan

Corresponding Author:

Mohammad Yasin

Department of Pulmonology,
Ayub Medical College,
Abbottabad - Pakistan
Email: yasinmohammadjan@yahoo.com

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ABSTRACT

Background: Before Covid-19 Pandemic, few studies speculated that early initiation of prone position in combination with NIV increases the probability of improved oxygenation in patients with ARDS.

Objective: We conducted an observational study to look for the beneficial effect of prone position combined with NIV in awake, non-intubated ICU/HDU patients presented with Covid19 associated ARDS and Pneumonia.

Methodology: We studied 120 Covid-19 positive patients admitted in ICU/HDU, FJ Institute of Chest Diseases, Quetta - Pakistan. They were subjected to PP combined NIV and observed for 4 weeks duration for primary outcome of improvement in SpO₂ and PaO₂/FiO₂ (P/F) ratio. Data for secondary outcomes like intubation rate, median stay in hospital and mortality rate were also noted.

Results: The study included 68% males and 32% female patients with median age of 60 years (IQR-18-80). After initiation of the standard PP, 80% of 120 subjects, the SpO₂ values improved from median 70% (IQR 60- 80) to median 93% (IQR 89-97) and P/F ratio from 100 (IQR 77-123) to 150 (IQR 123-177) within median 6 days (IQR 2-8) of admission. PP was adopted for median 12 hours/24 hours (IQR 4-16), and 90% were applied NIV for 12 hours/24 hours (IQR 6-18) with median 12 days (IQR 7-28). Mortality rate was 27% and 18% were intubated for invasive ventilators. Total hospital stay was 16 days (median -IQR 10-28).

Conclusions: Early awake self-prone combined with NIV application demonstrated improved oxygen saturation (SpO₂ & P/F ratio) and avoided intubation in our Covid19 related ARDS/Pneumonia Patients.

Keywords: Covid19; Prone position; Non-invasive Ventilation; Hypoxia; ARDS; Pneumonia

Introduction

The pandemic of SARS-Cov-2 (Covid-19) is a clinical condition which can manifest with a range of symptoms leading to severe acute respiratory illness (SARI) which began in the central Chinese city of Wuhan.¹ Till date no drugs or biologics have been recommended with proper approval by the FDA for the prevention or treatment of Covid-19.² Some antiviral agents, immune-therapies, and vaccines continue to be investigated and considered as potentially beneficial in its therapy.³ In early days of Covid-19 pandemic, the physicians were not much aware about the pathophysiology of this condition. In so many patients it was observed that the course of Covid-19 disease got complicated and a large number of patients developed pneumonia and ARDS causing high oxygenation deficits with severe hypoxia requiring hospitalization.⁴ That hypoxia was out of proportion to dyspnea associated with distress and anxiety.⁵

Routinely hypoxic patients are benefitted by receiving high flow of inspired oxygen (FiO₂) but in Covid19 infected patients with badly damaged lungs, positive pressure is required to deliver the required amount of oxygen.⁶ Such high flow is achieved by giving invasive or non-invasive ventilation (NIV). Ventilatory support is of great benefit and is mostly lifesaving by maintaining proper blood oxygenation and making patient getting rid of extra carbon dioxide. But the use of ventilator can have some bad effects like barotrauma and other so many complications.

The conventional alternatives to invasive mechanical ventilation are NIV and high flow nasal cannula (HFNC) which have been used successfully in Covid19 pneumonia patients but wide utilization of these modalities requires resources and the expertise.² NIV helps respiratory muscles in proper inspiration and improves oxygenation and SpO₂. This leads to the avoidance of endotracheal intubation in a lot patients. Therefore, combining prone positioning (PP) with NIV results in better effects on ventilation-perfusion mismatch, hence achieving better oxygenation in damages lungs in ARDS or Covid-19 pneumonia.⁷

We observed as the pandemic progressed, availability of beds with mechanical ventilation were difficult in our limited resources health care system in Pakistan. PP in awake, non-intubated patients is a low-risk intervention and can be used even in hospitals without the need for ICU. This therapy may enable the clinicians to manage such patients at secondary health care units and hence the burden on larger institutions can be reduced that are already overburdened in the current crisis of Covid19 pandemic surge. Therefore, many therapeutic modalities to prevent need for intubation were highlighted and

applied among which were prone position or posture in non-intubated patients were applied. Prone posture during invasive mechanical ventilation is used for ARDS patients and is almost the standard procedure.² Prone posture improved oxygenation in severe ARDS, and considerable mortality benefits were demonstrated.^{8,9} On the basis of previous studies done on ARDS patients due to different etiologies, it was speculated that proning of awake patients would improve patients' oxygenation and prevent or delay more invasive procedures like intubation.^{10,11} A recent study revealed significant improvement in oxygenation status by causing increase in lung recruitment in Covid19 associated ARDS patients who underwent mechanical ventilation.¹

Knowing the physiological benefits of PP in non-intubated patients if combined with NIV, we hypothesized that in Covid19 related ARDS/Pneumonia patients will gain in SpO₂ and P/F ratio and hence will reduce the rate of intubation. Therefore we conducted a prospective observational study to see the beneficial effects of proning in non-intubated patients with NIV as routine therapy.

Objective

We conducted an observational study to look for the beneficial effect of prone position combined with NIV in awake, non-intubated ICU/HDU patients presented with Covid19 associated ARDS and Pneumonia.

Methodology

This prospective observational study was conducted on convenience sample of patients in a 35-bed ICU & HDU at FJ Institute of Chest Diseases affiliated with Bolan University of Medical & Health Sciences, Quetta, Pakistan. Between 15th May 2020 to 30th July 2020, 120 adult patients with confirmed positive PCR testing for SARS-CoV-2 RNA or suspected cases were admitted primarily referred by government and private hospitals in the district Quetta. This hospital was the only hospital in whole province of Balochistan admitting and managing all Covid patients. The ethical approval was waived owing to the closed offices of institutional ethics review committee during the pandemic and due to the observational design of the study on Covid19 (Nasal- PCR) positive patients. Written informed consent was taken from every patient before enrolment in the study.

Apart from routine guidelines practices of Covid-19 patients management, we applied 2 interventions like PP and NIV and observed 120 patients for 4 weeks duration for primary outcome of SpO₂ improvement, and secondary outcomes like, mortality, mean ICU/HDU hospital stay among those who survived, and rate of Intubation among those who deteriorated during the course of prone and NIV intervention. Those Covid19 Positive patients with sepsis who could not tolerate NIV

and requiring Invasive ventilation, and also who were not able to prone position or refused to PP were excluded.

All patients tested positive for Covid-19 of age ≥ 18 years with early stage of ARDS and Covid19 pneumonia, critically ill patients presented with severe non-Hypercapnic Hypoxemic respiratory failure with SpO₂ $\leq 90\%$ in whom SpO₂ could not increase to $\geq 93\%$ despite receiving supplemental oxygen, and patients having PaO₂/FiO₂ ratio ≤ 300 were included.

Vital signs including SpO₂ were observed on cardiac monitor and noted on routine charts by duty staff 4 hourly. We included those who were not yet requiring mechanical ventilation in ICU and HDU units. Observing any deteriorating patients with low SpO₂ on monitor, they were asked to lie prone which was our routine protocol. Therefore we used to make awake patients prone for 2 to 4 hours as they tolerated prone and made them supine for 30 minutes and advised to avoid post meals prone. Our protocols included prone positioning of the patients for 30–120 minutes, followed by 30–120 minutes in left lateral decubitus, right lateral decubitus, and upright sitting position adopted by the protocol shown in Table 1. Positioning was guided by patient wishes. In every new position we noticed beneficial effects within 5–10 minutes. Care was taken of not maintaining a position that didn't improve the patients' breathing and comfort.

Patient's attendants were explained and demonstrated about position changes of the patient alternating every two hours between prone and supine position during the day time and to sleep in prone position at night, as tolerated. Afterwards nursing staff and chest physiotherapists reminded patient's attendant to maintain compliance and accuracy.

All patients receiving NIV with alternating body position demonstrated improved oxygenation and comfort leading to decreased minute ventilation and improved SpO₂ and P/F ratio on routine ABGs. Thus the combination of early application of NIV with self prone posture strategy caused avoidance of intubation and considerable improvement in SpO₂ and P/F ratio. All these daily observations were recorded in routine chart by doing arterial blood gases (ABGs) and P/F ratio (PaO₂/FiO₂) and improvement in oxygenation (SpO₂) was monitored by pulse oximeter on monitor. Almost all patients received empirical broad-spectrum antibiotics initially followed by switching over to the antibiotics according to microbial culture and sensitivity results. Study subjects were followed for 4 weeks and observations were recorded by the attending Pulmonary Physicians or Post Graduate Resident on call. Post-prone failure rates were defined as persistent SpO₂ of 90% with respiratory rate 30/minute or above and/or use of accessory muscles of respiration or altered sensorium

or raised level of PCO₂ in arterial blood. In those deteriorating patients decisions were taken to intubate them and start mechanical ventilation. Primary outcome measures were the change or improvement in SpO₂ on pulse oximeter, routine ABGs and P/F ratio after adopting prone position with applied NIV, or oxygen mask connected re-breathing bag. Secondary outcomes were intubation rate, length of ICU/HDU stay and mortality rate during 4 weeks hospital stay.

We estimated a total of 120 subjects with an expected SpO₂ improvement rate of 70% in the moderate to severe ARDS and Covid-19 Pneumonia patients with Prone Position and NIV support would have sufficient power to detect 35% improvement in SpO₂ ($35\% = 70\% \times [1-0.3]$) in the Prone Position patients with a confidence level $[1 - \alpha] = 95\%$ and power level $[1 - \beta] = 80\%$.

Quantitative continuous variables like age, breathing rate, heart rate, duration of Prone Position and NIV were expressed as means (SD) and medians (with inter-quartile ranges -IQR). These were compared via unpaired Student's t test or the Mann-Whitney test. The primary dependent variable was the SpO₂ before and after adopting prone position which was not normally distributed, reported of median value. And proportion of SpO₂ in those subjects failing in prone position and subsequently intubated. Qualitative or categorical variables like improvement in SpO₂, ABGs and PaO₂/FiO₂ ratio during week-1, week-2, and week-3 were compared with the chi-square test or Fisher's exact test. P values of less than 0.05 were considered as significant. All these analyses were done using SPSS software for Windows (21.00 versions)

Results

We observed a total 120 Covid (Nasal-PCR) positive patients, among which 68% were males and 32% females with median age 60 years (IQR-18 to 80). After initiation of the standard prone posture, there was improvement of SpO₂ and P/F ratio in 80% of subjects during 1st week of admission (median 6 days IQR 2 to 8) (Table 2). About 90% were applied NIV for 12 hours/24 hours (IQR 6-18) (Table 3). NIV was applied for median 12 days (IQR 7-28). After weaning from NIV, 35% were applied face mask alone or connected to re-breathing bags.

Mortality rate was 27% in those with prone position for an average of 12 hours/24 hours with 2 hours intervals of changing posture (IQR 4-16 hours/24hours) as presented in table 3. 18 % were intubated for invasive ventilators failing to PP with NIV and their outcome was not included in our data. Total hospital stay was median 16 days (IQR 10 to 28 days) for those who improved and discharged on domiciliary oxygen shown in Figure1. At the time of discharge, 94% required FiO₂ for home, and mean

Table 1. Timed position changes for patients undergoing conscious proning process¹²

<p>Timed Position Changes: If patient fulfils criteria for proning ask the patient to switch positions as follows. Monitor oxygen saturations 15 minutes after each position change to ensure oxygen saturation has not decreased. Continue to monitor oxygen saturations as per the National Early Warning Score (NEWS)</p> <ul style="list-style-type: none"> • 30 minutes to 2 hours lying fully prone (bed flat) • 30 minutes to 2 hours lying on right side (bed flat) • 30 minutes to 2 hours sitting up (30-60 degrees) by adjusting head of the bed • 30 minutes to 2 hours lying on left side (bed flat) • 30 minutes to 2 hours lying prone again • Continue to repeat the cycle.....

Adopted from: ICS Guidance for Prone Positioning of the Conscious COVID Patient 2020
<https://icmanaesthesiacovid-19.org/news/ics-guidance-for-prone-positioning-of-the-conscious-covid-patient-2020>
 [Accessed 10th Jun, 2020]

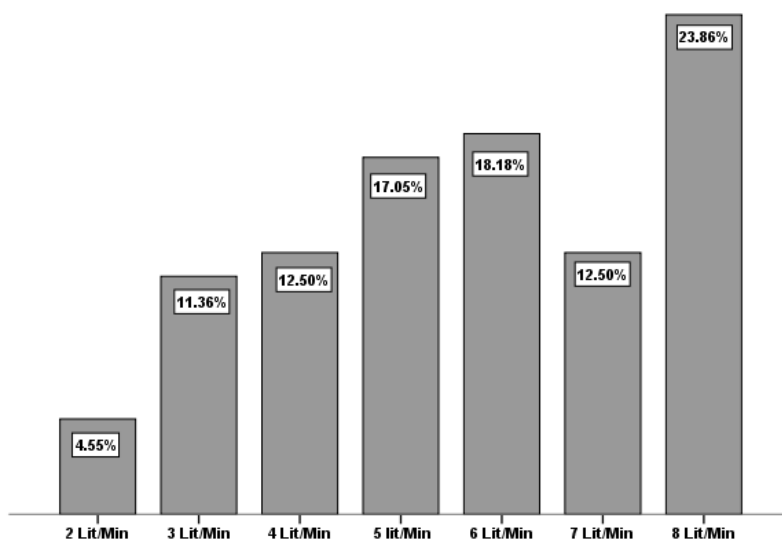


Figure 1. Domiciliary Oxygen Requirements

Table 2. SpO2, R/R, H/R, ABGs and Spo2/Fio2 before and after Prone position during 4-Weeks hospital stay

	Before Prone				After Prone						
	(on admission) (N=120)		1-Week (n=116)		2-Weeks (n=90)		3-Weeks (n =50)		4-Weeks (n = 18)		
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	
Spo2	70%	60- 80	93%	89-97	94%	92-96	95%	93-97	96%	94-98	
Respiratory Rate	35	29-41	21	17-25	20	16-20	20	18-22	18	14-22	
Heart Rate	100	84-116	90	80-100	80	75-85	80	76-84	80	78-82	
A	pH	7.45	7.36-7.54	7.38	7.31-7.45	7.33	7.28-7.38	7.30	7.27-7.33	7.30	7.28-7.32
B	PaCO2	22	14-30	32	22-42	38	36-40	40	36-42	40	35-45
G	PaO2	53	45-61	60	49-71	68	63-73	68	60-76	70	65-75
	HCO3	18	14-22	21	18-24	22	19-25	24	20-24	23	21-25
PaO2 / Fio2	100	77-123	150	123-177	180	150-210	185	165-205	200	185-215	

IQR- Interquartile Range, PaO2/Fio2 Ratio

Table 3. Proning Position and NIV during 4-weeks hospital stay.

	1-Week N = 120		2-Weeks n = 116		3-Weeks n = 90		4-weeks n = 18	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Adopting Proning Posture (hours/24 hours)	12	8-16	8	4-12	8	4-12	10	4-16
NIV applied - (hours/24 hours)	12	8-16	8	2-14	8	2-14	10	6-16

requirement was 6-liters/minute (SD \pm 2.00) presented in Figure 1.

Discussion

During this Covid19 Pandemic, several observations were made on prone position in emergency room (ER) for short duration and in most studies NIV was not combined.^{13,14} In this observational cohort study we have had collected data on those Covid19 (Nasopharyngeal swab-PCR) positive patients who adopted Prone Position/Posture (12 to 8 hours/24 hours) with applied NIV (median 12 to 8 hours/24 hours) shown in Table 3.

During 28 days of admission, we observed that SpO₂ values improved from median 70% (IQR 60- 80) to median 93% (IQR 89-97), P/F ratio from median 100 (IQR 77-123) to median 150 (IQR 123-177) within median 6 days (IQR 2-8) of admission with 18% intubations rate, length of hospital stay median 16 days (IQR 10-22) and mortality of 27%. As observed in previous studies on ARDS due to other etiologies it was suggested that PP may have beneficial effect in awake patients by improving oxygenation and may prevent or delay the need for mechanical ventilation.¹⁵⁻¹⁷ These findings were utilized by researchers in the management of Covid pneumonia patients and demonstrated encouraging results.^{13,18} The researchers also demonstrated that PP helped in improving oxygenation and survival rates in their Covid19 patients who presented with ARDS.^{19,20} The Formal Guide to the treatment of ARDS recommended the use of the proning position for 16 hours a day with P/F ratio < 150.^{6,17} In our analysis, we observed the mortality was 27% with PP adopted for on average of 8-12 hours/24 hours (table 3) with P/F ratio \geq 100 as shown in table-3. Awake patients who were very sick required a relatively more care than the patients on mechanical ventilation as most of them didn't tolerate staying in same position for long time and attempted to remove their oxygen masks.⁶ The safety of PP in awake non-intubated patients remained unclear and ongoing clinical trials are being done in Covid19 patients. Before this Covid pandemic, few studies observed that PP is of proven benefit in patients with ARDS with reduced rate of intubation but the resultant ventilator-induced lung damage to the patients was noted.^{9,16} Since proning is a simple maneuver as most of the patients are able to do this without any assistance. Also it is free of cost, and no resources are required for its use. Therefore it was recommended that PP may be used

for the improving oxygenation in a considerable majority of patients with Covid19 related ARDS and Pneumonia.¹³

In our tertiary care hospital, during the early stages of the Covid19 pandemic, many patients were brought to our hospital with hypoxia having median SpO₂ of 70% (IQR 10) (Table 1). During their management it was seen that some patients deteriorated very quickly and were started on mechanical ventilation. However, we observed a sub group of Covid19 patients whose oxygen saturations were low, but were not significantly distressed. They were markedly tachypnic with median respiratory rate 35 /min (IQR 6) and median heart rate of 100/minute (IQR 16). Most patients had chest X-ray findings consistent with ARDS and Covid19-Pneumonia and had severe hypoxemia which didn't respond to supplemental oxygen. Therefore as routine practices we installed them on NIV early in their hospital course and instructed to adopt them prone position/ posture to improve their oxygenation. Our experience suggests that the use of routine NIV when combined with rotating or proning, was a valuable tool in improving oxygenation with median SpO₂ was rise up to 93% (IQR-4) and decreasing respiratory effort with respirator rate fall of median rate 21/minute (IQR-4) during first week of adopting proning position/posture. Clinicians have used NIV and HFNC with successful results as an alternative to mechanical ventilation in Covid19 but its wide utilization was hindered by several factors.² Respiratory physicians in China and Italy managing the earliest cases of Covid19 had to manage severely hypoxemic patients and there were serious concerns about the spread of viruses during oxygen therapies like HFNC and NIV.^{21,22} This led to a recommendation to "intubate early approach" which was adopted in the first wave of critically ill Covid19 patients seen in New York City hospitals, but this strategy with early outcomes data was associated with high mortality for intubated patients, and secondly there was fear of resources scarcity if early intubation was continued with such rates.^{23,24} In addition to that the demand for ICU skilled health care workers and resources can limit its feasibility for the large number of patients during Covid surge.²⁵ These all observation forced the physicians to seek and adopt strategies in order to delay or prevent the initiation of mechanical ventilation in Covid19 patients.²⁶ Meanwhile debate started globally to acquire such strategies that could safely improve oxygenation without the need for additional resources.²⁷ In few recent studies, it has been observed that if NIV is combined with awake proning it will

result in marked improvement in oxygenation. The researchers also observed that intubation was avoided and oxygenation was improved in patients with moderate ARDS by early application of HFNC or NIV.^{28, 29, 30} These findings can be extrapolated to Covid19 positive patients with hypoxemic respiratory failure as we applied NIV to 90% patients which resulted in dramatic oxygenation improvements in 6 days and reduced to ICU/HDU stay to median 16 days (IQR 6). Since HFNC device was not available to all patients in our hospital, therefore its application and outcome was not included in this analysis. Previously before Covid19 Pandemic, NIV was increasingly used for acute respiratory failure management and reduced rates of intubation in patients with acute hypoxemic respiratory failure but had no impact on mortality (risk ratio [RR], 0.76, 95% CI: 0.55-0.99).³¹ NIV is still under investigation in various hypoxemic respiratory failures etiologies, such as asthma, pneumonia, immunosuppression and ARDS.²⁷

Therefore looking at the beneficial role and efficacy of NIV in severe hypoxic respiratory failure secondary to ARDS, we applied NIV to Covid19 patients (90%) with prone position for median period of 8 hours/24 hours (IQR 4-16) as shown in table 3.³² We observed the beneficial effects of NIV in term of Hypoxia improvement of SpO₂ from 70% to 93% and P/F ratio from 100 to 150 (IQR 123-177) in 1st week, and there often P/F ratio then increased to 180 (IQR 150-210) in 2nd week of admission. In addition to that total hospital course remained to 16 days (median) during second week and reduced the intubation rate to 18%, but prolonged hospital stay of 3 weeks had no significant effect ($p < 0.006$) on intubation and mortality rate.

Limitations of Study

Alternating body positioning improved lungs recruit ability but our findings do not imply that all patients with Covid19 related ARDS are poorly recruitable, hence no confirmed evidence can be drawn from these observations. Additionally as both the severity and management of these patients can differ remarkably among regions, therefore generalization of our findings needs further confirmation by observations made at different regions and in patients with different grades of severity.

Conclusions

Patients with moderate to severe hypoxemia related to Covid19 ARDS & pneumonia demonstrated an improvement in SpO₂ and P/F ratio after being placed in PP combined with NIV. Lung recruitability can be assessed at the bedside even in a very constrained environment which was low in patients with Covid19 induced ARDS. Until further studies demonstrate better alternative oxygenation strategies, we recommend early and frequent use of PP in addition to routine NIV

application to delay or prevent intubation in ARDS associated with high mortality of critically ill Covid19 patients. These findings might prompt clinicians to assess lung recruitability, respiratory mechanics, and add to evidence of the benefit of PP combined with NIV in this population of Covid19 related ARDS and pneumonia.

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