Effect of Prone Positioning in Patients with Moderate COVID-19 Pneumonia Admitted to Ward at a Tertiary Care Hospital

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Abstract

COVID -19 pneumonia can progress to severe disease in 5% of patients requiring intensive care management, which can put an excessive burden on health care systems. Prone positioning has been shown to improve oxygenation and decrease lung injury in patients with COVID-19 pneumonia and can be used as an adjunctive treatment to delay intubation. The objective of this study is to assess the effect of prone positioning in patients admitted to the COVID ward, with Moderate COVID-19 Pneumonia. This experimental study was conducted at Liaquat National Hospital. A quasi-experimental study design was applied. Patients with hypoxemia SpO_2 < 94% were assisted to prone and semi-prone for up to 2 hours at a time for multiple sessions. Parameters like SaO_2, PaO_2/FiO_2, hours of proning and changes and X-rays were recorded daily and pre and post-intervention values were compared. Paired t-test and Wilcoxon sign test were used to compare continuous parameters. A two-tailed p-value less than 5% of the level of significance was defined as statistically significant. 20 patients fulfilling the inclusion criteria were enrolled. Median hours of prone positioning were 48.5. The median hospital stay was 7.5 days. At baseline, mean PaO_2/FiO_2 ratio was 342±91.87 and at the time of discharge, it was 412.30±105.97 which is a statistically significant improvement from baseline (p=0.040). 50% of patients showed improvement in X-rays. One patient was intubated and all the patients were discharged. The sample collected in the current showed that prone positioning is a safe and feasible approach to improve oxygenation in moderate-severe COVID-19 pneumonias. However, studies with a larger sample size are recommended to further verify the findings of this study.

Keywords: *Awake proning, hypoxia, moderate COVID-19 pneumonia, prone position.*

BACKGROUND

COVID-19 pneumonia is a respiratory illness caused by SARS-COV2 that belongs to a family of Coronaviruses. Most people with the disease remain stable but 14% of those affected can develop severe disease requiring hospitalization and supplemental oxygen and 5% of these may require intensive care [WHO/2019-nCoV/SARI toolkit/2020]. 21-40% of these severely ill patients can develop acute respiratory distress syndrome (ARDS), a major complication of COVID-19 pneumonia, often leading to intubation and mechanical ventilation which puts a burden especially on resource-limited settings [1-4].

Awake proning in non-intubated patients with significant hypoxemia and no apparent respiratory distress has been tried in patients with COVID-19 pneumonia and studies have shown encouraging results with improvement in oxygenation and delaying intubation and mechanical ventilation [1-5]. Thus, this strategy could be especially helpful in settings with resource constraints and reduce the burden on intensive care settings.

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Received: October 16, 2021; Revised: November 29, 2021; Accepted: December 02, 2021
DOI: https://doi.org/10.37184/lnjpc.2707-3521.3.27

In 2020, Copo and colleagues reported that prone positioning in awake patients is feasible and safe in most of the patients and it significantly improves physiological measures of oxygenation; improving the ventilation-perfusion matching in dependent areas of lungs and also reducing lung injury in intubated patients, in a substantial fashion. The patients who were started earlier prone positioning in course of disease had sustained improvement in oxygenation even after resupination but there was no statistically significant difference in the rate of intubation among responder and non-responder [5].

Dubosh and colleagues from the USA demonstrated the positive relationship between early awake proning and improvement of hypoxia among 52 patients [6]. Another case series from Maryland hospital also showed good response in patients after awake proning in moderate Covid pneumonia and improves oxygenation and survival [7].

To the best of our knowledge, very few studies have been reported from Pakistan describing the effect of proning in COVID-19 patients presenting with hypoxemia [8, 9]. The aim of our study was to assess the effect of prone positioning on the oxygen saturation, PaO_2/FiO_2, total duration of prone positioning and improvement in Chest X-ray in patients with moderate COVID-19 pneumonia.

Operational Definition

Moderate COVID pneumonia: Oxygen saturation>90% but <94% and infiltrates on Chest X-ray involving <50% of lung fields requiring supplemental oxygen.

METHODOLOGY

This study was conducted in the COVID ward at Liaquat National Hospital, from July-August 2021. A Quasi-experimental study design and purposive sampling method were applied to recruit patients. After getting approval from Institutional Review Board (IRB) and hospital ethics committee (ERC), patients fulfilling the inclusion criteria *i.e.* both genders, 15 years in and above with PCR proven moderate COVID pneumonia, patients who were awake and willing to participate, were enrolled after getting informed consent. Patients with critical disease, having respiratory distress and requiring Non-Invasive Ventilation (NIV) / High Flow Nasal Cannula (HFNC) unable to prone because of discomfort or any other reason, and with contraindication to prone positioning as evidenced by a physician including pregnancy were excluded.

Patients were assisted to self-prone for 14-16 hours/24 hours after enrolling. Intermittent prone positioning for a maximum of 2 hours or until the patient could tolerate was advised. Lateral prone positioning to both sides was also acceptable. Patient's Oxygen saturation (SaO_2%), partial pressure of oxygen (PaO_2), oxygen requirement (FiO_2) and chest X-ray findings were recorded at the time of admission and before inclusion into the study and also noted at the time of completion of intervention/discharge and compared. Daily hours of proning and SaO_2 before and after proning were recorded in a chart. PaO_2/FiO_2 was also recorded daily and values before intervention and after cessation of intervention were compared. Chest X-ray findings along with other data including age, gender, co-morbidities, clinical features (moderate disease) were noted in a proforma by the investigator. Primary endpoints were: Oxygen saturation (SaO_2) at discharge, improvement in PaO_2/FiO_2 ratio before and at the end of the intervention, chest X-ray changes from baseline, length of hospital stay and outcome including discharge, mortality and shifting to ICU/HDU.

Data Analysis

Clinical data relating to enrolled patients were analyzed in the statistical package SPSS (version 20) for data analysis. Categorical variables such as gender, patients' outcome, ventilator use, co-morbid conditions, clinical manifestations, and chest X-ray findings, use of steroids, anti-coagulation, tocilizumab, and antibiotics were summarized as frequencies and percentages. Quantitative variables such as age, length of stay, duration of prone positioning, saturation level, PaO_2, FiO_2, the fraction of PaO_2 and FiO_2, duration of O_2 supplementation in the last 24 hours were presented as mean ± standard deviation or median with an inter-quartile range as appropriate. Shapiro-Wilk test was used to assess the assumption of normality. Paired t-test or Wilcoxon sign test was used to compare continuous parameters (such as saturation level, PaO_2, FiO_2, fraction of PaO_2 and FiO_2) at baseline and after the intervention. A two-tailed p-value less than 5% of the level of significance was defined as statistically significant.

RESULTS

A total of 20 patients' records were reviewed. The average age of study participants was 59.65±12.05 years. Three-fourth of the patients were males (n=15, 75%). The median hospital length of stay was 7.50 (IQR= 0.25 – 9.75) days. The majority of the patients had comorbidity (n=16, 80%), the most common was diabetes (n=11, 55%). Other common comorbidities and clinical features are presented in Table **1**.

Table 1: Clinical characteristics of patients with moderate COVID 19 pneumonia.

Clinical Characteristics	Number of Patients (n)	Percentage (%)
Co-morbid		
Diabetes	11	55
Hypertension	9	45
Ischemic heart disease (IHD)	8	40
Chronic liver disease	2	10
Osteoarthritis	1	5
Parkinson's diseases	1	5
Symptoms and Signs		
Fever	17	85
Shortness of breath	12	60
Myalgia	5	25
Diarrhea	4	20
Sore throat	3	15
Vomiting	2	10
Anosmia	1	5
Anxiety	1	5

All patients received steroids. Only 4(20%) patients received Tociluzimab, 15(75%) patients received Remidisivir and 18(90%) patients received antibiotics initially but were stopped later. Median prone positioning hours were 48.5hrs (Range: 5hrs - 70.5hrs).

At baseline 18(90%) had bilateral infiltrates on chest x-ray. 1(5%) had infiltration in the right lower zone and 1(5%) had no infiltration. On day 3, only 1(5%) patient showed improvement in chest x-ray and chest x-ray was further worsened in one patient (5%) whereas 18(90%) patients had no improvement in their chest x-rays. At the time of discharge, 10(50%) showed improvement in their chest x-ray. 8(35%) showed no improvement while 3(15%) showed worsened chest x-ray.

At baseline mean oxygen saturation level was 93.2±3, and at the time of discharge, the mean oxygen saturation was 94.55±4.47 and there was no significant difference (p=0.289). At baseline, the mean PaO_2/FiO_2 ratio was 342±91.87 and at the time of discharge, it

was 412.30±105.97 which is a statistically significant improvement from baseline (p=0.040).

No significant adverse event during proning was noted except for mild discomfort in elderly and obese patients. All of the patients were alive at the time of discharge. One patient worsened and was shifted to ICU and intubated, but he also recovered and was discharged.

DISCUSSION

In this study we observed the effects of proning and semi-proning in non-intubated, awake patients with moderate COVID-19 pneumonia, admitted to the ward. We found that prone positioning was able to reduce the PaO_2/FiO_2 significantly in patients who were able to tolerate it for a median of up to 48 hours in 5 days without any significant side effects.

Prone positioning (PP) results in a more uniform architecture of the alveoli, leading to decrease V/Q mismatch, increased recruitment of posterior zones so a proportion of alveoli for gas exchange increases and reduces lung injury by decreasing stress forces on the diaphragm. All these physiological effects lead to improved V/Q matching and low shunt fraction, thus improving oxygenation and potentially reducing mortality [10, 11].

Prolonged prone positioning (>12hrs/day) has already been proven as a useful tool in severe ARDS in non-COVID pneumonias in randomized controlled trials [12] and other studies [13] and is currently being used as adjunctive therapy in intubated patients with critical COVID pneumonias with encouraging outcomes [14, 15].

A limited number of international studies in pre-COVID era have proven the efficacy of PP in non-intubated patients with severe pneumonias and ARDS on NIV support mainly in the ICUs [14]. The study population between the studies was also heterogeneous. Data regarding PP in awake non-intubated patients with COVID-19 pneumonia has emerged, albeit largely comprising of case series and small observational cohort studies [1, 2, 4, 16]. Randomized control trials are also underway and the preliminary result of one multicenter trial has highlighted the feasibility and safety of this intervention in spontaneously breathing patients [17]. But, definitive results and recommendations from other RCTs as well, remain to be elucidated.

The major finding in our study was a statistically significant and sustained increase in the PaO2/FiO2 at the time of discharge. Existing literature supports our findings with several studies showing improvement in oxygenation and other physiological parameters after prone positioning [5, 11, 18-20]. However, certain studies found this improvement to be only transient, with PaO_2/FiO_2 reverting after re-supination [2, 5]. A large multicenter prospective study showed a sustained improvement in oxygenation post PP, but they had applied a high flow nasal cannula (HFNC) for providing oxygen therapy [21]. Similarly, Wearnels *et al.* also reported significant improvement in PaO_2/FiO_2 when PP was combined with CPAP [20]. Lack of sustained response in these studies could be attributable to the unspecified duration of prone positioning as no definitive guidelines currently exist regarding the number of hours of PP required in awake non-intubated patients with COVID pneumonia [5].

The duration and frequency of PP varied among the studies from <1 to >18 hours and was largely dependent on the patient's tolerability and primary physician's devised protocol and discretion [18]. Our patients were able to be prone for 1-2 hours for multiple sessions in a single day with some patients tolerating a maximum duration of up to 16 hours a day. Most of our patients had no apparent respiratory distress and were fairly stable, contributing to the sustainability of prolonged hours of prone positioning.

The role of PP in reducing the risk of intubation, the length of hospital stay and mortality is also not clearly defined as a majority of the studies did not involve a control group or had a small sample size [11, 14, 18]. Although, a large prospective study by Ding *et al.* in patients with severe ARDS requiring NIV/HFNC showed a reduced rate of intubation prior to the COVID-19 pandemic [22]. This further emphasizes the importance of larger randomized control trials (RCTs) for defining the role of PP in avoiding intubation. However, few studies showed a trend in delayed intubation after the institution of early awake PP in less severe diseases [18, 21]. Only one of the patients in our study was intubated but since we also did not have a control group and a small sample size hence, assessing the probability of avoiding intubation was difficult for our study. Another reason for this low rate of intubation could be related to the fact that most of our patients had a moderate disease. The majority of our patients also did not progress to severe disease and did not require NIV or HFNC either, showing that prone positioning can be a good adjunct to the standard treatment for moderate COVID pneumonia. However, this requires larger studies with an appropriate control group for further validation.

At the time of discharge half of our patients showed >25% improvement in their Chest X-ray. To the best of our knowledge, no existing study has reported the association between PP and changes in radiological findings. It is unclear from our data how much PP contributed to this change in X-ray findings as patients were also receiving anti-inflammatory and antiviral therapies.

Regarding the safety profile of PP, it was found to be a safe maneuver without any significant adverse events, except for mild discomfort and musculoskeletal pain, as noted in previous studies [11, 14, 18]. We also observed similar findings and the procedure was well tolerated by the majority of the patients.

We conducted this study with a quasi-experimental design without a control group. This study design enabled us to assess the differences in parameters, both pre and post-intervention in an accurate and subjective manner. There were several limitations to our study, firstly there was no control group and secondly, the sample size was small to draw any conclusive and significant inferences regarding the effect of prone positioning on the risk of intubation, length of hospital stay and mortality. Further research with control groups and randomization with a larger number of patients is required to evaluate these effects.

CONCLUSION

In conclusion, we found that PP is a feasible and safe adjunct to standard treatment in patients with COVID-19 pneumonia admitted in wards who do not require assisted ventilation. If instituted early and applied for an appropriate duration, it improves oxygenation and possibly reduces the risk of ICU transfer and the need for mechanical ventilation. We strongly recommend the initiation of multicenter RCTs in Pakistan for evaluation of PP, because if proven effective, it can greatly reduce the burden on the overwhelmed health care systems at times of crisis, especially in the intensive care units by decreasing the need for mechanical ventilation.

FUNDING

None.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

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