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ORIGINAL ARTICLE

Correlation of Arterial Blood Gas Parameters with the Duration of Proning in Awake Non-intubated COVID-19 Patients: A Retrospective Observational Study

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ABSTRACT

Background and aims: Prone positioning (PP), which has been known for decades to increase oxygenation in mechanically ventilated patients with moderate to severe acute respiratory distress syndrome (ARDS), was also practiced in Coronavirus disease (COVID-19) patients. We hypothesized that prone positioning in critically ill COVID-19 patients would improve oxygenation and ventilation and potentially translate into improved survival.

Methods: A retrospective, observational study was conducted in All India Institute of Medical Sciences, Rishikesh, from March 2021 to July 2021. SARS-CoV-2 reverse transcriptase – polymerase chain reaction (RT-PCR) positive adult patients admitted to the ICU on non-invasive ventilation were included in the study. Proning durations were categorised as adequately proned (at least six hours/day), inadequately proned (four to six hours/ day) and minimally proned (less than four hours/ day).

Results: The 30 included patients underwent 95 proning sessions. The change in $PaCO_2$ had no statistically significant correlation with the duration of proning in hours (rho= -0.11, p = 0.295). There was a statistically significant weak positive correlation between the change in PaO_2 and duration of proning in hours (rho = 0.22, p<0.05). For each hour of proning, percent increase in PaO_2 was by 0.44 percent**.** There was no significant difference between the groups in terms of time to intubation (days) (p = 0.407).

Conclusion: This study demonstrated that prone positioning in awake, non-intubated COVID-19 patients with acute respiratory failure improves oxygenation proportional to proning duration without affecting $PaCO_2$ levels.

Key words: *Arterial blood gas, non-invasive ventilation, prone positioning, severe acute respiratory distress syndrome Coronavirus-2*

INTRODUCTION

The severe acute respiratory distress syndrome coronavirus 2 (SARS COV 2), which has been linked to millions of confirmed cases and fatalities globally, is the cause of coronavirus disease 2019 (COVID-19). At the end of December 2019, a cluster of cases of pneumonia with an unknown etiology was discovered in Wuhan, a city in the Hubei Province of China which later caused a global pandemic.[1]

Prone positioning (PP), which has been known for decades to increase oxygenation in mechanically ventilated patients with moderate to severe acute respiratory distress syndrome (ARDS), was also used in patients with COVID-19. Following the publications of meta-analyses and the PROSEVA trial, which demonstrated a significant survival advantage in patients with ARDS, proning was widely accepted. Since then, prone positioning (PP) has become a common therapeutic option for patients with severe ARDS who are mechanically ventilated.[2]

Through a variety of mechanisms such as alveolar recruitment in the dorsal lung, lowering lung compression, form matching between the chest cavity and the lung, and increasing secretion clearance, prone positioning enhances pulmonary physiology and oxygenation.[3] Prone positioning was expected to be beneficial in awake, non-intubated patients with COVID-19 related ARDS, as it provides well-established physiological benefits in mechanically ventilated patients with ARDS. However, the available medical literature on prone positioning in non-intubated (PINI) COVID-19 in terms of the effects on the partial pressure of carbon dioxide ($PaCO_{2)}$ and oxygen ($PaO_{2)}$ and its clinical benefits require further investigation.

This study aimed to evaluate the effect of prone positioning duration on PaO_2 and $PaCO_2$ in non-intubated COVID-19 patients admitted to the ICUs. We hypothesized that prone positioning in critically ill COVID-19 patients would improve oxygenation and ventilation and potentially translate into improved survival.

METHODS

This study was approved by the Ethics Committee of All India Institute of Medical Sciences, Rishikesh, India (Letter No - AIIMS/IEC/22/211) on 22/04/2022 and registered in Clinical Trial Registry – India (CTRI Reg. No - CTRI/2022/07/043931 and Reference No. REFS/2022/06/055498) on 12/07/2022.

A retrospective, observational study was conducted in All India Institute of Medical Sciences, Rishikesh, from March 2021 to July 2021. SARS-CoV-2 reverse transcriptase – polymerase chain reaction (RT-PCR) positive (in nasal and pharyngeal swab) patients, aged more than or equal to 18 and admitted to the ICU on non-invasive ventilation were included in the study. Informed consent was waived off by the institutional ethical review committee due to the retrospective nature of the study.

Demographic data collected were age, gender, weight, body mass index, comorbidities, sequential organ failure assessment (SOFA) score, acute physiology and chronic health evaluation (APACHE) II score. An initial period of up to 12 hours was allowed for stabilisation. Continuous awake proning was encouraged during the night time. Arterial blood gases (ABGs) were obtained upon admission and subsequently recorded prior to each proning session at night and every morning post proning. The longest uninterrupted session of proning during each night was considered as the proning period. The duration of this proning session and the ABG parameters before and after these sessions were recorded. For the purpose of this study, proning durations at night were categorised as follows, i) adequately proned: patients proned for at least six hours, ii) inadequately proned: patients proned for four to six hours, and iii) minimally proned: patients proned for less than four hours. Data was collected for a maximum of 5 days or till patient was intubated. The ventilation methods employed, vital signs and ABG parameters were documented during the proning sessions. The time to intubation in days from the day of ICU admission among patients who got intubated was assessed. All treatment and proning decisions were as per the treating team. This included initiation or discontinuation of awake proning, decision for endotracheal intubation and mechanical ventilation. Radiometer ABL800FLEX was used for the ABG analysis.

We expected to detect a minimum correlation coefficient of 0.5 between change in $PaCO_2$ and duration of proning. Considering an alpha error of 0.05 and a power of 80%, the required sample size was calculated to be 29 patients. Spearman correlation coefficient (non-parametric test) were used to explore the correlation between percent change in PaO_2 (post-proning) and duration of proning. Similarly, percent change in $PaCO_2$ (post-proning) and duration of proning was also explored. Kruskal Wallis test was used for comparison of median time to intubation in different groups. Continuous variables were expressed as mean and standard deviation or median and interquartile range (IQR) depending on the normality of data distribution. The 95% confidence interval (CI) was reported where applicable. Kaplan Meier curve was used to compare the time to intubation between different proning groups. A p value of less than or equal to 0.05 was considered to be statistically significant. All the statistical analyses were performed using SPSS (version 17).

RESULTS

Out of 30 patients included in the study, the mean age was 57.37 ± 10.43 years. A total of 24 (80.0%) patients were males and 6 (20.0%) were females. The median SOFA and APACHE II score on admission were 4 [IQR 3-4] and 6.5 [IQR 5.5-7.5] respectively. The mean hours of proning were 6.03 ± 2.48 hours. Hypertension (46.7%) and diabetes mellitus (40%) were the most common comorbidities. Other comorbid conditions included chronic obstructive pulmonary disease/asthma (16.7%), obesity (16.7%), hypothyroidism (13.3%), and chronic liver disease (10%). No comorbidity was identified in 20% of the patients. The mean baseline PaO_2/ FiO_2 was 204±26 mm Hg. More than half of the cases (17 patients; 56.7%) were adequately proned (≥6 hours), 8 patients (26.7%) inadequately proned (4 – 6 hours), and 5 patients (16.7%) minimally proned (≤3 hours) (Table 1). All the patients got intubated at some point and the mean time to intubation was 9.27±4.49 days.

Table 1. Baseline characteristics of the patients

Variables	Incidence (%)
Age (years)	
21-30	1 (3.3)
31-40	0 (0)
41-50	6 (20.0)
51-60	11 (36.7)
61-70	9 (30.0)
71-80	3 (10.0)
Gender	
Male	24 (80.0)
Female	6 (20.0)
Adequacy of proning	
Adequate	17 (56.7)
Inadequate	8 (26.7)
Minimal	5 (16.7)

Overall, patients underwent 95 proning sessions during the study period. There was no significant correlation between the change in $PaCO_2$ after proning and the duration of proning in hours (rho = -0.11, p = 0.295). Similarly, no significant correlation was observed between percentage change in $PaCO_2$ and duration of proning (rho = -0.05, p = 0.621). There was a statistically significant weakly positive correlation between the change in PaO_2 and duration of proning in hours (rho = 0.22, p<0.05). Similarly, a weak positive correlation was observed between percentage change in PaO_2 and duration of proning (rho = 0.22, p = 0.035) (Figure 1).

The median time to intubation in days in adequately proned group was 9 [IQR 6-13], inadequately proned group was 9.5 [IQR 7.5-11] and minimally proned group was 6 [IQR 5-8]. There was no significant difference between the groups in terms of time to intubation in days (p = 0.407). Figure 2 depicts Kaplan Meier plot for time to intubation (days) in different groups of proning. The differences were not statistically significant (p = 0.38).

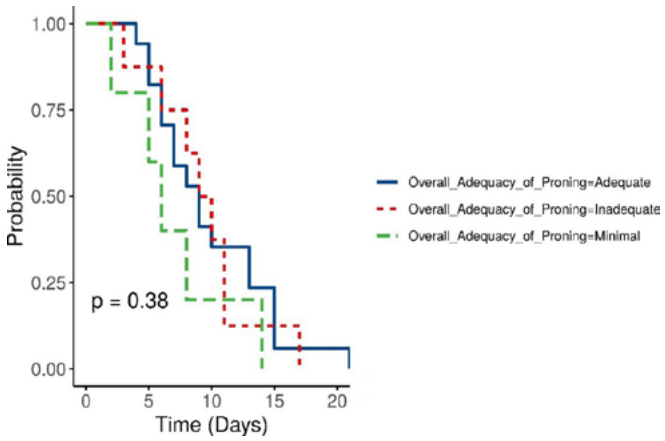

Figure 2. Kaplan Meier plot for time to intubation (days) in different proning groups.

DISCUSSION

The findings from this study suggests that duration of proning did not significantly impact $PaCO_2$ changes. Studies examining the relationship between prone positioning and $PaCO_2$ have shown mixed results. While some studies have found no significant changes in $PaCO_2$ during extended proning periods,[4] systematic review and meta-analysis of COVID-19 patients had demonstrated a significant decrease in $PaCO_2$ levels.[5] This could be partly explained by the differences in the duration and measurement points of $PaCO_2$. The patients were included early and followed till only five days. The measurements were obtained before and after each proning session. Proning could have been too short to get any significant changes. This is further corroborated by the

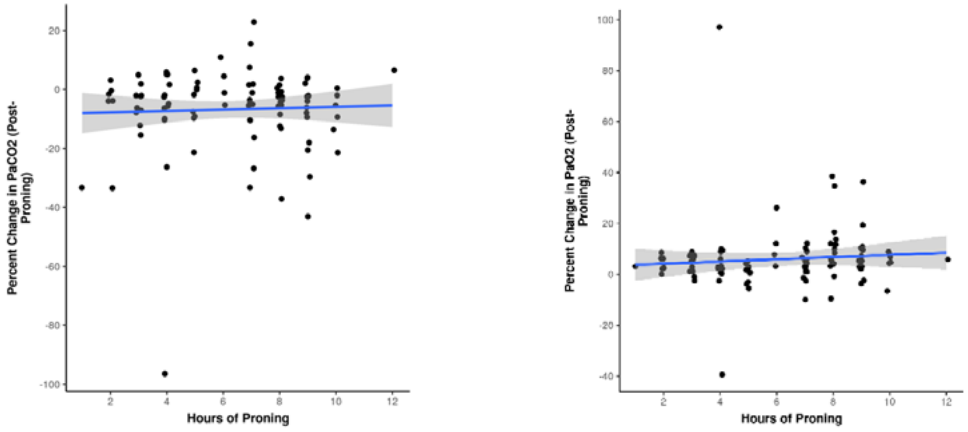

Figure 1. Scatter plot depicting the correlation between duration of proning and percentage change in $PaCO_2$ and PaO_2.

finding that all the patients had to be intubated eventually, pointing to a probable progressive nature of the disease in these patients.

The study demonstrated that duration of proning had statistically significant impact on oxygenation in these patients. However, this increase seems too small to be clinically significant and it couldn't be translated to benefit in terms of survival or need for mechanical ventilation. This could be due to the low average hours of proning which was only 6.03±2.48 hours. Whether or not more prolonged sessions of proning would be helpful remains unanswered by our study.

Results of previous studies on the effect of proning in patients with ARDS have shown otherwise. One study had showed improved oxygenation in ARDS patients with even 6 hours of daily proning.[6] Another, research on COVID-19 patients admitted in ICU had shown a 43.6% increase in PaO_2/FiO_2 ratio and 25% decrease in fraction of inspired oxygen (FiO_2) requirements.[7] Similarly, another retrospective study done among 15 non-intubated patients with hypoxemic acute respiratory failure treated with prone positioning, had concluded that it was feasible and enhanced oxygenation in non-intubated patients with ARF with PaO_2/FiO_2 of 124±50 mmHg, 187±72 mmHg, and 140±61 mmHg, during pre-proning, proning, and post-proning steps respectively, with p-value <0.001.[8]

All the patients (n=30) in this study got intubated and there was no significant difference between the groups in terms of time to intubation in days. This study did not support that prone positioning in COVID-19 patients could reduce the need for intubation. This result contradicts the result obtained by other studies which have found improvement of oxygenation parameters due to the prone position might be associated with a lower intubation rate in COVID-19 patients or even survival benefit due to a likely reduction in ventilator-induced lung injury.[5,9]

This discrepancy in the result obtained is partly due to intubation being a clinical decision and various parameters are involved other than ABG parameters when the attending physician makes a call for intubation. The hours of proning in different groups in this study was very less which could be the reason for no statistically significant difference in the time to intubation between the groups. Assessment of clinical benefits of proning based on the time for intubation needs standardization and better predictors of results due to proning need to be investigated.

This study has a few limitations. First, we decided to include individual sessions of proning only and the ABGs were accordingly taken before and immediately after those proning sessions. We included night time proning sessions only. This approach may have led to inclusion of patients with an overall inadequate proning duration over each 24 hours duration. Second, we didn't have standardized NIV settings. This could very well have led to confounding due to patient self-induced lung injury. Third, there were no standard definitions of treatment failure and the decision for intubation may have been subject to vary between clinicians. Fourth, though we did take the APACHE II and SOFA scores on admission, we did not take in to account the baseline lung pathology which could have been severe to start with since all the included patients had to be intubated. Despite these limitations, the findings do suggest that prone positioning improves oxygenation in patients with COVID-19, consistent with existing literature. Whether, this statistically significant increase in the PaO_2 translates to clinical significance is another discussion. Hence, we suggest early implementation of prone positioning to be continued. This approach may potentially delay intubation and reduce ventilator-induced lung injury and subsequently ventilator-associated pneumonia, both of which may delay disease progression though this was not seen in our study.

CONCLUSION

This study demonstrated that prone positioning in awake, non-intubated COVID-19 patients with acute respiratory failure improves oxygenation proportional to proning duration without affecting $PaCO_2$ levels. However, it did not reduce intubation rates or delay time to intubation. Further research is warranted to evaluate these results in a larger patient population.

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DISCLOSURE

No AI tools have been used in this study.

CONFLICT OF INTEREST

None.

FUNDING

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