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Awake proning in COVID-19 patients with acute hypoxic respiratory failure

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Abstract

Introduction: SARS-CoV-2 infection often experience hypoxic respiratory failure and invasive mechanical ventilation requirement. As pandemic progresses, ICU beds and mechanical ventilators may become rate-limiting factor. Prone positioning in conscious patients may improve oxygenation avoiding mechanical ventilation. We conducted retrospective study regarding proning in nonintubated patients in COVID ICU.

Objective:

Primary objective: change in SpO_2 and PaO_2 in ABG in non intubated COVID-19 patients who underwent awake prone positioning (PP).

Secondary objective: PaO_2 and $PaCO_2$ variation before and during PP or after resupination. Intubation incidence within 2 weeks of first PP trial.

Methodology: This retrospective study was conducted in SMCH from June – July 2020 among awake, nonintubated COVID 19 patients in ICU.

Inclusion criteria: Patients with SpO_2 >93 % with oxygen by face mask or nasal canula @ 2-10L/min.

Exclusion criteria: Altered mental status and impaired consciousness. We collected demographics, vitals, and position data.

Prone positioning: Placing patient on his or her stomach with head on side. Patient advised to remain in prone position as long as he can tolerate to maximum of 12hrs/day. Parameters such as HR, BP, SpO_2 and PaO_2 were measured before and during PP or after resupination at 30mins interval.

Result: Our retrospective study, suggest that in COVID-19 patients with mild to moderate acute hypoxic respiratory failure, conscious proning can lead to oxygenation improvement, less invasive ventilation requirement, shorter hospital stay length and better overall outcomes.

Keywords: COVID-19 patients, prone position, oxygenation

Introduction

The critical illness characterised by SARS-CoV-2 viral infection often results in respiratory symptoms leading to acute hypoxic respiratory failure necessitating mechanical ventilation. The initial mainstay of therapy is supplemental oxygen. COVID-19 pandemic has led to substantial increase in number of patients admitted to hospital with respiratory failure. Most of these patients require NIV support; however, the failure rate is extremely high and intubation is often necessary, rapidly saturating resources and availability of ICU beds, potentially leading to increased mortality. Prone positioning in spontaneously breathing, nonintubated patients seems to improve oxygenation because dorsal areas are no longer compressed by weight of the abdominal cavity and mediastinum, and can re-open, leading to recruitment of more gas-exchange-efficient regions and might decrease respiratory effort, which could be particularly beneficial in patients at increased risk of self-induced lung injury [1]. Therefore, this position might avoid or postpone tracheal intubation. Given the physiological benefits of prone positioning, we presupposed that patients with COVID-19 and respiratory distress, at high risk for intubation but not yet intubated, might benefit from prone positioning. This study describes examination of changes in oxygenation, as measured by PaO_2/FiO_2, across multiple episodes of prone positioning in conscious patients, with mild to moderate hypoxia, undergoing non-invasive ventilation following admission to ICU. In our retrospective case series, we describe 25 COVID-19 conscious patients requiring oxygen supplementation who underwent awake prone positioning, with mild to moderate hypoxia, describing the manoeuvre's effects on patients' oxygenation and outcomes [2-3].

Aim

To evaluate if there is improvement in oxygenation in COVID 19, non intubated patients who underwent awake prone positioning therapy in ICU.

Objectives

Primary objective: Change in PaO_2/FiO_2 ratio in non intubated COVID-19 patients who underwent awake prone positioning (PP).

Secondary objective: PaO_2 and $PaCO_2$ variation before and during PP or after resupination. Intubation incidence within 2 weeks of the first prone-positioning trial.

Methodology

Study Design and Participants

In this single-centre, retrospective study, we collected medical records of over 25 patients with COVID 19 pneumonia who are non intubated in Saveetha Medical College and Hospital from June 2020 to July 2020.

Inclusion criteria: aged 18–75 years, confirmed diagnosis of COVID-19-related pneumonia patients with SpO_2 >93 % requiring supplemental oxygen or non-invasive CPAP, and gave written or witnessed verbal informed consent.

Exclusion criteria: pregnant, altered mental status and impaired consciousness.

Procedures

- In all patients, COVID-19 diagnosis was made with RT-PCR using oral and nasal swab.
- Baseline data were collected (time point SP1) when enrolled, including demographic and anthropometric data, a baseline arterial blood gas measurement.
- Subsequently, each patient was helped into the prone position and data were collected again after approximately 10 min (time point PP1).
- The patient was then encouraged to maintain prone position for at least 3 h before being helped back into the supine position.
- 1 h after resupination (time point SP2) clinical data were collected again.
- Patients were free to resume supine position or maintain prone position at their discretion for up to 8 h in total at the end of 3 hr period.
- Data were retrospectively collected via hospital's health record.

Statistical Analysis

- Based on their distribution, calculated mean (SD) and median (IQR) for continuous variables.
- We describe discrete variables using percentages and frequencies.
- We used 95% CI according to the Clopper–Pearson method to estimate the probability of feasibility of the procedure
- For variables assessed repeatedly we then described data for the subset of patients for whom the procedure was feasible at the three time points SP1, PP1, and SP2
- Using the paired Student's t test on pairs of time points, we compared distributions of continuous variables between the three time points considering SP1 versus PP1 and SP1 versus SP2.
- McNemar's test for paired proportions on pairs of time points were used to compared proportions of dichotomous variables between several study time points.
- Using 95% Cis according to the Clopper–Pearson method we estimated the probability of response.
- We used unpaired Student's t test to compare distributions of continuous variables between subgroups defined by response
- Using univariate logistic regression models we validated this comparison on the binary outcome defined by the response (ie, response vs no response), considering the continuous variable as an explanatory variable.
- We used $\chi 2$ test to compare proportions of dichotomous variables between independent groups.
- p values of less than 0・05 considered to be significant.
- STATA software were used to do analysis.

Results

Between June 2020 to July 2020, 25 patients with COVID-19-related pneumonia were admitted to Saveetha Medical College and Hospital who underwent awake prone positioning.

Table 1: Baseline demographic and clinical characteristics of analysable population

	Analysable population (n=25)
Age, years	58 ± 4
Sex	
Female	6 (21 %)
Male	19 (79 %)
BMI, kg/m²	27 ± 5
Time between symptom onset and admission to hospital, days	7 ± 8
Time between admission to hospital and prone positioning, days	3 ± 5
Comorbidities	
Hypertension	11 (41%)
Chronic bronchopulmonary disease	1 (4%)
Diabetes	4 (14%)
chronic kidney disease	0
Ischemic heart disease	2 (7%)
Solid malignancy	1 (4%)
Oxygen delivery interface	

CPAP	2 (8%)
Reservoir mask	5 (20%)
Nasal cannula	18 (72%)

Data are n (%) or mean (SD). BMI=body-mass index. CPAP=continuous positive airway pressure.

Table 1 shows the characteristics of the study population.

- The mean age was 58 ± 4 years.
- The mean BMI was 27 ± 5 kg/m^2.
- 19 (79%) patients were male.
- Common comorbidities included hypertension and diabetes.
- Patients were admitted to hospital a mean of 7 ± 8 days after symptom onset, and were put into the prone position a mean of 3 ± 5 days after their admission to hospital.
- 2 (8%) patients were treated with CPAP, 5 (20%) with Reservoir mask and 18 (72%) with Nasal cannula.

Table 2: Study timepoint analysis among patients who tolerated prone positioning and had available data across the three study timepoints (n=25)

	SP1	PP1	SP2	SP1 vs PP1		SP1 vs SP2	
				Difference (95% CI)	p value	Difference (95% CI)	p value
FiO_2, %	68·9 (19·8)	68·9 (19·8)	65·9 (20·2)	0·0 (0·0 to 0·0)	1·0	3·0 (–0·7 to 6·8)	0·11
Arterial blood gas							
pH	7·46 (0·03)	7·46 (0·04)	7·46 (0·03)	0·0 (0·0 to 0·0)	0·50	0·0 (0·0 to 0·0)	0·08
PaO_2, mm Hg	117·1 (47·4)	200·4 (110·9)	121·4 (69·6)	83·3 (56·1 to 110·4)	<0·0001	4·3 (–13·2 to 21·6)	0·60
PaO_2/FiO_2 ratio, mm Hg	180·5 (76·6)	285·5 (112·9)	192·9 (100·9)	104·9 (70·9 to 134·0)	<0·0001	12·3 (–10·9 to 35·5)	0·29
$PaCO_2$, mm Hg	35·3 (4·9)	35·6 (4·5)	35·5 (4·4)	0·4 (–1·3 to 0·6)	0·48	0·3 (–0·9 to 1·4)	0·64
SaO_2, %	97·2 (2·0)	98·4 (1·3)	97·1 (2·0)	1·2 (0·8 to 1·7)	<0·0001	0·1 (–1·0 to 0·4)	0·35
SpO_2, %	97·2 (2·8)	98·2 (2·2)	97·1 (1·9)	1·0 (0·3 to 2·0)	0·01	0·1 (–0·8 to 1·0)	0·87
Respiratory rate, breaths per min	24·5 (5·5)	24·5 (6·9)	23·9 (6·3)	0·1 (–1·0 to 1·5)	0·71	–0·6 (–2·0 to 0·8)	0·40

Data are mean (SD) or n (%), unless otherwise indicated. p values were calculated using Student's t test for continuous variables and the χ^2 test for categorical variables. FiO_2=fractional concentration of oxygen in inspired air. $PaCO_2$=arterial partial pressure of carbon dioxide. PaO_2=arterial partial pressure of oxygen. SaO_2=arterial oxygen saturation of haemoglobin. SP1=baseline supine position. PP1=10 min after prone positioning. SP2=1 h after resuming supine position. SpO_2=peripheral oxygen saturation of haemoglobin.

Table 2 shows the arterial blood gas values and ventilation parameters of 25 patients who tolerated prone positioning at the three study time points.

Oxygenation improved on average by more than 50% from SP1 to PP1 (difference in PaO_2/FiO_2 ratio 104・9 mm Hg [95% CI 70・9 to 134・0]), although this improvement was on average not significant when supine position was resumed (SP1 vs SP2 difference in PaO_2/FiO_2 ratio 12・3 mm Hg [95% CI –10・9 to 35・5].

Table 3: Comparison between responders and non-responders

	Responders (n=13)	Non-responders (n=12)	Difference (95% CI)	p value
Age, years	58 ± 6	57 ± 4	2·7 (–7·0 to 1·7)	0·22
Sex				
Female	3 (24%)	3 (25%)	-	-
Male	10 (76%)	9 (75%)	-	-
BMI, kg/m²	27·3 (3·5)	27·4 (3·7)	–0·12 (–2·3 to 2·1)	0·92
Time between symptom onset and admission to hospital, days	8·1 (4·8)	7·4 (4·3)	–0·7 (–3·4 to 1·9)	0·58
Time between admission to hospital and prone positioning, days	2·7 (2·1)	4·6 (3·7)	–1·9 (–3·7 to 0·1)	0·04
Time between symptom onset and prone positioning, days	10·8 (4·9)	12·0 (4·3)	–1·1 (–3·9 to 1·6)	0·41
Comorbidities				
Hypertension	6 (46%)	5(41%)		
COPD	0	1 (8%)		
Diabetes	2 (15%)	2 (16%)		
chronic kidney disease	0	0		
Ischemic heart disease	0	2 (16%)		
Solid malignancy	1 (7%)	0		
Arterial blood gas at SP1				
pH	7·46 (0·0)	7·5 (0·0)	0·0 (0·0 to 0·0)	0·79
PaO_2, mm Hg	114·5 (49·1)	119·7 (46·7)	–5·2 (–33·6 to 23·3)	0·72
$PaCO_2$, mm Hg	35·1 (5·2)	35·4 (4·6)	–0·3 (–3·2 to 2·6)	0·85
SaO_2, %	97·1 (2·1)	97·3 (1·9)	–0·2 (–1·4 to 1·0)	0·73
Arterial blood gas at PP1				
pH	7·5 (0·0)	7·5 (0·0)	0·0 (0·0 to 0·0)	0·44
PaO_2, mm Hg	225·3 (112·6)	175·5 (105·8)	49·8 (–15·2 to 114·7)	0·13
$PaCO_2$, mm Hg	35·3 (5·4)	36·0 (3·6)	–0·7 (–3·4 to 2·0)	0·61
SaO_2, %	98·5 (1·4)	98·4 (1·3)	0·2 (–1·0 to 0·7)	0·72
Arterial blood gas at SP2				

pH	7·5 (0·0)	7·5 (0·0)	0·0 (0·0 to 0·0)	0·84
PaO_2, mm Hg	154·0 (84·9)	88·7 (21·8)	65·3 (28·4 to 102·1)	<0·0001
$PaCO_2$, mm Hg	35·1 (4·5)	36·0 (4·3)	–1·0 (–3·6 to 1·7)	0·47
SaO_2, %	97·8 (2·1)	96·4 (1·8)	1·4 (0·2 to 2·6)	0·03
Secondary outcomes				
Tracheal intubation	4(30%)	3 (26%)	4·3 (–30·7 to 21·6)	0·74
Duration of prone positioning, h	3·5 (3·0 to 4·0)	3·5 (3·0 to 4·0)	-	0·99
Prone positioning for >3 h	7(55%)	6(52%)	–4·3% (–33·1 to 24·4)	0·77
Number of prone positioning cycles	2 (1 to 3)	2 (1 to 3)	-	0·94
More than one prone positioning cycle	7(52%)	6(49%)	4·3% (–34·0 to 24·9)	0·76

Data are mean (SD) or n (%), unless otherwise indicated. Differences are not calculated for data presented as median (range) or for small proportions. p values were calculated using Student's t test for continuous variables and the $\chi 2$ test for categorical variables. BMI=body-mass index. FiO_2=fractional concentration of oxygen in inspired air. $PaCO_2$=arterial partial pressure of carbon dioxide. PaO_2=arterial partial pressure of oxygen. SaO_2=arterial oxygen saturation of haemoglobin. SP1=baseline supine position. PP1=10 min after prone positioning. SP2=1 h after resuming supine position. SpO2=peripheral oxygen saturation of haemoglobin.

- A comparison of baseline clinical and demographic data and secondary outcomes for the 13 patients who responded to prone positioning and the 12 patients who did not is shown in table 3.
- Prone positioning was done significantly earlier in patients who responded than in those who did not respond (2.7 days [SD 2.1] vs 4.6 days [3.7] from hospital admission; difference 1.9 days [95% CI 0.1 to 3.7]).
- Finally, incidence of tracheal intubation was not significantly different between responders and nonresponders (4 [30%] vs 3 [26%]; p=0.74),
- No adverse events related to the procedure were recorded.
- Overall, five deaths occurred in the whole that were not related to the procedure but to the underlying disease (COVID-19).

Discussion

In this retrospective study, we investigated the feasibility and effect of prone positioning in spontaneously breathing, non-intubated patients with COVID-19-related pneumonia. We found that prone positioning was safe and feasible in most patients, and that it substantially improved physiological measures of oxygenation, although this effect was lost after reverting to the supine position. We found that earlier prone positioning were associated with maintenance of improvement in oxygenation after resupination [4].

Finally, we showed that patients who responded to prone positioning had no significant difference in the rate of intubation compared with non-responders. Our data suggest that patients are more likely to respond to prone positioning if this procedure is done early after admission to hospital. One of the possible explanations for this finding is the typically higher proportion of potentially recruitable lung in early phases of ARDS compared with later phases. Another explanation is persistence of perfusion redistribution, with improved ventilation–perfusion matching [5]. Awake prone positioning did not seem to substantially improve long-term oxygenation in patients with COVID-19; however, it might decrease patients' oxygen requirements and allow the delay or avoidance of tracheal intubation, which might prove particularly valuable in scenarios where ICU bed capacity is reduced. An additional benefit of the reduction in FiO_2, allowed by the improved oxygenation, is the decrease in the risk of reabsorption atelectasis. Prone positioning could be used as an additional non-invasive tool in patients with a do-not intubate order.

Conclusion

With the global pandemic putting a strain on many countries resources, there is an urgency to find a low-risk, low-cost manoeuvre for non-intubated patients that halts disease progression, especially when this has the potential to reduce the need for labour-intensive care and prone ventilation in the ICU. In summary, we observed improvement in oxygenation during prone positioning, which was maintained upon resupination by half of the patients for at least 1 h. With minimal patient discomfort, prone positioning was found to be a useful and patient engaging technique to ameliorate blood gas parameters in the short term in patients with COVID-19-related pneumonia.

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