Irish Journal of Medical Science (1971 -) (2023) 192:811–815
https://doi.org/10.1007/s11845-022-03009-7

ORIGINAL ARTICLE

Efficacy and feasibility of awake proning in patients with COVID-19-related acute hypoxemic respiratory failure: an observational, prospective study

Tharwat Aisa[1] · Tidi Hassan[2] · Ehtesham Khan[1] · Khaled Algrni[3] · Muhammed Anwar Malik[1]

Received: 11 November 2021 / Accepted: 5 April 2022 / Published online: 14 April 2022

Abstract

Introduction Most of COVID-19 patients present with hypoxemic respiratory failure. Proning is one of the management options proven to improve oxygenation and reduce mortality in non-COVID-19-related acute respiratory distress syndrome. As a response to COVID-19 pandemic surge, a dedicated COVID-19 respiratory ward for the management of mild to moderate ARDS patients who require oxygen therapy, non-invasive ventilation (NIV), or high-flow nasal cannula (HFNC) was established. We adopted a policy of early awake proning in such patients.

Aims To determine the physiological changes, improvement in oxygenation, the need for intubation, alongside with the duration, tolerance, and adverse effects of awake proning.

Study design and methods Single-center, prospective observational cohort study. All awake, non-intubated, spontaneously breathing patients with COVID-19, and hypoxemic acute respiratory failure requiring oxygen supplementation, NIV, or HF

Results Fifty patients were enrolled. There was a significant improvement in oxygenation when turning the patients from supine to prone position with mean PFR was 85 (SD 13.76) in supine position which increased to 124 (SD 34.08) in prone position with substantial increase in mean PFR 1-h post proning to 138 (SD 28.01) and *P*-value 0.0001. Prone positioning was feasible in 41 (82%) patients (mean duration 8.5 (SD 3.13) h), and 38 (76%) patients reported that it was well tolerated.

Conclusion Awake proning was feasible, tolerable, and effective in improving oxygenation in patients with COVID-19-related pneumonia and acute hypoxemic respiratory failure in this prospective study.

Keywords ARDS · Awake proning · COVID19 · Feasibility · Hypoxic respiratory failure

Introduction and objectives

The COVID-19 pandemic has led to an increase in the number of patients admitted to hospital with acute respiratory failure [1]. Most of these patients present with hypoxemic respiratory failure which mandates the use of non-invasive respiratory support (NRS) such as high-flow oxygen or non-invasive ventilatory support; however, the failure rate due to either progression of disease or lack of improvement is extremely high, and intubation is often necessary.

Acute respiratory distress syndrome (ARDS) is a major complication of COVID-19 that occurs in 20–41% of patients with a severe disease [2, 3]. Proning is one of the management options proven to improve oxygenation and reduce mortality in non-COVID-19-related ARDS [4]. The improvement in oxygenation is due to improved ventilation–perfusion matching in the prone position due to recruitment of dorsal alveoli which are compressed by the weight of abdominal organs and mediastinum that leads to improved homogeneity of gas-exchange-efficient regions [5, 6].

It has been reported that application of self-proning in non-intubated patients treated with standard oxygen therapy and/or NRS was effective in reducing the work of breathing and improving oxygenation, thus decreasing the need for mechanical ventilation and subsequent admission to ICU [7–9].

✉ Tharwat Aisa
Tharwat40@yahoo.com

[1] Department of Anesthesia and Critical Care, Our Lady of Lourdes Hospital, Drogheda, Ireland

[2] Department of Respiratory Medicine, Our Lady of Lourdes Hospital, Drogheda, Ireland

[3] College of Public Health and Health Informatics, Umm Al-Qura University, Mecca, Saudi Arabia

The application of prone positioning in conscious, non-intubated patients (awake proning) during COVID-19 related-ARDS has shown to improve the respiratory parameters and improve oxygenation [10–12]. However, the reported duration of proning was short in some studies, and the sample size was small in others. Moreover, studies reporting its application and feasibility outside ICU settings are still lacking [9, 13, 14].

As a response to COVID-19 pandemic surge, we established together with the respiratory team, a dedicated COVID-19 respiratory ward for the management of mild to moderate ARDS patients who require oxygen therapy, non-invasive ventilation (NIV), or high-flow nasal cannula (HFNC). We adopted a policy of early awake proning in such patients and conducted a prospective observational study to report the physiological changes, improvement in oxygenation, the need for intubation, alongside with the duration, tolerance, and adverse effects of awake proning.

Methods

Study design and participants

In this single-center, prospective observational cohort study, we included all awake, non-intubated, spontaneously breathing patients with COVID-19 who are > 18 years old and with hypoxemic acute respiratory failure (peripheral oxygen saturation by pulse oximeter < 90% or PaO_2 < 10 kPa), requiring oxygen supplementation, NIV, or HFNC. The main exclusion criteria were acute respiratory failure requiring intubation, hemodynamic instability or decreased conscious level.

The main outcome was the improvement in oxygenation as indicated by the mean change of the partial pressure of oxygen to the fraction of inspired oxygen ratio (PFR) over time (before and post proning).

Secondary outcomes included improvement in the respiratory distress parameters heart rate (HR), respiratory rate (RR), blood pressure (BP), peripheral oxygen saturation by pulse oximeter (SpO_2), partial pressure of oxygen (PaO_2), the need for intubation, awake proning feasibility, patients' comfort, and adverse effects.

We enrolled all the patients who fulfilled the inclusion criteria. The study was approved by the National Research Ethics Board (reference 20-NREC-COV-001) and consent signed. A paper format guidance on awake proning was given while nurse or physician-led assistance and/or anxiolytics may be considered. Some patients required a small dose of sedatives to alleviate the hypoxia-related anxiety and to facilitate the proning.

Physiological parameters; HR, RR, and BP were recorded pre-proning and post proning. Arterial blood gases were measured just before proning, 30 min and 1-h post proning. Wherever possible, oxygen delivery interface and positive end–expiratory pressure (PEEP) were not changed between before or after proning; however, a fraction of inspired oxygen (FiO_2) was titrated according to the response of the patients to achieve the target oxygenation parameters based on the attending physician decision. The duration of proning achieved in the first 24 h and any complications or adverse effects were recorded. We observed the patients for improvement of the signs of respiratory distress (improvement in tachycardia, tachypnea, nasal flare, and working accessory muscles of respiration).

The subsequent prone positioning sessions were allowed according to the clinicians' discretion. The patients were followed up until ICU discharge for occurrence of intubation, time to intubation, and its duration.

If the patients tolerated the prone position > 3 h without adverse effects, discomfort or asking for supination, the prone position was considered feasible. Comfort was assessed on a scale of "well tolerated", "somewhat tolerated", or "untolerable".

Statistical analysis

We have used analysis of variance with repeated measures designed to assess the significance of change over time (ANOVA). All significant levels were set to P value < 0.05. All the analyses were performed using SPSS for windows version 18.00 (SPSS Inc., Chicago, IL., USA) program.

Results

In the period between January 9 and April 1, 2021, we enrolled 50 patients, of whom 23 (46%) were males while 27 (54%) were females with mean age 56.20 (SD 11.91) years and mean body mass index of 29.46 (SD 3.77). Table 1 shows the baseline characteristics of the patients.

There was a significant improvement in oxygenation when turning the patients from supine to prone position alongside with NIV and HFNC; mean PFR was 85 (SD 13.76) in supine position which increased to 124 (SD 34.08) in prone position with substantial increase in mean PFR 1-h post proning to 138 (SD 28.01) and P-value 0.0001. These findings were reported in 43 (86%) patients of our sample. Moreover, there was a significant improvement in SpO_2, HR, and RR over time with proning; P-value 0.001 (Table 2). Furthermore, 7 (14%) patients required intubation at a mean of 1.57 (SD 0.78) days and a mean duration of ventilation 16.5 days (Table 2).

In addition, we monitored the nasal flaring and sternomastoid muscle retraction which were observed in 22 patients pre-proning, while it was observed in 11 patients only post proning. There was no statistically significant difference (P-value was 0.49).

Table 1 Baseline characteristics of the patients ($n = 50$)

Variable	Mean (SD)
Mean age (years)	56.20 (11.91)
Mean BMI	29.46 (3.77)
Time spent proning (hours)	8.5 (3.13)
Time to intubation (days)	1.57 (0.78)
Gender (*n* and %)	
Male	23 (46%)
Female	27 (54%)
Hypertension (*n* and %)	18 (56%)
COPD (*n* and %)	4 (8%)
Chronic kidney disease (*n* and %)	6 (12%)
Asthma (*n* and %)	13 (26%)
Autoimmune disease (*n* and %)	2 (4%)
Smoker (*n* and %)	2 (4%)
% Intubated (*n* and %)	7 (14%)

Data are presented as mean and standard deviation (SD)

BMI body mass index, *COPD* chronic obstructive pulmonary disease, *n* number

Prone positioning was feasible in 41 (82%) of the patients (mean duration 8.5 (SD 3.13) h), and 38 (76%) reported that it was well tolerated. Only 5 (10%) patients had complications in the form of back pain, anxiety, or agitation.

Discussion

In our study, we investigated the efficacy and feasibility of prone positioning in spontaneously breathing, non-intubated patients (awake proning) with COVID-19-related pneumonia and acute hypoxic respiratory failure. We found that awake proning was effective, tolerable, and feasible in most patients, and that it substantially improved oxygenation parameters. Additionally, we showed that it decreased the rate of intubation in the patients in whom it was feasible and effectively improved the oxygenation.

This study adds to the growing evidence that awake proning may have a role in the management of ARDS in the context of COVID-19 infection. It supports previous findings in this group [8–10] and it was delivered effectively outside of the intensive care setting. The effect of prone positioning in the awake, spontaneously breathing patients was studied before. Valter and coauthors [7] reported improvement in oxygenation when awake proning was used with intubation avoidance.

We reported a significant improvement in the oxygenation during proning which was observed in the significant increase in the PFR. This improvement was associated with significant reduction in the HR and RR as well.

These findings are in line with the previous studies conducted on patients with COVID-19; Sartini et al. [11] reported a significant improvement in oxygenation when they used the awake proning alongside with continuous positive airway pressure (CPAP) in the medical ward. Caputo et al. [13] showed a significant increase in peripheral oxygen saturation in COVID-19 patients who attended the emergency department when they have been proned. Furthermore, Elharrar and coauthors [10] found that oxygenation improved only in six (25%) of the 24 patients who were enrolled when they applied prone positioning; however, they measured only the PaO_2, and it was a small sample size study.

Winearls et al. [14] reported a significant increase in the PFR and ROX index in a retrospective study on 24 patients with COVID-19-related acute hypoxemic respiratory

Table 2 Effects of awake proning on physiological parameters and oxygenation

Variable	Pre-proning mean (SD)	30 min Post proning mean (SD)	1 h Post proning mean (SD)	*P*-value
SpO_2 (median and IQR)	82% (IQR 72–85)	93% (IQR 90–94)	94% (IQR 90–95)	0.0001
PaO2 (KPA)	10 (1.84)	11 (1.18)	11 (1.23)	0.43
Respiratory rate (RR)	38 (4.37)	31 (4.84)	30 (4.60)	< 0.0001
FiO_2	0.90 (0.11)	0.67 (0.12)	0.62 (0.12)	< 0.0001
PFR	85 (13.76)	124 (34.08)	138 (28.01)	< 0.0001
Systolic BP	132 (9.10)	130 (7.44)	129 (8.6)	0.07
Diastolic BP	71 (9.07)	70 (6.70)	69 (6.80)	0.19
Heart rate (HR)	100 (7.05)	94 (8.86)	93 (10.20)	< 0.0001
Nasal flaring/sternomastoid retractions (*n*)	22	20	11	0.49*

ANOVA analysis with repeated measures was to assess the changes in parameters overtime. The significant level was set to 0.05

*The *P*-value is based on chi-square test

Data are presented as mean and standard deviation (SD) or median and interquartile (IQR)

failure who were treated in a high-dependency unit with awake proning alongside with CPAP.

In another study on 20 patients with moderate to severe ARDS, Ding et al. [9] used the awake proning alongside with the high-flow nasal cannulae and non-invasive ventilation, and they found that that procedure prevented intubation in 11 patients with a significant improvement in oxygenation. However, these findings are limited by the retrospective design and small sample size in the former study and by the small sample size in the other one. Our study had a prospective design with a good sample size and standardized ventilation interface before and during proning.

Prone positioning was feasible in most of the patients (82%), and they tolerated the proning for a mean duration of 8.5 h, and the majority of them reported good tolerability to the prone positioning. Only few of the patients reported adverse effects in the form of back pain in one patient and anxiety/agitation in the other 4 patients which could be related to the hypoxemia, as those patients ended up with intubation. In total, 7 (14%) patients required intubation after 36 h because they remained hypoxic. These findings are consistent with the findings of Coppo A. and colleagues [12] who reported that prone positioning in patients with COVID-19 was feasible in 47 patients (83.9%) outside the intensive care environment. Moreover; in the study conducted by Scaravilli et al. [8] in 2015, they found that the awake proning was feasible in 95% of cases with a significant improvement in oxygenation between before prone positioning and after resupination. Winearls et al. [14] found that the use of awake proning alongside continuous CPAP therapy was both feasible and tolerated in a respiratory high-care unit with few resources; however, they did not mention the parameter they used to measure feasibility. Our results support the existing available evidence that awake proning could be safely and effectively used outside the critical care area with minimal resources and staffing during the pandemic, where the ICUs and the resources are overwhelmed by the surge of cases.

Our findings suggest that the application of proning is a valuable tool in improving oxygenation and decreasing respiratory effort in many patients with moderate or severe COVID-19. Awake proning is a simple procedure which does not require additional resources or staff (most of the patients can prone themselves, without the need for assistance) and is costless.

Limitations

Our study is a single center, observational study. Although ts is prospective; however, it lacks randomization and control group. Thus, it might be difficult to generalize our findings, and the design does not allow to accurately estimate the patients' outcome such as the mortality or the need for tracheal intubation, in addition to lack of adjustment for the confounders in the analysis (such as other available treatment options in COVID-19 patients). Although it adds to the growing evidence that awake proning has physiological benefits and help improve oxygenation in such patients; however, further randomized controlled trials are warranted to explore its effects on patient outcomes in terms of morbidity, mortality, and avoidance of intubation and in decreasing the need for ICU admissions.

Conclusion

Awake proning was feasible, tolerable, and effective in improving oxygenation in patients with COVID-19-related pneumonia and acute hypoxemic respiratory failure in this prospective study. Further studies are required to determine the outcome of awake proning and whether it could be adopted as a standard strategy rather than a rescue therapy in patients with Covid-19 and non-Covid-19-related acute hypoxic respiratory failure.

Abbreviations ARDS: Acute respiratory distress syndrome; COVID-19: SARS-CoV-2 infection; HFNC: High-flow nasal cannula; NIV: Non-invasive ventilation; ICU: Intensive care unit; PFR: Partial pressure of oxygen to the fraction of inspired oxygen ratio; CPAP: Continuous positive airway pressure

Declarations

Conflict of interest The authors declare that they have no competing interests.

References

1. Grasselli G, Zangrillo A, Zanella A et al (2020) Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region. Italy JAMA 323:1574–1581
2. Wang D, Hu B, Hu C et al (2020) Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan. China JAMA 323:1061–1069
3. Wu C, Chen X, Cai Y et al (2020) Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020; published online March 13. https://doi.org/10.1001/jamainternmed.2020.0994
4. Guérin C, Reignier J, Richard JC et al (2013) Prone positioning in severe acute respiratory distress syndrome. N Engl J Med 368:2159–2168

5. Mure M, Glenny R, Domino K et al (1998) Pulmonary gas exchange in pigs improves in the prone position with abdominal distension. Crit Care 2(suppl 1):122
6. Albert RK, Hubmayr RD (2000) The prone position eliminates compression of the lungs by the heart. Am J Respir Crit Care Med 161:1660–1665
7. Valter C, Christensen AM, Tollund C et al (2003) Response to the prone position in spontaneously breathing patients with hypoxemic respiratory failure. Acta Anaesthesiol Scand 47:416–418
8. Scaravilli V, Grasselli G, Castagna L et al (2015) Prone positioning improves oxygenation in spontaneously breathing non intubated patients with hypoxemic acute respiratory failure: a retrospective study. J Crit Care 30:1390–1394
9. Ding L, Wang L, Ma W et al (2020) Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study. Crit Care 24:28
10. Elharrar X, Trigui Y, Dols A-M et al (2020) Use of prone positioning in nonintubated patients with COVID-19 and hypoxemic acute respiratory failure. JAMA
11. Sartini C, Tresoldi M, Scarpellini P et al (2020) Respiratory parameters in patients with COVID-19 after using noninvasive ventilation in the prone position outside the intensive care unit. JAMA
12. Coppo A, Bellani G, Winterton D et al (2020) Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study. Lancet Respir Med 8:765–774
13. Caputo ND, Strayer RJ, Levitan R (2020) Early self-proning in awake, non-intubated patients in the emergency department: a single ED's experience during the COVID-19 pandemic. Acad Emerg Med 27:375–378
14. Winearls S, Swingwood EL, Hardaker CL et al (2020) Early conscious prone positioning in patientswith COVID-19 receiving continuous positive airway pressure: a retrospective analysis. BMJ Open Resp Res 7:e000711