Effect of Awake Prone Positioning in Hypoxaemic Adult Patients with COVID-19: a single centre pilot cohort study

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Abstract

Although advocated in patients with COVID-19, evidence supporting awake prone positioning (APP) is limited. We investigated the effect of APP on 17 hypoxaemic patients with COVID-19. APP was associated with an increase in SpO_2/FiO_2 ratio (27.8 [6.3-82.3]; p<0.001), SpO_2/FiO_2 x respiratory rate^{-1} (ROX index), (3.1 [1.4-4.1]; p<0.001) and PaO_2/FiO_2 ratio (9.8kPa, [2.2-13.1]; p=0.016, p.adj=0.047). Estimated shunt fraction decreased whilst prone (-8.9% [-18.2- -7.3]; p=0.031, p.adj=0.094), but reverted to baseline levels upon supination. In conclusion, APP effectively improves respiratory physiology and clinical trials are required to evaluate the clinical effectiveness.

Introduction

The optimal non-invasive strategy to manage the profound hypoxaemia associated with COVID-19 remains unknown. Prone positioning has recognised benefit in management of invasively mechanically ventilated (IMV) patients with moderate to severe acute respiratory distress syndrome (ARDS)[1] and is reportedly effective in COVID-19.[2] Awake Prone Positioning (APP) has been proposed,[3] however, evidence remains limited both in the general,[4, 5] and COVID-19 population.[6–8] The aim of this study was to explore the effect of APP on the acute respiratory physiology of COVID-19 patients' and relationship with clinical outcomes.

Methods

A retrospective observational cohort study was conducted as a service evaluation, using routinely collected data, at an 1100 bed university-affiliated hospital. The study occurred between 1/4/2020 and 20/5/2020. APP was prescribed for adult patients with suspected or confirmed COVID-19, requiring an inspired fractional concentration of oxygen (FiO_2) ≥0.28 to maintain peripheral oxygen saturations (SpO_2) 92-96%, in line with national guidelines.[3] Following local protocol, we excluded patients requiring immediate intubation, with cardiovascular instability, altered consciousness or other factors rendering proning unsafe. Patients were required to independently self-prone and were free to cease at any stage for comfort. APP was commenced in the Emergency Department or level 1 wards, aiming for 30 minutes with immediate supervision. Site of subsequent APP was dependent on escalation status; either in critical care (*Group 2*: for full escalation) or a designated ward supervised by the attending medical/physiotherapy team (*Group 1*: ward-based therapy only). Observations were recorded at baseline, 5 and 30 minutes. If tolerated and of benefit, the protocol aimed to continue prone and/or lateral positioning for up to 2-4 hours, twice a day. Decisions regarding intubation were at the discretion of the attending physician.

Data was extracted from the electronic medical record. Shunt fraction and PaO_2/FiO_2 ratio was calculated from arterial blood gas (ABG) data. ROX index was calculated as SpO_2/FiO_2 x respiratory rate^{-1}.[9] Statistical analysis was performed using R (version 4.0.0, http://www.r-

project.org). Data are presented as median and interquartile range [IQR], or n and percentage (%). Wilcoxon signed-rank tests were used for paired comparisons, Friedman test with Bonferroni correction for >2 sequential comparisons and Mann-Whitney-Wilcoxon tests for unpaired data. All tests were two-sided and P< 0.05 was considered significant.

Results

19 patients received APP, two were excluded from further analysis following negative COVID-19 tests. Baseline characteristics are shown in *Table 1*.

Table 1: Baseline Characteristics for all patients with confirmed COVID-19 (n=17). Incomplete data for BMI (n=13), Elixhauser Score (n=11), FiO_2 (n=16) and respiratory rate (n=16). Imaging refers to Chest X-Ray in all patients, with additional CT pulmonary angiogram available for 5 patients and CT chest in 1. *BMI; body mass index. SpO_2; peripheral oxygen saturations*. *FiO_2; inspired fractional concentration of oxygen.*

Male	15 (88.2)
Age (years)	63.0 [55.0 - 69.0]
Ethnicity	
White: British	6 (35.3)
White: Other	2 (11.8)
Black	3 (17.6)
Asian	1 (5.9)
Other Ethnic Group	1 (5.9)
Not Specified	4 (23.5)
BMI	26.1 [24.4 - 28.1]
Elixhauser Score	0 [-2.0 - 7.0]
Time from admission to first proning session (hours)	94.8 [19.8 - 145.0]
Baseline Observations	
SpO_2 (%)	93.0 [92.0 - 94.0]
FiO_2	0.6 [0.4 - 0.8]
Respiratory Rate (breaths/minute)	22.0 [19.8 - 27.3]
Temperature (°C)	37.2 [37.1 - 38.2]

Imaging appearances	
Patchy bilateral opacification	6 (35.3)
Diffuse bilateral opacification	10 (58.8)
Bilateral focal consolidation	1 (5.9)
Pulmonary emboli	1 (5.9)

Baseline ABG were available for nine and sequential pre-, prone and post-APP ABGs for seven patients, SpO_2/FiO_2 calculated in 16 and ROX index[9] in 13, due to missing data. Group 1 comprised four patients and Group 2 13, one of whom had subsequent limitation of escalation. Duration of the initial trial was 55.0 [30.0-116.3] minutes and total APP days was 3 [1-3] days with total duration for days one to three of 9.2 [5.2-17.6] hours in 5 [2.8-10.0] sessions. Patient positioning during APP varied; 12 patients (70.6%) laid both prone and laterally during sessions, 5 (29.4%) laid prone only. APP was generally well tolerated with only one patient declining therapy beyond their initial session. All patients were hypoxic at initiation (SpO_2/FiO_2 156.7, [123.8-232.5]). Following APP, SpO_2/FiO_2 (27.8, [6.3-82.3]; p< 0.001) (*Figure 1A*) and ROX increased (3.1, [1.4-4.1]; p<0.001) (*Figure 1B*). In the subgroup with ABG data, PaO_2/FiO_2 increased (9.8kPa, [2.2-13.1]; p=0.016, p.adj=0.047) and shunt decreased (-8.9% [-18.2- -7.3]; p=0.031, p.adj=0.094). Following supination, both PaO_2/FiO_2 (-3.0 [-3.3- -1.6]; p=0.016, p.adj=0.047)) and shunt (8.6% [5.6-18.3]; p=0.016, p.adj=0.047) reverted to pre-APP levels (*Figure 1C*)**.** Baseline characteristics of Group 2 patients, with no limits of escalation, are shown in *Table 2*.

Table 2: Baseline characteristics for Group 2 patients with no limitations of treatment n=12, presented by intubation status. Intubated n=5, not intubated n=7. Incomplete data for BMI (n= 9), Elixhauser Score (n=8), FiO_2 (n=11) and respiratory rate (n=11). Baseline ABG available, and therefore P/F ratio and shunt fraction calculable, for 8 patients (4 in each group). Imaging refers to Chest X-Ray, which was reviewed in all patients, with additional CT pulmonary angiogram available for 4 patients and CT chest in 1. *BMI; body mass index. SpO_2, peripheral oxygen*

saturations. FiO_2; inspired fractional concentration of oxygen. ROX index; ([SpO_2/FiO_2]/RR), PaO_2; arterial partial pressure of oxygen.

	All	Intubated	Not Intubated
Male sex	11 (91.7)	5 (100.0)	6 (85.7)
Age (years)	58.0 [54.8 - 64.3]	58.0 [58.0 - 64.0]	58.0 [51.0 - 64.0]
Ethnicity			
White: British	5 (41.7)	2 (40.0)	3 (42.9)
White: Other	2 (16.7)	1 (20.0)	1 (14.3)
Black	2 (16.7)	2 (40.0)	0 (0.0)
Asian	1 (8.3)	0 (0.0)	1 (14.3)
Other Ethnic Group	1 (8.3)	0 (0.0)	1 (14.3)
Not Specified	1 (8.3)	0 (0.0)	1 (14.3)
BMI	27.8 [25.6 - 28.1]	27.9 [27.9 - 33.4]	25.9 [24.7 -27.6]
Elixhauser Score	0 [-4 - 2]	4 [2.0 - 6.0]	-2 [-4.0 - 0.0]
Time from admission to first proning session (hours)	76.2 [19.8 - 145.0]	22.9 [1.6 - 168.7]	94.8 [56.6 - 117.1]
Baseline Observations			
SpO2 (%)	93 [91.5 - 94.3]	93 [92.0 - 93.0]	94 [91.5 - 94.5]
FiO2	0.6 [0.4 - 0.7]	0.6 [0.6 - 0.8]	0.5 [0.4 - 0.6]
Respiratory Rate (breaths/minute)	22 [19.5 - 27.5]	23 [22.0 - 27.0]	21 [18.5 - 26.5]
Temperature (°C)	37.6 [37.1 - 38.2]	37.7 [37.1 - 38.3]	37.4 [37.1 - 38.1]
Baseline SpO_2/ FiO_2	158.3 [135.8 - 228.8]	146.7 [125.0 - 153.3]	192.5 [158.8 - 230.6]
Baseline ROX index	7.8 [6.1 - 8.6]	5.7 [5.3 - 6.6]]	8.2 [7.9 - 8.7]
Baseline PaO_2/FiO_2 ratio	14.7 [12.9 - 17.7]	13.0 [11.8 - 14.4]	19.0 [15.6 -21.8]
Imaging appearances			
Patchy bilateral	6 (50.0)	1 (20.0)	5 (71.4)
Diffuse bilateral	6 (50.0)	4 (80.0)	2 (28.6)
Bilateral focal consolidation	0 (0.0)	0 (0.0)	0 (0.0)
Pulmonary emboli	1 (8.3)	1 (20.0)	0 (0.0)

In those subsequently intubated the change in shunt fraction was -6.9%, [-7.3- -3.2] versus -18.2%, [-24.4- -13.0] in those not requiring intubation (p=0.06) (*Figure 1D*). Time from APP trial to intubation was 32.3, [8.7-90.9] hours; 2 patients required emergency intubation. Critical Care length of stay was 4 [3.5-6.5] days in not-intubated and 20 [20-23] days in intubated patients, with duration of IMV 19 [17-19] days. 2 patients have ongoing IMV requirements. Of 14 patients who have been discharged, hospital mortality was 35.7% (5/14); Group 2 mortality was 27.3% (3/11).

Discussion

These data demonstrate that APP is a generally safe and effective technique to improve acute respiratory physiology in hypoxaemic patients with COVID-19. Implementation was straightforward and the process is potentially transferable to low resource settings with appropriate precautions. Although consistent with other studies[6–8], this is the first to specifically report the timing and effect of APP in patients designated to ward based care only; improving the generalisability to a wider population. In addition, we have shown that 9 hours of APP delivered in the first three days was tolerable and associated with an improvement in oxygenation, as demonstrated by an increase in SpO_2/FiO_2, and ROX index. This would equate to a reduction in FiO_2 from 0.6 to 0.5 upon APP trial for the typical patient. Whilst our shunt and PaO_2/FiO_2 data represents a smaller subgroup, it indicates that improvement in oxygenation is non-sustained, consistent with previous studies of APP.[4] We hypothesise that the reduction in shunt is due to immediate redistribution of perfusion, rather than lung recruitment, and propose that APP is predominantly a supportive measure rather than modifying the underlying disease process. This is supported by the need for repeated APP sessions over a number of days at the peak of disease severity. Notably, 45% of patients who were for escalation failed APP and required IMV; we therefore recommend that for patients in whom escalation is appropriate, APP only occurs within a structured framework, in a critical care environment where prompt intubation is deliverable. Whilst APP may prevent intubation, it may also delay IMV, thus risking severe hypoxaemia or a prolonged period of patient self-induced lung injury.[10] Thus, whilst the intervention is clinically appealing, APP must be evaluated in the context of clinical outcome, in

particular intubation rates, length of stay and mortality. We acknowledge that conclusions are limited from this single centre study and prospective trials are required to demonstrate clinical efficacy in addition to physiological improvement.

Declarations

No Competing Interests, no funding declarations.

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