Appendix C

**EFFECTIVENESS AND SAFETY OF A NEW HELMET CPAP CONFIGURATION ALLOWING TIDAL VOLUME MONITORING**

**IN PATIENTS WITH COVID-19**

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|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Treatment** | **All patients**  **(n=35)** | **h-CPAP**  **success**  **(n=23)** | **h-CPAP failure**  **(n=12)** | **p-value** |
| Helmet CPAP N. (%) | 35 (100) | 23 (100) | 12 (100) | 1.00 |
| CPAP cmH2O (IQR) | 12 (10-12) | 10 (10-12) | 12 (10.5-14.5) | 0.06 |
| Prone position N. (%): | 24 (68.6) | 16 (69.6) | 8 (66.7) | 1.00 |
| >6 h/die | 13 | 11 | 2 |  |
| <6 h/die | 6 | 3 | 3 |  |
| Prone position failure | 5 | 2 | 3 |  |
| Hydroxychloroquine N. (%) | 33 (94.3) | 22 (95.7) | 11 (91.7) | 1.00 |
| Corticosteroids N. (%): | 26 (74.3) | 19 (82.6) | 7 (58.3) | 0.22 |
| Dexamethasone | 11 | 6 | 5 |  |
| Methylprednisolone | 15 | 13 | 2 |  |
| Darunavir/cobicistat N. (%) | 19 (54.3) | 11 (47.8) | 8 (66.7) | 0.47 |
| Remdesivir N. (%) | 3 (8.6) | 2 (8.7) | 1 (8.33) | 1.00 |
| Tocilizumab N. (%) | 22 (62.9) | 13 (56.5) | 9 (75.0) | 0.46 |
| Heparin N. (%) | 21 (60) | 12 (52.2) | 9 (75.0) | 0.28 |
| Azithromycin N. (%) | 8 (22.9) | 7 (30.4) | 1 (8.3) | 0.22 |
| Antibiotics N. (%) | 33 (94.3) | 22 (95.7) | 11 (91.7) | 1.00 |
| Dialysis N. (%): | 4 (11.5) | 2 (8.7) | 2 (16.7) | 0.59 |

**Table C.1. Treatments**

CPAP Continuous Positive Airway Pressure



**Figure C.1. Tidal volume trend of included patients**

Vt trend of the 35 patients recorded three times a day until the start of the weaning, then once a day. Black line for patients who successfully completed h-CPAP; red line for patients who failed h-CPAP (intubation or death).

|  |  |
| --- | --- |
| **Adverse event** | |
| Deep Vein Thrombosis N. (%) | 0 (0) |
| Cardiovascular events N. (%): | 15 (42.9) |
| Hypotension | 0 |
| Bradycardia | 13 |
| Atrial fibrillation | 2 |
| Pulmonary embolism N. (%) | 3 (8.6) |
| Other complications N. (%) | 11 (31.4) |
| Blood stream infection | 5 |
| Acute kidney injury | 2 |
| Immune thrombocytopenia | 1 |
| Epileptic seizure | 1 |
| Major bleeding | 1 |
| Perforated diverticulitis | 1 |
| Pneumothorax and/or pneumomediastinum N. (%) | 0 (0) |

**Table C.2. Secondary endpoints results - Adverse events not related to the helmet configuration**

|  |  |  |
| --- | --- | --- |
|  | **Parameters at the start of weaning**  **Median (IQR) (n=23)** | **Parameters at the end weaning**  **Median (IQR) (n=23)** |
| pH | 7.44 (7.42-7.51) | 7.47 (7.45-7.51) |
| PaCO2, mmHg | 39 (36-44) | 39 (35-42) |
| PaO2:FiO2, mmHg | 276 (245-310) | 322 (284-378) |
| HCO3-, mmol/l | 28 (24-30) | 28 (25-30) |
| RR, bpm | 20 (17-24) | 18 (15-22) |
| BORG | 0 (0-1) | 0 (0) |
| FiO2 | 0.6 (0.5-0.7) | 0.6 (0.4-0.6) |
| CPAP, cmH2O | 10 (10-12) | 10 (8-10) |
| Vt, ml | 360 (290-400) | 350 (300-400) |
| ml/kg IBW | 5.2 (4.8-5.9) | 5.3 (4.0-5.9) |

**Table C.3. Respiratory parameters at the start and at the end of helmet CPAP weaning**

PaCO2 arterial partial pressure of carbon dioxide, PaO2 arterial partial pressure of oxygen, FiO2 fractional inspired oxygen, HCO3- bicarbonate, RR respiratory rate, BORG Modified Borg Dyspnoea Scale (MBS), Vt Tidal volume, IBW Ideal Body Weight

|  |  |
| --- | --- |
|  | **Deaths in RICU**  **Median (IQR)**  **(n=3)** |
| pH | 7.40 (7.39-7.44) |
| PaCO2, mmHg | 33 (30-34) |
| PaO2:FiO2, mmHg | 73 (70-91) |
| HCO3-, mmol/l | 20.0 (17.5-23.5) |
| RR, bpm | 24 (23-25) |
| BORG | 3 (2-3) |
| FiO2 | 0.7 (0.7-0.9) |
| CPAP, cmH2O | 12 (11-12) |
| Vt, ml | 650 (610-675) |
| ml/kg IBW | 10.5 (9.3-10.5) |

**Table C.4. Respiratory parameters of patients died in RICU (patients with do-not-intubate decision)**

PaCO2 arterial partial pressure of carbon dioxide, PaO2 arterial partial pressure of oxygen, FiO2 fractional inspired oxygen, HCO3- bicarbonate, RR respiratory rate, BORG Modified Borg Dyspnea Scale (MBS), Vt Tidal volume, IBW Ideal Body Weight

|  |  |
| --- | --- |
| **Parameters pre-intubation**  **Median (IQR) (n=9)** | |
| PaCO2 mmHg | 35 (34-43) |
| PaO2:FiO2 mmHg | 100 (66-130) |
| RR bpm | 30 (26-30) |
| BORG | 3 (3-5) |
| FiO2 | 0.80 (0.60-0.85) |
| CPAP cmH2O | 13 (11-14) |
| Vt ml | 455 (355-500) |
| ml/kg IBW | 6.5 (5.8-7.9) |

**Table C.5. Respiratory parameters of intubated patients**

PaCO2 arterial partial pressure of carbon dioxide, PaO2 arterial partial pressure of oxygen, FiO2 fractional inspired oxygen, RR respiratory rate, BORG Modified Borg Dyspnea Scale (MBS), Vt Tidal volume, IBW Ideal Body Weight.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | T0 | | | T6 | | | T24 | | | ∆T0-T6  p-value | | ∆T0-T24  p-value | |
|  | S | F | p-value | S | F | p-value | S | F | p-value | S | F | S | F |
| PaCO2, mmHg (IQR) | 32 (29-36) | 32 (29-36.5) | 0.93 | 35 (31-38) | 34 (31-36.5) | 0.45 | 35 (35-42) | 38 (31.5-40) | 0.99 | 0.02 | 0.18 | <0.001 | 0.01 |
| PaO2:FiO2, mmHg (IQR) | 133 (104-178) | 98 (81.5-165.5) | 0.18 | 226 (134-280) | 162 (136-184) | 0.08 | 257 (181-319) | 171 (133-225) | 0.02 | 0.001 | 0.03 | <0.001 | 0.03 |
| RR, bpm (IQR) | 32 (28-35) | 32.5 (28-40) | 0.50 | 28 (23-30) | 26.5 (20.5-34) | 0.93 | 25 (20-28) | 25 (20-30) | 0.60 | 0.001 | 0.01 | <0.001 | 0.003 |
| BORG (IQR) | 3 (2-3) | 3 (2-5) | 0.30 | 2 (1-3) | 2.5 (2-4) | 0.24 | 1 (0-2) | 2 (1-2) | 0.08 | 0.001 | 0.01 | <0.001 | 0.01 |
| CPAP, cmH2O (IQR) | / | / | / | 10 (10-12) | 12 (10.5-14.5) | 0.06 | 12 (10-15) | 12 (10-13) | 0.88 | / | / | / | / |
| Vt, ml/IBW (IQR) | / | / | / | 5,6 (4,5-6,5) | 6,2 (5,7-8,1) | 0.12 | 5,7 (4,8-6,3) | 5,9 (4,0-7,6) | 0.65 | / | / | / | / |
| Vt, ml (IQR) | / | / | / | 360 (290-440) | 427 (358-553) | 0.14 | 390 (300-420) | 390 (305-478) | 0.96 | / | / | / | / |
| Ve L/m (IQR) | / | / | / | 9  (7.5-12) | 10.2  (7.7-14.8) | 0.42 | 8.4  (7.8-10.1) | 9.8 (6.9-10.5) | 0.51 | / | / | / | / |

**Table C.6. Comparison of respiratory parameters of helmet CPAP success (S, n=23) and helmet CPAP failure (death and/or intubation) (F, n=12) at admission in RICU (T0), and after 6 hours (T6), and after 24 hours (T24)**

CPAP continuous positivie airway pressure, IBW ideal body weight, PaCO2 arterial partial pressure of carbon dioxide, PaO2 arterial partial pressure of oxygen, FiO2 fractional inspired oxygen, RR respiratory rate, BORG Modified Borg Dyspnea Scale (MBS), Vt Tidal volume, Ve minute volume