

Monitoring astronauts' status through Non-Invasive Positive Pressure Ventilation

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Background:

Many hospitalized patients with respiratory failure are treated with non-invasive positive pressure ventilation (NiPPV). In many cases non-invasive ventilation can be used to successfully treat patients and subsequently avoid endotracheal intubation. Recent literature and clinical practice have shown that in patients who are protecting their airway, and in whom the pH is not dangerously low, the use of non-invasive positive pressure ventilation can be effective (1). Additional studies argue that NiPPV in more severely ill patients (pH < 7.2) with chronic obstructive pulmonary disease (COPD) is no worse than endotracheal intubation (2,3) with regard to mortality, lengths of stay and readmission rates. Furthermore, better outcome was confirmed for patients who succeeded NiPPV and avoided endotracheal intubation. Thus, the non-invasive mode of ventilation can assist patients in ventilating equally or more effectively, and in many cases can be used to avoid the more invasive endotracheal intubation.

Many studies have evaluated treatment failures of NiPPV. Failure rates range from 30-80% depending on the cause of respiratory failure and underlying medical condition(s) of patient population (4). Other studies have looked at factors which predict NiPPV failure, such as physiologic scoring (age, severity of underlying illness) and presence of acute respiratory distress syndrome (ARDS) or community acquired pneumonia (CAP) (5). Having an objective and real time means of early identification of patients that will fail NiPPV would greatly benefit patients by helping physicians intervene early with endotracheal intubation when indicated.

The current modality of evaluating patients with respiratory failure on NiPPV is via analysis of arterial blood gas (ABG). Arterial blood is obtained via invasive radial or femoral artery puncture, and in some cases arterial catheters are placed to allow for frequent ABGs. Treating physicians may use ABG data (PaCO₂ and PaO₂ values) to make adjustments to NiPPV settings (ie, adjustment to IPAP or EPAP, inspiratory/expiratory positive airway pressure). Over time, data trends of ABG analytes may be followed and adequacy of ventilator therapy can be assessed. During successful treatment with NiPPV guided by ABG assessment, clinicians may adjust NiPPV settings, or physicians may change modes of ventilation. Improvements in trends of ABG data resulting from successful treatment may lead to discontinuation of NiPPV in favor of face-mask or nasal cannula oxygen delivery. If ABG values trend in a worsening direction, NiPPV may be viewed as a treatment failure and the patient may require intubation and mechanical ventilation.

It would be preferable to provide early identification of patients for whom NiPPV is likely to fail, and to do so without performing and waiting for the results of ABG analysis. ABG analysis is invasive, expensive and slow to respond to changes in NiPPV therapy settings. Additionally, the routine use of indwelling arterial catheters (IAC) for ICU patients has recently been challenged since the information IACs provide can almost always be obtained without them and they introduce risk of blood infection and vascular complications (6). Ideally, noninvasive measures of patient status could be used to predict future success or failure of NiPPV therapy in

a more timely fashion. In addition, it would be beneficial to avoid ABG analysis in space and NASA headquarters could monitor trends more easily with a non-invasive system.

One noninvasive parameter that is an indicator of PaCO₂ is end-tidal CO₂ (etCO₂). End-tidal CO₂ is obtained by analyzing the CO₂ concentration in the expired gas. It is assumed that a gas sample taken at the end of expiration, or end-tidal gas, is pure alveolar gas and that the CO₂ concentration is indicative of the arterial CO₂ level. Prior studies have compared ABG PaCO₂ values to EtCO₂ values, though much of the literature involves intubated patients on mechanical ventilation. The data on the correlation between PetCO₂ and PaCO₂ values in intubated patients has been mixed (7, 8), though much of the literature shows that the correlation is not strong and argues against the use of PetCO₂ monitoring in this patient population (9).

In mainstream volumetric capnography (MVC) the infrared measurement takes place at the airway, in line with the respiratory gas stream. The capnometer interfaces directly with extension tubing inserted into the NiPPV circuit without altering the airflow or NiPPV mask fit. The lightweight and easy to use device can easily be attached to the NiPPV system without any detriment or discomfort to the patient. The infrared data signal could then be passed via electrical cable directly to the ventilator providing the positive pressure. Some noninvasive ventilators are already equipped with an input for capnometer data.

To our knowledge, no prior studies have exclusively evaluated patients on NiPPV in assessing the use of mainstream volumetric capnometry monitoring. It is not known whether the use of mainstream volumetric capnography monitoring is useful in the management of patients with respiratory failure on NiPPV.

Patient Selection Criteria:

The population evaluated was patients with respiratory distress or respiratory failure who are on non-invasive positive pressure ventilation and are inpatients in the medical intensive care unit (MICU), the surgical intensive care unit (SICU), the neurologic critical care unit (NCC), the intermediate care unit (IMCU) or the Huntsman Hospital ICU (HICU) at the University of Utah Hospital. Any patient on noninvasive ventilation at any time during the hospitalization may be considered. This includes intubated patients on invasive mechanical ventilation who may be extubated to NiPPV. A total of 60-120 subjects will be studied prospectively. All patients will be monitored using mainstream volumetric CO₂. Monitoring will be conducted in the MICU, SICU, NCC, HICU and IMCU. After a research team member discusses the study with the patient or medical decision making representative and invites the patient to participate, the patient will be allowed as much time as necessary to decide whether or not to participate.

Exclusion Criteria:

1. Age < 18
2. Pregnant women
3. Patient's inability to tolerate NiPPV mask
4. Prisoners
5. Lack of informed consent
6. Use of a NiPPV mask that does not completely cover the mouth and nose (ie nasal pillows)
7. Attending Physician feels enrollment could interfere with optimal patient care

8. Patient is Do Not Intubate (DNI)
9. V60 ventilator not available for NiPPV

Instrumentation and Patient Set-Up:

The mainstream volumetric CO₂ collecting device will be the Capnostat® 5 (Philips Respironics, Wallingford, CT). The device measures CO₂ in the NiPPV tubing via infrared spectroscopy. The Capnostat 5 may either be attached to a mouthpiece for a PetCO₂ measurement or attached to a tube extension that is placed inline between the NiPPV tubing and mask. A new mouthpiece collecting device and extension tubing will be used for each patient. Each new device will be calibrated prior to data collection for each patient. The Capnostat 5 will be connected to the NM3 Volumetric Capnometer (Phillips-Respironics, Wallingford, CT) by the signal cable and pressure sensing tubing.

Enrolled patients will have their mask fitted according to the judgment of the respiratory therapist (RT) which is the current standard; the investigators will not be involved in mask selection. If the patient has already been enrolled at the time of initiation of BiPAP ventilation, immediately prior to placement of the mask and initiation of non-invasive ventilation, the patient will be asked to breathe for several breaths via a mouthpiece connected to the Capnostat 5 sensor in order to establish a reference PetCO₂ measurement. After a mask is selected and fitted, the study team will record the mask type and size.

The patients will be ventilated using the V60 BiPAP ventilator (Phillips).

If the clinical team allows the patient to remove the non-invasive mask at any time (administration of medications, mask breaks, etc), we will request the patient to breathe normally for several breaths directly into the Capnostat 5 sensor via mouthpiece.

The patient will be asked to wear an additional pulse oximeter finger probe that will be connected to the NM3 for collection of peripheral oxygen saturation (SpO₂) and heart rate. By default the screen of the NM3 to not be readily accessible/viewable to the clinician since she/he likely already has an available display monitor for heart rate and peripheral oxygen saturation. However, if the clinician feels it is in the best interest in the patient to view the NM3 display screen he/she may do so. There is no guarantee that the heart rate and saturation displayed on screen accurately represent true clinical parameters.

There will be no use of investigational devices in this study.

We anticipate there will be study patients enrolled after NiPPV has already been initiated for respiratory distress/failure. After consent is obtained and patients are enrolled, we will request that the RTs assist us in placing the Capnostat 5 sensor inline to ensure there is no adverse impact on patient therapy by the brief (<5 second) disconnect of the ventilation circuit.

Measurement of end-tidal CO₂ (etCO₂) during noninvasive positive pressure ventilation is difficult because of gas mixing in the mask, loss of expired gas due to leak and dilution of the expired gas by ventilator flow during expiration. We have tried a number of methods to

compensate for these error sources including placing the sample port near the patients nose and periodically disabling the ventilator flow during expiration. Neither of these methods allows for measurement of the volume of excreted CO₂ (VCO₂) along with etCO₂. We have also pursued a method of mathematically compensating for the effect of gas mixing and leak so that etCO₂ and VCO₂ can be calculated from the CO₂ and flow signals obtained by placing volumetric capnography sensors (flow and CO₂) between mask port and the exhalation port during NPPV. Earlier tests have demonstrated that this compensation method works when tested using a mock patient setup on the bench. In bench tests we can directly measure the true etCO₂ by placing a second sensor in the simulated trachea. In bench tests we have been able to successfully compensate for the effects of mask leak and gas mixing in the mask using the following equation to calculate etCO₂:

$$\text{etCO}_2\text{comp} = \text{etCO}_2\text{raw} / [1 - \exp(-TV/V_{\text{mask}})]$$

Where:

etCO₂comp is the compensated end tidal CO₂ value

etCO₂raw is the end tidal CO₂ measured at the mask port without any compensation,

TV is non-leak compensated expired tidal volume as measured at the mask port and

V_{mask} is the volume of the space between the patient's face and the mask.

This model assumes that the mask volume represents a perfect mixing chamber and that mixing in the mask is a first-order system where the volume of the mask equals one time (volume) constant.

Testing this method is more challenging in a clinical setting. The first problem is that we cannot directly measure the true etCO₂. We can only periodically measure the partial pressure of arterial CO₂ (PaCO₂) by taking an arterial blood gas sample. PaCO₂ is similar to etCO₂ in normal healthy patients who do not have severe ventilation perfusion (V/Q) mismatch problems. In most cases, it is expected that the etCO₂ would be less than the PaCO₂ and should sometimes be much less than PaCO₂ depending on the severity of the lung disease.

Arterial blood gas samples:

We will request that patients allow the collection of two ABG. If the patients already have an indwelling arterial catheter (IAC) the two ABGs will be drawn from the catheter to avoid additional arterial punctures. If the patients do not have IACs we will have the pulmonary lab technicians perform the arterial punctures to obtain the ABGs.

We will not recommend or encourage the placement of IAC by clinicians. We will not recommend or encourage any additional lab draws other than the two post enrollment blood gases. The first ABG will be approximately one hour (60 minutes) after enrollment and the other approximately two hours after the first (180 minutes after enrollment). The cost of these ABGs will be covered as part of the study expenses. If the clinical team has ordered an ABG independent of our study protocol within +/- 30 minutes of our expected draw, we will forego the study protocol ABG to avoid additional arterial punctures and/or additional loss of blood.

The clinical team (including the attending physician) will be preferentially blinded to the results of the study protocol ABGs. We believe the blinding is necessary to prevent alteration in normal clinical behavior due to increased availability of ABG data which would not normally have been available. However, if any ABG results meet critical criteria, the values will be reported to the clinical team as they normally would per policy. For example, any $\text{pH} \leq 7.25$ or ≥ 7.6 , $\text{PaCO}_2 \leq 20$ or ≥ 60 mmHg, $\text{PaO}_2 \leq 40$ will be called to the clinical team.

If enrollment occurs sometime after initiation of NiPPV, then both study ABGs would be for research purposes only. This assumes that the patient is tolerating the NiPPV well and not demonstrating concerning clinical signs that would otherwise warrant an ABG request.

Variables to be Recorded:

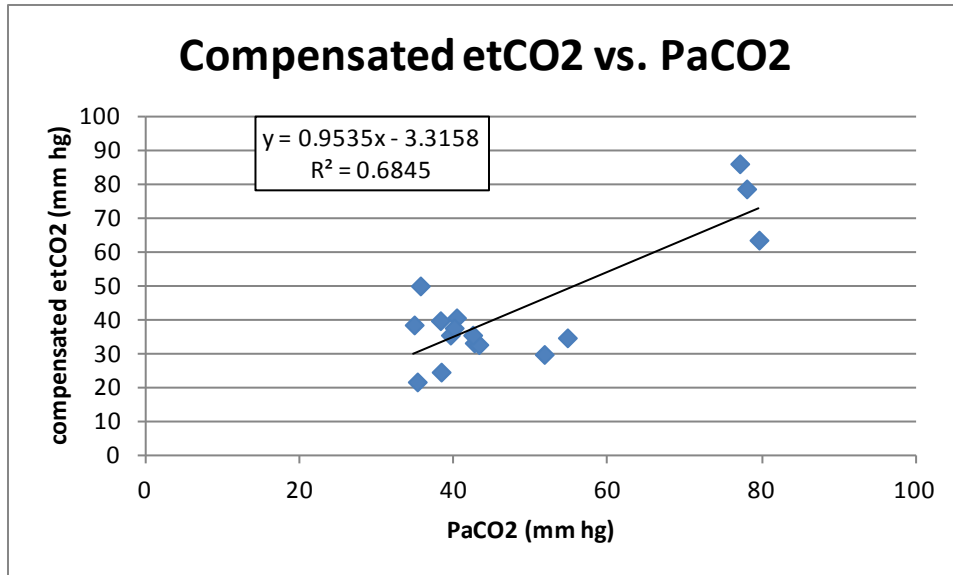
The NM3 monitor will record mainstream volumetric CO₂, airway pressure, pulse oximeter and heart rate data. The V60 ventilator calculates ventilation related variables, such as, but not limited to, return tidal volume (T_v), leak rate, set pressures (IPAP, EPAP), respiration rate (R), set FiO₂, and peak pressures. NiPPV variables can either be transmitted via cable to a personal computer in the case of the V60 ventilator or recorded from the display screen of the NiPPV ventilator. Data for the NM3 is collected at 100 Hz and the V60 at 50 Hz and stored on a laptop computer.

Additional data (lab values and vitals) will be recorded or retrieved from the patient medical chart (Powerchart). These data include, but are not limited to, diagnosis, body temperature, blood gas values, temperature (T), pulse rate (P), blood pressure (BP), and oxygen saturation (SpO₂). Examples of laboratory values which will be retrieved from the patient chart will include serum creatinine, bilirubin, lactate, and venous and arterial pH. If the clinical staff collects any body temperature, blood gas values, or vital signs during the data collection session, we may also record or retrieve those values. We will also record any treatments administered to the patient during the study as chosen by the clinical staff. We will not recommend or take part in clinical decision making based on the non-invasive CO₂ measurements that are observed or recorded.

Results: In analyzing the data from the first 7 test patients for whom PaCO₂ measurements were available we found the following results:

Mask Type	Average uncompensated difference (raw etCO ₂ – PaCO ₂)	Average -compensated etCO ₂ difference (comp etCO ₂ – PaCO ₂)
Full Face	-38.1 ± 22.3.8 mm Hg	-4.6±7.8 mm Hg
Mouth and Nose	-29.6 ± 6.9 mm Hg	-6.5±12.8 mm Hg
Combined data	-33.8±16.5 mm Hg	-5.6±10.3 mm Hg

There were 15 total blood gas comparisons in the data set, 8 were in patients with full face NPPV masks and 7 with a nose and mouth mask. The plot below shows the results when compensated etCO₂ is plotted against PaCO₂



Conclusions:

The overall average error appears to be effectively compensated using this method. There appears to be a correlation between the etCO2 and PaCO2; however, if one of the patients that had a high PaCO2 is removed, there is no correlation in the data. The method seems to do an acceptable job in processing noisy clinical data. It also requires a combination flow and CO2 sensor placed between the mask and the exhalation port. This is beneficial for astronauts in that their ventilation status can be accurately monitored in space. There is currently more data being collected for further analysis.

References and Appendices

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