Study Title

Research Protocol

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BACKGROUND AND SIGNIFICANCE

Patients presenting to emergency departments and hospitals for various medical conditions often require non-invasive ventilation (breathing support). For example, a person with shortness of breath as a complication of COPD (chronic obstructive pulmonary disease) may be treated with a BiPAP machine, one type of non-invasive ventilation.

However, in the current environment of COVID-19, aerosols produced by a BiPAP machine in a COVID-19 positive patient pose serious potential harms to healthcare providers and other patients. All patients with similar symptoms to COVID-19 are presently treated as positive until definitive testing determines otherwise. The best test available for COVID-19 takes up to 4 hours to determine the patient's status, which is too long to delay application of BiPAP in a distressed patient. This could lead to either a delay in care or the need for invasive breathing measures (intubation), which requires intense resource utilization, may not be in line with a patient's goals of care, and could cause serious harms (i.e. infection, medication reactions, etc.) in patients who do not need it.

As well, the lack of BiPAP as an option in the clinician's arsenal leads to increased ventilator days that would previously have been bridged with a BiPAP machine. The use of a closed-loop BiPAP machine in which no expired air is released into the environment would solve these problems. Building off the experiences of a similar approach that was trialed in Italy in response to the COVID-19 crisis, this project will develop and test a novel BiPAP mask that reduces mask leaks and thus aerosolization.

Few studies have been done on the potential harm caused by aerosolization from non-invasive ventilation[1]. The data available suggest that caution must be taken with acute respiratory infection (ARI) patients when placing them on non-invasive ventilation such as CPAP or BiPAP due to excess risk to health care workers[1–4]. This advice is being heterogeneously applied during the recent COVID-19 pandemic, with some practitioners advocating the use of non-invasive ventilation[5].

There is a role for non-invasive ventilation in COVID-19 negative patients during the pandemic, although practitioners are reluctant to initiate these measures because of the slow speed, lack of reliability and lack of availability of the viral swab confirming corona virus status. This study seeks to ensure that an easy-to-produce, specifically-engineered mask and circuit has the ability to maintain non-invasive ventilatory support without aerosolizing viral particles. If successful, this will return an important tool to the clinician’s arsenal.

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STUDY OBJECTIVE(S); INCLUDING SPECIFIC AIMS AND/OR HYPOTHESES

To validate that an easy-to-produce, specifically-engineered mask and circuit has the ability to maintain non-invasive ventilatory support while reducing aerosolization of viral particles

The primary objective of this study is to assess if the mask device leaks when attached to a patient's face in real-world use.

This outcome will be measured by recording data from the ventilator about the total leak volume over the study period at various intervals. This volume is a normal output of modern ventilators. The researcher will also assess the physical seal on the patient four times throughout the device's use.

The secondary objective of the study is to assess markers of ventilation and perfusion in patients, including pH, pCO2, pO2, respiratory rate, heart rate and level of consciousness (via GCS).

These markers will be measured through routine vital signs monitoring (respiratory rate, heart rate and GCS) and an arterial or venous blood gas (pH, pCO2, pO2).

METHODS

Study Design

This study is an opportunistic prospective randomized controlled trial.

If experimental non-invasive ventilation masks are available in the patient's expected size, patients will be randomized to control masks or experimental. If experimental masks are not available, the patient will be consented and entered into the control arm. Patients who receive BiPAP or CPAP with the mask are assessed for several variables over time to ensure adequate treatment and assess leaks.

Study Population

The study population will include patients in the Emergency Department or an in-patient in a monitored or ICU setting requiring non-invasive ventilation for respiratory distress or hypercapnia at both London Health Sciences Centre. This population will include both the Victoria Hospital site and University Hospital site. The local sample size is n=50.

Inclusion Criteria:

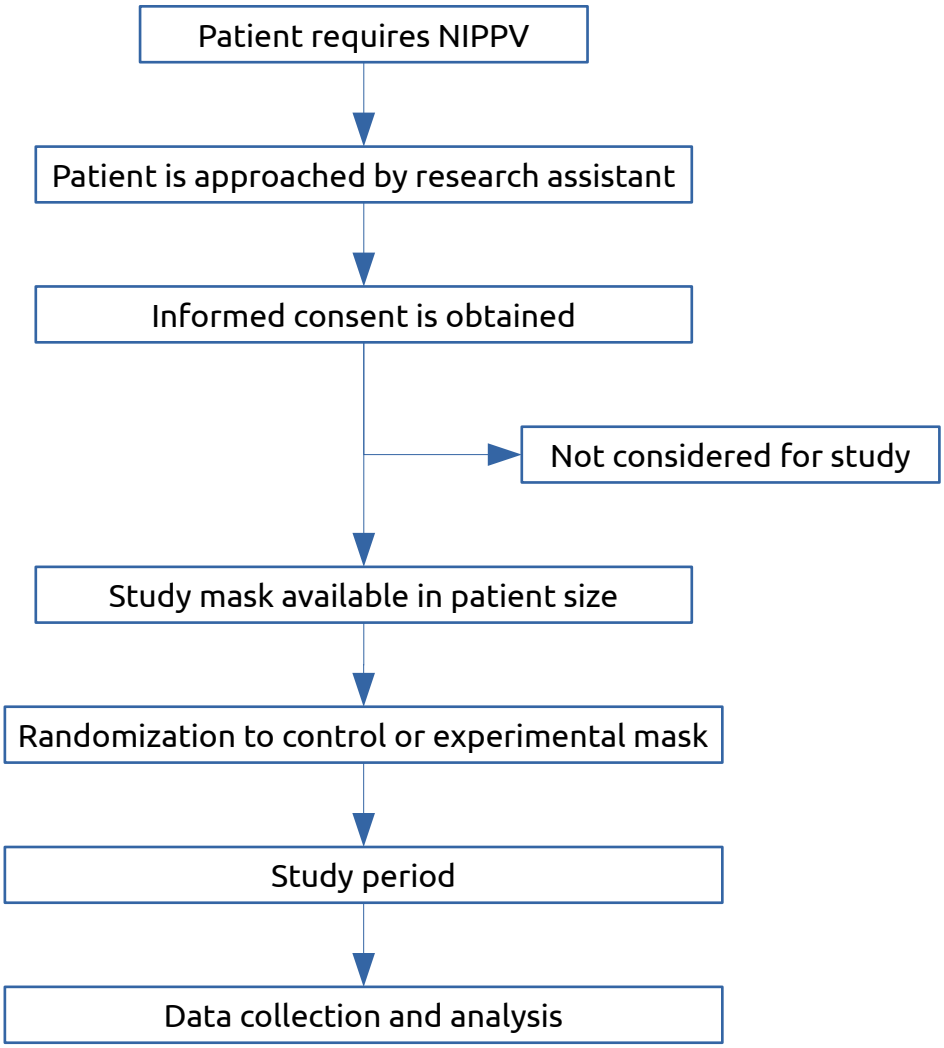
- Patient with respiratory failure due to primary pulmonary pathology.
- Patient who is selected for BiPAP or CPAP by the health care provider

Exclusion Criteria:

- Age <18 years.

- Respiratory failure due to non-pulmonary pathology.
- Impaired consciousness (Glasgow coma scale <10).
- Patients with contraindications of NIV.
- Severe upper gastrointestinal bleeding.
- Chest trauma.
- Agitated or violent patient.

Study Procedures



DATA COLLECTION

Demographic Data: age, sex, height, weight, presence or absence of dentures, presence or absence of facial hair

Clinical Data: arterial or venous blood gas measurements (pC02, pH, Hc03, and p02), vital signs (body temperature, pulse, respirations, blood pressure, oxygen saturation).

Note: no additional blood work beyond standard patient care will be required for the study.

Safety Data: From initiation to completion of non-invasive ventilation using the standard or non-aerosolizing mask, any reports of : nasal or oral bleeding, pneumothorax, ulcers.

Note: The electronic medical record (Power chart) will be accessed to review this data

All data will be tracked by the DSMC to ensure safety of patients. Where possible, the committee will analyze data to ensure patients are ventilating as expected by compiling and reviewing all bloodwork results found in the blood gases.

DATA ANALYSIS

Data will be entered directly into a study-specific LibreOffice database (The Document Foundation, Berlin, Germany). All data analyses will be performed using R (R Foundation, Vienna, Austria). All identifying patient data will be kept separate from study data.

For Data Analysis, the means and standard deviations of the Glasgow coma scale (GCS), respiratory rate, heart rate, pH, $PaCO_2$, and PaO_2 will be calculated for each time period.

Participants will be assigned a subgroup of control or experimental depending on which mask the patient received. These two subgroups will be compared using an analysis of variance (ANOVA) to detect differences between outcome parameters. A subgroup analysis will also be taken based on COVID-19 culture status regardless of the type of respiratory failure. This analysis will be performed with an ANOVA on the outcome parameters.

The critical importance of mask leaking means that these data will be displayed as a sum of all incidents. As these are binomial, a subgroup and time comparison will also be carried out using a generalized linear model of the binomial family (logistic regression). Leak volumes will be compared with an ANOVA.

ETHICS AND PRIVACY

The research team will seek approval from Wester Health Sciences Research Ethics Board.

All data collected will be maintained on the LHSC "P" Drive in a password protected folder. Investigators will only look at or analyze data on LHSC computers. Data will only be passed between investigators on encrypted memory sticks or through secure FTP sites. Hard copies will be stored in a locked filing cabinet in a secured location. Data will be coded with unique identifiers and the master list containing any identifiers will be stored separately from the collected data.

There will be no additional information stored on any external hard drives, laptops, or portable devices.

This study data will be retained for 15 years as per Health Canada policy. After this 25 year period, paper records secured in a locked filing cabinet at LHSC will be destroyed according to institutional protocols, which includes placing the records in locked, confidential shredding bins. The bins are then collected by an outsourced company (Shred-It) and the contents are shredded. Computer and electronic records will be encrypted and secured for 25 years and then all study files will be destroyed according to institutional protocols of data deletion including clearing all memory sticks. This will be done in consultation with the IT department for current protocols.

PLANS FOR DISSEMINATION OF FINDINGS

The source code for the device, anonymized data from the study, and preprints will be stored in a local repository and submitted for publication.

The investigators will also disseminate findings through mass media and peer-reviewed publication.

References

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