OXYGEN EFFICIENT RESPIRATORY AID (OXERA™) DEVICE A SAFETY STUDY

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A research report submitted to the Faculty of Health Sciences, University of Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Internal Medicine

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Declaration:

I, Midhun Thomas John, do hereby declare that this research report is my unaided work. It is being submitted for the degree of Master of Medicine in the branch of Internal Medicine. This research report is submitted in the publishable format as recognized by the Faculty of Health Sciences. I further declare that this work has not been submitted for any other examination or degree at this or any other University.

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Signed on the ……

Dedication:

To my lovely Wife, Aishwarya, for her patience, infinite support, understanding, and love.

To my parents, Thomas John, Siju John, Binu Luke, and Sushmitha Varghese for their infinite support, love, and prayers in everything that I do and achieve.

To my siblings and nephew, Mithra, Shane, Ashwin, and Zane, for always showing support and well wishes in everything I do.

Lastly, to my incredible supervisors, to whom without, this report would never materialise in the manner it has.

Publications and presentations arising from this research report:

The author intends to publish this research report in a reputable, peer-reviewed journal.

Ethical considerations:

Permission for this study was granted before data collection commenced by Dr. JML Tsitsi (Head of Department Internal Medicine, Chris Hani Baragwanath Academic Hospital), the Medical Advisory Committee (MAC), and hospital (see Appendix) management at this institution as well as the Human Research Ethics Committee (Medical) at the University of the Witwatersrand HREC Ref No: M210222. National Research Database Reference Number GP 202107013. All participants signed informed consent.

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- To all the healthy participants who dedicated their time

Abstract

Background: Severe Coronavirus Disease 2019 (COVID-19) can develop pneumonia with acute respiratory distress, acute hypoxia, and/or death. The Oxygen Efficient Respiratory Aid (OxEra™) device has been granted SAHPRA approval for emergency COVID-19 pandemic use. The device has the potential to be used widely in the healthcare sector due to its efficient oxygen supply and adjustable wall positive expiratory pressure (PEP).

Objectives: We assessed whether the OxEra™ device was safe to use in a healthy adult volunteer population. Our primary objective was to ensure there was no asphyxiation, as assessed by changes observed from baseline End Tidal Carbon Dioxide ($ETCO_2$) exceeding 6.3 mmHg and above the 45mmHg threshold. We also monitored changes in vital organ signs and assessed the pain and comfort of the participant at various intervals with changes in PEPs.

Methods: This was an experimental safety study of the OxEra™ Device on 30 healthy participants at the Intensive Care Unit training centre of Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa. Each participant had basic vital signs, $ETCO_2$, and Oxygen saturation percentages (SpO_2%) taken at baseline until the end of 2 hours. In the first 20 minutes, the PEP was increased by 5cmH_20 every 5 minutes to a maximum of 20 cmH_20. Then continued for the rest of the time on a PEP of 5 cmH_20. At each interval, vital signs, subjective comfort, pain, and visual scores were measured.

Results: Thirty healthy participants were enrolled for the experimental study. There was no significant difference in $ETCO_2$ from baseline until 2 hours. No participant experienced an increase in measured $ETCO_2$ greater than 45 mmHg and no increase in $ETCO_2$ from baseline was greater than 6.3mmHg. The median increase in $ETCO_2$ over the study period was 2mmHg.

There were no significant changes in respiratory rate. The heart rate decreased significantly from a median of 73(IQR 65-87) to 68.5(IQR 63-75) at the end of the 2 hours. There were no significant changes in the blood pressure over the study. The visual analogue scale (VAS) score and comfort score had a significant increase over the 2 hours from baseline of 0 to 2 at maximum; however, the pain analogue scale (PAS) scores showed no significant increase.

Conclusion: Overall the OxEra™ device achieved the safety endpoints set out. There was no sign of asphyxiation and there were appropriate physiological responses to changes in PEP once applied. The comfort of the mask did worsen over the 2 hours; however, the scores were minimally worse on PEP application but improved once-off PEP. No adverse event were recorded at all.

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CHAPTER 1: Protocol and Extended Literature Review

CHAPTER 1

INTRODUCTION

Background

Coronavirus Disease 2019 (COVID-19) is a highly contagious virus caused by a new β coronavirus called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV 2)[1]. The outbreak was first documented in a small city by the name of Wuhan, in the Hubei Province, China, in December 2019[1]. Since the first case, the virus has spread throughout the world. This new coronavirus is closely related to the 2003 Severe Acute Respiratory Syndrome and the 2012 Middle East Respiratory Syndrome Coronavirus, of which caused severe respiratory distress, cytokine storm, and severe lung injury[1].

Globally the virus has spread to more than 85 million people and has taken the lives of more than 1.8 million, (as of the 26th of January 2021)[2]. It has spread to more than 200 countries and has affected both the lives and livelihoods of the populations of these countries[2].

On the 5th of March 2020[2], South Africa had recorded the first case of COVID-19. This infection then spread over the following months, culminating in over 1.1 million infections and 29 000 lives lost as of 26th January 2021. South Africa has now joined the top twenty nations with the highest case burden[2].

The clinical impact of COVID-19 is mainly on the pulmonary system but has also been documented to affect the extra-pulmonary system (cardiovascular, renal, hepatic, gastrointestinal, ocular, dermatologic, and neurological)[3]. The most common clinical symptoms reported are a dry cough, dyspnoea, sore throat, and fever. The more severe cases develop into pneumonia with acute respiratory distress syndrome (ARDS), acute hypoxic respiratory failure, and/or death[3]. It has been well documented that the target of entry for the virus is the angiotensin-converting enzyme 2 receptors (ACE-2)[4]. These receptors are found in type 1 and type 2 alveolar cells and epithelial cells. Once the virus enters the cell, it initiates a series of pro-inflammatory mediators such as interleukin 6, tumour necrosis factor, and interleukin 1β. In comparison to the SARS-CoV-1, SARS-CoV-2 has a much higher affinity to the ACE 2 receptor, thus resulting in a greater inflammatory response and pulmonary injury[4].

Hypoxia in COVID-19

Mortality in moderate to severe COVID-19 is generally secondary to hypoxia. These patients usually present as a 'happy hypoxic'[5]. This is interpreted as having a low concentration of oxygen distribution throughout the body due to a ventilation/perfusion mismatch in the lungs without the associated respiratory distress and anxiety[5].

It has been documented that the mechanism surrounding this hypoxia is often seen early in the disease process and is due to intrapulmonary shunting (this involves oedema and atelectasis); loss of lung perfusion regulation; intravascular thrombi; reduced lung compliance; increased dead space; increased consolidation complicated by super-added infection; carbon dioxide retention; and anxiety with fatigue[5].

Hypoxaemia Management Options

The management of hypoxaemia revolves around the provision of supplemental oxygen either in an invasive or non-invasive manner using oxygen delivery systems.
Oxygen delivery systems are categorised into low-flow and high-flow systems; both systems have been extensively used in the battle against COVID-19[5].
Both of the above systems have their advantages and disadvantages, which are particularly important in a resource-limited setting such as South Africa. For example, a nasal cannula is cheap and easy to use for the patient and provider, but it is limited to 6 litres per minute of oxygen flow and is classified as a low flow system.

In response to this major demand on oxygen during the pandemic, the South African trade and industry minister announced that a consortium of companies (Council for Scientific and Industrial Research (CSIR) and the South African Ventilatory Emergency Project (SAVE-P)) under the National Ventilator Project (NVP) would join hands in providing extra ventilatory support. SAVE-P manufactured 18000 Venturi-type CPAP devices and an additional 2000 blender-type Continuous Positive Airway Pressure (CPAP) devices[6].

These devices are all high flow devices that require high volumes of oxygen (over 60L per minute) to provide a single patient with adequate oxygen support. This creates a huge demand for the oxygen supply in the ward, where there is a fixed diameter of oxygen piping and hence a fixed supply[7].

Besides the need for oxygen, these devices need well-trained staff and time to deliver oxygen support satisfactorily. The second wave in South Africa has highlighted the lack of trained staff members such as doctors and nurses[7]. Many small local healthcare facilities rely on a limited stock of oxygen that is replenished regularly, often time with oxygen cylinders. With the surge in numbers, we face the harsh reality of potentially not being able to meet the demand due to supply constraints[8].

With the concerns raised above, the nation needs a device that is user-friendly and simple, being oxygen efficient and effective at low oxygen flows. Furthermore, patients are unable to be transported or moved on such high flows, as they require attachment to wall piped oxygen, or specialised adaptors to enable oxygen cylinder use. This is often a limiting factor when patients need to move to other wards or areas of care, and when special investigations are required, such as computerised tomography scans.

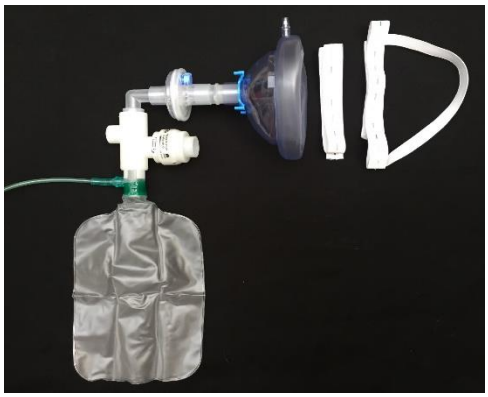
Oxygen Efficient Respiratory Aid: OxEra™ - a solution?

This growing demand and lack of resources led to the development of an Oxygen Efficient Respiratory Aid Device called OxEra™.
OxEra™ is an oxygen delivery device that has been designed and developed by a consortium named Umoya for emergency use in the COVID-19 pandemic. Umoya is a group of volunteers inclusive of engineers, doctors, designers, 3D printing specialists, and programme managers that have collaborated to find solutions in the COVID-19 pandemic [9]. After having developed OxEra™, Umoya then attained emergency accreditation for use in this COVID-19 pandemic. Gabler is a third-party company that has partnered with Umoya to take charge of the distribution of the OxEra™. Umoya, the developer, is a collaborator in the device and is not involved in the distribution of the device.

The rationale behind the OxEra™ device is its ability to delay the need for ventilation as much as possible.

The OxEra™ claims to be a simple, cost-effective, and oxygen-efficient device that uses an anaesthetic mask with an adjustable mechanical Positive Expiratory Pressure (PEP) valve.

The device is made of a custom-designed main housing, that has an adjustable mechanical PEP valve providing between 5-20 cm H_2O end-expiratory pressure, and an anti-asphyxiation valve for safety. This device is then connected to the wall oxygen supply via an oxygen hose and adapter on the one end, and to a mask and head strap at the other end, thereby providing the patient with a pressurised oxygen supply.



OxEra™ can provide oxygen at low flow rates (15L/min) but with the benefit of adjustable positive pressure which when transmitted to the lung alveoli, prevents them from collapsing (atelectasis). This results in an improvement in oxygenation, a decrease in barotrauma, and a reduced effort of breathing[9]. Another advantage of this device is that the incoming oxygen collects in the bag during expiration and is therefore also available during inspiration, together with the oxygen flow in the line, thereby minimising oxygen wastage. This is in comparison to other commonly used devices such as loose venturi masks, nasal prongs, High Flow Nasal Cannula (HFNC), and CPAP units, where there is no accumulation of unused oxygen, thus resulting in wasted oxygen as it escapes before it is inhaled[10]. The device is locally designed and manufactured, thus allowing the device to be cost-effective. Lastly, to ensure a patient's safety, there is an anti-asphyxiation valve, which, in cases of disconnection or if oxygen runs out, opens, and allows ambient air entry into the device. This ensures that the patient does not suffocate should they not be able to remove the mask themselves. To ensure the safety of those around the patient, the port that allows exhaled air to be expelled during expiration, is fitted with a viral filter.

Assessment of Oxygen Delivery Devices

Oxygen delivery devices are often measured and assessed by their ability to provide adequate oxygen concentration to the patient, or to produce good ventilation of well-perfused lung tissue, whilst ensuring the best comfort possible for the patient. Evaluating the safety of an oxygen delivery device can be performed by using pulse oximetry and end-tidal carbon dioxide values[11].

Pulse oximetry is a bedside tool that is used to indirectly measure the oxygen saturation of haemoglobin in arterial blood (SpO_2). The pulse oximeter uses the different wavelengths of light from light-emitting diodes through the skin and into the tissue[11]. These wavelengths then reflect oxygenated and deoxygenated blood to the pulse oximeter where it converts the signals into an electrical signal[11]. This method is very useful in both spot check and continuous monitoring of a patient's arterial haemoglobin oxygenation. There are three main types of pulse oximeters, namely, fingertip, portable handheld, and tabletop/stand-alone oximeter. All three of the devices work well but one of the main differences is in performance and accuracy due to the different hardware as well as signal processing algorithms. The stand-alone device is the most accurate and is commonly seen in high care and intensive care units. Normal SpO_2 should be more than 95%[11]. The pulse oximeter will function well when it detects a change in transmitted light. However, if there is decreased perfusion or obstruction of the light (in the case of nail polish), the signal will be decreased and show a false reading[12].

End-tidal carbon dioxide ($ETCO_2$) is the amount of carbon dioxide that is exhaled at the end of each breath. It represents the adequacy of carbon dioxide that is carried in the blood back from the lungs and exhaled out of the body. Evidence shows that it can indicatative of cardiac output and pulmonary blood flow[13].
Capnometry and capnography are non-invasive methods that are available to measure $ETCO_2$. Capnometry provides a numerical value whereas capnography provides a waveform on the monitor as well as a numerical value. By measuring $ETCO_2$ with the help of a monitor attached to the oxygen device, one is equipped with the ability to monitor breathing in real-time and respond adequately to changes in the clinical conditions of patients. This value is more commonly seen in intubated patients in Intensive Care Units (ICU), high care units, and theatres. The normal value is usually between 35 mmHg and 45 mmHg[13].

Most CPAP systems run the risk of inducing rebreathing in case of failure[14]. The OxEra™ device has a built-in safety valve to avoid rebreathing. In the case of rebreathing a significant rise in $ETCO_2$ will occur[15]. This may be accompanied by a decrease in oxygen saturation[15].

Positive pressure delivered through a non-invasive device may present challenges regarding patient comfort and acceptance[16]. The ability of a patient to tolerate the device is therefore vital to the utility of such a device and necessitates the objective assessment of pain and discomfort. Pain and discomfort are notoriously difficult to assess in severe or critically ill patients[16]. It is clear that appropriate assessment of pain is key to its management[18]. Tracking physiological parameters including heart rate (HR) and blood pressure together with the use of validated pain tools like the Numerical Rating Scale (NRS) and the Visual Analogue Scale (VAS) are required to objectively assess comfort and pain[19]. The NRS looks at a score of 0-10 where 0 means no pain and 10 is the most pain the patient has ever felt. The VAS is used predominantly in the paediatric population and uses images to describe a patient's subjective emotion in response to a stimulus[19].

The OxEra™ has received approval by SAHPRA for emergency use in COVID-19 hypoxaemic patients. (See Appendix) While a multidisciplinary team at the CSIR (Council for Scientific and Industrial Research) has evaluated the device with a significant amount of testing around the calibration and reliability of the device, there has been no clinical human evaluation.

Rationale for the Safety Study

Given the potential for the widespread utilisation of this oxygen device in a resource-limited setting, we performed a clinical assessment study. To evaluate the safety and patient acceptance of the OxEra™ device, we evaluated the device on a group of healthy volunteers and monitored $ETCO_2$, oxygen saturation, physiological variables related to pain, and we performed an objective pain assessment using more than one pain tool.

OBJECTIVES

Aim:

Using a healthy volunteer population, we assessed the safety and user acceptance of the OxEra™ device.

Objectives:

- Primary Objective: Monitor for an increase in $ETCO_2$:
  - Less than 6.3 mmHg change from baseline $ETCO_2$ and no $ETCO_2$ above the 45mmHg threshold

- Secondary Objectives: Monitoring changes in vital signs:
  - Maintenance of normal pulse oximetry saturation readings (above 93%)
  - Changes in Blood Pressure, Mean Arterial Pressure, Respiratory Rate, and Heart Rate

- Tertiary objectives: Pain and comfort score assessment
  - To assess the comfort and pain scores while using the OxEra™ at each time interval with varying PEPs

METHODOLOGY

a) Study design
This is an experimental safety study of the OxEra™ Delivery device on healthy subjects at the ICU training centre in Chris Hani Baragwanath Academic Hospital.

b) Sample population
Inclusion criteria
  - Age ≥ 18years
  - All volunteers are healthy with no known cardiac or respiratory co-morbidities.

Exclusion criteria
  - Respiratory co-morbidities such as Asthma, Chronic Obstructive Pulmonary Disease
  - Smoking
  - Pregnancy
  - Body Mass Index >30
  - Cardiac co-morbidities
  - Beard/facial hair
  - Facial abnormalities
  - Previous thoracic surgery

c) Sample size
The sample size calculation is based on the primary objective.

The calculation is a standard calculation for sample size estimation for a single mean estimate, (N = [(Z score x SD)/ D]2)[20]. To detect a change in $ETCO_2$ of above 45mmHg with 95% confidence and a precision of 5%, we require a minimal sample size of 30 patients. A threshold of 45mmHg plus a standard deviation of 6,3mmHg was used. This change was based on the accuracy data of $ETCO_2$ monitors[21].

d) Study site, procedure, and data collection

The study was performed at the ICU training center at Chris Hani Baragwanath Academic Hospital. Thirty (30) participants will be recruited as per the criteria above, by the principal investigator.

The study, with its accompanying data collection, was planned to take 7 days. The various parameters for each of the 30 participants were taken at baseline with the OxEra™ set at 15 L/min oxygen and a minimum PEP of 5 cmH_20. Using a 5-minute interval, the PEP was increased by 5cmH_20 until a maximum of 20 cmH_20. Five minutes after the maximum PEP of 20 cmH_20, the PEP was reduced to 5 cmH_20 for the remainder of the study (2 hours).

The principal investigator will be present during the entire data collection process. This will involve:

- Preparation of the ICU training facility with all the equipment and necessary documents.
- Supervising each safety test session.
- Recording each participant's details on the datasheet.
- Provide detailed explanations to the participants about the study.
- Collecting all data individually from all 30 participants throughout the safety test session that will run over 7 days.
- All data to be collected and organized in a streamlined manner.

Data will be collected using the equipment provided by the ICU training centre at Chris Hani Baragwanath Academic Hospital. An ICU nurse will be present to ensure support to the Principal Investigator.

The following data will be collected:

- Demographics of the participant: Height, weight, age, race, gender.
- Oxygen Saturation, $ETCO_2$ (using Capnostream™ Portable Respiratory Monitor),, Respiratory rate, Blood Pressure, Mean Arterial Pressure, Heart Rate, PAS, VAS, NRS, Adverse events, Comfort Score, FiO_2, and PEP (see table 1).

DATA ANALYSIS AND STATISTICS

a) Data Record Keeping

Study data were collected and managed using REDCap® electronic data capture tools hosted at the University of Witwatersrand (Research Electronic Data Capture), and Microsoft Excel®.

b) Statistical analysis

Continuous data will be described using the mean and standard deviation or medians and interquartile ranges depending on the distribution of the data. Continuous data will be compared using either the dependent T-test or the Wilcoxon matched-pairs test (dependent data). A 5% significance level will be used for all comparisons between changes at each time interval with each PEP setting.

FUNDING

The costs include stationery and printing costs, and assistance with data collection, and will be covered by the principal investigator.
The devices will be donated to the principal investigator and his supervisors by Gabler.

Gabler had no role in the study design, the collection, analysis, and interpretation of data, in writing of the report, or in the decision to submit the article for publication.

ETHICS APPROVAL

Written informed consent will be mandatory before study inclusion. Permission from the Human research ethics committee, medical (HREC) approval has been obtained. The reference number is M210222. National Research Database Reference Number GP 202107013.

GANTT CHART

	Literature Search	Protocol Development	Protocol Assessment	Ethics Application	Funding application	Data collection	Data analysis	Research report compilation	Submission for publication
Jan- March 2021									
March-May 2021									
June-July 2021									
Aug 2021									
Sept 2021									
Oct-Dec 2021									

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CHAPTER 2: Proposed Manuscript

BACKGROUND

Coronavirus Disease 2019 (COVID-19) is a highly contagious disease caused by a new β coronavirus called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV 2)[1]. This new coronavirus is closely related to the 2003 Severe Acute Respiratory Syndrome (SARS) and the 2012 Middle East Respiratory Syndrome (MERS) Coronavirus, of which caused severe respiratory distress, cytokine storm, and severe lung injury[1]. The clinical impact of COVID-19 is mainly on the pulmonary system but has also been documented to affect the extra-pulmonary systems[2].

Non-invasive ventilation has had a successful role in the management of patients with acute hypoxemic respiratory failure[3]. In response to the pandemic, a local volunteer initiative called Umoya collaborated to create the Oxygen Efficient Respiratory Aid ™ (OxEra™) device which very simply is a simple CPAP device that only requires an oxygen flow rate of 15L/min. The collaboration included engineers, doctors, designers, 3D printing specialists, and programme managers. The OxEra™ device has received approval by SAHPRA for emergency use in COVID-19 hypoxemic patients. While a multidisciplinary team at the CSIR has evaluated the device relating to the calibration and reliability of the device, there has been no clinical human evaluation.

Most CPAP systems run the risk of inducing rebreathing in case of failure[3]. The OxEra™ device has a built-in safety valve to avoid rebreathing. In the case of rebreathing a significant rise in $ETCO_2$ will occur [4, 5]. This may be accompanied by a decrease in oxygen saturation[5].

Another important challenge related to positive pressure ventilation delivered through a non-invasive device relates to patient comfort and acceptance[6]. The ability of a patient to tolerate the device is therefore vital to the utility of such a device and necessitates the objective assessment of pain and discomfort. Pain and discomfort are notoriously difficult to assess in severe or critically ill patients[7]. Appropriate assessment of pain is key to its management[7]. Tracking physiological parameters including heart rate (HR) and blood pressure together with the use of validated pain tools like the Numerical Rating Scale (NRS) and the Visual Analogue Scale (VAS) are required to objectively assess comfort and pain[8].

Given the potential for the widespread utilisation of this oxygen device in a resource-limited setting we performed a clinical assessment study. To evaluate the safety and patient acceptance of the OxEra™ device, we evaluated the device on a group of healthy volunteers and monitored $ETCO_2$, oxygen saturation, physiological variables related to pain, and we performed an objective pain assessment using three different pain and comfort tools.

OBJECTIVES

Aim:

Using a healthy volunteer population, we assessed the safety and user acceptance of the OxEra™ device.

Objectives:

- Primary Objective: Monitor for an increase in $ETCO_2$:
    - Less than 6.3 mmHg change from baseline $ETCO_2$ and no $ETCO_2$ above the 45mmHg threshold

- Secondary Objectives: Monitoring changes in vital signs:
    - Maintenance of normal pulse oximetry saturation readings (above 93%)
    - Changes in Blood Pressure, Mean Arterial Pressure, Respiratory Rate, and Heart Rate

- Tertiary Objectives: Pain and comfort score assessment
    - To assess the comfort and pain scores while using the OxEra™ at each time interval with varying PEPs

METHODS

Study Design and Setting

We performed an experimental safety study of the OxEra™ Device at the Intensive Care Unit training centre of the Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa. This is a large academic facility affiliated with the University of the Witwatersrand. The protocol was approved by the University of Witwatersrand's Human Research Ethics Committee (HREC No: M210222). National Research Database Reference Number GP 202107013. Written informed consent was obtained from each participant.

Study population, procedure, and data collection

Population

Thirty (30) healthy adult participants were included in the study. Exclusion criteria included smoking, pregnancy, body mass index (BMI) greater than 30, respiratory and cardiac co-morbidities, beards, facial abnormalities, and previous thoracic surgery.

Procedure

An initial safety brief, demonstration, and face mask test to ensure an appropriate seal was followed by the application of the CPAP facemask, an oxygen flow rate of 15l/min but no positive end-expiratory pressure (PEP=0). Baseline data (T0) was collected. Data was then collected at the following time points; T1 (5 minutes, PEP =5 cmH¬20), T2 (10 minutes, PEP =10 cmH¬20), T3 (15 minutes, PEP =15 cmH¬20), T4 (20 minutes, PEP =20 cmH¬20), T5 (30 minutes, PEP =5 cmH¬20), T6 (45 minutes, PEP =5 cmH¬20), T7 (60 minutes, PEP =5 cmH¬20), T8 (90 minutes, PEP =5 cmH¬20) and T9 (120 minutes, PEP =5 cmH¬20). The data was collected by a a trained study doctor and nurse.

Study data

Demographic data of each patient included: height (cm), weight (kg), age (years), race, and gender. The following clinical data were collected at each study time point: $ETCO_2$ (using Capnostream™ Portable Respiratory Monitor), oxygen saturation percentage, respiratory rate, heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, and any adverse events were noted. The visual assessment score (VAS), pain assessment score (PAS), and the comfort score were also taken at each time point. See Appendix I and II for VAS and PAS scores.

Statistical Analysis

All continuous data were described using median and interquartile range (IQR) while categorical data were described using number (n) and percentage (%). Dependent data were compared using the Wilcoxon matched-pairs test (2 groups) or the Friedman ANOVA tests for more than 2 groups. A p-value < 0.05 was considered significant.

Sample Size

The sample size was based on the calculation of a single mean estimate. In the case of rebreathing a significant rise in $ETCO_2$ will occur[5]. This may be accompanied by a decrease in oxygen saturation[5]. We, therefore, used an $ETCO_2$ mean threshold value of 45mmHg and a standard deviation of 6.3mmHg. Using a 5% precision we required sample size of 30 participants.

Outcomes

The main outcome was to determine if there was a significant increase in $ETCO_2$ using a threshold of 45mmHg or an increment of 6.3mmHg for the study duration. Secondary and tertiary outcomes included changes in pulse oximetry saturation readings, blood pressure, respiratory rate (RR), heart rate (HR), and pain and comfort scores for the duration of the study.

RESULTS

Participant Description

The thirty participants had a median age of 30 with the youngest being 25 years of age and the oldest being 41 years of age. The median weight was 71.5 kilograms with an interquartile range from 61 kilograms and 80 kilograms. The median height measured was 170 cm with an interquartile range of 167 cm to 176 cm. Therefore, the median Body Mass Index (BMI) was 24.7 kg/m^2, with interquartile ranges of 21.9 kg/m^2 and 25.9 kg/m^2.

Main Outcome

There was no significant difference in $ETCO_2$ from baseline until T9 at 2 hours. (p=0.13) No participant experienced an increase in measured $ETCO_2$ up to a value greater than 45 mmHg. No participant experienced an increase in measured $ETCO_2$ greater than 6.3 mmHg. The median increase in $ETCO_2$ (Δ $ETCO_2$) over the study period was 2 mmHg (IQR, 0-1). See Figure 1.

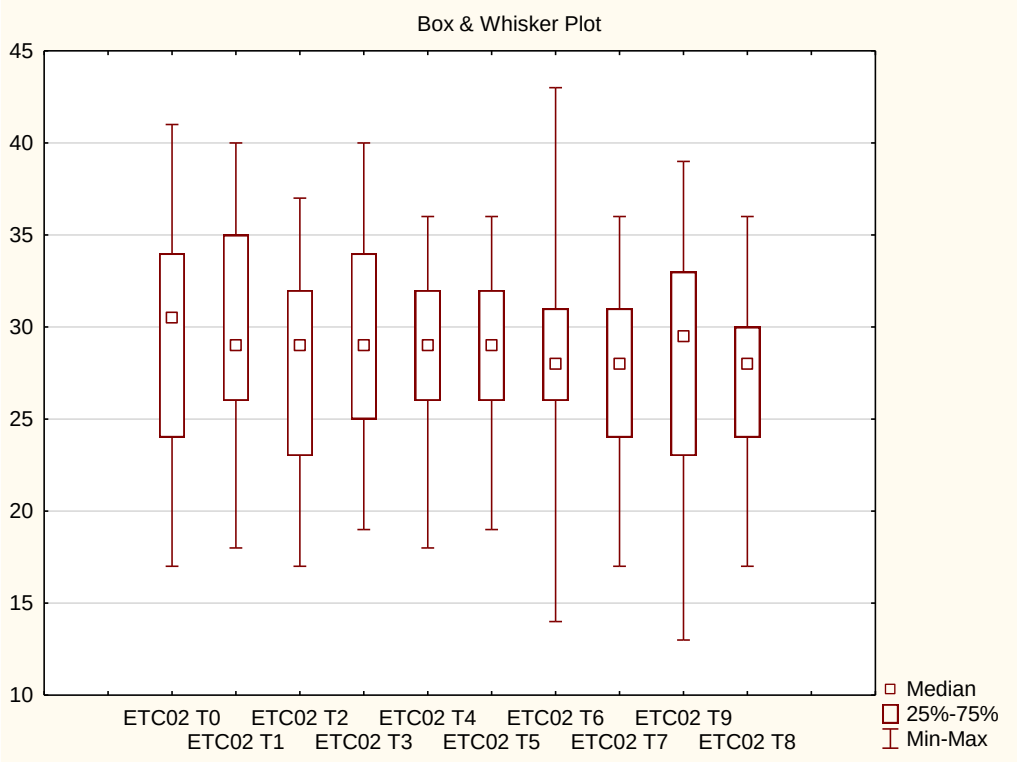

Figure 1: Box and Whisker Plot of $ETCO_2$ from start to end.

Other Outcomes

Description of changes in Respiratory Parameters

Pulse Oximetry (SpO_2%)
Sixteen (16 out of 30) participants had a SpO_2% reading of 100% at baseline, while 14 participants had a value of between 94 and 99% at baseline. Thirteen (13/14) had an increase in SpO_2% by 5 minutes on the OxEra™ and one (1/14) had an increase by 20 minutes.

Table 1: SpO_2% readings from baseline to the end of the study

Variable	Valid N	Median	Minimum	Maximum	25.000th Percentile	75.000th Percentile
Sp02 T0	30	100	94	100	97	100
Sp02 T1	30	100	96	100	99	100
Sp02 T2	30	100	97	100	99	100
Sp02 T3	30	100	95	100	99	100
Sp02 T4	30	100	98	100	99	100
Sp02 T5	30	100	97	100	99	100
Sp02 T6	30	100	97	100	99	100
Sp02 T7	30	100	98	100	99	100
Sp02 T8	30	100	97	100	100	100
Sp02 T9	30	100	99	100	100	100

Respiratory Rate (RR. Friedman ANOVA)
There were no significant changes in respiratory rate from baseline to 2 hours (T9), p=0.32. See Figure 2. The median RR at T0 was 16 (IQR 14-17), while the median RR at T9 was 16.5 (IQR 13-18)

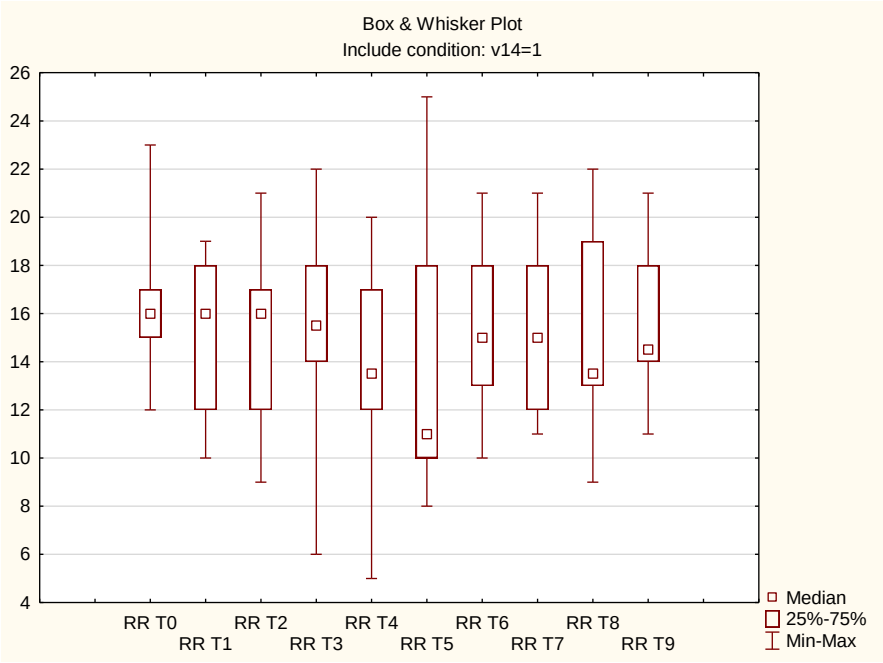

Figure 2 RR from start to the end of the study

Description of changes in Hemodynamic Parameters

Heart Rate (HR)
The median HR decreased significantly from 73 (IQR 65-87) at T0, to 68.5 (IQR 63-75) at T9, p=0.000. See Figure 3.

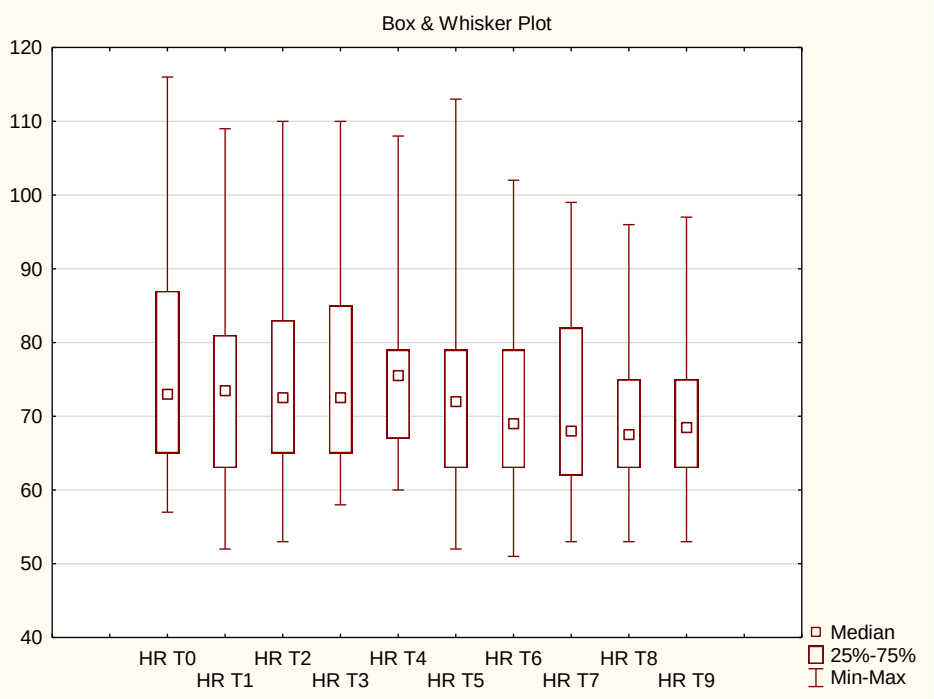

Figure 3 HR from start to the end of the study

Mean Arterial Pressure (MAP)
There were significant changes in the MAP from baseline to 2 hours (T9), p=0.21. See Figure 4.

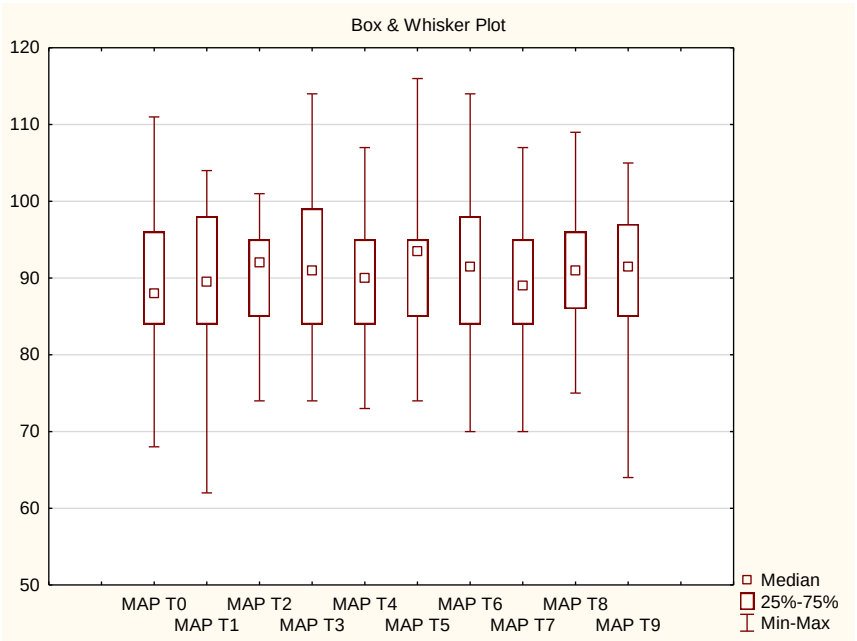

Figure 4. MAP from start to the end of the study

Systolic Blood Pressure (SBP)
There were no significant changes in SBP from baseline to 2 hours (T9), p=0.14. See Figure 5.

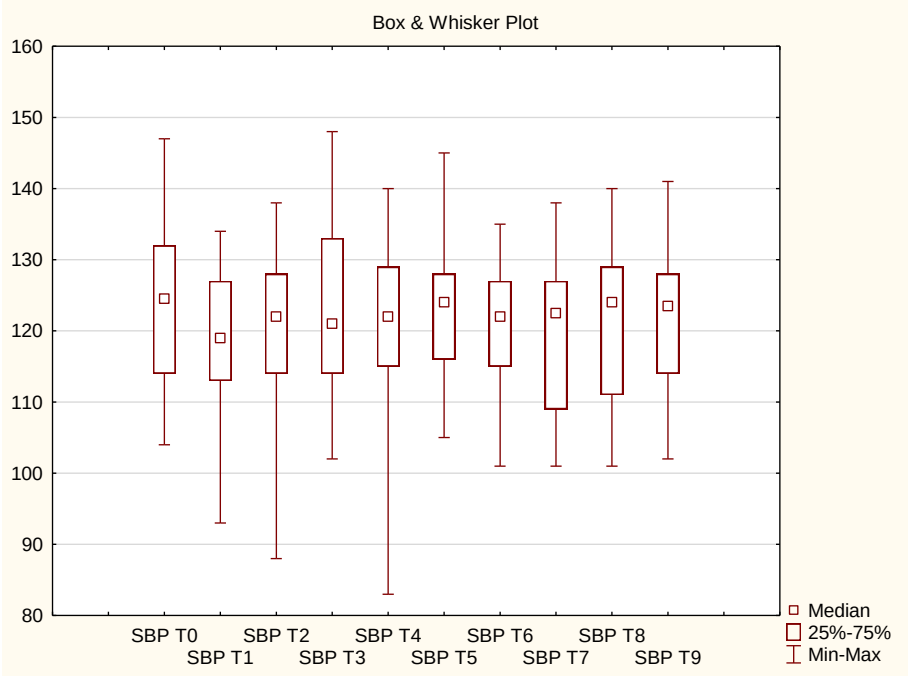

Figure 5. SBP from start to the end of the study

Diastolic Blood Pressure (DBP)
There were no significant changes in DBP from baseline to 2 hours (T9), p=0.33. See Figure 6.

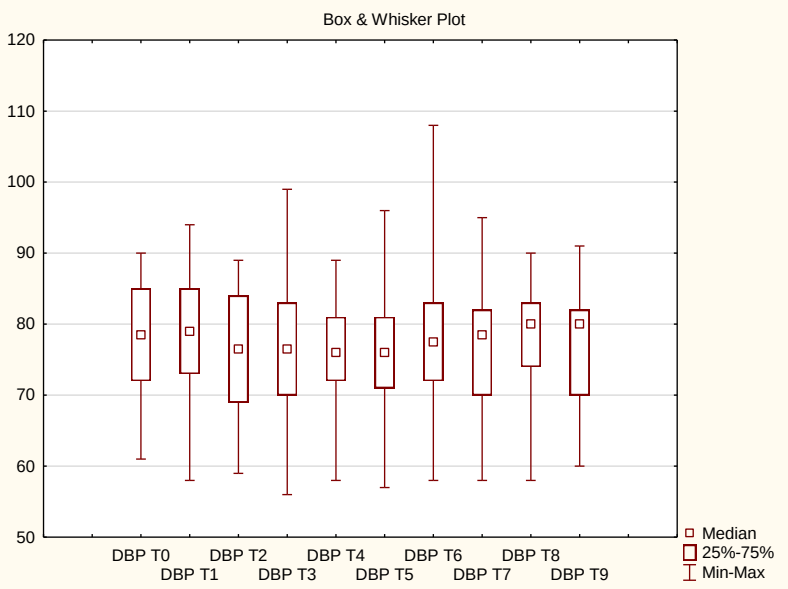

Figure 6. DBP at the start to the end of the study

Pain and Comfort Scores

VAS Score

The VAS score had a significant increase from T0-T9, p=0.000. The worst median VAS score was 2 at T3, T4, and T5. This decreased to a median VAS score of 1 by T9. See Figure 7.

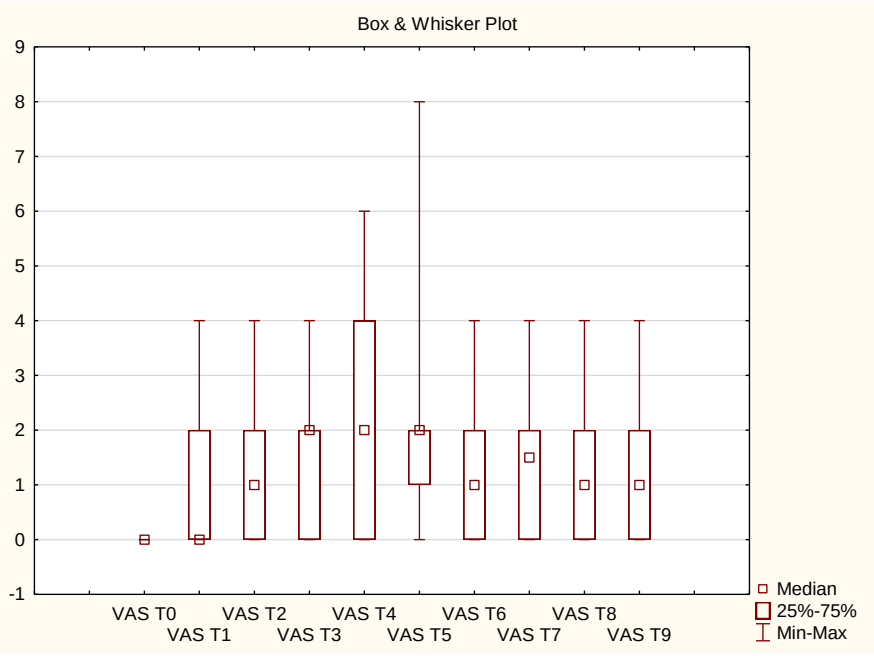

Figure 7. VAS score from start to the end of the study

PAS Score

There was no significant increase in PAS scores from T0 to T9, p=0.09. See Figure 8.

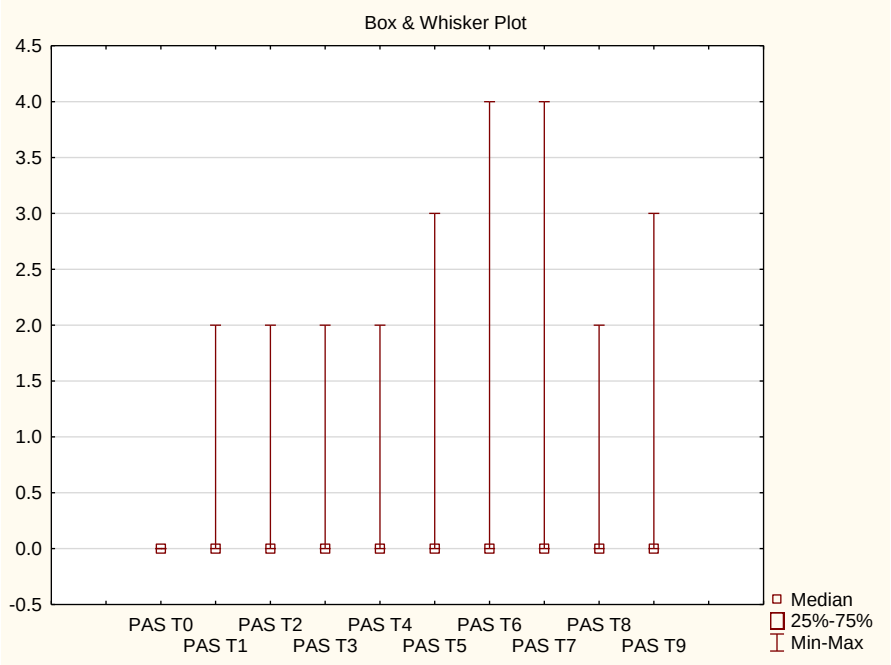

Figure 8. PAS scores from start to the end of the study

Comfort Score

There was a significant increase in comfort scores from T0-T9, p=0.000. The worst median comfort score was 2 at T4 and T5 (i.e., the comfort was worst on average at this stage). This decrease to a median comfort score of 1 by T7. See Figure 9.

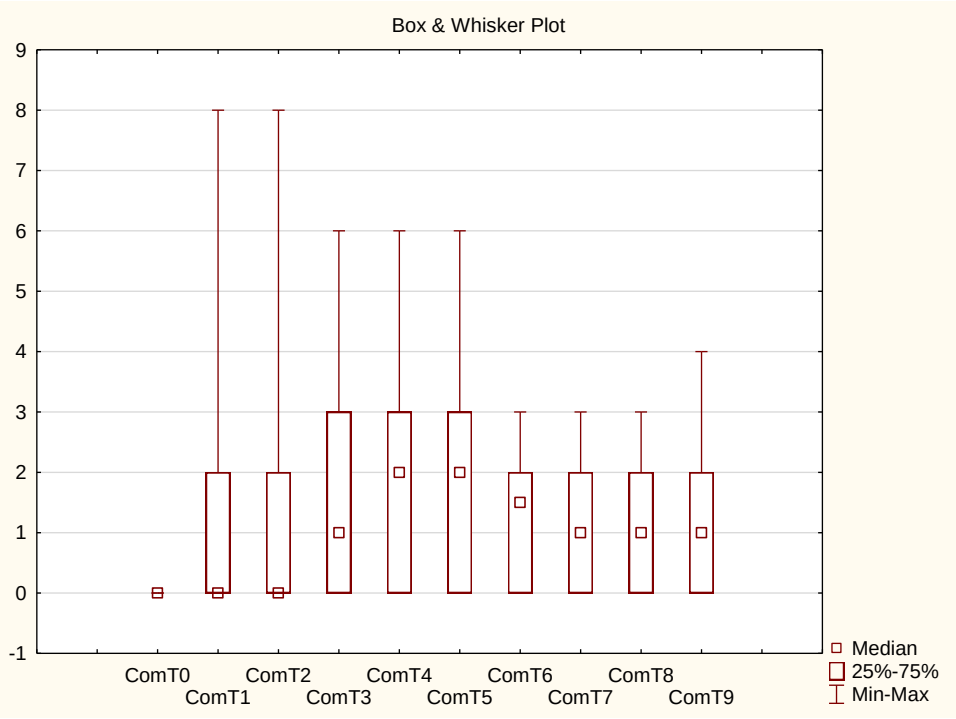

Figure 9. Comfort score from start to the end of the study.

DISCUSSION

A) SAFETY

The main aim of this study was to assess the safety of the OxEra™ device concerning to the risk of rebreathing. This safety aspect is key among many characteristics on which a CPAP system is selected. In our limited resource setting, safety, portability, comfort, ease of use, and the ability to reduce oxygen requirements are key[9]. The risk of rebreathing is a well-established risk and design features suggest the inclusion of a passive/ safety valve[10]. Capnography is a useful tool to detect changes in $ETCO_2$ that may be caused by rebreathing[8]. The clinical consequences of exposing patients to rebreathing and increased work of breathing must be avoided, and clinical studies are required to understand these issues[11].

The main finding of our study showed no significant difference in $ETCO_2$ from baseline until the end of the study. No participant experienced an increase in $ETCO_2$ above the upper reference limit. In addition, no participant experienced an increase in $ETCO_2$ greater than the imprecision of the measurement device (capnography devices). This finding confirms the safety of the OxEra™ device concerning to rebreathing.

B) TOLERANCE OF OXERA™ DEVICE

Discontinuation of PEP will occur in a significant proportion of patients due to pain and discomfort. A recent study during the SARS CoV-2 pandemic demonstrated that 12% of patients on CPAP discontinued due to pain and discomfort[12]. A CPAP trial showed that 70-80% who were placed on CPAP, continued whereas 5-30% abandoned them. The reasons attributed to abandonment were mainly lacked benefit but also included mask discomfort, anxiety, pain, and noise[13]. In another study, 15% of the participants abandoned CPAP mainly due to its discomfort with the mask [14].

A multi-variable approach to pain and discomfort may be superior to any one method of detection[15]. The normal physiological change in the cardiac system with PEP is a decrease in cardiac output and mean arterial pressure[16].
Respiratory physiological changes of PEP are usually monitored in studies with invasive methods. These studies observed that the work of breathing is shown to be reduced in unhealthy patients with increases in PEP from as little as $5cmH_2O$[17]. Healthy individuals are not meant to decrease the work of breathing. As expected in our healthy participants, there were no changes in the respiratory rate in the participants in the study. There were no significant changes in mean arterial pressure, systolic blood pressure, or diastolic blood pressure. Similarly, we did not find an increase in heart rate or respiratory rate. The lack of significant changes in these physiological markers suggest tolerance of the OxEra™ device.

C) PAIN/DISCOMFORT

Pain and discomfort are notoriously difficult to assess in severe or critically ill patients[18]. Appropriate assessment of pain is key to its management[19]. Validated pain tools like Numerical Rating Scale (NRS, also known as Pain Assessment Score (PAS)) and the Visual

Analogue Scale (VAS) are required to objectively assess comfort and pain[20]. There was no significant change in the pain score (PAS). The changes in the VAS score did not reach the threshold required to initiate acetaminophen or anti-inflammatory drugs making them unlikely to result in the termination of CPAP therapy[21]. These changes are simply managed by reassurance and observation. The comfort score increased marginally but once again it did not reach the threshold for activating a formal pain assessment. These elevations in the VAS and comfort score occurred at positive pressure levels of $20cmH_20$. The combination of the lack of physiological changes of pain and the lack of significant indicators of pain using objective scoring systems suggest that the OxEra^{TM} device was well tolerated on a positive pressure as high as $20cmH_20$ and discontinuation due the pain or discomfort is unlikely.

LIMITATIONS

Although we used an imprecision documented in the literature, we did not measure this in the capnograph instrument used for the study.
Secondly, we did not measure the positive pressure generated by the OxEra^{TM} device in our subjects however, this has been previously done for SAHPRA approval.
Lastly, we could have improved on the average age of participants. An older population would have distributed the sample size to a greater general population.

CONCLUSION

The OxEra^{TM} device is an innovative oxygen delivery device that has many benefits, especially in this era of COVID-19. Currently, it has SAHPRA approval to be used in the COVID-19 pandemic for emergency use.

The OxEra^{TM} device demonstrated safety in terms of risk of rebreathing and was well tolerated up to a positive pressure of 20 cmH_20 in this clinical evaluation amongst healthy participants.

With approval for the safety of this device, the OxEra^{TM} may have use in various fields of medicine involving respiratory diseases, specifically in resource and oxygen-limited settings.

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CHAPTER 3: APPENDIX

APPENDIX A
ABBREVIATIONS

ABBREVIATIONS

ACE-2	Angiotensin-converting enzyme 2
ARDS	Acute Respiratory Distress Syndrome
Bi-PAP	Bi-level positive airway pressure
COVID-19	Corona virus disease 19
CPAP	Continuous positive airway pressure
$ETCO_2$	End-tidal carbon dioxide
HFNC	High flow nasal cannula
ICU	Intensive Care Unit
LED	Light emitting diodes
MERS	Middle East Respiratory Syndrome
NIV	Non-Invasive Ventilation
NRS	Numerical Rating Scale
NVP	National Ventilator Project
OxEra™	Oxygen Efficient Respiratory Aid
PAS	Pain Analogue Score
PEP	Positive expiratory pressure
SARS COV 2	Severe Acute Respiratory Syndrome Coronavirus 2
SARS	Severe Acute Respiratory Syndrome
SAVE-P	South African Ventilatory Emergency
SpO_2	Oxygen saturation of haemoglobin in arterial blood
VAS	Visual Analogue Scale

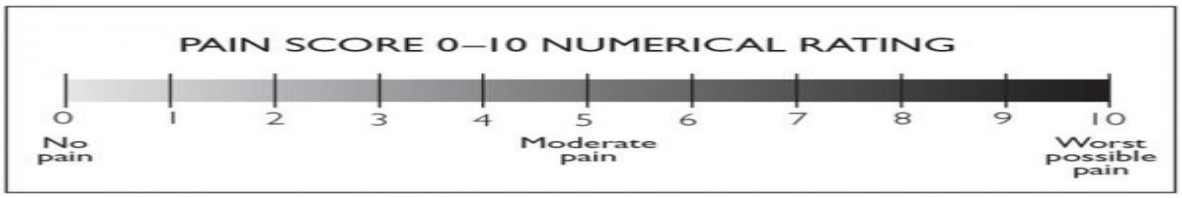
APPENDIX B
DATA COLLECTION SHEET

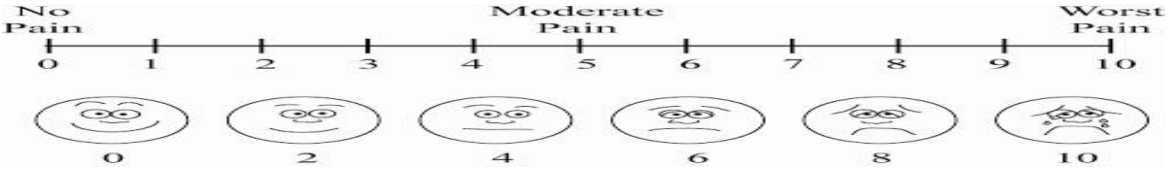
DATA COLLECTION SHEET

Participant No: ……
Height: ……
Weight: ……
Age: ……
Race: ……
Gender: ……

Variables	Time	T0 : Start	T1: 5 min	T2: 10 min	T3: 15 min	T4: 20 min	T5: 30 min	T6: 45 min	T7: 1 hour	T8: 1.5 hours	T9: 2 hours
	PEEP	0 cm H20	5 cm H20	10 cm H20	15 cm H20	20 cm H20	5 cm H20	5 cm H20	5 cm H20	5 cm H20	5 cm H20
BP											
MAP											
RR											
HR											
Sats											
VAS											
PAS											
ETCO2											
Adverse Events											
Comfort Score											

Comfort Score: Very Comfortable being 0 and Very Uncomfortable being 10





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APPENDIX C
APPROVAL LETTERS MEDICAL ADVISORY COMMITTEE

APPROVAL LETTERS MEDICAL ADVISORY COMMITTEE

[redacted]

GAUTENG PROVINCE

HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 14th January 2021

TITLE OF PROJECT:

OxEra: Oxygen Delivery Device – A Safety Study

UNIVERSITY: Witswatersrand

Principal Investigator: Dr M John

Department: Internal Medicine

Supervisor : Dr SA van Blydenstein

Permission Head Department (where research conducted): Yes

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Academic Hospital. The CEO / management of Chris Hani Baragwanath Academic Hospital is accordingly informed and the study is subject to:-

- **Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.**
- The Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- The MAC will be informed of ary serious adverse events as soon as they occur
- Permission is granted for the duration of the Ethics Committee Approval.

.....
Recommended
(On behalf of the MAC)
Date: 14/1/2021

.....
Approved/~~Not Approved~~
Hospital Management
Date: 15/01/2021

APPENDIX D
HUMAN RESEARCH ETHICS COMMITTEE APPROVAL

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research and Postgraduate Affairs)

TO:	Dr MH John School of Clinical Medicine Department of Medicine Division of Internal Medicine Medical School University E-mail: johnmidhun8@gmail.com
CC:	Supervisor: Drs SA van Blydenstein & J Bruins; Prof S Omar <savanblydenstein@gmail.com> and <HREC-Medical Research Office@wits.ac.za>
FROM:	Mr Iain Burns Human Research Ethics Committee (Medical) Tel: 011 717 1252 E-mail: Iain.Burns@wits.ac.za
DATE:	2021/04/29
REF:	R14/49
PROTOCOL NO:	**M210222** (This is your ethics application reference number. Please quote it in all enquiries, oral or written, relating to this study.)
PROJECT TITLE:	*Oxygen Efficient Respiratory Aid-a safety study*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to Government funding of the University.

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

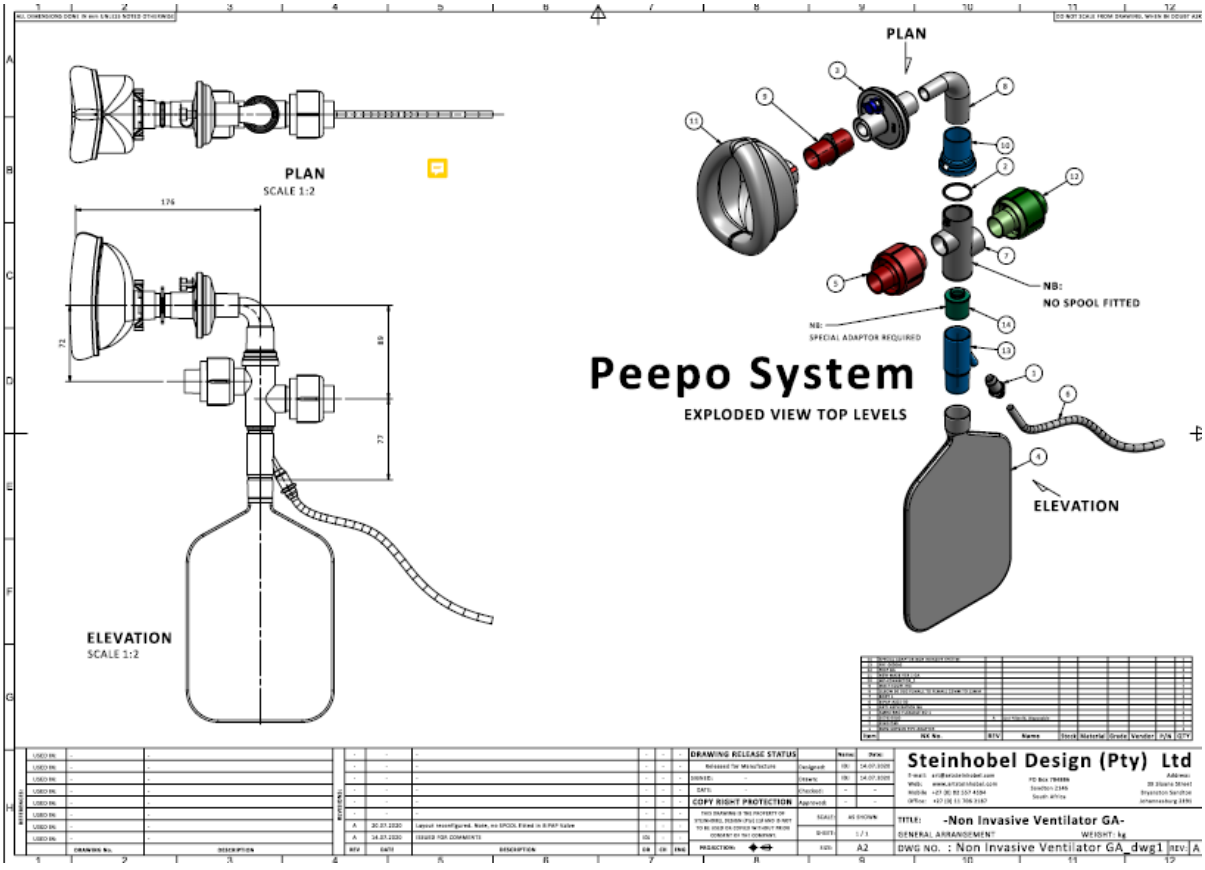
R49 Dr MH John

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M210222

NAME: (Principal Investigator)	Dr MH John
DEPARTMENT:	School of Clinical Medicine Department of Medicine Division of Internal Medicine Medical School University
PROJECT TITLE:	*Oxygen Efficient Respiratory Aid-a safety study*
DATE CONSIDERED:	2021/02/26
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Drs SA van Blydenstein & J Bruins; Prof S Omar
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2021/04/29

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

APPENDIX E
PROTOTYPE, INFORMATION LEAFLET AND SAHPRA APPROVAL


PLAN
SCALE 1:2
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NB:
NO SPOOL FITTED
NB:
SPECIAL ADAPTOR REQUIRED
Peepo System
EXPLODED VIEW TOP LEVELS
ELEVATION
DRAWING RELEASE STATUS
COPY RIGHT PROTECTION
Steinhobel Design (Pty) Ltd
TITLE: -Non Invasive Ventilator GA-
GENERAL ARRANGEMENT
DWG NO. : Non Invasive Ventilator GA_dwg1
A2

SAHPRA
South African Health Products Regulatory Authority

SAHPRA Head Office
Building A
Loftus Park
2nd Floor
Kirkness Road
Arcadia
0083

Enquiries: Medical device Unit
Email: mdadmin@sahpra.org.za
Ref: MDF 00015
Licence: 00000468MD_v2

Gabler Medical Cape Town (Pty) Ltd
22 – 24 Thor Circle
Viking Place
Cape Town
7640
Email: dmiller@gablermedical.com

ATTENTION: Mr D Miller

Dear Sir,

RE: SECTION 21 AUTHORISATION – RAPIDLY MANUFACTURED VENTILATOR / RESPIRATORY DEVICES

BACKGROUND

1. Section 21 of the Medicines and Related Substances Act, 1965 (Act 101 of 1965) makes provision for the South African Health Products Regulatory Authority (SAHPRA) to authorise the sale of unregistered medicines, medical devices or in-vitro diagnostics (IVDs) for certain purposes.
2. The Authority may in writing authorise any person to sell during a specified period to any specified person or institution a specified quantity of any particular medicine, medical device or IVD which is not registered.
3. Any medicine, medical device or IVD sold in pursuance of any authority granted under Section 21(1) may be used for such purposes and in such manner and during such period as the Authority may in writing determine.
4. The Authority may at any time by notice in writing withdraw any authority granted in terms of Section 21(1) if effect is not given to any determination made in terms of Section 21(2).
5. SAHPRA's intent is to foster the continued availability of safe and effective medical devices while being flexible regarding modifications made to ventilators, anaesthesia gas machines and other respiratory devices, and their accessories, in response to the COVID-19 public health emergency.

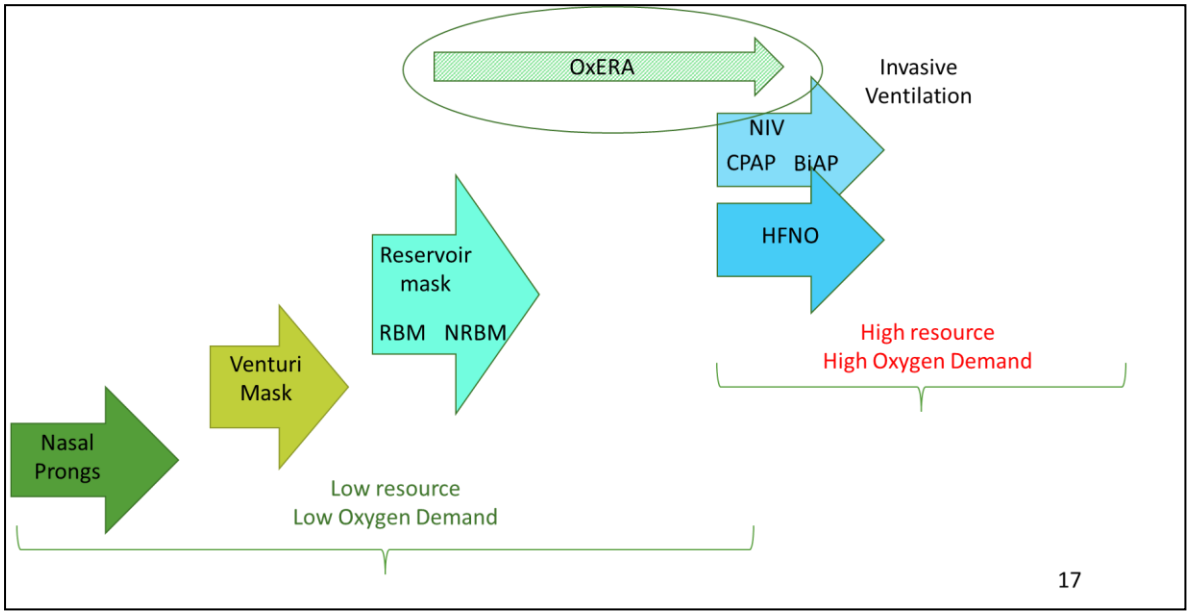
SECTION 21 AUTHORISATION

6. The following unregistered medical device has been granted authorization for sale in terms of Section 21 of Act 101 of 1965, by the following SAHPRA licensed manufacturer, only:

PRODUCT NAME	Fairovent Cpap
LOCAL MANUFACTURER	Gabler Medical (Pty) Ltd
SAHPRA LICENCE HOLDER	Gabler Medical Cape Town (Pty) Ltd
AUTHORISED REPRESENTATIVE	Mr D Miller

OxEraTM ®
Oxygen Efficient Respiratory Aid

South Africa, like many developing countries, finds itself burdened with a high Covid-19 patient load but with a lack of skilled staff, ICU and high care facilities and bulk oxygen supplies to be able to effectively manage patients.
Umoya sought to extend the spectrum of care available in these low resource settings and to bridge the gap between standard oxygen mask therapy and ventilation strategies such as High flow nasal cannulas, BiPAP and CPAP. This resulted in the development of the OxEra™ device.



OxEra™ bridges the gap between the two resource environments and extends the care available at small hospitals and clinics.

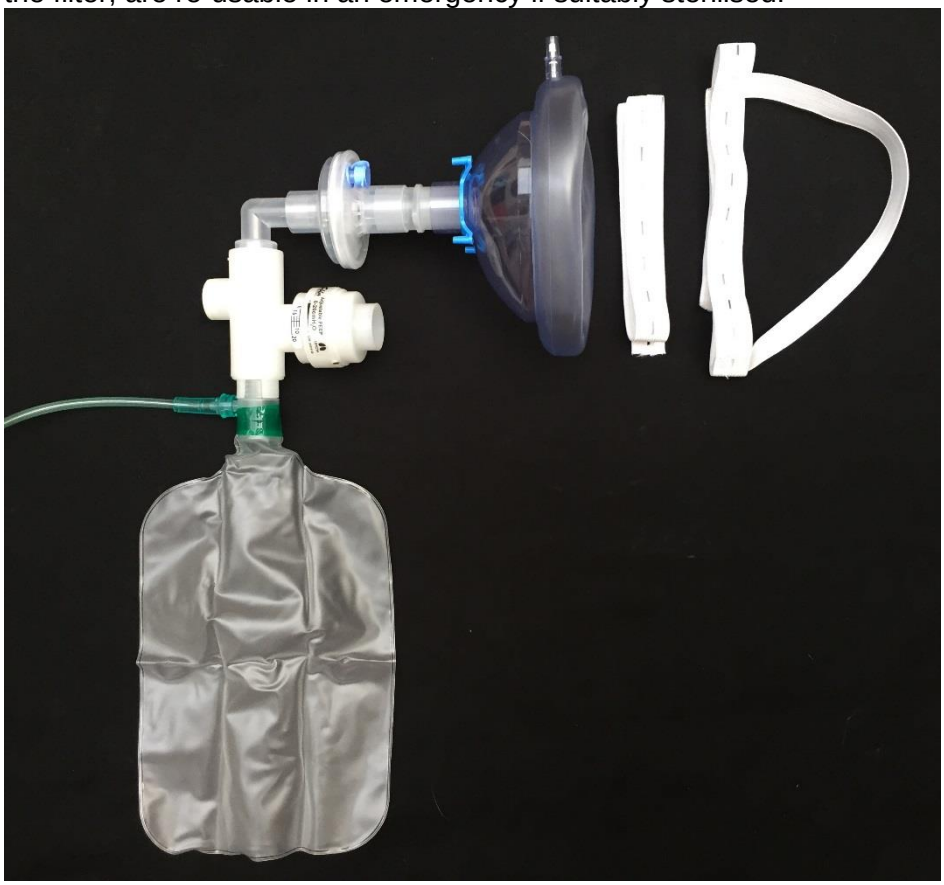
The innovative OxEra™ device is an all-in-one device using an anaesthetic mask and an adjustable mechanical PEEP valve that is simple, cost effective and oxygen efficient. Tests have shown that not only can consistently high levels of oxygen be delivered with the critical benefit of PEEP, but less oxygen is usually needed as supply can be titrated to patient demand rather than having to be left fully open to compensate for leaks. In our oxygen resource constrained environment this is a game changer and allows even the most basic facilities that are dependent on bottled oxygen or small oxygen concentrators to provide a higher level of clinical care than they are currently able to. It also means that the device is suitable for use in transferring patients in ambulances where other options are limited.

How does it work?

The OxEra™ device assists patients by providing high percentage (up to 100%) oxygen plus maintaining slight pressure to keep their lungs from collapsing during expiration via adjustable PEP. This reduction in atelectasis improves oxygenation, decreases trauma to the alveoli and reduces the work required to re-open the alveoli and hence the work of breathing.

It comprises a custom main housing, incorporating the adjustable PEP (5 – 20 cm H2O), anti-asphyxiation valve (for safety) and oxygen supply via a hose and accumulator bag. The oxygen hose can be connected to any available source of oxygen.

Commercial medical devices such as an anaesthetic mask and viral filter complete the package together with simple but effective elastic head straps. All components, other than the filter, are re-usable in an emergency if suitably sterilised.



OxEra™ device

Key to the devices efficient use of oxygen is the fact that incoming oxygen is accumulated in the bag during expiration and is therefore available during inspiration together with the flow in the line. In loose fittings masks and especially nasal prongs, high flow nasal canulae and even CPAP units, the lack of any accumulation of oxygen in a sealed system means that large percentages (up to 66%) of the feed oxygen are simply wasted making them very oxygen inefficient. Under our Covid-19 conditions with so many patients requiring oxygen at the same time this is a major problem.

Key benefits:

Clinically effective – Able to provide superior levels of care than can be provided by standard non-rebreather oxygen mask.

Low oxygen consumption – Maximum 15l/min required but can operate at any oxygen flow rate below this by entraining extra room air as required through the anti-asphyxiation valve. This is no more than the standard oxygen masks already being used.

Efficient oxygen consumption – through the snug fitting mask and accumulator bag, all the oxygen flowing down the line is available to the patient rather than being wasted when the patient exhales.

Cost effective – locally designed and manufactured and off-the-shelf items used as far as possible. Pricing based on our social enterprise objectives of providing affordable medical devices to the developing world.

Simple to use – All levels of hospital staff and GPs quickly become familiar with using the device, meaning it can be used anywhere.

Safe to use – Equipped with an anti-asphyxiation safety device in case oxygen supply runs out or is disconnected. Expired air filtered to keep environment safe for health care workers. Fully approved for Covid-19 emergency use.
Portable – Can be used anywhere where a suitable oxygen source is available ranging from home and ambulances to tertiary hospital level.

Now SAHPRA approved for use during Covid-19 with production gearing up in early January 2021.

Contact:

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Gabler Medical Devices
Reiner Gabler
0828899269
rgabler@gablermedical.com

Umoya (https://umoya.org.za).

APPENDIX F
PARTICIPANT INFORMATION SHEET AND CONSENT FORM

OxEraTM®: Oxygen Delivery Device – a safety study

PATIENT INFORMATION FORM TO USE OXERA™ OXYGEN DELIVERY DEVICE

PROTOCOL: OxEraTM®: Oxygen Delivery Device – a safety study
SHORT TITLE: OxEraTM®: Oxygen Delivery Device – a safety study
STUDENT: Dr MT JOHN

TELEPHONE: 0713828185

INTRODUCTION
Good day, my name is Dr John, I am a doctor at the Chris Hani Baragwanath Academic Hospital.

I would like to ask you if you would be willing to be part of a study. You are a candidate for the study as a volunteer to test the safety of the OxEra™ Oxygen Delivery Device. If you would like to hear more about this part of the study, I will explain it to you before you decide whether you are willing to be part of this section of the study.

WHY ARE WE DOING THIS STUDY?
All over the world people are admitted to hospital with COVID-19 and some are dying in hospital, while some do well and get discharged. Most patients that are admitted into hospital are patients that are hypoxic. Supplemental oxygen is provided to these patients with the available resources that we have.
The OxEra™ Oxygen Delivery Device is a device that is shown to provide oxygen with adjustable Positive End Expiratory Pressure (PEEP) with low oxygen requirements. It currently has SAHPRA approval for emergency COVID use only. With this study, I hope to find a better solution for the management of hypoxic patients in a low resource setting like ours. We hope to establish the safety of the device in order to use it in the general medical discipline.

YOU CAN CHOOSE TO BE PART OF THIS STUDY
It is your own decision to be in the study. You can refuse to be in the study at any time and you do not have to tell me why.

IF YOU AGREE TO THIS STUDY
I shall attach the OxEra™ device onto your face and I shall have continuous monitoring take place for at least 2 hours. We shall be measuring blood pressures, respiratory rate, oxygen saturations, end tidal carbon dioxide levels and subjective comfort scores. None of the above will be invasive and I shall always be with you during the data collection.

THE RISKS AND DISCOMFORTS OF THE STUDY PROCEDURES
There are no risks expected in the use of the device and constant monitoring will be ensured while using the device. If any discomfort is felt during the study, you are welcome to pull out from the study if you so wish to.

BENEFITS TO BEING IN THE STUDY
I hope that by doing this research I will be able to assess and establish use for the OxEra™ oxygen device. Thus, allowing it to be supplied and used in low resources settings like our healthcare in South Africa. Due to the pandemic, oxygen demands are increasing. This device would solve that issue and save many lives in the process.

REIMBURSEMENT
There is no cost for you to be in this study.

WITHDRAWAL FROM THE STUDY
If you change your mind you can decide to leave this study at any time without causing a problem.

WE WILL KEEP YOUR INFORMATION PRIVATE
I will keep your information confidential. Study pictures will be labelled with a unique study identification number. Study records may only be reviewed by study staff. Any publication of this study will not use your name.

PERSONS TO CONTACT FOR PROBLEMS OR QUESTIONS
If you ever have questions about this study or in case you feel that you were not treated fairly or were misled by study staff during your participation in this research study, you should contact Dr Midhun Thomas John (Investigator) at the Chris Hani Baragwanath Hospital on 0119339168 (office hours)/0713828185 and Dr Alex van Blydenstein (Supervisor) on 0119338000 (office hours)/0718937056

ETHICAL APPROVAL
This study was submitted to the University of the Witwatersrand, Human Research Ethics Committee (HREC) and written approval received for the study by that Committee,

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg ("Committee"). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.

If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Dr Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Thank you for reading this Study Information Sheet.

OxEra™®: Oxygen Delivery Device – a safety study

PROTOCOL: OxEraTM®: Oxygen Delivery Device – a safety study
SHORT TITLE: OxEraTM®: Oxygen Delivery Device – a safety study
STUDENT : Dr MT JOHN

TELEPHONE: 0713828185

STATEMENT OF CONSENT AND SIGNATURES

- I have read this form or had it read to me.
- I was able to discuss the information with study staff.
- I understand that my decision to be part of the study is voluntary.
- I understand that I may withdraw from the study at any time.

I am:
More than 18 years' old

Participant's name (print) _____

Participant's signature _____

Date & Time _____

APPENDIX G
TURNITIN REPORT AND SUPERVISOR LETTER

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2013
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GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

25 August 2021

Re: TurnItIn Similarity Report for MMED Student Midhun John

MMED: OXYGEN EFFICIENT RESPIRATORY AID (OXERA) DEVICE - A SAFETY STUDY

To whom it may concern

The above student has completed his MMED and is submitting it for examination.

I have noted that he has run it through TurnItIn, and it has a 19% similarity index. The similarities identified are related to medical definitions found in multiple sources, and from standard layout. There is no evidence of plagiarism. This letter serves to confirm that I have reviewed his MMED with the TurnItIn report and approve for submission.

Sincerely

Dr Alex van Blydenstein
Supervisor
Specialist Physician, Pulmonologist
Chris Hani Baragwanath Hospital

533057:Midhun_John_MMed_Latest.pdf

ORIGINALITY REPORT

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