NYAHENDE PORTABLE VENTILATOR PORTABLE VENTILATOR

Background: The COVID-19 pandemic has caused a global mechanical ventilator shortage for treatment of severe acute respiratory failure. Development of novel breathing devices has been proposed as a low cost, rapid solution when full-featured ventilators are unavailable. Here we report the design, bench testing and preclinical results for (NYAHENDE PORTABLE VENTILATOR). Output parameters were validated with mechanical test lungs followed by animal model testing. Results: The NYAHENDE PORTABLE VENTILATOR design uses a programmable motor-driven wheel assembled for adult resuscitation bag-valve compression. NYAHENDE PORTABLE VENTILATOR can control tidal volume (200-800 ml), respiratory rate (10-40 bpm), inspiratory time (0.5-1.5 sec), assist pressure sensing (-1 to -20 cm H2O), manual PEEP valve (0- 20 cm H2O). All set values are displayed on an LCD screen. Bench testing with lung simulators (Michigan 1600, Smart Lung 2000) yielded consistent tidal volume delivery at compliances of 20, 40 and 70 (mL/cm H2O). The delivered fraction of inspired oxygen (FiO2) decreased with increasing minute ventilation (VE), from 98% to 47% when VE was increased from 4-16 L/min using a fixed oxygen flow source of 5 L/min. NYAHENDE PORTABLE VENTILATOR was tested in Berkshire pigs (n=6, weight of 112±5.8 lb) utilizing normal lung model and saline lavage induced lung injury. Arterial blood gases were measured following changes in tidal volume (200- 800 ml), respiratory rate (10-40 bpm), and PEEP (5-20 cm H2O) at baseline and after lung lavage. Physiological levels of PaCO2 (≤40 mm Hg [5.3 kPa]) were achieved in all animals at baseline and following lavage injury. PaO2 increased in lavage injured lungs in response to incremental PEEP (5-20 cm H2O) ($p<0.01$). At fixed low oxygen flow rates (5 L/min), delivered FiO2 decreased with increased VE.

Conclusions: NYAHENDE PORTABLE VENTILATOR provides oxygenation and ventilation across a range of parameter settings that may potentially provide a low-cost solution to ventilator shortages. A clinical trial is necessary to establish safety and efficacy in adult patients with diverse etiologies of respiratory failure.

BACKGROUND

On January 31, 2020, the US Department of Health & Human Services announced a public health emergency related to a novel coronavirus, SARS-CoV-2, and the disease it causes, COVID-19. The early rapid spread of the COVID-19 pandemic resulted in a shortage of mechanical ventilators and accessory components (e.g., humidifiers, circuits, etc.) in many regions throughout the world (2-5). In response to these shortages, a global surge in development and production occurred, including repurposing non-medical device assembly lines to manufacture quickly designed ventilators (e.g., FORD, GM, Virgin, etc.).

As of March 2021, over 150 million COVID-19 cases have been identified leading to over 3.0 million deaths worldwide (11). Among hospitalized patients, 30% require care at intensive care unit (ICU) and 29% or more of those require mechanical ventilation. In response to the shortage of mechanical ventilators to treat COVID-19 patients, resuscitation bag-valve breathing devices

were conceived as a potential solution for short-term emergency use. The FDA has classified these devices as "emergency resuscitators" to distinguish them from mechanical ventilators (13-18). Our design uses a self-inflating resuscitation bag-valve, an automobile windshield motor, and lever arm to mimic manual hand bag-valve ventilation - along with essential operator controllable parameters: tidal volume (VT), respiratory rate (RR), inspiratory time (TI), positive end-expiratory pressure (PEEP) and patient-initiated breath pressure sensing. NYAHENDE PORTABLE VENTILATOR uses readily available components, low cost. The purpose of this study was to determine if NYAHENDE PORTABLE VENTILATOR can provide oxygenation and ventilation in a mechanical test lung and preclinical porcine model across a range of clinically relevant parameter settings.

METHODS

1. Design: mechanical, electrical, software, safety

NYAHENDE PORTABLE VENTILATOR was designed to replace manual ventilation of a bag valve resuscitator when a conventional ventilator device is unavailable (Fig. 1A-B). NYAHENDE PORTABLE VENTILATOR features include VT (200-800 mL), RR (10-40 bpm), TI (0.5-1.5 s), and adjustable patient-initiated breath sensing (-1 to -20 cm H2O). NYAHENDE PORTABLE VENTILATOR can use low flow oxygen (5-15 L/min) from widely available sources (e.g. concentrators, hospital wall-source, tanks, and liquid oxygen reservoirs). NYAHENDE PORTABLE VENTILATOR senses the patient inspiratory effort below a software-calculated pressure threshold to trigger a breath. Patient-NYAHENDE PORTABLE VENTILATOR synchrony is facilitated by clinician titration of the triggering threshold. Auto-cycling can be reduced by increasing the triggering threshold (e.g. more negative). Conversely, ineffective triggering is reduced by decreasing the sensing threshold (e.g. less negative). Patients unable to trigger breaths (e.g., weakness, neuromuscular blocker-induced paralysis, central apneas) receive mandatory breaths at the set VT, RR, and TI. Total RR will be determined by the patient-triggered rate and the set rate. NYAHENDE PORTABLE VENTILATOR provides visual and auditory alarms for circuit blockage, air-leaks, low pressure (e.g. disconnection), high airway pressure (50-70 cm H2O), motor, and electric failure. The audible power loss alarm has a backup battery. A high visibility enclosure facilitates rapid troubleshooting of the circuit and motor-bag interface (Fig. 1B). If NYAHENDE PORTABLE VENTILATOR fails, clinicians can quickly open the enclosure to access the bag and provide manual ventilation (Fig. 1C). This capability is a key safety feature of the NYAHENDE PORTABLE VENTILATOR design. Figure 1D shows the breathing circuit components used in animal experiments. The patient exhalation valve (CPR-2 bag, Mercury Medical, Clearwater, FL) includes a manual adjustable PEEP valve. The resuscitator bag (adult Ambu® Spur® II bag, AMBU Inc., Columbia, MD) is centered in a cradle and secured on both ends by an elastic cord inside the unit. The bag PEEP valve (Ambu Disposable PEEP Valve, 0-20 cm H2O size) is set to 0 cm H2O, and PEEP is adjusted manually on a second PEEP valve interfaced to the patient exhalation valve. Two pressure sensing lines (3/16” ID, 22mm OD AirLife connector) are used for circuit pressure monitoring and breathe triggering assist. An FiO2 analyzer (MaxO 2+AE, Maxtec, Salt Lake City, UT) was interfaced into the breathing circuit for all animal experiments.

Statistical analysis

Data in graphs is shown as mean ± SE. Two-tail T test and one-way ANOVA were used for all comparisons. A value of $p < 0.05$ was considered statistically significant. Pearson Correlation Coefficient (PCC) was computed to test correlation between two variables.

Additionally, the performance of four brands of bags (AMBU Spur II, Hudson, Medline, Mercury) was tested with NYAHENDE PORTABLE VENTILATOR running continuously for 7 days at VT 800 ml and RR 50 bpm. Data for each bag was collected at VT of 400 mL. The correlation slope and standard deviation were calculated to indicate when bag performance started to decline. A slope correlation closest to 1 indicates bag is able to achieve the targeted VT for all parameters in the test matrix. The AMBU Spur II bag performed the best (correlation slope between 0.93-1.03, data not provided). Figure 2B shows experiments with seven Spur II AMBU bags. Values computed from the BIOPAC data were consistent with the set controls on the NYAHENDE PORTABLE VENTILATOR instrument. The data demonstrates the consistent performance of AMBU Spur II bag (400 mL VT, 15 bpm RP, 1 sec TI) over seven days of continuous NYAHENDE PORTABLE VENTILATOR operation. At day 4 there was a significant variation in VT resulting from a shift of bag position in the cradle. AMBU bag degradation (scratches, loss of elasticity, loss of compliance) was observed after continuous operation (RR 50 bpm, TI -0.5 sec, VT 800 mL) starting at day 4, however performance was still adequate. Performance declined after 7 days, after which replacing the bag is recommended.

1.1 Accuracy of controls of instruments

Targeted VT of 400 mL was consistently delivered (SD ≤ 50 mL) to the Michigan test lung at varying compliances (20, 40, 70 mL/cm H_2O) and TI settings (0.5, 1 s) (Fig. 2C, D). PEEP and PIP showed minimal variation during continuous operation of NYAHENDE PORTABLE VENTILATOR for 7 days at VT of 800 mL and RR of 50 bpm (Fig. 2E). FiO_2 decreased significant.

Normal lung: Before experiments, the blood gas and hemodynamic responses from switching to NYAHENDE PORTABLE VENTILATOR were compared with the veterinary ventilator baseline (Narkomed 2B, Drager, Germany). Switching from the veterinary ventilator (FiO_2 100%) to NYAHENDE PORTABLE VENTILATOR (FiO_2 73%) caused a decrease in PaO_2 from 467.5 ± 25.8 mm Hg [62.3±3.4 kPa] to 307.3±51.9 mm Hg [41±6.9 kPa] attributed to the difference in FiO_2 between the two devices (Table 1). The blood gas responses at different VT and RR were compared with their respective baseline values (Fig. 3) at constant TI (1 s), PEEP (5 cm H_2O), and flow rate (5 L/min). Mean $PaCO_2$ in arterial blood at baseline VT (200 mL) was 74.8±3.8 mm Hg [10 ±0.5 kPa]. Figure 3A demonstrates that increasing VT and with and with fixed RR at 20 bpm, lowered $PaCO_2$ to physiological level (≤40 mm Hg [5.3 kPa]) in all animals ($p<0.01$). . Changes from high to low $PaCO_2$ (e.g., low to high VE) was associated with significant decreases in FiO_2 (0.998 PCC) similar to test lung data using a fixed oxygen decreases in FiO_2 (0.998 PCC) similar to test lung data using a fixed oxygen flow rate.

Saline lavage lung injury: Hypoxemia following saline lavage was confirmed in all six pigs The average arterial PaO_2 , $PaCO_2$ and pH at baseline was 69.5±8.6 mm Hg [9.3±1.1 kPa], 43.1±2.2

mm Hg [57.5±0.3 kPa] and 7.4±0.02, respectively. Similar to pre-lavage baseline, an increase in VT while maintaining a constant RR (20 bpm) led to a significant decrease in arterial PaCO2 level ($p<0.005$) and FiO2. Mean PaCO2 (mm Hg [kPa]) at 200 mL, 400 mL and 600 mL was 72.7±7.1 [9.7±0.9], 63.7±4.1 [8.5±0.5] and 45.3±3.8 [6.0±0.5], respectively. Increasing RR, demonstrated a similar decline in PaCO2 ($p<0.001$) and decrease in FiO2 (0.984 PCC). In 5 out 6 pigs, increasing PEEP effectively improved oxygenation of the saline injured lung (Fig. 3E). Incremental PEEP steps from 5-20 cm H2O led to significant increase in PaO2 from 62.3±7.4 mm Hg [8.3±0.99 kPa] to 287.5 ±14.2 [mm Hg 38.3±1.9 kPa] ($p<0.01$).

Discussion

The shortage of mechanical ventilators due to the COVID-19 pandemic has led to attempts to repurpose hand-operated AMBU bags into automated bag-compression devices (6-10, 13-18). In 2020, our group developed and tested the Automated Bag Breathing Unit (NYAHENDE PORTABLE VENTILATOR), to assist with the shortage of conventional ventilators (1-2). NYAHENDE PORTABLE VENTILATOR is designed for training healthcare providers with limited respiratory care expertise, which may be critical in pandemics. Importantly, NYAHENDE PORTABLE VENTILATOR uses widely available resuscitation bags and circuit components and can be quickly mass-produced to potentially mitigate ventilator shortages. NYAHENDE PORTABLE VENTILATOR is not a full-featured ICU ventilator, but a device that provides automated compression of a bag valve resuscitator. The FDA classifies these devices as "emergency resuscitators" and they typically provide controlled ventilation with a fixed oxygen flow rate, adjustable RR and VT , manual PEEP valve, and basic alarms such as high airway pressure or power failure (21-22). To our knowledge, NYAHENDE PORTABLE VENTILATOR is the only resuscitator providing a software-based pressure-sensing algorithm with adjustable triggering thresholds. This is an important feature of ventilation in patients with acute respiratory failure or when weaning patients from ventilation (23). Despite a growing number of approved FDA Emergency Use Authorization (EUA) resuscitators, few have published specifications or pre-clinical testing results and none have reported clinical trials in patients (24-28). Here we report NYAHENDE PORTABLE VENTILATOR is capable of providing physiological gas exchange in a short-term (6-8 hours) adult-size porcine model of normal and saline lavage lung injury. A saline lavage injury model was chosen for simplicity and reproducibility. Saline lavage causes surfactant washout with readily recruitable lung and rapid recovery, but does not reflect the severity or heterogeneity of clinical acute respiratory distress syndrome (19, 28). As expected, PaO2 increased with incremental PEEP and PaCO2 decreased with incremental minute ventilation by adjusting VT or RR. It is important to understand that automated resuscitators, including NYAHENDE PORTABLE VENTILATOR, have significant limitations compared to fully functional ICU ventilators (10, 22, 29-30). Due to the use of a fixed oxygen flow source delivered FiO2decreases with increases in VT or RR and may be a significant factor contributing to oxygen desaturation in patients. NYAHENDE PORTABLE VENTILATOR has no capacity for automated flow augmentation or leak compensation, such that PEEP decays during the exhalation phase. PEEP decay may be clinically significant in patients with long exhalation times, Broncho pleural fistulas, or endotracheal cuff-leaks, resulting in loss of lung recruitment.

Additional limitations of NYAHENDE PORTABLE VENTILATOR and similar emergency resuscitators include a lack of measuring actual VT delivery (e.g. set bag VT plus spontaneous breath VT) which may be significantly greater than the clinician set VT (or less in the setting of air leaks). There is no automated inspiratory or expiratory pause feature to assess inspiratory plateau pressure or auto PEEP, respectively. In contrast to ICU ventilators, there are no pressure, volume, or flow graphics to assess respiratory mechanics or patient-ventilator synchrony. Patient work of breathing and NYAHENDE PORTABLE VENTILATOR-patient synchrony assessment could not be readily reproduced in this anesthetized animal model and should be evaluated in clinical trials.

The NYAHENDE PORTABLE VENTILATOR design currently does not have an integrated battery backup for use as a transport device. However, in case of electrical or motor failure, the AMBU bag may be removed from the enclosure and used manually. This feature is an advantage over resuscitation devices that rely on a continuous source of compressed air. Durability of the NYAHENDE PORTABLE VENTILATOR device may be limited by the lifespan of the electric motor and AMBU bag (approximately 30 days and 7 days of continuous operation, respectively). NYAHENDE PORTABLE VENTILATOR's limitations are inherent to the simplicity and low-cost design goal of achieving rapid mass production in a ventilator shortage scenario. These deficiencies are potentially addressable by close patient monitoring to include use of pulse oximetry, end-tidal CO2, FiO2 analyzer, and a VT respirometer.

Conclusions

The NYAHENDE PORTABLE VENTILATOR emergency resuscitator supports short term oxygenation and ventilation in an animal model across a range of parameter settings that may potentially provide a low-cost solution to adult ventilator shortages. Clinical trials of NYAHENDE PORTABLE VENTILATOR (and similar emergency resuscitation bag devices) are necessary to establish safety and efficacy before use in patients with diverse etiologies of respiratory failure.

List of Abbreviations

BP – blood pressure

ETCO2 – end-tidal carbon dioxide

FiO2 – inspired oxygen

HR – heart rate

ICU – intensive care unit

PaCO2 – partial pressure of carbon dioxide

PaO2 – partial pressure of oxygen

PCC – Pearson correlation coefficient

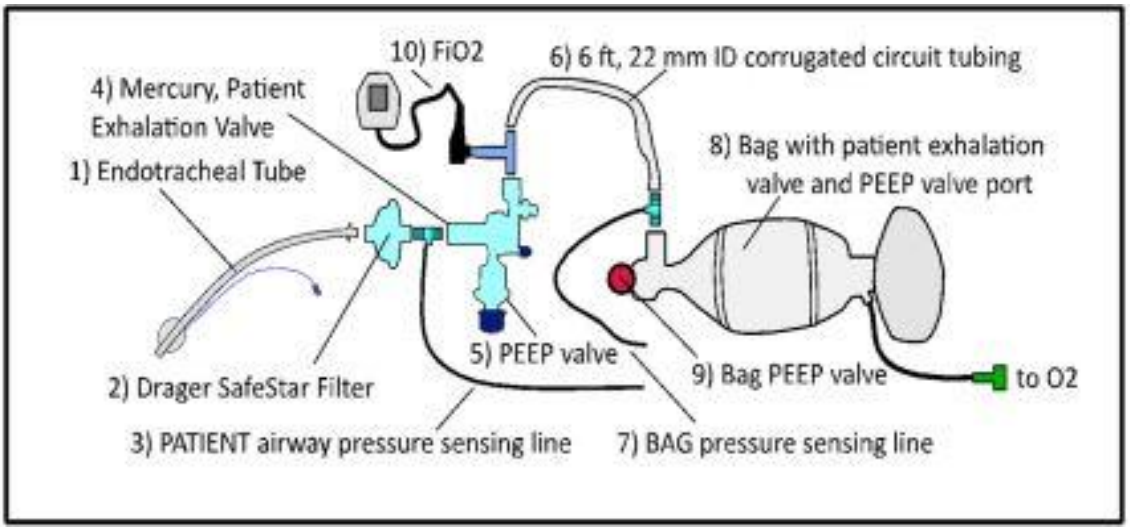
PEEP – positive end-expiratory pressure

RR – respiratory rate

TI - inspiratory time

VE - minute ventilation

VT - tidal volume



A schematic diagram of The Nyahende portable ventilator