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EXPERIMENTAL PAPER

Increasing ventilator surge capacity in disasters: Ventilation of four adult-human-sized sheep on a single ventilator with a modified circuit☆

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Summary
Objective: Recent manmade and natural disasters have focused attention on the need to provide care to large groups of patients. Clinicians, ethicists, and public health officials have been particularly concerned about mechanical ventilator surge capacity and have suggested stockpiling ventilators, rationing, and providing manual ventilation. These possible solutions are complex and variously limited by legal, monetary, physical, and human capital restraints. We conducted a study to determine if a single mechanical ventilator can adequately ventilate four adult-human-sized sheep for 12 h.
Methods: We utilized a four-limbed ventilator circuit connected in parallel. Four 70-kg sheep were intubated, sedated, administered neuromuscular blockade and placed on a single ventilator for 12 h. The initial ventilator settings were: synchronized intermittent mandatory ventilation with 100% oxygen at 16 breaths/min and tidal volume of 6 ml/kg combined sheep weight. Arterial blood gas, heart rate, and mean arterial pressure measurements were obtained from all four sheep at time zero and at pre-determined times over the course of 12 h.
Results: The ventilator and modified circuit successfully oxygenated and ventilated the four sheep for 12 h. All sheep remained hemodynamically stable.

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Conclusion: It is possible to ventilate four adult-human-sized sheep on a single ventilator for at least 12 h. This technique has the potential to improve disaster preparedness by expanding local ventilator surge capacity until emergency supplies can be delivered from central stockpiles. Further research should be conducted on ventilating individuals with different lung compliances and on potential microbial cross-contamination.

Introduction

The World Trade Center attacks, South and Central Asian Earthquakes, Indian Ocean Tsunami, SARS epidemic, and H5N1 influenza have focused attention on the need to provide care to large groups of patients during disasters. Public health planners and emergency and critical care providers have been particularly concerned about the availability of mechanical ventilation.[1–3] This concern is based on experience with the 1918 influenza pandemic,[4] 2001 anthrax attacks,[5] 2003 SARS outbreak,[5] and human H5N1 influenza cases,[5,6] which have all been characterized by rapidly progressive, severe, and often fatal respiratory failure.

Clinicians, ethicists, and public health officials have suggested rationing mechanical ventilation, providing manual ventilation, and stockpiling ventilators.[2,3,7,8] Each of these possible solutions are complex and variously limited by legal, monetary, physical, and human capital restraints.[2] A number of groups have proposed modifications of ventilator circuits that would permit a single ventilator to support multiple patients.[9–11] In some cases, these adaptations have been tested using lung models and other simulators. No previous work has demonstrated the feasibility of multiple patient adaptations in a biologically relevant model using standard equipment. We conducted a study using four adult-human-sized sheep to test whether it is possible to provide mechanical ventilation to multiple patients using a single ventilator and commonly available equipment.

Methods

Study design

This study used a large animal (sheep) model to determine whether multiple adult patients can be ventilated simultaneously using a single ventilator. We chose sheep for several reasons, including the availability of adult-human-sized animals and our group's earlier experience working with this species.[12] Most importantly, sheep respiratory physiology is similar to human physiology[13,14] and the animals have been used to model respiratory changes in a variety of states, including pregnancy,[14] asthma,[15] emphysema,[16] respiratory distress syndrome,[17] and acute lung injury.[18]

Animal participants

Female 69—75 kg sheep (*Ovis aries*) were supplied by Barton West End Facilities in Oxford, NJ. After delivery the sheep were maintained in livestock pens with free access to food and water. The animals were fasted for 8 h before the experiment. A temperature of 20—23 °C and a 12:12 h light/dark cycle were maintained in the housing area. This study was approved by the SUNY Downstate Medical Center Animal Care and Use Committee and followed American Association for Laboratory Animals care guidelines.

Preparation and anesthesia

The animals were pre-medicated with IM glycopyrrolate 0.02 mg/kg (A.H. Robins, Richmond, VA). After 10 min, the sheep were sedated with IM ketamine 10 mg/kg (Fort Dodge Animal Health, Fort Dodge, IO) and IM xylazine 0.1 mg/kg (Bayer, Shawnee Mission, KA). After the sedatives took effect, the animals were weighed, placed on the operating table, and attached to cardiac monitoring and pulse oximetry leads. A jugular venous line was inserted, and a 3 mg/kg bolus of thiopental (Abott, North Chicago, IL) was administered to facilitate laryngoscopy and intubation. The sheep were then intubated orotracheally with a 9 mm internal diameter cuffed endotracheal tube (Rusch, Chicago, IL) and manually ventilated with 100% oxygen separately during the set-up phase. The femoral artery was cannulated with a 16-gauge single lumen catheter. This line was used for blood pressure measurements and arterial blood gas sampling. Invasive blood pressure, pulse oximetry, and heart rate were recorded using Propaq #106 monitors (Protocol Systems, Beaverton, OR). Sedation was maintained throughout the remainder of the experiment with intravenous thiopental and boluses of xylazine. At the time that all four animals were ready to be placed on the mechanical ventilator, vecuronium bromide (Bedford labs, Bedford, OH) 0.15 mg/kg bolus was administered and re-bolused each hour. Neuromuscular blockade was carefully maintained to ensure that the animals were fully dependent on the ventilator and to prevent asynchronous breathing and high peak airway pressures.

Ventilation

A four-limb ventilator circuit was created using components employed in routine patient care at SUNY Downstate Medical Center. This circuit was similar to that described by Neyman and Irvin[9] but the configuration differed slightly as pictured (Figure 1). The circuit is composed of four standard unheated ventilator circuits with four microbial filters on each expiratory limb. The inspiratory and expiratory flow was split using a single aerosol 'T' adaptor and 2 male/female 'T' adaptors (Hudson Respiratory Care Inc., Temecula, CA). The circuit was attached to a single Servo-i ventilator loaned to us by Maquet Critical Care (Solno, Sweden) for the purpose of this experiment. We chose this model because it is currently in use in our institution and would be employed in the event of a disaster. The institution contracted with Maquet Critical Care before this project was conceived.

Table 1 Initial characteristics of subjects

Subject	pH	pO_2 (mmHg)	pCO_2 (mmHg)	MAP (mmHg)	HR (bpm)	O_2 saturation (%)
A	7.35	473	43	100	150	100
B	7.42	81	40	94	72	96
C	7.49	420	37	116	157	100
D	7.49	420	37	116	157	100

MAP, mean arterial pressure, HR, heart rate.

All four animals received 12 h of simultaneous mechanical ventilation. We chose 12 h because ventilators from US Strategic National Stockpile can be delivered within this time frame.[19,20] The initial ventilator settings were: synchronized intermittent mandatory ventilation with a respiratory rate of 16 breaths/min, tidal volume of 6 ml/kg combined sheep weight, 5 cmH_2O of positive end-expiratory pressure (PEEP) and fraction of inspired oxygen of 100%. As is common in human critical care, we anticipated that it might be necessary to provide suctioning, change tidal volume and respiratory rate, add additional PEEP and provide occasional short (60 s) periods of manual ventilation to recruit alveoli in individual animals. We recorded all such interventions.

Positioning

Positioning is an important issue in this experiment, because supine ventilation has been shown to worsen respiratory variables significantly in this species relative to prone ventilation.[21] In contrast, prone positioning failed to benefit humans with hypoxemic respiratory failure in a randomized controlled trial[22], and supine positioning is standard in humans. In addition, we were able to provide adequate supine ventilation to sheep for a short period of time in our previous work[12]. Given all these considerations, we decided to initiate the experiment with supine positioning and turn the animals into the prone position if they experienced problems with ventilation and oxygenation that our veterinarian consultant deemed to be species-specific and position-dependent.

Figure 1 Modified ventilator circuit.

Data collection

The time that all sheep were placed on the ventilator using the initial settings was called time zero ($t = 0$). We obtained arterial blood gases from a femoral arterial line (pH, pCO_2, pO_2) and recorded heart rate (HR) and mean arterial pressure (MAP) at $t = 0$ and every 15 min during the first hour of the experiment, every 30 min for the 2nd and 3rd hours, and every 60 min until the 12th hour. We used a Gem Premier 3000 (Instrumentation Laboratory, Lexington, MA) for blood gas analysis. Data was recorded in real time.

Data analysis

The data were reported as means ± standard deviations calculated using Excel X for MAC Service Release 1 (Microsoft Co., Seattle, WA, USA). Independent sample t-tests were calculated using Analyze-It Version 1.73, Analyze-It Software Ltd., UK.

Results

Base line respiratory and hemodynamic characteristics of the four subjects were similar except for sheep B which became apneic during induction and was resuscitated (Table 1).

Figure 2 graphs the subjects' ventilatory status as measured by pCO_2 over 12 h. At the beginning of the experiment each subject had a very similar pCO_2 (range 37—43 mmHg). As the experiment progressed over the first 6 h, each supine subjects' pCO_2 increased variably from baseline. At the end of the first quarter of the experiment, our veterinarian determined that CO_2 retention resulted from the subjects' supine position. Sheep B, A, D and C were sequentially repositioned from the supine to the prone position. This repositioning resulted in a large and sustained decrease in pCO_2 in all the subjects (Figure 2).

Figure 3 describes each subject's oxygenation over the experimental period. Sheep A, C, and D had very little variability in oxygenation at time = 0. Sheep B suffered significant hypoxia before intubation secondary to an adverse reaction to the induction agents. We provided less than 1 min of manual ventilation to this animal at 1 h and 30 min. We were not able to optimize oxygenation in sheep B until it was repositioned (supine to prone) at 3 h and 25 min. All sheep demonstrated a significant ($p < 0.002$) increase in oxygenation when we compared pO_2 pre- to post-repositioning.

Because repositioning each sheep from supine to prone was labor- and time-intensive and thus could only be done sequentially, the individual animals sharing this circuit had

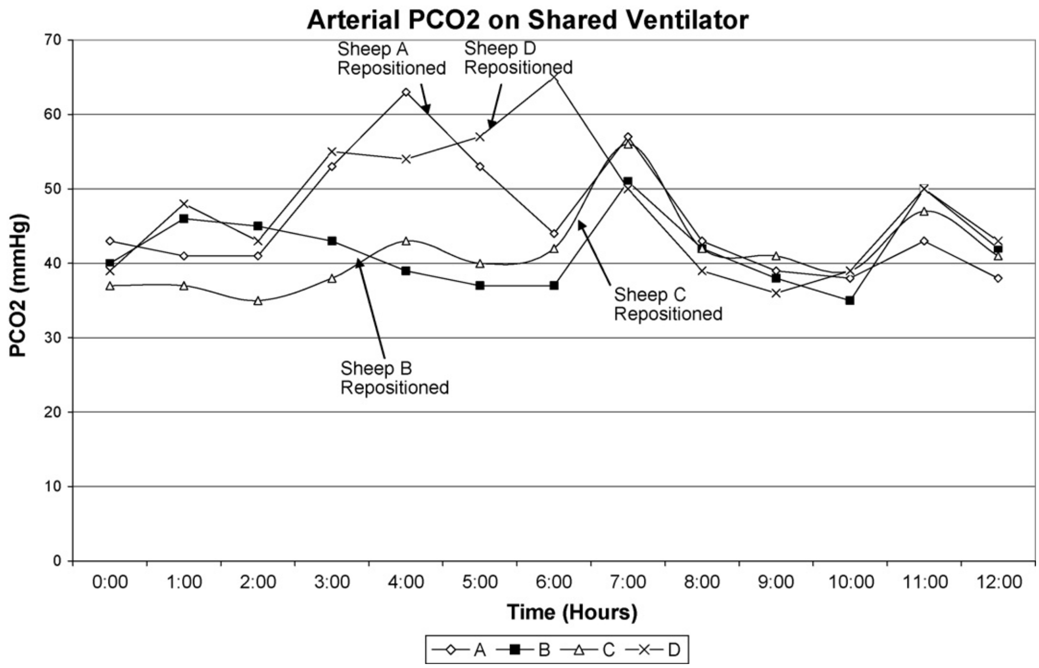

Figure 2 Arterial pCO_2.

different respiratory mechanics for several hours. As demonstrated by following Figures 2 and 3 over the full 12 h trial period, the circuit succeeded in ventilating and oxygenating all subjects despite these differences.

Discussion

In this trial, our group demonstrated that it is possible to simultaneously ventilate four adult-human-sized sheep for at least 12 h using a single mechanical ventilator. We employed a circuit proposed by Neyman and Irvin[9] and tested only with artificial lungs. Writers commenting on this system questioned whether it would function for anything more than ''very short-term positive pressure ventilation augmentation.''[23] We believe that this trial begins to address these issues and is a significant step in the development of a multi-patient ventilation strategy for the initial response to disasters involving a surge of patients with acute respiratory failure.

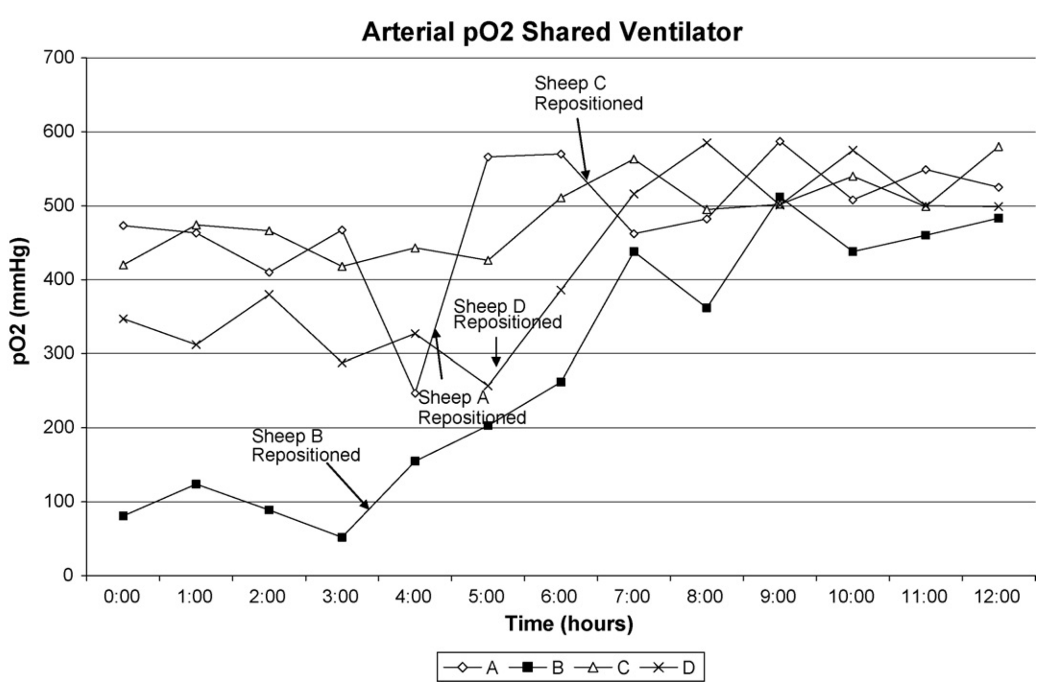

Figure 3 Arterial pO_2.

To insure that this trial would be clinically relevant, we used a standard full-feature ventilator, a simple volume-controlled ventilation strategy, and equipment that is readily available in hospitals in the US, Europe and other countries with well-developed critical care resources. Because it is not logistically or financially possible for hospitals to stock many spare ventilators for emergencies,[3] it is critical that each one be used maximally in a disaster. Although ventilating multiple patients on a single full-feature ventilator effectively prevents the application of the most advanced functions, the loss of these features for a single patient has to be weighed against the likely death of other patients who are denied any positive pressure ventilation because available resources are not fully employed. The Working Group on Emergency Critical Care and others recognize the need for clinicians to use inexpensive ventilators and simple ventilatory strategies during public health crises.[2,3] As noted above, the 12 h period that we chose for our experiment is sufficient to allow US National Security Stockpile ventilators to be delivered.[19,20] At that point, depending on the magnitude of the event and individual circumstances, local providers could decide whether it is appropriate to re-deploy the full featured ventilators back to individual patients.

Limitations

This trial was designed only to evaluate whether a modern ventilator can maintain multiple adult-human-sized animals for a significant period of time. The study leaves several issues to be addressed in future research. Chief among these are the effect of differential lung compliance on the distribution of ventilation, and cross-contamination.

In a disaster, it is possible and even likely that patients needing ventilation will have suffered similar respiratory insults. Despite this, lung compliance may differ so much between individuals that adequate ventilation of the least compliant patients on a circuit may not be achievable,[23] even during the interval proceeding ventilator delivery from the SNS. While this is a major concern, it must be weighed against the inability of existing equipment and personnel to provide any ventilation at all to certain patients. In addition, there are several factors that may limit problems that do arise.

First, patients with poor lung compliance tolerate and even benefit from low-volume hypercapnic ventilation.[24] Although patients with better lung compliance would receive a greater share of tidal volume, this process can be controlled by setting conservative (e.g. 40—45 cmH_2O) peak pressure limits for the circuit as a whole. In addition, Neyman and Irvin have suggested that this problem can be minimized by assigning groups of patients to common ventilators based on lung compliance.[9]

Because of the inevitable differences between individual animals, the sheep in our study exhibited differences in pCO_2 and other measures. It is likely that this variation is at least in part attributable to differential compliance and flow resistance, and this did not compromise the overall function of the circuit. Future research using a model that intentionally creates flow resistance and compliance differences will allow this issue to be thoroughly addressed. Finally, we anticipate that further research will allow us to test whether simple real-time modifications along specific limbs of the circuit may mitigate the magnitude of asymmetric ventilation.

Although the study was not designed to address microbiological issues, there are several factors that reduce the likelihood of microbial cross-contamination on this circuit. First, the ventilator we used provides bias flow at 2 l/min, which ''maintains a positive flow from the ventilator to the y-piece at all times, leaving the inspiratory side uncontaminated.''[25] Because significant patient-sourced colonization of the expiratory limbs of respiratory circuits has been documented,[26] we isolated the individual expiratory limbs in our circuit with standard antimicrobial filters. Although the effectiveness of these filters varies significantly,[27] high quality ceramic filters could be employed and positioned anywhere on the circuit. As with all other issues in disaster medicine, clinicians must balance concerns about cross-contamination against the need to ration mechanical ventilation and the feasibility of other options. Although manual ventilation of individual patients during disasters has been discussed,[2,3] earlier work suggests that manual resuscitators can be a significant source of microbial contamination that may place patients and rescuers at risk.[28,29] Further research is needed to fully evaluate the risk of cross-contamination, as well as the usefulness of different filters[27] and other protective measures.

Conclusion

In this study, we demonstrated that it is possible to ventilate four adult-human-sized sheep on a single full-feature ventilator for at least 12 h. We employed standard equipment and an easy-to-construct circuit that was first tried in an artificial lung model.[9] This technique has the potential to extend local ventilatory support resources until emergency supplies can be delivered. Further research should be conducted on differential lung compliance and microbial cross-contamination.

Conflict of interest

The authors have no conflicts of interest to disclose.

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