Transtracheal ventilation with a novel ejector-based device (Ventrain) in open, partly obstructed, or totally closed upper airways in pigs†

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Abstract

Background: Transtracheal access and subsequent jet ventilation are among the last options in a ‘cannot intubate–cannot oxygenate’ scenario. These interventions may lead to hypercapnia, barotrauma, and haemodynamic failure in the event of an obstructed upper airway. The aim of the present study was to evaluate the efficacy and the haemodynamic effects of the Ventrain, a manually operated ventilation device that provides expiratory ventilation assistance. Transtracheal ventilation was carried out with the Ventrain in different airway scenarios in live pigs, and its performance was compared with a conventional jet ventilator.

Methods: Pigs with open, partly obstructed, or completely closed upper airways were transtracheally ventilated either with the Ventrain or by conventional jet ventilation. Airway pressures, haemodynamic parameters, and blood gases obtained in the different settings were compared.

Results: Mean (sd) alveolar minute ventilation as reflected by arterial partial pressure of CO2 was superior with the Ventrain in partly obstructed airways after 6 min in comparison with traditional manual jet ventilation [4.7 (0.19) compared with 7.1 (0.37) kPa], and this was also the case in all simulated airway conditions. At the same time, peak airway pressures were significantly lower and haemodynamic parameters were altered to a lesser extent with the Ventrain.

Conclusions: The results of this study suggest that the Ventrain device can ensure sufficient oxygenation and ventilation through a small-bore transtracheal catheter when the airway is open, partly obstructed, or completely closed. Minute ventilation and avoidance of high airway pressures were superior in comparison with traditional hand-triggered jet ventilation, particularly in the event of complete upper airway obstruction.

Key words: airway obstruction; equipment, ventilator; ventilation, transtracheal

A ‘cannot intubate–cannot oxygenate’ (CICO) scenario characterizes the clinical situation of multiple failed attempts at tracheal intubation combined with an impossibility to ventilate or oxygenate the patient with non-invasive techniques and special airway manoeuvres. In this life-threatening situation, recovery of spontaneous breathing is commonly recommended but not always reliably possible. When the oxygen saturation begins to reduce, a percutaneous transtracheal airway needs to be established immediately.

Several techniques for transtracheal access have been described. Anaesthetists usually prefer a needle cricothyrotomy to more invasive surgical techniques because of their daily experience in puncture and Seldinger techniques. After needle cricothyrotomy, oxygenation can be maintained by transtracheal
jet ventilation, and several types of high-pressure jet ventilators are available for this purpose. These devices are able to generate an adequate inspiratory flow even through a small-bore catheter, but the upper airway must be unobstructed to ensure the egress of gas. Unfortunately, in a CICO scenario it is commonly not known whether there is an underlying or concomitant upper airway obstruction. In the event of a totally obstructed upper airway, conventional jet ventilation via a narrow-bore catheter is potentially life threatening because passive expiration through the small-lumen cannula is limited as a result of its high resistance. Barotrauma and haemodynamic impairment can result from the increasing intrathoracic pressure.

In such a situation, active expiratory assistance is necessary so that gas can egress through the same small lumen in order to avoid intrathoracic air trapping. Decades ago, the application of negative pressure to augment expiration was suggested, but not a single specific ventilation device is available for CICO management in clinical practice so far. However, ejector pumps for industrial use have been designed to generate subatmospheric pressures, based on Bernoulli’s principle. Recently, a small number of studies were able to demonstrate the generation of an adequate minute volume through a small-lumen transtracheal catheter. This was achieved by expiratory ventilation assistance in simulated upper airway obstruction using a modified industrial ejector. A subsequent development is the Ventrain (Dolphys Medical, Eindhoven, The Netherlands), a handy, single-use, manually operated, high-pressure source ventilator for emergency use. The Ventrain has become commercially available and was specially designed to ventilate through a small-bore transtracheal catheter. The aim of the present study was to evaluate the Ventrain in simulated clinical situations of open, partly obstructed, and totally closed upper airways using an in vivo model.

**Methods**

**Animals and preparation**

After approval of the study protocol by the institutional review board (No. 02-052/10), 10 female pigs with a mean body weight of ~30 kg were obtained from a commercial farm source (Fraitz Brothers, Pölzig, Germany). The experiments were conducted at the animal research facility of the Jena University Hospital, and relevant aspects of the ARRIVE guidelines were followed. Animals were housed in group pens at a temperature of 20°C and a 12 h–12 h light–dark cycle. The animals had free access to water and were fed regularly (grist).

The animals were fasted overnight before preparative surgery, but had free access to water. Premedication was ketamine (1200 mg i.m.) and midazolam (10 mg i.m.), and general anaesthesia was induced with sufentanil (1 μg kg⁻¹), propofol (3 mg kg⁻¹), and pancuronium (0.2 mg kg⁻¹) via a peripheral vein. Anaesthesia was maintained with a continuous infusion of propofol (20 mg kg⁻¹ h⁻¹), sufentanil (1 μg kg⁻¹ h⁻¹), and pancuronium (0.1 mg kg⁻¹ h⁻¹). The adequacy of anaesthesia and analgesia was assured by monitoring of haemodynamic parameters and clinical signs, and relatively high doses of anaesthetic drugs were administered continuously during the experiment. After the onset of anaesthesia, a tracheal tube of 6 mm internal diameter (Hi-Lo Endotracheal tube; Covidien-Nellcor, Boulder, CO, USA) was inserted orally. The cuff was initially blocked with 50 cm H₂O. Pressure-controlled ventilation (Servo Ventilator 900C; Siemens AG, Nürnberg, Germany) was adjusted to maintain the end-expiratory CO₂ tension at 35–40 mm Hg. The fraction of inspired oxygen was 0.4, with a PEEP value of 5 cm H₂O. The right internal jugular vein was dissected and a three-lumen central venous catheter (Cerofix; B. Braun, Melsungen, Germany) inserted. The right carotid artery was cannulated (Arterial Leader Cath 2.7 Fr; Vygon, Ecouen, France) to allow blood gas analysis and invasive measurement of blood pressure. The ECG, pulse oximetry (Datex AS/3; Datex-Ohmeda, Helsinki, Finland), body temperature, haemodynamic, and ventilatory parameters were recorded at different time points. After dissection and exposure of the trachea, a transtracheal catheter of 2 mm internal diameter and 7.5 cm length (Emergency Transtracheal Airway Catheter; Cook Medical, Bloomington, IN, USA) was inserted into the trachea below the distal end of the tracheal tube. A second, identical catheter was inserted one transtracheal cartilage above the primary cannula to measure the airway pressure. The correct positions of both transtracheal catheters were verified by fibre-optic bronchoscopy (LF-2; Olympus Europa GmbH, Hamburg, Germany). A balanced electrolyte solution (Jonosteril; Fresenius Kabi AG, Bad Homburg, Germany) was administered to compensate for fluid loss. During each individual experiment, arterial blood samples were withdrawn at specific time points (0, 2, 4, and 6 min) for blood gas analysis. Baseline values were obtained during ventilation via a tracheal tube at a fractional inspired O₂ of 0.4. At the end of the experiments, the animals were killed with a lethal dose of potassium chloride.

**Experimental protocol**

After establishing a stable haemodynamic and respiratory situation for at least 15 min, the ventilator was disconnected from the tracheal tube and different predefined upper airway situations were simulated in random order (open, partly obstructed, or totally closed upper airway). The randomized order was generated by a freely available Internet-based randomization tool (random.org). However, the scenario ‘manual jet ventilation with a totally closed upper airway’ was always performed last because pilot studies had shown a potentially fatal outcome of jet ventilation in these conditions (Table 1). Each simulated airway situation was applied to all animals for 6 min. Between the scenarios, each animal was allowed a recovery phase of ~15 min in order to re-establish the baseline haemodynamic and pulmonary status. This was confirmed by blood gas analysis and arterial blood pressure measurement. A partly closed airway was simulated by using a PEEP valve set at 20 cm H₂O (Ambu GmbH, Bad Nauheim, Germany), and a completely closed upper airway was obtained by clamping the tracheal tube at the proximal end. During these sequences, the cuff of the tracheal tube was blocked at 80 cm H₂O. Oxygenation through the transtracheal catheter was achieved using either the Ventrain (Dolphys Medical) or an emergency manual jet ventilator (Manujet III; VBM Medizintechnik, Sulz a. N., Germany). Both devices were driven with 100% oxygen. For the Ventrain, a pressure-compensated flowmeter was used.
with an oxygen flow of 15 litres min\(^{-1}\), the respiratory frequency was set at 12 bpm, and the inspiratory-to-expiratory (I:E) ratio was 1:1. In a separate series of experiments, the expiratory time was prolonged (I:E ratio 1:2) to analyse the effect of the inspiratory-to-expiratory time ratio on airway pressures during ventilation with the Ventrain. Jet ventilation using the Manujet was carried out with a driving pressure of 0.5 bar, a frequency of 12 bpm, and an I:E ratio of 1:4. The prolonged expiratory time was chosen because pilot studies showed an incompatibility with survival in the situation of ventilation with the Manujet whilst applying an I:E ratio of 1:1 in totally closed upper airways. The airway devices were always operated by the same investigator using an electronic metronome (Seiko SQ-70; Seiko Instruments Inc., Torrance, CA, USA) to ensure a precise I:E ratio.

### Table 1

|------------|---------------------------------|---|---------------------------------|---|---------------------------------|---|---------------------------------|---|---------------------------------|---|---------------------------------|---|
| 1          | 4                                | 2 | 1                               | n.d. | n.d. | 3 | 5 | 6 | 1                               | n.d. | n.d. | 3 | 5 | 6 
| 2          | 5                                | 1 | 3                               | n.d. | n.d. | 2 | 4 | 6 | 1                               | n.d. | n.d. | 2 | 4 | 6 
| 3          | 5                                | 3 | 2                               | n.d. | n.d. | 1 | 4 | 6 | 1                               | n.d. | n.d. | 1 | 4 | 6 
| 4          | 2                                | 3 | 5                               | n.d. | n.d. | 4 | 1 | 6 
| 5          | 1                                | 2 | 5                               | 4 | 3 | 6 | 7 | 8 | 1                               | 5 | 6 | 4 | 2 | 8 
| 6          | 1                                | 6 | 7                               | 5 | 3 | 2 | 4 | 8 | 1                               | 5 | 6 | 4 | 2 | 8 
| 7          | 7                                | 5 | 6                               | 1 | 4 | 3 | 2 | 8 | 1                               | 5 | 6 | 4 | 2 | 8 
| 8          | 4                                | 5 | 6                               | 7 | 2 | 1 | 3 | 8 | 1                               | 5 | 6 | 4 | 2 | 8 
| 9          | 2                                | 7 | 1                               | 4 | 6 | 5 | 3 | 8 | 1                               | 5 | 6 | 4 | 2 | 8 
| 10         | 5                                | 4 | 6                               | 3 | 1 | 7 | 2 | 8 | 1                               | 5 | 6 | 4 | 2 | 8 

Fig 1. Arterial oxygen partial pressure (P\(_{aO2}\)) during transtracheal ventilation with Ventrain or manually hand-triggered jet ventilation (Manujet). Data are mean (SD) for both devices in open, partly obstructed, or totally closed upper airways (n=10). *P<0.05 vs Ventrain in totally closed upper airways.
Statistical analysis

A power calculation performed a priori showed that a sample size of n=10 would be required to detect changes in blood gases of 20% (σ) at β=0.8. Statistical analysis was performed using the Sigma-Plot 12.0 software package (Jandel Scientific, San Rafael, CA, USA), and data are presented as the mean (±) after undertaking the Shapiro–Wilk test to assess data distribution. The results obtained at the end of each specific airway situation managed with both ventilation devices were tested using Student’s unpaired t-test. The time course within an experimental group was evaluated by one-way analysis of variance (ANOVA) followed by pairwise multiple comparison procedures according to the Holm–Sidak method. A value of P<0.05 was considered statistically significant.

Results

Blood gas analysis

Arterial oxygen partial pressure

The inspiratory oxygen fraction of 0.4 at baseline was increased to 1.0 at the beginning of transtracheal ventilation. Transtracheal oxygenation with both ventilation devices resulted in an overall increase in arterial oxygen partial pressure (PaO₂). Highest values were seen during ventilation in partly obstructed airways with both devices, and after use of the Ventrain in completely closed airways. The PaO₂ was slightly lower but still supranormal during transtracheal ventilation with both the Manujet and the Ventrain in open upper airways. However, when using the Manujet in a completely closed airway, PaO₂ decreased below the baseline at the end of the experiment (at time point 6 min), and thus lay significantly below the PaO₂ values achieved with the Ventrain in the same conditions (Fig. 1).

Arterial carbon dioxide partial pressure

Transtracheal ventilation in an open upper airway situation led to a significant increase in arterial carbon dioxide partial pressure (PaCO₂) with both ventilation devices, whereby at the end of the 6 min period the PaCO₂ was significantly higher with the Manujet compared with the Ventrain (Fig. 2).

Manual jet ventilation during partial upper airway obstruction resulted in a moderate but significant increase in PaCO₂ compared with baseline. In contrast, ventilation with the Ventrain led to a significant decrease in PaCO₂ in comparison with both baseline values and values generated with the Manujet in the same airway conditions.

Thus, carbon dioxide elimination, which is largely dependent on alveolar ventilation, was most effective when using the Ventrain in a completely closed upper airway situation. In this condition, PaCO₂ values remained significantly below baseline at all points in time and were also significantly lower compared with all other ventilation arrangements of the experiment. Ventilation with the Manujet in a closed airway resulted in a
Pa$_{CO_2}$ that remained steady at baseline throughout the time course (Fig. 2).

**Peak airway pressure**

An I:E ratio of 1:1 was used during ventilation with the Ventrain, whereas an I:E ratio of 1:4 was chosen using the Manujet. In comparison with mechanical ventilation via a tracheal tube, which was taken as baseline peak airway pressure (PAW), ventilation with a high-pressure gas source through a transtracheal cannula in open upper airway conditions resulted in distinctly lower airway pressures. No differences in PAW were observed when comparing the Ventrain with the Manujet in open upper airway situations. With a partly closed airway and using the Manujet, PAW was almost unaffected compared with baseline and remained stable throughout the observation time. In contrast, ventilation with the Ventrain in the same conditions led to a moderate decrease in PAW compared with baseline, and these pressures were significantly lower than the ones generated by the Manujet. The complete closure of the upper airway markedly increased airway pressures during the use of both devices. However, while the Ventrain generated PAW values around 30 mbar, the Manujet led to significantly higher pressures of 50 mbar (Fig. 3).

In a separate experiment, PAW was measured for Ventrain ventilation in partly obstructed or completely closed upper airways accompanying a shorter expiration time (I:E 1:1) was not observed when the expiratory phase was prolonged (I:E 1:2; Fig. 4).

**Impact on haemodynamics**

Transtracheal ventilation with a high-gas-pressure source in totally closed airways resulted in a profound decrease in mean arterial blood pressure (MAP) during the observation period of 6 min no matter which device was used (Fig. 5). The MAP decreased from baseline values of ~60 mm Hg to below 30 mm Hg. During partial obstruction of the upper airway, MAP was significantly higher at the end of the observation period when the Ventrain was used compared with the Manujet values and lay slightly above the baseline value. In open upper airways, MAP was slightly above the baseline value with either ventilation device (Fig. 5).

The central venous pressure (CVP) as a surrogate parameter for intrathoracic pressure decreased minimally from baseline during ventilation with both devices in open upper airway conditions (Fig. 6) and remained almost identical throughout the experimental time course in both groups. When the upper airway was partly obstructed, CVP did not change during ventilation with the Ventrain, whereas use of the Manujet led to a moderate increase of CVP. After complete obstruction of the upper airway, ventilation with the Ventrain resulted in a significant increase of the CVP to ~12 mm Hg. However, a marked increase in CVP to values approaching 25 mm Hg for the entire observation period...
Discussion
In this experimental study, the novel ventilation device Ventrain was used for transtracheal ventilation in anaesthetized pigs during three different scenarios of open, partly obstructed, or completely closed upper airways. The effects of the Ventrain with respect to airway pressures, blood gases, and haemodynamic parameters were compared with conventional jet ventilation using the manually operated device, Manujet.

In a CICO scenario, the underlying anatomical situation is largely unclear; it is usually not known whether the upper airway is open, partly obstructed, or completely closed. In the worst-case scenario, the initially life-saving jet ventilation can turn rapidly into a life-threatening action, because it may result in barotrauma and cardiocirculatory failure. Therefore, any device applied in a CICO situation should be able to ensure both inspiratory and expiratory gas flow. Keeping in mind the known limitations of high-pressure jet ventilation in this respect, our experiment was designed to investigate whether the Ventrain device might perform differently in a variety of airway scenarios.

First of all, our results showed that, at least for the limited duration of the experiments, oxygenation was maintained in each airway scenario, with the exception of the situation ‘conventional jet ventilation in a closed airway’, where $P_{aO_2}$ decreased significantly below baseline towards the end of the experiment. Still, it is reassuring that the goal of oxygenation in a CICO situation can probably be achieved with either device as long as there is not a completely obstructed airway. In this situation, however, the Ventrain may outperform the Manujet.

In the present study, peak airway pressure markedly increased during transtracheal ventilation in animals with totally closed upper airways. The average peak airway pressure was $\sim 20$ mbar lower during ventilation with the Ventrain however, and reached values around $30$ mbar compared with the Manujet, where it approached $50$ mbar. The most convincing explanation for the advantageous effects of the Ventrain on airway pressures is the principle of augmented expiration by expiratory ventilation assistance. While the Manujet does not allow the egress of gas through the infraglottic catheter during the expiratory phase and is therefore dependent on an open upper airway for expiration, the Ventrain is able to work as a bidirectional airway. In the event of an obstructed airway, both the delivery of oxygen to the lungs and the egress of respiratory gas can take place through the same lumen. Thus, the risk of hyperinflation and subsequent barotrauma is substantially reduced.

Changes in the ratio of inspiratory to expiratory time during use of the Ventrain in completely obstructed upper airways resulted in pronounced differences in airway pressure. As mentioned above, for hand-triggered jet ventilation with Manujet an I:E ratio of 1:4 was chosen for all experiments because a shorter expiration time has been shown to result in fatal outcomes. An I:E ratio of 1:1 during ventilation with Ventrain led to a moderate increase in peak airway pressures only in closed upper airways. In this situation, extension of the expiratory time with an I:E ratio of 1:2 resulted in a marked decrease in airway pressures. This pressure was comparable with that generated in a partly
obstructed airway. While up to this point in time there have not been any in vivo studies investigating the effect of a prolonged expiration time with the Ventrain, our study shows that prolongation of the expiratory phase in Ventrain ventilation will lead to only a minor increase in peak airway pressure even in complete upper airway obstruction. Thus, if hyperinflation occurs during use of the Ventrain it is necessary to adjust the I:E ratio. Careful clinical assessment (e.g. watching chest movements, listening, and feeling for gas flow) during ventilation may help to prevent hyperinflation on the one hand and the development of a negative intrathoracic pressure on the other.

A high intrathoracic pressure may not only cause lung injury but may also result in haemodynamic impairment. In animals with completely closed airways, CVP increased considerably with both ventilation devices, whereby CVP values with the Manujet significantly exceeded those with the Ventrain. Correspondingly, MAP markedly decreased during transtracheal ventilation in completely obstructed airway situations with either device. However, as PAW and CVP were significantly lower with the Ventrain, one would have expected a less extensive decrease in MAP. The reason for the similar reduction in MAP with both devices is not entirely clear. Most probably, the increase in intrathoracic pressure in either instance was sufficient to cause marked hypotension in these particular animals at the given hydromechanical status and depth of anaesthesia. Maybe, a moderate intravascular volume deficit was revealed despite the infusion of a balanced electrolyte solution during the whole experiment. Interestingly, during an I:E ratio of 1:2 with the Ventrain in closed airways, MAP was almost unaffected compared with a shorter length of expiration (I:E ratio of 1:1; data not shown). Despite the critical decrease in MAP, all animals of the Ventrain group with totally closed upper airways recovered within a few minutes, whereas three animals died during conventional jet ventilation in the same conditions.

Finally, the present study shows that in situations of complete upper airway obstruction, expiratory ventilation assistance eliminates carbon dioxide more efficiently than conventional jet ventilation. In all airway scenarios, ventilation with the Ventrain resulted in significantly lower $P_{A\text{CO}_2}$ values at the end of the experiment compared with traditional jet ventilation. Generally, the least efficient elimination of carbon dioxide was observed in animals with open airways, because in these animals ventilation is not very effective as a result of the partial back stream of gas through the upper airway. During ventilation with the Ventrain, however, the elimination of carbon dioxide tended to be the more efficient the more the airway was obstructed. Recently, Berry and colleagues compared the impact of the Ventrain and the Manujet on physiological outcome during transtracheal ventilation in an obstructed airway model in postapnoeic sheep. Both devices achieved rapid reoxygenation in this model, but only the Ventrain provided effective ventilation at low airway pressures when the airway was critically obstructed.

Although our experimental study has provided some interesting and relevant results, there are some important limitations. One limitation of the present study lies in the moderate weight of the animals. The results obtained cannot necessarily be applied to adult patients with a much higher body weight and a higher required respiratory minute volume. We assumed that

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**Fig 5** Invasively measured mean arterial blood pressure (MAP) during transtracheal ventilation with Ventrain or manually hand-triggered jet ventilation (Manujet). Data are mean (±SEM) for both devices in open, partly obstructed, or totally closed upper airways (n=10). *P<0.05 compared with ventilation with Manujet in partly obstructed upper airways.
oxygen consumption in smaller pigs would be considerably higher compared with humans. Several experimental studies that quantified oxygen consumption in pigs with a body weight of ~30 kg found oxygen consumption at rest to be 7–8 ml kg$^{-1}$ min$^{-1}$. Thus, the required minute volume can be estimated to be within the range of that of an average adult. Moreover, a bench study of a lung model has shown the Ventrain to achieve the remarkable minute volume of up to 7.1 litres min$^{-1}$ through a catheter of 2 mm internal diameter. This minute volume would indeed be adequate for adult patients. In addition, providing 7000 ml of pure oxygen per minute should be adequate to oxygenate even obese patients in a CICO situation.

A further limitation of our study concerns the methodology. In order to minimize the number of laboratory animals, all experiments were conducted in each animal in random order, but hand-triggered jet ventilation in combination with totally obstructed airways was always performed last in the series of experiments without randomization because of the possibility of fatal outcomes as a result of barotrauma.

In conclusion, our experiments using the Ventrain in live pigs with varying degrees of airway obstruction have shown that even in the worst case of an unforeseeable completely closed airway, sufficient oxygenation and ventilation through a small-bore catheter, accompanied by only moderately increased airway pressure, is eminently possible. The minute volume generated by the Ventrain is not only adequate for reoxygenation but also able to prevent hypercapnia.

Authors’ contributions
Study design: M.P., N.P.P., R.G.
Data analysis: M.P., T.R., A.S.
Writing the paper: M.P.
Revising the paper: all authors.

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Declaration of interest
None declared.

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