Resuscitation 84 (2013) 1150–1155

Contents lists available at SciVerse ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Experimental paper

The effects of an automatic, low pressure and constant flow ventilation device versus manual ventilation during cardiovascular resuscitation in a porcine model of cardiac arrest☆,☆☆

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ARTICLE INFO

Article history:
Received 24 November 2012
Received in revised form 8 February 2013
Accepted 15 February 2013

Keywords:
Cardiac arrest
Ventricular fibrillation
Cardiopulmonary resuscitation
CPR
Oxylator

ABSTRACT

Background: Cardiac arrest is an important cause of mortality. Cardiopulmonary resuscitation (CPR) improves survival, however, delivery of effective CPR can be challenging and combining effective chest compressions with ventilation, while avoiding over-ventilation is difficult. We hypothesized that ventilation with a pneumatically powered, automatic ventilator (Oxylator®) can provide adequate ventilation in a model of cardiac arrest and improve the consistency of ventilations during CPR.
Methods/results: Twelve pigs (~40 kg, either sex) underwent 3 episodes each of cardiac arrest and resuscitation consisting of 30 s of untreated ventricular fibrillation, followed by 5 min of CPR, defibrillation, and ~30 min of recovery. During CPR in each episode, pigs were ventilated in 1 of 3 ways in random balanced order: manual ventilation using AMBU bag (12 breaths/min), low pressure Oxylator® (maximum airway pressure 15 cmH_2O with 20 L/min constant flow in automatic mode [Ox15/20]), or high pressure Oxylator® (maximum airway pressure 20 cmH_2O with 30 L/min constant flow in automatic mode [Ox20/30]). During CPR, both Ox15/20 and Ox20/30 resulted in higher levels of positive end expiratory pressure than manual ventilation. Ox15/20 ventilation also resulted in higher arterial pCO_2 than manual ventilation. Ox20/30 ventilation yielded higher arterial pO_2 and a lower arterial–alveolar gradient than manual ventilation. All pigs were successfully defibrillated, and no measured haemodynamic variables were different between the groups.
Conclusion: Ventilation with an automatic ventilation device during CPR is feasible and provides adequate ventilation and comparable haemodynamics when compared to manual bag ventilation.

1. Introduction

Approximately 400,000 people have an out-of-hospital cardiac arrest each year in North America, and survival to hospital discharge is less than 10% [1]. Cardiopulmonary resuscitation (CPR), consisting of chest compressions and ventilations, improves survival [2]. However, the optimum sequence, timing and coordination of chest compressions and ventilation is not known.

Chest compressions are often delayed or interrupted to allow for securing an airway, or delivery of ventilations [3]. The latest ILCOR guidelines recommend interrupting chest compressions (albeit briefly) in order to ventilate, although recent data show that interruptions in chest compressions during CPR lowers survival [4,5]. Even when CPR is performed by a team of professionals and delays are minimal, manually ventilated patients are often hyperventilated, which lowers survival [6]. "Chest compression only" CPR has been suggested as a means to reduce the deleterious effects of compression interruptions and hyperventilation. However, CPR

☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at http://dx.doi.org/10.1016/j.resuscitation.2013.02.017.
☆☆ St. Michael's Hospital Animal Care Committee Protocol Number – ACC 742.
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http://dx.doi.org/10.1016/j.resuscitation.2013.02.017

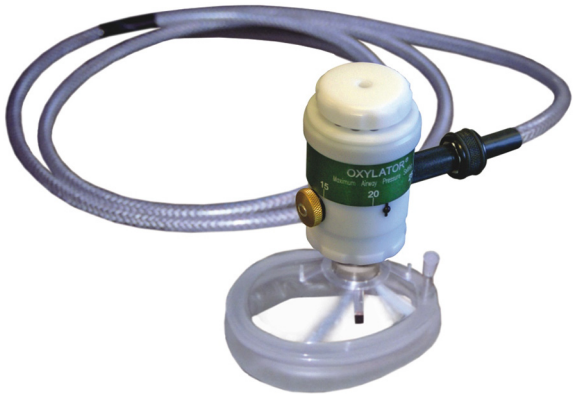

Fig. 1. The Oxylator® device. Image downloaded from www.cprmedic.com with the permission of CPR Medical Devices Inc.

without ventilation adversely affects survival in animal studies, and the American Heart Association does not support removal of ventilations from CPR [3,7,8]. Thus there is a need for a method of ventilation which can be applied with minimal delay, does not lead to hyperventilation, and which does not require cessation of chest compressions.

In this study, we tested the Oxylator®, an automatic ventilation device, in experimental CPR (see Fig. 1) [9–12]. This simple-to-use, non-electronic device can be applied with minimal delay using a mask or an endotracheal tube. The device is powered by compressed gas and delivers constant inspiratory flow when airway pressure is below a preset value (2 mmHg). Once a maximum preset pressure during the inspiratory phase is reached, flow stops and passive exhalation takes place until airway pressure falls to ~2 mmHg, triggering a new inspiratory cycle. During continuous CPR this typically results in short, small bursts of ventilation delivered between compressions (during decompression). We hypothesized that this automatic ventilation device (Oxylator®) would provide adequate ventilation and increase the efficiency of CPR despite maintaining constant positive airway pressure.

2. Methods

2.1. Surgical preparation

This prospective randomized controlled study was performed according to the guiding principles of the Canadian Council on Animal Care and approved by the Animal Care Committee of St. Michael's Hospital. Twelve healthy Yorkshire pigs (39.7 ± 4.4 kg) of either sex were fasted overnight except for free access to water, and sedated with ketamine (20 mg/kg i.m. ['Ketalean' Bimeda-MTC Animal Health Inc., Cambridge, ON]). Anesthesia was induced with thiopental sodium (8 mg/kg i.v. [Hospira Healthcare Corp., Saint-Laurent, QC]) and maintained with isoflurane (1–4% via inhalation [Pharmaceutical Partners of Canada Inc., Richmond Hill, ON]) for the duration of the surgical procedure. Pigs were placed in the dorsal recumbent position and intubated by standard endotracheal intubation technique. Mechanical ventilation was provided by an Ohmeda® ventilator (Ohio Medical Products, Madison, WI), with a tidal volume and rate set to maintain the arterial pH, pCO_2 and pO_2 in the physiological range (pH 7.35–7.45, pCO_2 35–45 mmHg, pO_2 > 100 mmHg) measured via arterial blood samples. Core temperature was maintained between 36.5 °C and 38.5 °C using a heating blanket (Micro-Temp® Pump, Charlottesville, VA). Normal saline was infused at a rate of 2–4 mL/kg/hr to prevent hypovolemia. Defibrillation patch electrodes (EDGE Quik-Combo®, Physio-Control, Redmond, WA) for defibrillation and cardiac monitoring were adhered to the left and right chest. A monophasic action potential (MAP) catheter (EP Technologies Inc., Sunnyvale, CA) was positioned at the apex of the right ventricle via the right femoral vein to allow for pacing and inducing VF. Two micromanometer-tipped catheters (Mikro-Tip® Transducer, Millar Instruments Inc., Houston, TX) were placed in the aortic arch via the right femoral artery to allow for the recording of aortic pressure (AoP), and in the right atrium via the left femoral vein for the recording of the right atrial pressure (RAP). A catheter sheath attached to a pressure transducer (Cobe CDX3, Lakewood, CA) was inserted in the left femoral artery for arterial pressure monitoring and for drawing arterial blood gas samples during the experiment. Once all introducing sheaths were in place, 2500 IU of heparin (Sandoz, Boucherville, QC) were administered in order to fully anti-coagulate the animal. A pressure transducer was connected to a side port of the ET tube for measuring airway pressure. Three limb leads of the surface electrocardiogram, the endocardial MAP catheter, AoP, RAP and airway pressure were amplified using a custom-made amplifier (Cartesian Labs, Toronto, ON) and recorded using a custom-made software program (Electrophysiological Recording System – Acqui II, Cartesian Labs, Toronto, ON). End tidal CO_2 ($ETCO_2$), positive end-expiratory pressure (PEEP) and oxygen saturation (SpO_2) were measured with a CO_2SMO Plus (Novametrix Medical Systems Inc., Wallingford, CT). Arterial blood gases were collected before the induction of VF (baseline) and after 4 min of CPR in each episode.

2.2. Experimental procedure

Each pig underwent 3 episodes of cardiac arrest as follows. VF was induced using a 2 s, 7.5 V, fully rectified, 60 Hz current via the right atrial endocardial MAP catheter. The ET tube was immediately disconnected from the mechanical ventilator and ET tube cuff pressure was assessed to ensure that the trachea was sealed. After 30 s of untreated VF, CPR was performed for 5 min followed by defibrillation and then 20–30 min of rest before starting the next episode (see Supplementary Data Figure 1). Pigs were assigned to 1 of 3 different ventilation methods during CPR in each episode in a computer generated, random, balanced order:

(1) Manual ventilation using AMBU bag (12 breaths/min; Ambu Inc., Glen Burnie, MD)
(2) Low pressure Oxylator® (maximum airway pressure 15 cmH_2O with 20 L/min constant flow, CPR Medical Devices Inc., Markham, ON) (Ox15/20)
(3) High pressure Oxylator® (maximum airway pressure 20 cmH_2O with 30 L/min constant flow (Ox20/30).

During the inspiratory phase, the Ox15/20 device delivers gas at a constant rate of 20 L/min until airway pressure rises to 11 mmHg (15 cmH_2O). At this point flow ceases and passive exhalation takes place (expiratory phase) until airway pressure reaches ~2 mmHg which triggers a new inspiratory phase. Similarly, the Ox20/30 device delivers air at 30 L/min until airway pressure rises to 15 mmHg (20 cmH_2O). Both devices can function in an "automatic" mode (described above), a "manual assist" mode or a "constant flow" mode.

2.3. Resuscitation protocol

After 30 s of untreated VF, closed-chest standard chest compressions were delivered continuously with a pneumatically-driven automatic piston device (CPR Controller, Ambu Inc., Glen Burnie, MD). The compression rate was 95 min^{-1} with an 8 cm circular compression pad positioned over the sternum; compression depth was 4–6 cm (approx. 25%) of the anterior-posterior diameter of the chest wall. After each compression the chest wall was allowed to recoil

Table 1
Ventilatory parameters.

	Baseline			After 4th min of CPR			Recovery		
	Manual	Ox15/20	Ox20/30	Manual	Ox15/20	Ox20/30	Manual	Ox15/20	Ox20/30
AWPp (mmHg)	16 ± 5	15 ± 4	15 ± 4	36 ± 7	13 ± 2**	18 ± 3**	14 ± 4	15 ± 3	17 ± 4
AWPt (mmHg)	2.4 ± 3.1	2.1 ± 2.5	2.0 ± 3.0	0.6 ± 1.3	1.3 ± 2.1	4.2 ± 3.1*	2.2 ± 3.1	1.3 ± 2.8	1.9 ± 3.2
AWPm (mmHg)	6.1 ± 2.5	5.5 ± 2.8	5.6 ± 2.5	3.7 ± 2.4	5.9 ± 2.2*	8.3 ± 2.0**	5.3 ± 3.1	5.4 ± 1.7	6.6 ± 2.7
$ETCO_2$ (mmHg)	40 ± 2	40 ± 3	39 ± 2	22 ± 5	33 ± 6**	25 ± 5	39 ± 2	41 ± 2	39 ± 2
a-pH	7.39 ± 0.07	7.42 ± 0.05	7.41 ± 0.07	7.54 ± 0.08	7.45 ± 0.09*	7.51 ± 0.09	7.40 ± 0.06	7.36 ± 0.03#	7.36 ± 0.06
a-pCO_2 (mmHg)	41 ± 3	40 ± 2	40 ± 5	24 ± 4	36 ± 8**	26 ± 6	39 ± 5	42 ± 3	42 ± 3
a-pO_2 (mmHg)	441 ± 59	469 ± 67	444 ± 45	302 ± 71	343 ± 90	418 ± 36**	456 ± 57	420 ± 54	419 ± 57
A-a-O_2 gradient	220 ± 57	194 ± 67	218 ± 44	381 ± 73	326 ± 88	262 ± 37**	208 ± 57	241 ± 51	242 ± 58
PEEP (cmH_2O)	3.8 ± 1.2	3.5 ± 1.1	3.8 ± 0.8	1.1 ± 0.6	2.7 ± 0.8**	3.3 ± 1.3**	4.2 ± 0.8	3.1 ± 0.8	4.01 ± 0.2
SpO_2 (%)	98 ± 2	99 ± 1	98 ± 1	91 ± 7	92 ± 5	91 ± 9	98 ± 1	97 ± 1	98 ± 2

AWP: airway pressure; $ETCO_2$: end tidal CO_2; a-: arterial; A-a: arterial–alveolar; PEEP: positive end expiratory pressure; SpO_2: saturation pressure O_2; *p*: peak; t: trough; m: mean. All baseline comparisons NS, CPR comparisons.
* $P < 0.01$ compared to Manual group during same time point.
** $P < 0.001$ compared to Manual group during same time point.
\# $P < 0.01$ compared to baseline time point in same group.

Table 2
Haemodynamic parameters.

	Baseline			After 4th min of CPR			Recovery		
	Manual	Ox15/20	Ox20/30	Manual	Ox15/20	Ox20/30	Manual	Ox15/20	Ox20/30
CPP (mmHg)	67 ± 20	68 ± 19	69 ± 17	20 ± 7	25 ± 9	23 ± 11	61 ± 11	61 ± 12	61 ± 15
AoPs (mmHg)	91 ± 21	94 ± 18	93 ± 22	57 ± 17	57 ± 14	62 ± 22	88 ± 11	81 ± 15	87 ± 21
AoPd (mmHg)	66 ± 18	68 ± 15	70 ± 16	23 ± 5	24 ± 5	27 ± 14	64 ± 7	60 ± 9	63 ± 14
AoPm (mmHg)	74 ± 18	76 ± 15	77 ± 18	32 ± 7	32 ± 7	43 ± 22	75 ± 9	68 ± 11	71 ± 18

CPP: coronary perfusion pressure; AoP: aortic pressure; s: systolic; d: diastolic; m: mean. All comparisons NS.

completely without any impedance from the compression device. Ventilation proceeded via one of the methods described above and compressions were never interrupted with any method. When in use, the automatic ventilation devices were attached to the end of the ET tube and powered by a small tank containing 100% O_2. With these devices, airway pressure climbed steeply every time a compression occurred leading to cessation of inspiratory airflow soon after the start of compression. At the end of the 5 min CPR period, animals were defibrillated with an external defibrillator (Medtronic-PhysioControl Lifepak 12™, Medtronic Inc, Redmond, WA) using 200J, 250J, 300J and 360J × 3 shocks as needed. Following return of spontaneous circulation (sinus rhythm and aortic systolic pressure ≥50 mmHg [ROSC]), the mechanical ventilator was reconnected at baseline settings. No other therapeutic interventions were performed before, during, or after CPR.

2.4. Data analysis

Parameters measured during CPR were averaged over 30 s starting after 4 min of CPR had elapsed. Coronary perfusion pressure (CPP) was calculated as the difference between diastolic AoP and diastolic RAP.

2.5. Statistics

All results are expressed as the mean ± standard deviation. All three groups were compared to each other via one way ANOVA using GraphPad Prism 5 for Windows (v5.04, GraphPad Software Inc., La Jolla, CA). A Dunnett's multiple comparison post-test was used to compare the Ox15/20 and Ox20/30 groups to Manual. A *P*-value < 0.05 was regarded as significant.

3. Results

There were no significant differences in any baseline parameters between the groups (see Tables 1 and 2).

3.1. Ventilation

During CPR, adequate ventilation with the automatic ventilation devices (Oxylator®) was achieved at lower airway pressures relative to standard manual bag ventilation. The end tidal CO_2 was higher with the automated ventilator. Arterial blood gases demonstrated that there was less hyperventilation with the automatic ventilator. In the Ox15/20 group, a lower arterial pH, and higher arterial pCO_2 were measured relative to manual bag ventilation ($P = 0.0459$, 0.0001 respectively). In the Ox20/30 group, there was a higher arterial pO_2, and a lower arterial alveolar gradient than manual bag ventilation ($P = 0.0010$, 0.0009 respectively, see Table 1 and Fig. 2). Both automatic ventilators produced significantly higher levels of PEEP than manual bag ventilation. Manual bag ventilation produced significantly higher peak, lowest trough and mean airway pressure relative to the automatic devices. Peripheral oxygen saturation was not different between any of the ventilation methods. After defibrillation in each episode when the animals had been reconnected to the mechanical ventilator for 15 min,

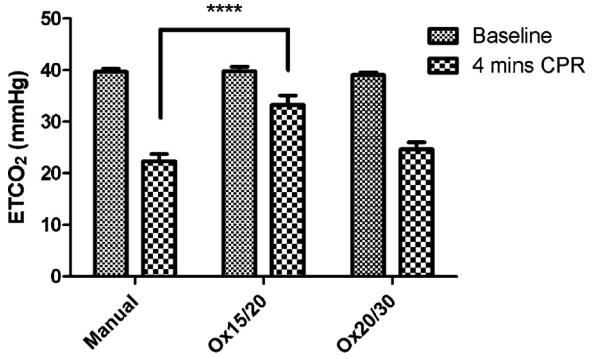

Fig. 2. End tidal carbon dioxide at baseline and after 4 min of CPR. ***$P < 0.001$ compared to Manual.

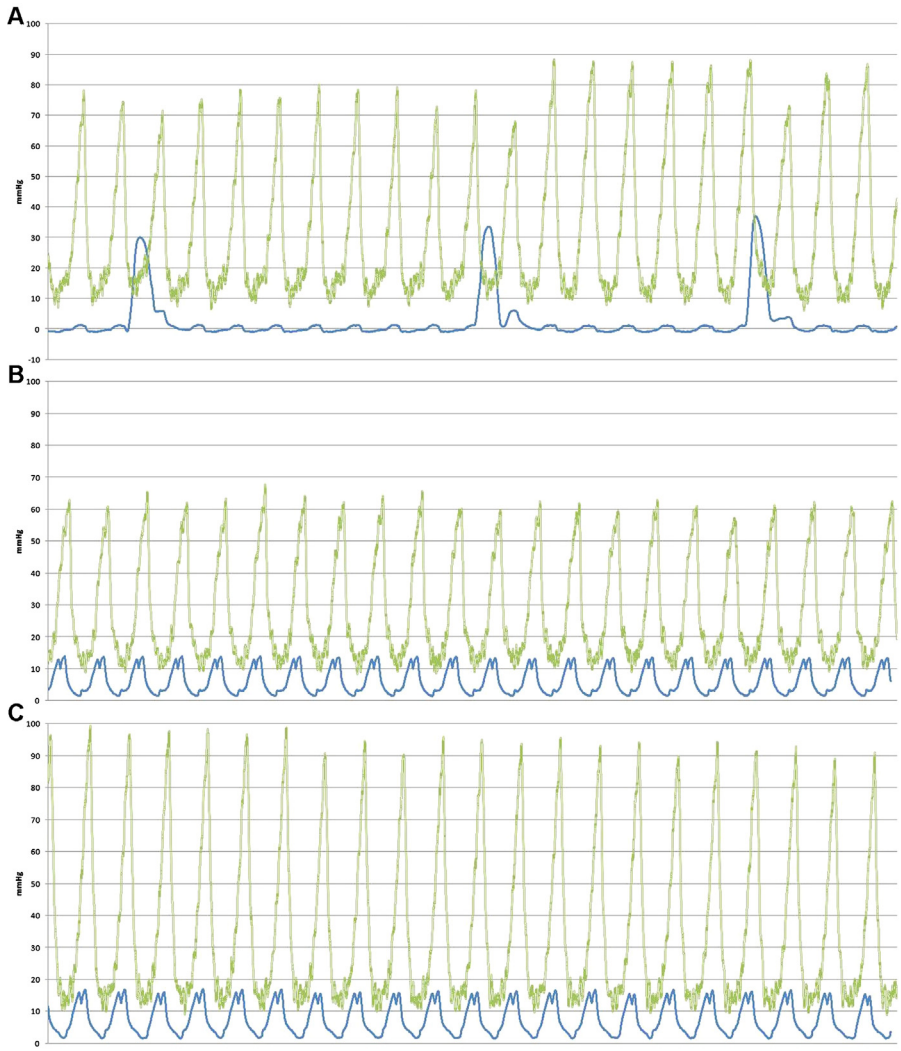

Fig. 3. Airway pressure and aortic pressure over 15 s. Fifteen seconds of representative superimposed airway pressure (dark blue line) and AoP (light green line) curves and AoP curves during the 4th min of CPR for each ventilation method. A = manual bag ventilation, B = Ox15/20, C = Ox20/30. In the manual group, each squeeze of the bag resulted in a transient drop in peak AoP. Both automatic ventilator groups show similar patterns of ventilation. In both groups, ventilation rate during CPR is identical to compression rate. When AoP was at a minimum, the devices began to deliver flow causing a rise in airway pressure. Airway pressure rose quickly as both the force of the compression and the inspiration by the device coincided. Flow ceased when pressure reached the maximum threshold leading to a transient drop in airway pressure. This drop was quickly reversed by the continuing force of the compression leading to a second peak in the airway pressure curves. Both AoP and airway pressure dropped as the compression finished. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

ventilatory parameters were not different from baseline values with the exception of arterial pH in the Ox15/20 group.

3.2. Haemodynamics

There were no significant differences between the groups in terms of CPP or AoP during CPR (see Table 2). After 15 min of recovery, haemodynamic variables were not different from baseline values. During CPR, the Ox15/20 and Ox20/30 devices "cycled" with each compression-decompression cycle, providing inspiratory flow during decompression and passive expiration during compression (see Fig. 3).

3.3. Defibrillation

All episodes of VF were successfully defibrillated. There were no significant differences between the groups in terms of number of shocks required for defibrillation, cumulative defibrillation energy or total duration of VF (see Table 3). Use of the Ox15/20 or Ox20/30 device does not reduce defibrillation success.

4. Discussion

This study shows that ventilation with the automatic devices provided adequate ventilation without changing defibrillation requirements or haemodynamic measurements during CPR. Potential advantages of ventilation with these automated devices include ventilation with lower airway pressure, reduced hyperventilation and improved arterial oxygenation during CPR. As with other ventilatory strategies, the increase in PEEP achieved with these automated ventilators may have been responsible for the reduced A-a gradient and improved arterial oxygenation.

Table 3
Defibrillation parameters.

	Total shocks	Cumulative energy (J)	VF duration (s)
Manual	1.8 ± 1.6	458 ± 498	362 ± 25
Ox15/20	1.4 ± 1.2	327 ± 367	355 ± 19
Ox20/30	1.8 ± 1.2	414 ± 376	358 ± 19

VF: ventricular fibrillation. All comparisons NS.

The Ox15/20 device (max. pressure 11 mmHg, flow 20 L/min) is capable of producing adequate oxygenation during CPR, while yielding a significantly higher $ETCO_2$ than manual bag ventilation, and preserving pH in the normal range. $ETCO_2$ has been shown to correlate directly with cardiac output in low flow states and, according to current guidelines, can be used as a marker of CPR quality [8,13]. The Ox20/30 device (max. pressure 15 mmHg, flow 30 L/min) produces a significantly higher arterial pO_2 than manual bag ventilation and also significantly less ventilation perfusion mismatch (as estimated by the alveolar–arterial O_2 gradient).

The most recent AHA guidelines do not recommend the use of automatic (including pressure controlled) ventilators during CPR, citing lack of research and the possibility of increasing PEEP which may reduce perfusion (Class III indication) [14]. Current theory suggests that good CPR requires negative intrathoracic pressure during decompression to "suck" blood back to the heart so that it can be pumped out by the subsequent compression [15,16]. Ventilation increases airway pressure, a surrogate of intrathoracic pressure, thus according to the theory, ventilation resulting in positive airway pressure during decompression is undesireable [17]. It is likely true that high intrathoracic pressure during decompression can impede venous return and thus lower perfusion pressures, however, the relationship between airway pressure and intrathoracic pressure is not perfectly linear [18]. Although high levels of airway pressure and PEEP are likely detrimental to CPR quality, it may be that low, but positive, levels do not significantly impair venous return. Thus low levels of airway pressure and PEEP may still allow adequate perfusion while protecting against atelectasis and pulmonary edema which may also be important factors in improving CPR quality [19].

The idea that a method of automated ventilation could be useful in CPR is not novel; other high flow or high frequency, but low pressure ventilation methods have been tested before. The Boussignac valve, jet ventilation and constant positive airway pressure ventilation (CPAP) have all been used in CPR with beneficial results [20–22]. A 2002 study by Kleinsasser et al. used CPAP in combination with pressure support ventilation (PSV) in a pig model of VF and CPR [23]. PSV detects a patient triggered inspiration and helps ventilation by delivering a preset amount of inspiratory pressure support. During CPR, PSV was triggered by the onset of the decompression phase which resulted in a form of ventilation similar to what is delivered by the Ox15/20 and Ox20/30 devices. This resulted in significantly higher arterial pO_2 and O_2 uptake (VO_2) than traditional or CPAP alone ventilation. The advantage of the devices used in the current study over these aforementioned modes of ventilation is their ability to ventilate during ROSC (which would be problematic for the Boussignac valve), and the small size of the unit (in comparison to CPAP machines and jet ventilators). Ease-of-use has also been tested in the Ox15/20 and Ox20/30 devices; a recent study demonstrated that first responders could more easily ventilate patients with these devices than with a bag-mask system even while distracted [11,12]. These devices are FDA and Health Canada approved, and are currently in routine use by EMS personnel in several jurisdictions [11,12].

The use of these automatic ventilation devices in CPR should be further studied. Given the complexity and difficulty in providing uninterrupted chest compressions while adequately ventilating (without hyperventilating) with a limited number of rescuers during a cardiac arrest, technologies that simplify this process would be a welcome addition. These devices are inexpensive, portable, non-electric, and function automatically without assistance. They make single rescuer CPR (in an intubated patient) effective, and allow a second rescuer to perform other tasks such as intravenous line insertion and drug administration. There is no need for a change in ventilation equipment or technique if ROSC occurs. The option to easily switch the device function between automatic mode (exclusively used in this study), manual assist mode and constant flow mode provides further ventilation flexibility. The results of this study may indicate that guidelines suggesting the use of any mechanical ventilators during CPR are a class III indication may need to be re-evaluated.

4.1. Limitations

The pigs used in this study were young, healthy and have none of the pathologies that lead to cardiac arrest in humans. Additionally, each pig underwent 3 cardiac arrests and results from later episodes may be affected by incomplete recovery from previous cardiac arrest(s). However, the order of experiments was random and balanced. Although the focus of this work was cardiac resuscitation, it has been shown that ventilation with PEEP can negatively affect cerebral blood flow [24]. Conflicting results have been published and the level of PEEP at which these effects appear is likely in excess of 5 cmH_2O (greater than the ~3 cmH_2O delivered by the automatic devices) [25,26]. Nevertheless it is a limitation of this study that carotid and cerebral blood flow was not measured.

5. Conclusion

Ventilation with an automatic, low inspiratory pressure, passive exhalation ventilation device during CPR is feasible and resulted in improved arterial oxygenation relative to manual bag ventilation.

Conflicts of interest

None declared

Acknowledgements

We are grateful for the technical assistance of Romeo Warner (CPR Medical Devices). This study was supported by the Keenan Research Centre in the Li Ka Shing Knowledge Institute of St. Michael's Hospital, the Heart and Stroke Foundation of Ontario and by an unrestricted grant from CPR Medical Devices Inc. (Markham, ON). Dr. Ramadeen was supported by a Heart and Stroke Foundation of Canada Jump Start Resuscitation Fellowship and Dr. Hare was supported by a Merit Award from the Department of Anesthesia, University of Toronto (Toronto, ON).

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.resuscitation.2013.02.017.

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