Clinical paper

Intrathoracic pressure regulation during cardiopulmonary resuscitation: A feasibility case-series

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Aim of the study: Intrathoracic pressure regulation (IPR) is a novel, noninvasive therapy intended to increase cardiac output and blood pressure in hypotensive states by generating a negative end expiratory pressure of −12 cm H₂O between positive pressure ventilations. In this first feasibility case-series, we tested the hypothesis that IPR improves End tidal (ET) CO₂ during cardiopulmonary resuscitation (CPR). ETCO₂ was used as a surrogate measure for circulation.

Methods: All patients were treated initially with manual CPR and an impedance threshold device (ITD). When IPR-trained medics arrived on scene the ITD was removed and an IPR device (CirQLATOR™) was attached to the patient’s advanced airway (intervention group). The IPR device lowered airway pressures to −9 mmHg after each positive pressure ventilation for the duration of the expiratory phase. ETCO₂ was measured using a capnometer incorporated into the defibrillator system (LifePak™). Values are expressed as mean ± SEM. Results were compared using paired and unpaired Student’s t test. p values of <0.05 were considered statistically significant.

Results: ETCO₂ values in 11 patients in the case series were compared pre and during IPR therapy and also compared to 74 patients in the control group not treated with the new IPR device. ETCO₂ values increased from an average of 21 ± 1 mmHg immediately before IPR application to an average value of 32 ± 5 mmHg and to a maximum value of 45 ± 5 mmHg during IPR treatment (p <0.001). In the control group ETCO₂ values did not change significantly. Return of spontaneous circulation (ROSC) rates were 46% (34/74) with standard CPR and ITD versus 73% (8/11) with standard CPR and the IPR device (p <0.001).

Conclusions: ETCO₂ levels and ROSC rates were significantly higher in the study intervention group. These findings demonstrate that during CPR circulation may be significantly augmented by generation of a negative end expiratory pressure between each breath.

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1. Introduction

The primary objective of cardiopulmonary resuscitation (CPR) is to provide sufficient blood flow to the heart and brain to facilitate return of spontaneous circulation (ROSC) and long-term restoration of vital organ function. In an effort to improve outcomes after cardiac arrest, intrathoracic pressure regulation (IPR) therapy was recently described. IPR therapy provides a negative end expiratory pressure during all or part of the time interval after a positive pressure breath. The negative end expiratory pressure results in a reduction of intrathoracic pressure to levels below atmospheric values and is associated with enhanced venous return to the heart and reduced intracranial pressure (ICP). During CPR these mechanisms enhance cardiac and cerebral perfusion. These physiological principles, which are also part of normal breathing, have been previously described. IPR therapy may be particularly beneficial during standard CPR. With standard CPR negative intrathoracic pressures develop only to a minimal degree with each chest wall recoil; this is the main force that draws blood back to the thorax and refills the heart after each chest compression. This is not an efficient process and it is one of the important reasons circulation is so poor during standard CPR. Animal studies have shown that circulation to the heart and brain can be significantly enhanced during standard CPR with IPR therapy.
In this feasibility case series, we tested the hypothesis that IPR therapy during CPR improves End tidal carbon dioxide (ETCO2). ETCO2 was measured as a surrogate marker of circulation.

2. Methods

This prospective feasibility case-series was performed from March to November 2010 in the Lucas County, OH (USA), emergency medical services (EMS) system. All adult patients treated with CPR for a non-traumatic out-of-hospital cardiac arrest of presumed cardiac etiology were treated according to American Heart Association CPR 2005 guidelines, including use of an impedance threshold device (ITD; ResQPodTM; Advanced Circulatory Systems Inc; Roseville, MN), carried by basic (B) and advanced (A) life support (LS) teams, and used on all patients, per protocol.8 The IPR device was utilized by two paramedic supervisors, only when they were on active duty, as part of this feasibility case-series. In response to the 911 call for help, CPR was provided by the first BLS team on site. When ALS personnel arrived additional advanced care was provided per AHA Guidelines recommendation. The IPR device (CirQLATOR™; Advanced Circulatory Systems Inc; Roseville, MN), was applied upon arrival of one of the two paramedic supervisors. IPR application was delayed until the supervising medic arrived. All other routine care, including the delivery of chest compression and ventilation, was performed by the on scene BLS and ALS team members. The supervising paramedic assured the IPR device was applied and used as intended. The Institutional Review Board at ProMedica approved the process of gathering and publishing data on this device evaluation.

Inclusion criteria included (a) adult patients in cardiac arrest with ongoing CPR by rescue personnel and (b) successful endotracheal intubation or successful King tube intubation. Exclusion criteria included (a) patients with preexisting do-not-resuscitate orders, and (b) patients who had return of spontaneous circulation (ROSC) before application of the IPR device. Immediately prior to placement of the IPR device, the ITD was removed from the patient’s airway.

The IPR therapy used in this evaluation requires a continuous vacuum source, a means to provide intermittent positive pressure ventilation and a switching mechanism (CirQLATOR™; Advanced Circulatory Systems Inc; Roseville, MN, USA). The device has been described previously.1,2,4 It is inserted between the patient and a ventilation source. This new device was cleared for use in patients with poor circulation by the U.S. Food and Drug Administration under the 510K process. It is connected to an advanced airway and a ventilation source, in this case a standard resuscitator bag, and it is also connected to a vacuum source and a pressure manometer, as shown in Fig. 1. After each positive pressure breath an internal mechanical switch immediately closes providing a means to actively withdraw respiratory gases at a pressure of –9 mmHg relative to atmospheric pressure. During this evaluation positive pressure ventilations were delivered with a resuscitator bag at a rate of 10/min with supplemental oxygen of 101/min, and a tidal volume of ~600 ml/breath, per AHA Guidelines.8

ETCO2, the primary evaluation endpoint, was recorded routinely (Medtronic; Redmond, WA, USA) and electronically measured using a Lifepak® 12 or 15 (Medtronic Physiocontrol, USA) monitor/defibrillator and recorded every 3 min, after intubation. ETCO2 was recorded continuously during both ITD and IPR device use. Additional data collected included patient age, gender, initial cardiac rhythm, time of 911 call, EMS arrival, and IPR placement, ROSC rates, type of advanced airways. Potential adverse device effects were monitored, in particular device malfunction, pulmonary edema as demonstrated by blood in the advanced airway during CPR or on first emergency department chest X-ray, and arrest with device still in position.

Fig. 1. Intrathoracic pressure regulation (IPR) device in a resuscitation bag circuit and effect of intrathoracic pressure regulation. The device is connected to a bag valve mask (BVM), a vacuum source, a manometer, and to the patient through an advanced airway.

2.1. Statistical analysis

The primary end point, determined a priori, in the 11 case series patients that acted as their own controls, was the comparison of ETCO2 values from immediately before device placement to the maximum value recorded during performance of CPR with the device. Secondary endpoints included comparison of mean ETCO2 values during CPR with the ITD versus mean ETCO2 values with the IPR device in the 11 case series patients, with each patient serving as their own control. In addition, the mean ETCO2 values during standard CPR with the IPR device in the 11 case series patients were measured and compared with mean ETCO2 values from 74 concurrent and consecutive controls treated with CPR and the ITD (referred herein as the control population) who were not treated with the new IPR device. All values with a normal distribution are expressed as mean ± SEM. Results were compared using a paired or unpaired Student’s t test as appropriate. A p value of <0.05 was considered statistically significant.

3. Results

A total of 11 patients were treated with the new IPR device. Demographic data, bystander CPR rates, initial cardiac rhythms and time from 911 call to first team on site and from 911 call to IPR placement are detailed in Table 1. ETCO2 values increased from an average of 21 ± 1 mmHg immediately before IPR application to an average value of 32 ± 5 mmHg and to a maximum value of 45 ± 5 during IPR treatment (p < 0.001). In the consecutive 74 patient control group ETCO2 values did not change significantly. A comparison of ETCO2 values during CPR between patients treated with the IPR device and concurrent controls is shown in Fig. 2.

It is noteworthy that while all patients received epinephrine per the AHA Guidelines recommendations that a lower total dose of epinephrine was used in the patients treated with IPR therapy (1.9 ± 0.2 mg) versus controls (2.9 ± 0.1 mg; p = 0.007). The type of advanced airway did not appear to affect the measured ETCO2 values or other outcomes that were measured. No adverse effects were
Table 1

Comparison of demographic data, bystander CPR rates, timing, End tidal (ET) CO₂ (mmHg), initial cardiac rhythms, epinephrine dose, return of spontaneous circulation rates (ROSC) and potential adverse effects between intervention and control groups.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>IPR therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>74</td>
<td>11</td>
</tr>
<tr>
<td>Age</td>
<td>64 ± 2</td>
<td>63 ± 4</td>
</tr>
<tr>
<td>Female</td>
<td>29 (39%)</td>
<td>7 (64%)</td>
</tr>
<tr>
<td>Bystander CPR</td>
<td>37 (30%)</td>
<td>4 (36%)</td>
</tr>
<tr>
<td>Time from dispatch to first team on site</td>
<td>9 min 0 s ± 25 s</td>
<td>8 min 27 s ± 43 s</td>
</tr>
<tr>
<td>Time from dispatch to IPR therapy on</td>
<td>N.A.</td>
<td>16 min 0 s ± 10 s</td>
</tr>
<tr>
<td>Total time of CPR</td>
<td>12 min ± 1 min</td>
<td>21 min ± 3 min</td>
</tr>
<tr>
<td>Total time of IPR therapy</td>
<td>N.A.</td>
<td>26 min ± 3 min</td>
</tr>
<tr>
<td>ETCO₂ prior to the study device intervention</td>
<td>21 ± 1</td>
<td>21 ± 3</td>
</tr>
<tr>
<td>Maximum ETCO₂</td>
<td>33 ± 2</td>
<td>45 ± 5</td>
</tr>
<tr>
<td>Mean ETCO₂</td>
<td>22 ± 1</td>
<td>32 ± 5</td>
</tr>
<tr>
<td>Initial cardiac rhythm</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Asystole</td>
<td>39 (53%)</td>
<td>7 (64%)</td>
</tr>
<tr>
<td>Pulseless electrical activity</td>
<td>21 (28%)</td>
<td>2 (18%)</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>14 (19%)</td>
<td>2 (18%)</td>
</tr>
<tr>
<td>Total dose of epinephrine</td>
<td>2.9 ± 0.1 mg</td>
<td>1.9 ± 0.2 mg</td>
</tr>
<tr>
<td>Type of airways</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endotracheal tube</td>
<td>40</td>
<td>5</td>
</tr>
<tr>
<td>Ring tube</td>
<td>32</td>
<td>6</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Patients with ROSC</td>
<td>34 (46%)</td>
<td>8 (73%)</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>0</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

reported with IPR use. Further, there were no logistical issues associated with use of the new device.

4. Discussion

The data from this feasibility case series confirmed that the generation of negative end expiratory pressure between positive pressure ventilations results in an augmentation of ETCO₂ during CPR. Circulation, measured indirectly by ETCO₂, was significantly enhanced during CPR with the study device. The increase in ETCO₂ levels is consistent with studies in animals demonstrating increased ETCO₂ and increased survival rates with this technology.⁵ The increased levels of circulation were also associated with increased ROSC rates in patients treated with the new IPR device. The lower epinephrine amount needed in the intervention group to obtain ROSC is also a reflection of an increase in circulation obtained with the study device. While the IPR device has been previously observed to increase cardiac output in patients prior to bypass surgery,⁶ this is the first clinical evaluation of this approach in patients undergoing CPR. Since the IPR device is attached only to an advanced airway and to a vacuum source, it has the potential to be easily deployed by BLS and ALS personnel.

These new findings are consistent with animal studies demonstrating that IPR therapy augments venous preload, refills the heart after each compression, and lowers intracranial pressures during CPR.⁷ Achieving the physiologic goal of significantly increasing negative intrathoracic pressure on the upstroke of CPR with the ITD is not only dependent on complete chest recoil by the rescuer performing chest compressions, but on the intrinsic elastic recoil of the chest wall. One recent study utilizing an active compression decompression CPR device and an ITD resulted in a significant increase in survival with favorable neurological function compared with standard CPR alone.⁸ One of the potential advantages of this new IPR technology seems to be the potential to achieve this physiologic goal of subatmospheric pressure irrespective of the intrinsic elastic recoil of the chest. As with any technology for patients in cardiac arrest, the study device should be placed as rapidly as possible to derive meaningful clinical benefit. In this regard, a larger long-term evaluation is needed to determine the relative clinical benefit of IPR therapy compared with other approaches.

Prior animal studies have shown that IPR treatment decreases intracranial (ICH) and right atrial (RAP) pressures, increases mean arterial pressure (MAP), improves vital organ perfusion pressures and increases 24h neurologically intact survival rates compared with controls treated with positive pressure ventilation alone.⁹,¹⁰,¹¹,¹² While we were limited to measurement of ETCO₂ as a surrogate for circulation in this case-series, the nearly normal ETCO₂ values observed during CPR and IPR application support this concept and are consistent with the augmentation in circulation previously observed in animal studies.

Active generation of negative intrathoracic pressure during CPR may provide further benefit when CPR is not performed optimally. During standard CPR the chest should be allowed to fully recoil, thereby generating a small vacuum within the thorax to draw more blood back into the heart. It has been demonstrated that rescuers often fail to allow the chest to fully recoil at the end of each compressions.¹³,¹⁴ The constant positive intrathoracic pressure that results from this common error has been demonstrated to result in lower coronary and cerebral perfusion pressures in animals.¹⁴,¹⁵ By contrast, IPR treatment results in a significant decrease in intrathoracic pressure after each chest compression even if the chest is not allowed to fully recoil. We speculate that complete chest wall recoil may be less critical to providing adequate circulation during CPR with IPR use.

This study has a number of limitations. It is possible that unmeasured differences between patients in the intervention and control groups exist that contributed to the observed differences in ETCO₂ given that the intervention group was severely limited in size. Both the control and intervention group received treatment with an ITD, a passive valve that also lowers the intrathoracic pressure during chest wall recoil (to a lesser degree than IPR therapy) and results in an increase in ETCO₂ levels. Thus, the significant increase in ETCO₂ demonstrated with IPR therapy may have been influenced by pre-treatment with an ITD. Further, the study was prospective but not randomized or blinded. Tidal volume and ventilation frequency were not controlled, but were provided by the same BLS and ALS personnel throughout this evaluation. While ROSC rates increased from 46% in the control group to 73% in the IPR therapy group, it is premature to conclude that the IPR device will provide long-term benefit. In this regard additional studies are needed.

5. Conclusion

This first feasibility case-series of utilizing IPR therapy during CPR demonstrates that this therapy has the potential to significantly enhance ETCO$_2$, a surrogate measure for circulation, in patients in cardiac arrest. A larger study is needed to assess the potential long-term clinical benefit of this approach.

Statement of authorship

All authors have participated to the conception, design and writing of this manuscript. This manuscript represents valid work and that neither this manuscript nor one with substantially similar content under our authorship has been published or is being considered for publication elsewhere.

Conflict of interest statement

None.

Ethical adherence

The study was approved by the Institutional Review Board at Promedica approved this evaluation.

Prior publication

None.

Copyright constraints

None.

References