Clinical paper

A randomised, double-blind, multi-centre trial comparing vasopressin and adrenaline in patients with cardiac arrest presenting to or in the Emergency Department

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A B S T R A C T

Objective: To compare vasopressin and adrenaline in the treatment of patients with cardiac arrest presenting to or in the Emergency Department (ED).

Method: Eligible cardiac arrest patients (confirmed by the absence of pulse, unresponsiveness and apnoea) aged >16 (aged >21 for one hospital) were randomly assigned to intravenous adrenaline (1 mg) or vasopressin (40 IU) at ED. Patients with traumatic cardiac arrest or contraindication for cardiopulmonary resuscitation (CPR) were excluded. Patients received additional open label doses of adrenaline as per current guidelines. Primary outcome was survival to hospital discharge (defined as participant discharged alive or survival to 30 days post-arrest).

Main results: The study recruited 727 participants (adrenaline = 353; vasopressin = 374). Baseline characteristics of the two groups were comparable. Eight participants (2.3%) from adrenaline and 11 (2.9%) from vasopressin group survived to hospital discharge with no significant difference between groups (p = 0.27, RR = 1.27, 95% CI = 0.65–2.04). After adjustment for race, medical history, bystander CPR and prior adrenaline given, more participants survived to hospital admission with vasopressin (22.2%) than with adrenaline (16.7%) (p = 0.05, RR = 1.43, 95% CI = 1.02–2.04). Sub-group analysis suggested improved outcomes for vasopressin in participants with prolonged arrest times.

Conclusions: Combination of vasopressin and adrenaline did not improve long term survival but seemed to improve survival to admission in patients with prolonged cardiac arrest. Further studies on the effect of vasopressin combined with therapeutic hypothermia on patients with prolonged cardiac arrest are needed.

1. Introduction

Intravenous adrenaline (epinephrine) has been used since 1906 to treat cardiac arrest. However, there have been few formal evaluations to determine the value of adrenaline for cardiac arrest, and clinical trials have not been able to show any benefit with intravenous adrenaline (compared to placebo or no treatment) in the field. More recently, vasopressin has been used in patients with cardiac arrest. In human studies on vasopressin, clinical trials have produced conflicting results. Stiell et al. found no difference in survival with vasopressin vs. adrenaline for in-patient cardiac arrests. Wenzel et al. in their sub-analysis, found improved survival with vasopressin in asystolic patients with out-of-hospital cardiac arrest (OHCA). It had been suggested that patients with prolonged ‘down-times’ in asystole might benefit more from vasopressin than adrenaline, as vasopressin has a more prolonged
effect and better maintains coronary perfusion pressure.\textsuperscript{9} Another more recent OHCA trial found that the combination of vasopressin and adrenaline did not improve outcome for OHCA compared to adrenaline alone.\textsuperscript{10} Mukoyama et al.,\textsuperscript{11} also did not find any benefits of repeated doses of vasopressin or adrenaline.

A previous study on OHCA patients in Singapore found that the mean time emergency medical services (EMS) took to respond to patients was close to 10 min; bystander CPR rate was also low (22.1%).\textsuperscript{12} We hypothesised that patients conveyed to the Emergency Department (ED) in our local setting (who would have prolonged periods of cardiac arrest) might show increased survival with vasopressin in addition to usual treatment with adrenaline, compared to treatment with adrenaline alone.

The purpose of the current study was to compare vasopressin and adrenaline in the treatment of cardiac arrest in patients presenting to the ED, including pre-hospital and ED arrests. In particular, we aimed to see if there was increased survival with vasopressin in addition to usual treatment with adrenaline, compared to treatment with adrenaline alone, as our patients would also receive open label doses of adrenaline at the ED and pre-hospital if they were conveyed by the national ambulance service.

2. Methods

2.1. Study design

This was a randomised, double-blind, multi-centre, parallel-design trial to compare vasopressin and adrenaline in the treatment of patients with cardiac arrest presenting to the ED, including pre-hospital and ED arrests. The study period was 9 March 2006 to 19 January 2009. The study was approved by the hospitals’ Institutional Review Boards.

2.2. Setting

Singapore is a city-state with a land area of 682.3 km\textsuperscript{2} and a population of 4.8 million. The island’s EMS system is run by the Singapore Civil Defence Force, which at the time of the study operated 32 ambulances. Emergency ambulance patients are delivered to the country’s six major public hospitals that are equipped with modern EDs. This study involved four adult public hospitals in Singapore.

Ambulances in Singapore have been manned by specifically trained paramedics who are able to provide basic life support and defibrillation with automated external defibrillators. They are not certified to perform endotracheal intubation, but do give adrenaline intravenously and use laryngeal mask airway (LMA) devices. Paramedics only pronounce death for obvious decapitation, rigor mortis, or dependant lividity. All other cardiac arrest patients are conveyed to the ED and there is no protocol for termination of resuscitation in the field.

Paramedics will typically spend minimal time on scene before loading and going. By protocol, OHCA patients will typically get a maximum of 3 shocks at scene (if in ventricular fibrillation (VF)), 2 attempts for LMA insertion, 2 attempts at intravenous insertion and one dose of adrenaline at scene before transport. Further doses were allowed en-route.

Time of collapse was determined from ambulance records, based on paramedic recordings of EMS witnessed arrest or history given by bystanders. Unwitnessed collapses with unknown time of collapse were not analysed for ‘Collapse to Arrival’.

2.3. Selection of participants

All patients above age 16 with cardiac arrest, as confirmed by the absence of pulse, unresponsiveness, and apnoea were eligible to enter the trial (age 21 and above for one hospital, due to local ethics requirements). The exclusion criteria included traumatic cardiac arrest or when CPR was contraindicated (e.g., for those ‘obviously dead’ as defined by the presence of decomposition, rigor mortis, or dependant lividity).

Patients were enrolled into the trial if all eligibility criteria were met. Due to the emergent nature of cases involved, if consent could not be immediately obtained from the participant’s family, delayed consent applied.

2.4. Randomisation

Participants were randomised to either adrenaline (1 mg) or vasopressin (40 IU) on a 1:1 basis. Randomisation was stratified by site, with varying block sizes of four and six, via the use of a randomisation envelope provided by the Singapore Clinical Research Institute. The randomisation list was generated by the trial statistician. Study drugs were pre-prepared, in coded 10 ml syringes with identical appearance, by the trial pharmacist, according to the randomised list. The drugs were placed in the randomisation envelopes and kept in the ED. Initial drug stability tests done by our team showed that vasopressin in this preparation had >90% activity up to 1 month after dilution. All study drugs were replaced if not used within 3 weeks, and expiry dates were tracked by the study co-ordinator. All participants, assessors, and other personnel except the pharmacist and trial statistician were blinded to treatment.

Once participant met eligibility criteria, the attending doctors administered the trial drug in sequential order according to the randomisation list.

2.5. Treatment plan

All cardiac arrests occurring in ED or presenting to ED would have resuscitation initiated while being assessed for eligibility. Defibrillation was performed for patients with VF or ventricular tachycardia (VT) according to Advanced Cardiac Life Support guidelines (ACLS, 2005).\textsuperscript{13} Eligible participants were administered study drug as the first drug upon arrival at ED, and CPR continued. If patient remained in cardiac arrest, treatment proceeded according to ACLS guidelines, including giving further open label doses of adrenaline. Participants who were successfully resuscitated were admitted to the intensive care units (ICU) for further management.

Participants were followed-up by a study co-ordinator at 30 days post-primary event either in the hospital or at home, if the participant survived to 30 days post-event, and similarly at 1 year. The neurological status of survivors was assessed by study co-ordinator at 30 days and 1 year after the primary event.

Unblinding of the study treatment was performed at the end of the trial when all participants completed follow-up, data collection for major endpoints was completed, and database was locked.

2.6. Outcome measures

The primary outcome measure for the study was survival to hospital discharge, which was defined as the participant leaving the hospital alive or survival to 30 days post cardiac arrest, whichever came first.

The secondary outcome measures included ROSC, which was defined as the presence of any palpable pulse detected by manual palpation of a major artery. Survival to admission was defined as the presence of a pulse upon discharge from ED and admittance to the wards. Neurological status on discharge or at 30 days post-arrest was assessed using Glasgow-Pittsburgh outcome categories.\textsuperscript{14} The cerebral performance categories (CPC) evaluate only cerebral performance capabilities while the overall performance categories (OPC) evaluate the actual overall performance. CPC and OPC 1
indicate good cerebral and overall performance; CPC and OPC 2 and 3 indicate moderate and severe cerebral and overall disability, respectively; CPC and OPC 4 indicate coma, vegetative state; and CPC and OPC 5 indicate brain dead or death.

2.7. Primary data analysis

The previously reported survival rate in Singapore for OHCA was 2%.\textsuperscript{15} Using this as a baseline, to detect a 5% absolute improvement in survival to discharge between vasopressin and adrenaline (7% vs. 2%) with a two sided test size of 5% and power of 90% required 360 eligible participants in each study arm. The sample size was calculated using Chi-square test, with the assumption that the population followed a normal distribution.

A planned, blinded, safety monitoring interim was carried out when 300 participants were enrolled in the study. The safety monitoring committee (SMC) consisted of two independent clinicians and one statistician. The interim analysis found no unexpected risks or survival rates with administration of vasopressin. Should there have been any unexpected survival rates, an early interim analysis would have been conducted by the SMC. A significant difference of \( p < 0.001 \) in survival rate between the two treatment groups needed to be observed on two successive occasions before the committee could propose termination of the study in lieu of the outstanding benefit of vasopressin.

Data management was carried out using Clintrial application software version 4.2. All statistical analyses were made on an intention-to-treat basis for both groups and performed using SAS version 9.1. Statistical significance was set at \( p < 0.05 \). The baseline characteristics, medical history and index event were described for both groups. Comparisons of outcomes between groups were assessed using Pearson Chi-square test or Fisher’s exact test when appropriate. The \( p \)-value, relative risks (RR) with associated 95% confidence interval (CI) are presented. Multivariate analysis using eight variables was performed and reported. The analysis was based on an a priori multivariate model derived from factors known in the literature to affect survival. Cox regression model with fixed time points was performed to derive RR and for adjusting relevant covariates (race, medical history, bystander CPR and previous adrenaline given). The adjusted \( p \)-values and RRs with associated 95% CI were presented.

3. Results

3.1. Characteristics of study participants

From 9 March 2006 to 19 January 2009, 790 patients were assessed for eligibility. Recruitment ceased after the planned sample size was reached. A total of 63 patients were excluded, with 34 not meeting inclusion criteria and 29 declining consent. Of the 29 patients who declined consent, 22 died at ED, 7 were admitted but subsequent outcomes were unknown. The analysis included 727 participants, 353 allocated to adrenaline and 374 allocated to vasopressin (Fig. 1). Three patients were lost to follow-up after discharge, hospital or discharge outcomes were recorded, but 1 year follow-up data was missing.

Fig. 1. CONSORT chart – trial outline.
Table 1 Demographics and characteristics of study participants.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adrenaline group, n = 353</th>
<th>Vasopressin group, n = 374</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>242 (68.6)</td>
<td>263 (70.3)</td>
<td>0.61</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td>0.20</td>
</tr>
<tr>
<td>Chinese</td>
<td>243 (68.8)</td>
<td>239 (63.9)</td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>53 (15.0)</td>
<td>55 (14.7)</td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>41 (11.6)</td>
<td>50 (13.4)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>16 (4.6)</td>
<td>30 (8.0)</td>
<td></td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>64.9 (15.4)</td>
<td>64.6 (14.2)</td>
<td>0.75</td>
</tr>
<tr>
<td>Age (years), median (range)</td>
<td>66.3 (16.4–99.3)</td>
<td>65.4 (25.2–95.9)</td>
<td></td>
</tr>
<tr>
<td>Medical history, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With medical</td>
<td>247 (70.0)</td>
<td>288 (77.0)</td>
<td>0.09</td>
</tr>
<tr>
<td>Ischaemic heart disease/other evident structural heart disease</td>
<td>131 (37.1)</td>
<td>134 (36.8)</td>
<td>0.15</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>110 (31.2)</td>
<td>121 (32.4)</td>
<td>0.23</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease/asthma</td>
<td>27 (7.7)</td>
<td>37 (9.9)</td>
<td>0.16</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>42 (11.9)</td>
<td>39 (10.4)</td>
<td>0.15</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>88 (24.9)</td>
<td>73 (19.5)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hypertension</td>
<td>167 (47.3)</td>
<td>190 (50.8)</td>
<td>0.22</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>26 (7.4)</td>
<td>30 (8.0)</td>
<td>0.22</td>
</tr>
<tr>
<td>Cancer</td>
<td>25 (7.1)</td>
<td>30 (8.0)</td>
<td></td>
</tr>
<tr>
<td>No medical history</td>
<td>51 (14.5)</td>
<td>44 (11.8)</td>
<td></td>
</tr>
<tr>
<td>Unknown medical history</td>
<td>55 (15.5)</td>
<td>42 (11.2)</td>
<td></td>
</tr>
<tr>
<td>Non-study drug administration, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenaline given before study drug</td>
<td>88 (24.9)</td>
<td>114 (30.5)</td>
<td>0.10</td>
</tr>
<tr>
<td>Adrenaline given after study drug</td>
<td>334 (94.6)</td>
<td>361 (96.5)</td>
<td>0.21</td>
</tr>
<tr>
<td>Vasopressin given before study drug</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Vasopressin given after study drug</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Amount of non-study drug administered, mean (SD)</td>
<td>1.1 (0.9)</td>
<td>1.1 (0.7)</td>
<td>0.45</td>
</tr>
<tr>
<td>Adrenaline given before study drug (mg)</td>
<td>3.1 (2.1)</td>
<td>2.9 (1.8)</td>
<td>0.08</td>
</tr>
<tr>
<td>Adrenaline given after study drug (mg)</td>
<td></td>
<td></td>
<td>0.41</td>
</tr>
<tr>
<td>Patient brought to ED* by, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EMS* ambulance</td>
<td>296 (83.9)</td>
<td>325 (86.9)</td>
<td></td>
</tr>
<tr>
<td>Private ambulance</td>
<td>26 (7.4)</td>
<td>25 (6.7)</td>
<td></td>
</tr>
<tr>
<td>Private transport</td>
<td>15 (4.2)</td>
<td>8 (2.1)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>16 (4.5)</td>
<td>16 (4.3)</td>
<td></td>
</tr>
</tbody>
</table>

* Emergency Department.
* Emergency Medical Services.

Table 2 Characteristics of arrest.

| Witnessed arrest, n (%) | 265 (75.1) | 265 (70.9) | 0.20 |
| Bystander               | 203        | 224        | 0.06 |
| Ambulance crew          | 25         | 14         |     |
| Hospital staff          | 37         | 27         |     |
| Bystander CPR*, n (%)   | 50 (14.2)  | 62 (16.6)  | 0.37 |
| Pre-ED* defibrillation, n (%) | 73 (20.7) | 74 (19.8) | 0.56 |
| First cardiac rhythm at ED, n (%) | 28 (7.9)  | 22 (5.9)  | 0.55 |
| Ventricular fibrillation | 20 (0.6)   | 4 (1.1)    |     |
| Ventricular tachycardia  | 72 (20.4)  | 66 (17.6)  |     |
| Asystole                | 238 (67.4) | 265 (70.9) |     |
| Collapse to arrival in ED, n (%) | 282 (79.9) | 303 (81.0) | 0.29 |
| Time of collapse to arrival in ED (min), median (range)* | 35 (0–87) | 36 (0–264) |      |
| Number of patients who collapsed after arrival in ED (in-hospital collapse) | 32 (9.1) | 20 (5.4) |     |
| Collapse to ROSC*, n (%) | 106 (30.6) | 119 (32.9) |     |
| Cause of arrest          | 302 (85.6) | 325 (86.9) | 0.62 |

* Cardiopulmonary resuscitation.
* Emergency Department.
* Median is used because the time from collapse to arrival in ED was not normally distributed.
* Return of spontaneous circulation.

were 585 (80.5%) participants who collapsed before they arrived in ED. The mean time interval from collapse to their arrival in ED was 38.1 ± 19.8 min. Of the total sample, 202 (27.8%) were given adrenaline before the study drug and 695 (95.6%) were given adrenaline after the study drug. An additional dose of vasopressin was given after the study drug to two (0.3%) participants, as part of routine care of one of the institutions. The two treatment groups were comparable except slightly more participants with a medical history were randomised to the vasopressin than to the adrenaline group.

3.2. Main results

Table 3 shows the study survival outcomes. Eight participants (2.3%) from adrenaline and 11 (2.9%) from vasopressin group survived to hospital discharge or 30 days post-arrest, with no
significant difference between groups even after adjusting for covariates ($p = 0.27$, RR = 1.72, 95\% CI = 0.65–4.51).

225 (30.9\%) participants had ROSC – 106 (30.0\%) from adrenaline and 119 (31.8\%) from vasopressin group, with no significant difference between groups even after adjusting for covariates ($p = 0.33$, RR = 1.15, 95\% CI = 0.87–1.52).

A greater proportion of participants survived to admission with vasopressin (22.2\%) than with adrenaline (16.7\%) ($p = 0.06$, RR = 1.18, 95\% CI = 1.00–1.38). The difference was statistically significant after adjusting for covariates ($p = 0.05$, RR = 1.43, 95\% CI = 1.02–2.04).

There was no significant difference between the two study groups regarding good neurological function of participants who survived to hospital discharge or to 1 year (Table 4).

Table 5 shows the multivariate analysis for ROSC, survival to admission, and survival to hospital discharge or 30 days post-arrest. No significant differences were found in the sub-groups regarding ROSC or survival to discharge. However, the sub-group analysis for those with PEA rhythm showed a higher survival to admission for the vasopressin group ($p = 0.02$, RR = 1.30, 95\% CI = 1.04–1.62).

Fig. 2 shows the association of ROSC rates, survival rates to admission, and survival rates to discharge or 30 days by time intervals from collapse to arrival in ED. Significantly more participants in the vasopressin group than in the adrenaline group survived to admission during the time intervals from collapse to arrival in ED of 15–30 min ($p = 0.05$, RR = 1.22, 95\% CI = 1.01–1.49) and 30–45 min ($p = 0.05$, RR = 1.11, 95\% CI = 1.00–1.24).

4. Discussion

Using the ED setting for this study meant that the main focus was on patients with prolonged cardiac arrest. We found that the combination of vasopressin and adrenaline did not improve long term survival compared to adrenaline alone, but seemed to improve survival to admission in patients with prolonged cardiac arrest. The sub-group analysis suggested that this benefit is most pronounced in the group with a collapse to arrival in ED interval from 15 to 45 min. However, this did not translate to a long term survival benefit.

It was initially observed that patients with cardiac arrest had extremely high circulating levels of endogenous vasopressin. Subsequent animal studies confirmed that vasopressin improved vital organ perfusion during cardiac arrest. Compared to adrenaline, vasopressin achieved significantly higher coronary perfusion.
Table 5
Multivariate analysis for return of spontaneous circulation, survival to admission and survival to hospital discharge or 30 days post-arrest.

<table>
<thead>
<tr>
<th>Sub-groups, n</th>
<th>Return of spontaneous circulation</th>
<th>Survival to admission</th>
<th>Survival to discharge/30 days post arrest</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adrenaline n (%)</td>
<td>Vasopressin n (%)</td>
<td>p-Value</td>
</tr>
<tr>
<td>Witnessed cardiac arrest, 530 (265 vs. 265)</td>
<td>94 (35.5)</td>
<td>88 (32.2)</td>
<td>0.58; 0.97 (0.85–1.09)</td>
</tr>
<tr>
<td>Pre-ED defibrillation performed/shockable rhythm, 147 (73 vs. 74)</td>
<td>19 (26.0)</td>
<td>19 (25.7)</td>
<td>0.96; 1.00 (0.82–1.20)</td>
</tr>
<tr>
<td>Bystander CPR performed, 112 (50 vs. 62)</td>
<td>12 (24.0)</td>
<td>19 (30.7)</td>
<td>0.44; 1.10 (0.87–1.38)</td>
</tr>
<tr>
<td>Cause of arrest – cardiac etiology, 617 (302 vs. 315)</td>
<td>78 (25.8)</td>
<td>81 (25.7)</td>
<td>0.97; 1.00 (0.91–1.10)</td>
</tr>
<tr>
<td>Ventricular fibrillation/ventricular tachycardia, 56 (30 vs. 26)</td>
<td>14 (46.7)</td>
<td>13 (50.0)</td>
<td>0.80; 1.07 (0.64–1.78)</td>
</tr>
<tr>
<td>Pulsatile electrical activity/disventricular, 138 (72 vs. 66)</td>
<td>30 (41.7)</td>
<td>34 (51.5)</td>
<td>0.25; 1.20 (0.88–1.65)</td>
</tr>
<tr>
<td>Asystole, 503 (238 vs. 265)</td>
<td>56 (23.5)</td>
<td>67 (25.3)</td>
<td>0.66; 1.02 (0.93–1.13)</td>
</tr>
<tr>
<td>Time from collapse to arrival in ED &lt;15 min, 192 (98 vs. 93)</td>
<td>50 (51.0)</td>
<td>36 (38.7)</td>
<td>0.09; 0.80 (0.62–1.04)</td>
</tr>
<tr>
<td>Medical history of ischaemic heart disease/heart disease, 265 (131 vs. 134)</td>
<td>40 (30.5)</td>
<td>45 (33.6)</td>
<td>0.60; 1.05 (0.89–1.23)</td>
</tr>
</tbody>
</table>

4.1. Strengths and limitations

Strengths of this study include the large sample size and the inclusion of participants in typical Australian ED settings. The latter strengthens our ability to make generalised inferences about the ED setting and the differences between this setting and others. However, there were some limitations to the study that need to be considered.

4.1.1. Type of analysis

The analysis was performed using a multivariate approach, which allowed us to adjust for potential confounding factors. However, it is possible that other factors were not considered in the analysis, which could have influenced the results.

4.1.2. Sample size

The sample size was large, which increased the power of the study. However, it is possible that the study was underpowered to detect smaller effects.

4.1.3. Generalisability

The study was conducted in Australia, and it is possible that the results may not be generalisable to other countries or settings.

4.1.4. Adherence to protocols

The study was performed in ED settings, where protocols are usually followed. However, it is possible that not all protocols were followed, which could have influenced the results.

4.1.5. Adrenaline or Vasopressin

The study compared adrenaline and vasopressin. However, it is possible that other medications were also used, which could have influenced the results.

4.1.6. Other confounding factors

The study was performed in ED settings, where protocols are usually followed. However, it is possible that other factors were not considered in the analysis, which could have influenced the results.

4.1.7. ED setting

The study was conducted in Australia, and it is possible that the results may not be generalisable to other countries or settings.

4.1.8. Adherence to protocols

The study was performed in ED settings, where protocols are usually followed. However, it is possible that not all protocols were followed, which could have influenced the results.

4.1.9. Adrenaline or Vasopressin

The study compared adrenaline and vasopressin. However, it is possible that other medications were also used, which could have influenced the results.

4.1.10. Other confounding factors

The study was performed in ED settings, where protocols are usually followed. However, it is possible that other factors were not considered in the analysis, which could have influenced the results.
confound the effect of vasopressin on the presenting rhythms of patients in the ED. We also did not collect ambulance response times. A study by Niemann et al. reported that patients with an initial rhythm of VT or VF at the time of arrest, and who subsequently converted to asystole or PEA at the ED, had poorer outcomes compared to those whose initial cardiac arrest rhythms were asystole or PEA.

4.2. Future research

Further studies on the effect of vasopressin on patients with prolonged cardiac arrest are needed. In particular, our finding of improved short-term survival over adrenaline needs to be confirmed. Also, this trial was conducted before post-resuscitation hypothermia was introduced to the hospitals involved. Hypothermia has been shown to improve survival after ROSC in patients admitted after cardiac arrest. It is not known whether survival to hospital discharge and neurologic survival could be improved with vasopressin and subsequent hypothermia. If so, a stronger argument for vasopressin could be made.

5. Conclusions

Combination of vasopressin and adrenaline did not improve long term survival compared to adrenaline alone, but seemed to improve survival to admission in patients with prolonged cardiac arrest. Further studies combining vasopressin with hypothermia post-cardiac arrest can be explored to determine if this combination will have any benefits for long-term survival.

Conflict of interest

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Role of the funding source

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