Sudden cardiac arrest pharmacotherapy with prefilled syringes improves adherence to Advanced Life Support protocol in understaffed resuscitation pre-hospital care teams

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Abstract

Every procedural facilitation or a change in available equipment in treatment of out-of-hospital arrest (OHCA) by two-person teams may significantly enhance their performance quality. The aim of this study was to assess the impact of adrenaline in prefilled syringes on improving the adherence to Advanced Life Support protocol by understaffed teams. The research was based on a randomized cross-over high-fidelity simulation study. Two-person teams took part in two 10-minute simulation scenarios featuring sudden cardiac arrest in ventricular fibrillation (VF). The control group (group C) had at its disposal standard ampoules, whereas the experimental group (group E) prefilled syringes. The execution times of CPR start, defibrillation shocks, intravenous (IV) access, epinephrine and amiodarone doses were measured. Additionally, the chest compression fraction (CCF) was calculated. The designed two-minute loops were considerably prolonged in group C. Nineteen teams (31.1%) in group C but 49 (80.3%) in group E carried out the fifth defibrillation (P < 0.001). After two minutes of CPR nobody in group C switched to perform chest compressions. IV access was obtained significantly earlier in group E (114.7 ± 52.2 sec) than in group C (150.2 ± 68.6 sec) (P = 0.002). Two doses of adrenaline were administered in group E, whereas its second dose only by 12 teams in group C. The simulation study has proved that for understaffed teams a use of prefilled syringes not only did enhance the flow of ALS procedure, but it also improved the quality of cardiopulmonary resuscitation.

Keywords

Sudden cardiac arrest; Cardiopulmonary resuscitation; Simulation; Prefilled syringes; Epinephrine; Paramedic

1. Introduction

Sudden cardiac arrest (SCA) it becoming the most common cause of death in the developed countries. It occurs particularly often to patients with preexisting cardiac pathologies [1-3]. A recent study EuReCa ONE conducted in 27 European countries estimated the incidence rate at 84.0 for 100 000 [2]. The survival of patients depends crucially on the quality of pre- and in-hospital phases of first aid [4]. In Polish Medical Emergency System there are usually two-person teams, who are obliged to follow the Advanced Life Support (ALS) procedures [5].

All contemporary guidelines on resuscitation recommend routine pharmacotherapy in SCA- mostly indicating epinephrine (for all SCA cases) and amiodarone (in ventricular fibrillation/pulseless ventricular tachycardia VF/pVT cases that do not respond to initial shocks). There is no evidence that this pharmacotherapy significantly improves the outcome in out-of-hospital cardiac arrest (OHCA), nevertheless it is a routinely recommended medical treatment in 2015 European Resuscitation Council (ERC) guidelines and paramedics are expected to provide it when performing advanced life support [6, 7]. Preparing and administering epinephrine and amiodarone is time-consuming and thus it can possibly affect resuscitation quality when resuscitation team is understaffed, common in prehospital care [8]. Most European countries utilize two-person paramedical teams in prehospital emergency medical services, while ERC recommend six people in resuscitation team. It has been found, that two-member ambulance team is not able to adhere to ALS protocol, especially in terms of pharmacotherapy and when first dose of epinephrine is administered after 7 minutes of resuscitation [9].

European guidelines on resuscitation do not focus on the technical aspects of drug preparation for resuscitation teams, moreover it is not mentioned in the official document whether any specific type of storage and injectors should be favored.
There is a clear indication though that pharmacotherapy should be initiated when sufficient staff is present, unfortunately there is no clarification what number of medical professionals should be considered as sufficient [10].

Throughout recent years, the use of prefilled syringes has been analyzed in various fields of medicine. It has turned out that they have numerous advantages including better quality of cardiopulmonary resuscitation improved patients’ safety and optimal drug administration [11, 12].

The aim of this study was to assess the impact of adrenaline in prefilled syringes on improving the adherence to Advanced Life Support protocol by understaffed teams.

2. Materials and methods

2.1 Study group

We created a randomized, cross-over simulation study, which was analyzed by a local bioethics committee and confirmed to be a research not following into the category of medical experiment (KB 1075/19).

Sixty-three teams altogether, each consisting of two paramedics, were randomly assigned to take part in the study from the group of seventy teams available. Paramedics took part in the study voluntarily, but needed to demonstrate a minimum of 5 years of work experience in EMS. Their age rate varied from 23 to 45. Prior the study voluntary, written informed consent was obtained from each participant.

Each team took part twice in 10-minute scenarios featuring sudden cardiac arrest in ventricular fibrillation. The order both of the teams and scenarios was random and based on toss-up. There was no debriefing of any sort between simulations and a pause of at least 10 minutes was provided for each team to rest before another attempt. The high-fidelity simulation study was led by qualified medical simulation instructors. During the scenario, paramedics followed the European Resuscitation Council guidelines from 2015 [7].

2.2 Equipment and medicines

The simulated work environment and available equipment was compliant with the conditions of local ambulances and was based on ALS procedure. Each team had at their disposal a rescue bag equipped with supraglottic airway device (SAD), bag mask device with oxygen tube and tank, set of catheters and covers, clip style tourniquet, set of needles and syringes 1 mL, 10 mL, 20 mL, saline 500 ml with mini spike and glucose 5% 500 mL with mini spike, alcohol swab, and boxes for sharp objects. The instructors had two rescue bags with medicines. One was filled with standard ampoules with adrenaline 1 mg in 1 mL (Adrenalina WZF, Warsaw, Poland) and amiodarone 150 mg in 3 mL (Amiodarone InPharm/Sanofi, Ambares, France). The second one was equipped with prefilled syringes with adrenaline (Adrenaline, Aurum, Ramford, United Kingdom) 1 mg in 10 mL 1 : 10,000 and amiodarone (Amiodarone, Aurum, Ramford, United Kingdom) 300 mg in 10 mL both in plastic packaging.

Drugs and disposable elements have been received from local Emergency Medicine Station. The authors have not received any additional funds for the research. All the teams worked with the same defibrillator Zool M (Runcorn, UK) series, to which they have been introduced prior to the study.

2.3 Scenario

The paramedics took part in two scenarios featuring OHCA in ventricular fibrillation.

Control group (C) - standard procedures during SCA according to ALS protocol with drugs in standard ampoules;

Experimental group (E) - standard procedures during SCA according to ALS protocol with drugs in prefilled syringes.

Before the scenarios the teams were not instructed on the sequence of actions to be undertaken.

A randomization process in first shift (Experimental group - 33, Control group - 30). The participants in both groups did not differ significantly in the terms of age, gender and professional experience.

2.4 Simulator

To conduct the research a high-fidelity simulator MegaCode Kelly was used (Laerdal, Stavanger, Norway). The venous system of the simulator was filled with liquid imitating blood, so that paramedics trying to obtain intravenous access could assess whether it was correctly done. Throughout both scenarios the mannequin simulated SCA in ventricular fibrillation mechanism. The mannequin’s airways enable the use of SAD and during successful ventilation the movement of chest is observable.

2.5 Storing and processing data

In all the scenarios previously trained paramedics were present in order to measure the execution time of the most important steps during CPR and to put the results into a spreadsheet afterwards. All of the scenarios were recorded to verify the start time of the procedures. The following parameters such as time of CPR start, number of defibrillation shocks, time of intravenous (IV) access obtain, number and time of consecutive doses of epinephrine and amiodarone doses, breaks between electric shocks, chest compression fraction (CCF, defined as the period of time of uninterrupted CC) and time to achieve airways patency were analyzed and compared between groups.

2.6 Data processing and statistical analysis

All continuous variables were checked for normality by means of the Shapiro-Wilk W test and these normally distributed were expressed as means with standard deviation (mean ± sd) and then compared with the unpaired Student T test. Categorical data were presented as number (n) with percentage (%) and analyzed by means of Yates corrected $\chi^2$ test. A p value below .05 was considered as statistically significant. All calculations were done in the Statistica 10.0 software package (StatSoft, Tulsa, OK, USA).

3. Results

Sixty three paramedical teams participated in the simulator-based study and they carried out 126 scenarios. However, due to technical failure of the simulator, 4 of them had to
be excluded thus eventually 122 scenarios were entered into further analysis (61 in control and 61 in experimental group).

3.1 Adherence to CPR protocol

After initial assessment of the rhythm that lasted comparably between groups, the first shock applications were done at the same time, whereas the subsequent ones were applied earlier in the experimental group. Additionally, time between shocks differed markedly between all but one (exception between fourth and fifth). The breaks are presented graphically in Fig. 1. However, it must be pointed that only in 19 cases in group C (31.1%) but in 49 in group E (80.3%) the fifth electric shocks were carried out ($P < 0.001$).

Generally, paramedics in group C did not change regularly in chest compressions, which was also a more observable case in group E (see Fig. 2). In 2nd minute of CPR, nobody changed in group C whereas only in 10 (16.4%) scenarios in group E. The best adherence to CPR protocol was noted after 4 minutes in group C (45.8%; $n = 28$) and 2 minutes later in group E (75.4%; $n = 46$), then dropped, however more dramatically in group C.

Moreover, IV access was obtained significantly earlier in group E than in group C, despite of comparable time of its insertion (25.9 ± 15.9 sec and 24.8 ± 16.1 sec, in group C and group E, respectively; $P = 0.713$). This difference resulted from later starting point of IV access introduction. The detailed data are presented in Table 1.

Poor adherence to the CPR algorithm regarding optimal administration of emergency medicine (ie., epinephrine and
### TABLE 1. Detailed data regarding time and adherence to valid CPR protocol.

<table>
<thead>
<tr>
<th></th>
<th>Control group [n = 61]</th>
<th>Experimental group [n = 61]</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. CPR start</td>
<td>14.1 ± 4.6</td>
<td>14.4 ± 6.4</td>
<td>0.733 (NS)</td>
</tr>
<tr>
<td>2. Shock No.1</td>
<td>43.3 ± 15.6</td>
<td>39.8 ± 14.9</td>
<td>0.436 (NS)</td>
</tr>
<tr>
<td>3. IV access start obtained</td>
<td>124.3 ± 65.6</td>
<td>89.9 ± 43.9</td>
<td>0.001</td>
</tr>
<tr>
<td>4. Shock No.2</td>
<td>213.1 ± 65.6</td>
<td>158.1 ± 30.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>5. Shock No.3</td>
<td>366.6 ± 85.3</td>
<td>284.9 ± 32.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>6. Epinephrine 1st dose</td>
<td>438.8 ± 64.8</td>
<td>308.2 ± 41.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>7. Amiodarone 1st dose</td>
<td>476.3 ± 76.4</td>
<td>325.9 ± 48.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>8. Shock No.4</td>
<td>480.0 ± 53.9</td>
<td>412.2 ± 41.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>9. Epinephrine 2nd dose</td>
<td>542.6 ± 28.8</td>
<td>534.1 ± 23.1</td>
<td>0.356 (NS)</td>
</tr>
<tr>
<td>10. Amiodarone 2nd dose</td>
<td>551.9 ± 27.6</td>
<td>531.7 ± 48.8</td>
<td>0.051 (NS)</td>
</tr>
<tr>
<td>11. Shock No.5</td>
<td>559.1 ± 27.6</td>
<td>517.5 ± 25.5</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Continuous data (time) are expressed as the means with standard deviation, whereas categorical variable (&, number of scenarios with application of a given point of CPR algorithm) as number (n) with percentage (%).

* data were compared by the means of either unpaired Student T test (continuous data; upper rows) or Yates corrected χ² test (categorical data; lower rows).

Abbreviations: NA = non-applicable; NS = not statistically significant difference.

amiodarone) was obviously noted in group C. Although, the first dose of epinephrine was given in all scenarios in both groups, the second dose in all scenarios in group E, whereas only in 12 in group C. The worse situation regarded amiodarone injections in group C. During those, the first dose was administered in 75% and the second only in less than 20%.

Time to achieve airways patency did not differ significantly between groups and mean time was equal 128.9 ± 80.3 sec in group E and 132.9 ± 67.9 sec in group C (P = 0.767).

### 3.2 Quality of CPR

Although the detailed assessment of CPR quality was not a primary aim of our study, we additionally evaluated chest compression fraction (CCF). Its mean value was markedly higher in group E (75.0 ± 5.2%) than in group C (69.5 ± 4.3%) (P < 0.001). It resulted from longer total time of CCs, 450.2 ± 31.3 sec and 416.8 ± 25.7 sec, in group E and C, respectively (P < 0.001).

### 4. Discussion

In our simulation-based study prefilled syringe with adrenaline was chosen due to its easy availability and common use in daily clinical practice. Although its administration is recommended in SCA subjects in valid guidelines of the European Resuscitation Council (ERC), the outcomes of its use in these individuals are not consistent [13–16]. According to the aforementioned recommendations, the first dose of adrenaline should be administered immediately after insertion intravenous or interosseous cannula in initial non-shockable whereas after the third shock in the shockable rhythms [17]. Therefore, in our study we did not test the impact of adrenaline injection itself on CPR efficacy nor its outcomes, but we assessed the significance of two different and available methods of drug preparation prior to its application. These two methods could impact the adherence to all aspects of ALS protocol. We have tested not only appropriate time and number of recommended drug injections but also defibrillations, changes of paramedics in CCs, airways patency and eventually CPR quality expressed as CCF. Moreover, scenario of OHCA with initial shockable rhythm was assessed because it was found before that
paramedics committed most errors in SCA in ventricular fibrillation [18]. Of note, two-person prehospital resuscitation teams are common in some European countries. However, there are no specific guidelines for them to address the issue of such understaffed teams and also other types of limited prehospital resources.

It was found before that high-quality CCs and early defibrillation are the most important actions to be taken during SCA. It has been also proven that pauses during CCs significantly reduce the coronary vessels pressure, what inseparably leads to the decrease in the probability of returning the spontaneous circulation (ROSC) [19]. This issue was also stressed in 2015 Guidelines of the American Heart Association (AHA). AHA define the chest compression fraction (CCF) parameter as a proportion of time dedicated to continuant CCs and its value should exceed 60% [20, 21]. Current analysis has proven that teams working with prefilled syringes with adrenaline reached higher CCF rate than group C. With this facilitation the teams could focus on providing high-quality chest compressions. The changes between paramedics after every two minutes of CCs are crucial components of high-quality CPR [10]. Our study has proven that paramedics switched irregularly, especially during initial phase of CPR. Although those having prefilled syringes at their disposal followed ALS protocol better than in group C, they were still not optimal regarding this aspect of CC.

We have also noted two-person teams were not able to follow the ALS protocol regarding defibrillations. The delays resulted in the numbers of electric shocks, whereas introduction of prefilled syringes significantly improved adherence to guidelines. It is also interesting that paramedics using prefilled syringes controlled the 2-minute defibrillation loops, whereas those working with standard ampoules prolonged the loops even to 160 seconds, especially during first 2 changes. The time needed to draw, dissolve and inject the ampouled drug seemed to be an important contributing factor. The medicine preparation not only caused delay in the specific steps of the protocol, but also had significant impact of other crucial actions during CPR, particularly in OHCA scenario, such as airway management and uninterrupted chest compressions (CCF). The different time of obtaining the intravenous access may result from many factors. One of them can be psychological comfort having prefilled syringes at disposal. When decision is made to provide pharmacotherapy in shockable rhythm (at least initially) in group C, which is a reasonable approach and is encouraged by the guidelines, the teams of two professionals can reach acceptable parameters of CPR quality and all major steps of CPR are not delayed. Teams that decided to withhold the pharmacotherapy and focus on other parts of ALS had clearly better CPR quality and adherence to the protocol. Of note, such delay is not justified if initial rhythm is a non-shockable one [9].

The authors have not come across any similar analyses in the medical literature that would assess the impact of using prefilled syringes on following the ALS protocols by 2-membered teams. There are analyses however that clearly prove that the use of adrenaline in a prefilled syringe significantly fastens and facilitates drug administration [8]. Authors working on the impact of prefilled syringes on the quality of cardiopulmonary resuscitation in SCA patients in unshockable rhythms have reached similar conclusion. It turned out that the first dose of adrenaline was administered faster by the paramedics who had prefilled syringes at their disposal. Additionally, the improvement of chest compressions parameters was observed, followed by visible better implementation of ALS protocol [19, 22].

Paramedic Self-Reported Medication Errors has published a list of the most common errors committed by paramedics. Nearly 10% of the respondents confirmed to have made a mistake during drug administration in recent 12 months. More than 60% of those errors were related to the dose, 33% to administering drug discordantly to the protocol, 21% to the paramedics choosing the wrong administration method and 4% to a wrong drug administration [23]. Using prefilled syringes has its indisputable advantages. It facilitates faster drug administration as the method eliminates most of the phases related to preparation of proper doses [24]. Moreover, it increases safety both of the patient and the paramedic because it limits the probability of pricking with sharp elements of an ampoule. Furthermore, a prefilled syringe does not require using aspirating needle, what in turn eliminates the risk of paramedic pricking themselves [24]. Similar results were reported by Stevens et al. in a prospective randomized study in simulated scenario of SCA in children. Ready-to-use prefilled color-marked syringes have shortened the time of drug administration and enabled to eliminate the critical errors during simulation scenario featuring prehospital resuscitation [25].

5. Limitations of the study

The authors are aware of the limitations of the research. The scenarios were conducted in a high-fidelity simulation, which naturally cannot fully mirror the conditions of real life or clinical trials. The research enabled repeatability of the conditions, which is not possible in reality. Paramedics in prehospital situations act in different conditions with various equipment at their disposal. Often, the environment or the behavior of incident’s witnesses may lead to a stressful situation, what is minimized during simulation. There were no distractors planned for the simulation, which could impact the results. During simulation only one type of prefilled syringes was used. Currently on the market there are many manufacturers producing various prefilled syringes in different packaging. The described limitations may influence the studies parameters.

6. Conclusions

The simulation study has proved that for two-membered paramedic teams, having at their disposal standard ampoules, it is not possible to follow the international CPR guidelines. A usage of prefilled syringes not only does enhance the flow of ALS procedure, but it also improves the quality of CPR, what may increase the survival rate.
ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

AUTHOR CONTRIBUTION

(I) Conception and design: RZ, WT, MP. (II) Administrative support: RZ, MP, BP, LS, WT. (III) Provision of study materials or patients: RZ, WT, MP, LS. (IV) Collection and assembly of data: RZ, WT, MD. (V) Data analysis and interpretation: RZ, BP, MP, WT, LS. (VI) Manuscript writing: RZ, MP, WT, BP, LS, MD. (VII) Final approval of manuscript: RZ, MP, WT, MD, BP, LS.

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CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

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