

PRE-FILLED SYRINGES WITH ADRENALINE DURING CARDIOPULMONARY RESUSCITATION IN NON- SHOCKABLE RHYTHMS. PILOT RANDOMISED CROSS- OVER SIMULATION STUDY

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ABSTRACT

INTRODUCTION: Pre-filled syringes are increasingly popular in medicine, especially in emergency medicine, where fast intervention is crucial. Additionally, as indicated by numerous studies, the use of drugs in pre-filled syringes reduces the risk of medical errors associated with inadequate preparation of the drug and reduces the risk of contamination as a result of tissue injury due to rupture of a standard ampoule with the drug. The aim of the study was to compare the use of pre-filled syringes with adrenaline and standard adrenaline in ampoules during simulated CPR during simulated cardiopulmonary resuscitation in non-shockable rhythms performed by two-person teams.

MATERIAL AND METHODS: The study was a randomised cross-over study and was based on medical simulation. The study involved 40 paramedics assigned randomly to 20 two-person rescue teams. These teams were to perform 10-minute cardiopulmonary resuscitation in three research scenarios: Scenario A — During CPR, access to the median basilic vein and preparation and administration of adrenaline infusions from generally available ampoules at concentration 1:1000 were required (Adrenaline WZF 0.1%; Polfa, Warsaw, Poland) with a standard syringe; Scenario B — During resuscitation, the median basilic vein was accessed and adrenaline was to be administered from an adrenaline pre-filled syringe (Aguettant Santé, Lyon, France); Scenario C — During CPR, intraosseous tibial vascular access was obtained using a NIO Adult kit, and adrenaline was administered using a pre-filled syringe with adrenaline (Aguettant Santé, Lyon, France). Both the order of resuscitation and medication administration as well as the order of participants were random.

RESULTS: The time to obtain vascular access in the examined scenarios varied and was 240 sec [IQR; 220–265] for Scenario A, 236 sec [IQR; 210–270] for Scenario B, and 165 sec [IQR; 90–180] for Scenario C; A vs. C, ($p < 0.001$), B vs. C ($p < 0.001$). In scenarios A, B, and C, the duration of adrenaline administration varied and was 55 sec [IQR; 50–85] vs. 20 sec [IQR; 18–35] vs. 20 sec [IQR; 20–30] (A vs. B, and A vs. C, $p < 0.001$).

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CONCLUSIONS: A simulation study has shown that paramedics in two-person teams are unable to deliver adrenaline at the time recommended by CPR guidelines. The delay of CPM adrenaline supply compared to PFS adrenaline is statistically significant. In the opinion of paramedics participating in the study, adrenaline during resuscitation should be administered by means of pre-filled syringes, which eliminates the delays in rescue operations resulting from the time needed to prepare drugs as well as limited human resources in rescue teams.

KEY WORDS: cardiopulmonary resuscitation, medical simulation, pre-filled syringe, epinephrine, emergency medical service

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INTRODUCTION

Medical errors are a relatively frequent phenomenon in hospitals, especially related to the preparation and administration of medicines [1, 2]. Numerous studies, including those of Berdot et al. [3], Parshuram et al. [4], and Gokhman et al. [5], indicate that errors in drug preparation concern up to 48% of cases. Double-checking should be conducted, because this could reduce drug administration errors by about 20%, but collaborative efforts between all health-care professionals are essential [1]. As indicated by Hedlund et al., error types and reported rates vary substantially, including wrong drug (0% to 4.7%), wrong diluent solution (0% to 49.0%), wrong label (0% to 99.0%), wrong dose (0% to 32.6%), wrong concentration (0.3% to 88.6%), wrong diluent volume (0.06% to 49.0%), and inadequate aseptic technique (0% to 92.7%) [6].

The risk of error is all the more important in the aspect of emergency medicine, especially sudden cardiac arrest, where, according to the guidelines for resuscitation published by both the European Resuscitation Council and the American Heart Association, in the case of non-shockable rhythms, adrenaline should be administered as soon as possible after obtaining vascular access [7, 8]. During the cardiopulmonary resuscitation (CPR) there is a need to take quick action, and in the case of two-person emergency teams, therapeutic compromises are to be expected often.

The solution to this problem may be ready-made pre-filled syringes, which eliminate mistakes in the administration of the wrong drug, reduce the risk of the improper dose, and shorten the time to administer drugs [9]. An example of adrenaline in the form of progression-free survival (PFS) is the adrenaline from Aguetant Santé (Lyon, France), which is produced in 10 mL syringes with a standard Luer system, and the adrenaline itself is at a concentration

of 1:10,000, which facilitates its supply, especially in the context of paediatric patients, and allows for the infusion of the already diluted drug for both adults and children.

The aim of the study was to determine different methods of adrenaline supply during cardiopulmonary resuscitation in order to follow the adult resuscitation algorithm recommended by the American Heart Association 2015 [8].

MATERIAL AND METHODS

The trial was designed as a randomised cross-over simulation study. The study protocol was approved by the Institutional Review Board of the Polish Society of Disaster Medicine (Approval no. 07.10.2019 IRB). The study included 20 teams of two people composed of paramedics. Each of the study participants, having familiarised themselves with the study objectives, expressed a voluntary desire to participate in the study.

Prior to the study, all participants underwent one hour of theoretical training in adult advanced cardiopulmonary resuscitation based on the American Heart Association 2015 guidelines [8]. Next, training was carried out on how to obtain intraosseous access to the NIO Adult kit (PerSys Medical, USA) and the use of a pre-filled syringe with adrenaline (Aguettant Santé, Lyon, France; Fig. 1).

The order of participants as well as the selection of participants in two-person groups was random; for this purpose the Research Randomizer program was used. The participants were to perform 10-minute adult cardiopulmonary resuscitation based on the cardiopulmonary resuscitation algorithm. The rhythm accompanying cardiac arrest was asystole. The participants performed cardiopulmonary resuscitation in three scenarios:

Scenario A — During CPR, access to the median basilic vein and preparation and administra-



FIGURE 1. Example of pre-filled syringe with adrenaline

tion of adrenaline infusions from generally available ampoules at concentration 1:1000 were required (Adrenaline WZF 0.1%; Polfa, Warsaw, Poland) with a standard syringe.

Scenario B — During resuscitation, the median basilic vein was accessed, and adrenaline was to be

administered from an adrenaline pre-filled syringe (Aguettant Santé, Lyon, France).

Scenario C — During CPR, intraosseous tibial vascular access was obtained using a NIO Adult kit, and adrenaline was administered using a pre-filled syringe with adrenaline (Aguettant Santé, Lyon, France).

Vascular access was performed based on the principles of aseptic and antiseptic. In each scenario it was assumed that rescue teams would conduct resuscitation based on the AHA algorithm. According to the above algorithm, adrenaline will be administered in a dose of 1 mg every 3–5 minutes. After a 10-minute CPR procedure, the participants had a one-hour break and then performed CPR based on another scenario. The detailed randomisation procedure is presented in Figure 2.

In each scenario, the time of access, measured from the diagnosis of cardiac arrest and start of resuscitation, and the time of supply of the first dose of adrenaline, measured as the time between

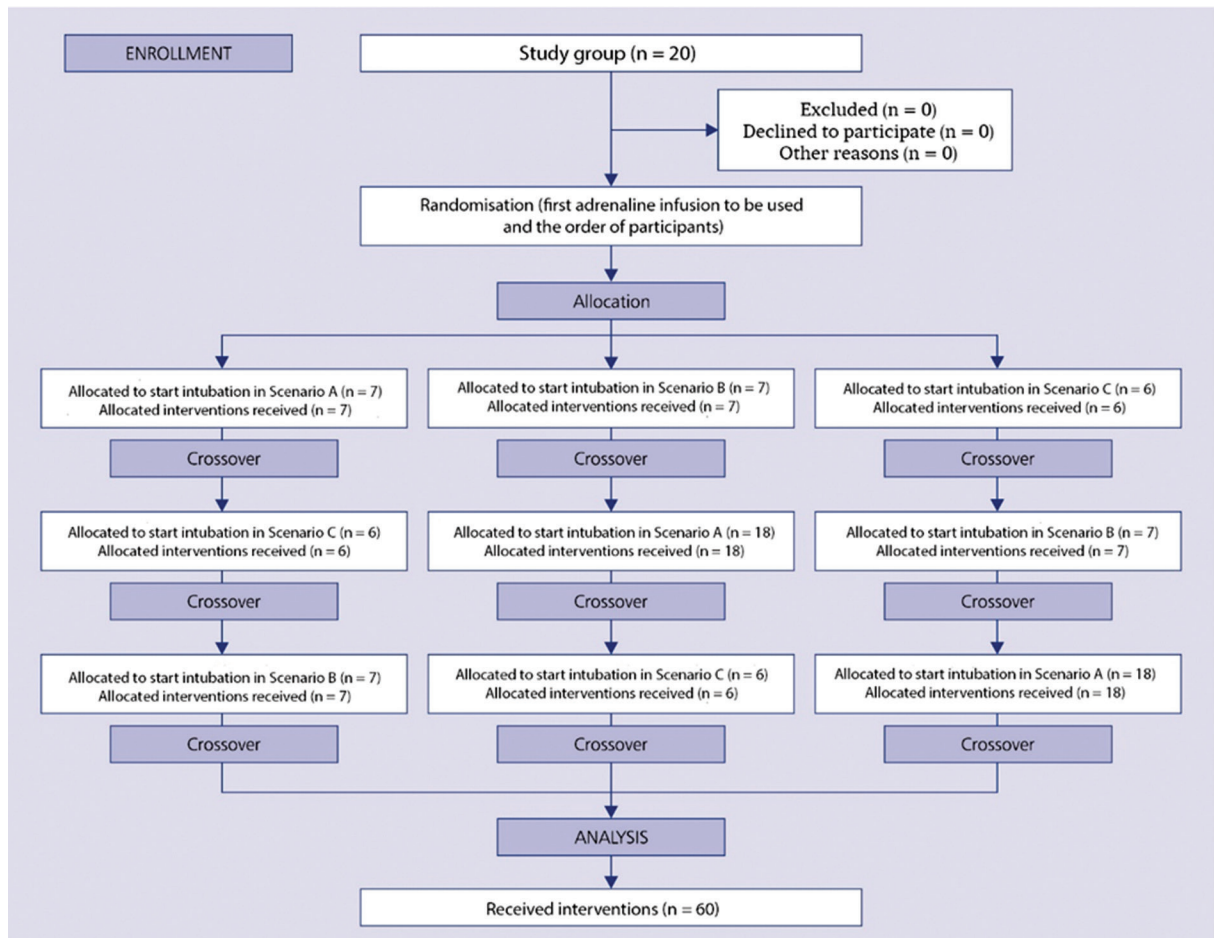


FIGURE 2. Randomisation flow chart

cardiac arrest and the end of 1 mg of adrenaline supply, were assessed. The reference point was the algorithm of advanced resuscitation in adults [8], according to which in non-shockable rhythms adrenaline should be administered as soon as possible. Additionally, after the completion of the study, rescuers were asked to determine the preferences concerning the method of adrenaline administration during resuscitation.

The data were collected by the instructors using a previously prepared study protocol. Statistical analysis was conducted using Statistica 13.3 EN statistical package (Tibco Inc., Tulsa, OK, USA). The results were considered statistically significant at $p < 0.05$.

RESULTS

The study involved 40 paramedics, who formed 20 two-person resuscitation teams. The average age of the study participants was 32.5 ± 4 years, while the average length of service in emergency medicine was 9.6 ± 7.3 years. None of the participants had previously had to deal with pre-filled syringes with adrenaline during CPR. All participants declared clinical experience in cardiopulmonary resuscitation as well as the ability to perform intraosseous access.

Time to obtain vascular access

The time to obtain vascular access in the examined scenarios varied and was 240 sec [IQR; 220–265] for Scenario A, 236 sec [IQR; 210–270] for Scenario B, and 165 sec [IQR; 90–180] for Scenario C. There were significant statistical differences in the time to obtain vascular access between Scenarios A and C ($p < 0.001$), and between Scenarios B and C ($p < 0.001$).

Time of administration of the first dose of adrenaline

The analysis to determine the time of adrenaline administration, measured from the moment of access to the vascular system, through preparation of adrenaline for infusion, to the moment of notification of 1 mg of adrenaline, was performed in each of the examined scenarios. In scenarios A, B and C, the duration of adrenaline administration varied and was 55 sec [IQR; 50–85] vs. 20 sec [IQR; 18–35] vs. 20 sec [IQR; 20–30], respectively. Statistically significant differences were noted between scenarios

A and B ($p < 0.001$), as well as between scenarios A and C ($p < 0.001$).

Self-assessment

The study participants unanimously stated that the first dose of adrenaline during CPR should be administered with a pre-filled syringe. At the same time, all participants of the study also stated that the optimal method of accessing the vascular system during CPR is an intraosseous access.

DISCUSSION

Rapid implementation of advanced resuscitation procedures, including vascular access and adrenaline administration, is one of the key elements in the context of non-shockable rhythms. As indicated by the CPR guidelines for asystole or pulseless electrical activity (PEA), rapid adrenaline administration is one of the key elements of management. The main focus of the study was to compare the duration of PFS adrenaline and CPM adrenaline; the time parameters of intraosseous and intravenous access under simulated cardiopulmonary resuscitation were also examined.

Currently, many drugs in the form of pre-filled syringes are available on the medical market. They are particularly appreciated in anaesthesia. As indicated by Saliba et al. [10], the use of pre-filled saline syringes significantly reduced peripheral venous catheter failure and increased catheter dwell time. In turn, in research by Jenson et al., in a review of 80 incidents, use of PFS with thiopental was shown to result in fewer dose and substitutional errors [11]. Benhamou et al. carried out an analysis in which they compared the cost and occurrence of medical errors between the use of atropine in standard ampoules and PFS atropine [12]. Preliminary results showed that atropine CMP is much more expensive than atropine PFS. This relationship applies to all drugs in the form of PFS. However, Benhamou points out that if medical errors and overall preparation of the drug for administration are also taken into account, it turns out that PFS adrenaline can reduce hospital costs. Saving would mainly relate to a reduced number of medication errors and the elimination of wastage in concentration with atropine syringes prepared in advance. Also, Larmené-Beld et al., in their analysis of the cost of medicines, showed that the use of PFS compared to CPM leads to a significant cost reduction,

which results in an improvement of the medical unit's budget [13]. The cost reduction, as in the Benhamou et al. study, is related to reductions in the number of medication errors and contaminations of parenteral medications.

In the simulation study, preparation of the drug was much shorter in the case of adrenaline in the form of PFS compared to CPM adrenaline. This may affect the change of rhythm during CPR in real-life conditions. [14, 15]. Another key element that was also shown in the study was the fact that an intraosseous access is a much faster method of obtaining a vascular access than an intravenous one.

Baert et al. suggest that intraosseous access is a comparably effective alternative to peripheral intravenous access for treating OHCA patients in matched populations [16]. Therefore, CPR drugs can be administered both by the intraosseous access and intravenously with the same efficacy, but the key element is the time taken to gain vascular access. In this regard, intraosseous access is the quickest method of obtaining vascular access [17], and is recommended especially for cardiopulmonary resuscitation [18] or hypovolaemic shock when the vascular bed is collapsed [19–21]. Holloway et al. indicated that humerus intraosseous versus intravenous provides rapid and reliable access to administer life-saving medications during cardiac arrest [22]. In turn, Rose et al., in the setting of out-of-hospital cardiac arrest, showed that the time to administer the first dose of epinephrine was faster in the IO access group when compared to the peripheral intravenous access group [18].

Among the limitations of the study, one can specify the fact that the study was conducted under medical simulation conditions and not under real (clinical) resuscitation; however, it is the medical simulation that allows for full standardisation of the obtained procedure conditions. Additionally, by means of medical simulation, medical procedures can be performed many times without potential harm to the patient. The possibility of measurements was an additional aspect that supported the use of medical simulation in the study. Another limitation was to carry out the study only in relation to paramedics; however, such a procedure was also purposeful and dictated by the fact that paramedics working in two-person teams in pre-hospital conditions must have technical solutions which will optimise the performance of the resuscitation.

CONCLUSIONS

A simulation study has shown that paramedics in two-person teams are unable to deliver adrenaline at the time recommended by CPR guidelines. The delay of CPM adrenaline supply compared to PFS adrenaline is statistically significant. In the opinion of the paramedics participating in the study, adrenaline during resuscitation should be administered by means of pre-filled syringes, which eliminates the delays in rescue operations resulting from the time needed to prepare drugs and from limited human resources in rescue teams.

Conflicts of interest: The authors declare no conflicts of interest regarding the publication of this paper.

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