Clinical paper

Effects of intra-resuscitation antiarrhythmic administration on rearrest occurrence and intra-resuscitation ECG characteristics in the ROC ALPS trial☆

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ABSTRACT

Background: Intra-resuscitation antiarrhythmic drugs may improve resuscitation outcomes, in part by avoiding rearrest, a condition associated with poor out-of-hospital cardiac arrest (OHCA) outcomes. However, antiarrhythmics may also alter defibrillation threshold. The objective of this study was to investigate the relationship between rearrest and intra-resuscitation antiarrhythmic drugs in the context of the Resuscitation Outcomes Consortium (ROC) amiodarone, lidocaine, and placebo (ALPS) trial.
Hypothesis: Rearrest rates would be lower in cases treated with amiodarone or lidocaine, versus saline placebo, prior to first return of spontaneous circulation (ROSC). We also hypothesized antiarrhythmic effects would be quantifiable through analysis of the prehospital electrocardiogram.
Methods: We conducted a secondary analysis of the ROC ALPS trial. Cases that first achieved prehospital ROSC after randomized administration of study drug were included in the analysis. Rearrest, defined as loss of pulses following ROSC, was ascertained from emergency medical services records. Rearrest rate was calculated overall, as well as by ALPS treatment group. Multivariable logistic regression models were constructed to assess the association between treatment group and rearrest, as well as rearrest and both survival to hospital discharge and survival with neurologic function. Amplitude spectrum area, median slope, and centroid frequency of the ventricular fibrillation (VF) ECG were calculated and compared across treatment groups.
Results: A total of 1144 (40.4%) cases with study drug prior to first ROSC were included. Rearrest rate was 44.0% overall; 42.9% for placebo, 45.7% for lidocaine, and 43.0% for amiodarone. In multivariable logistic regression models, ALPS treatment group was not associated with rearrest, though rearrest was associated with poor survival and neurologic outcomes. AMSA and median slope measures of the first available VF were associated with rearrest case status, while median slope and centroid frequency were associated with ALPS treatment group.
Conclusion: Rearrest rates did not differ between antiarrhythmic and placebo treatment groups. ECG waveform characteristics were correlated with treatment group and rearrest. Rearrest was inversely associated with survival and neurologic outcomes.

Table 1
Descriptive Statistics by Rearrest and ROSC Status.

	ROSC, Rearrest	ROSC, No Rearrest	No ROSC	Overall
N	503	641	1237	2381
Male, n (%)	399 (79.3%)	483 (75.4%)	1028 (83.1%)	1910 (80.2%)
Age				
Median (IQR)	66 (19.0)	63 (20.0)	63 (20.0)	64 (20.0)
< 40 yrs, n (%)	16 (3.2%)	41 (6.4%)	60 (4.9%)	117 (4.9%)
40–60 yrs, n (%)	154 (30.6%)	228 (35.6%)	434 (35.1%)	816 (34.3%)
≥60 yrs, n (%)	333 (66.2%)	372 (58.0%)	743 (60.1%)	1448 (60.8%)
Witness Status				
Bystander, n (%)	351 (69.8%)	448 (69.9%)	785 (63.5%)	1584 (66.5%)
EMS, n (%)	14 (2.8%)	27 (4.2%)	58 (4.7%)	99 (4.2%)
None, n (%)	138 (27.4%)	166 (25.9%)	394 (31.9%)	698 (29.3%)
Bystander CPR, n (%)	314 (62.4%)	392 (61.2%)	674 (54.5%)	1380 (58.0%)
Initial rhythm				
VT/VF, n (%)	497 (98.8%)	635 (99.1%)	1231 (99.5%)	2363 (99.2%)
PEA, n (%)	3 (0.6%)	3 (0.5%)	2 (0.2%)	8 (0.3%)
Asystole, n (%)	2 (0.4%)	2 (0.3%)	4 (0.3%)	8 (0.3%)
No shock advised, n (%)	1 (0.2%)	1 (0.2%)	0 (0.0%)	2 (0.1%)
Episode location				
Public, n (%)	341 (67.8%)	423 (66.0%)	869 (70.3%)	1633 (68.6%)
Private, n (%)	162 (32.2%)	218 (34.0%)	368 (29.7%)	748 (31.4%)
First agency arrival time				
< 6 min, n (%)	316 (62.8%)	444 (69.3%)	760 (61.4%)	1520 (63.8%)
≥6 min, n (%)	187 (37.2%)	197 (30.7%)	477 (38.6%)	861 (36.2%)
ALPS Treatment Arm				
Placebo, n (%)	155 (30.8%)	206 (32.1%)	472 (38.2%)	833 (35.0%)
Lidocaine, n (%)	192 (38.2%)	228 (35.6%)	366 (29.6%)	786 (33.0%)
Amiodarone, n (%)	156 (31.0%)	207 (32.3%)	399 (32.3%)	762 (32.0%)
Number of Shocks, mean (SD)	*6.2 (3.5)*	*4.6 (2.4)*	*6.9 (4.2)*	*6.2 (3.8)*
Site				
A, n (%)	3 (11.1%)	5 (18.5%)	19 (70.4%)	27
B, n (%)	44 (11.7%)	70 (18.6%)	263 (69.8%)	377
C, n (%)	40 (24.8%)	48 (29.8%)	73 (45.3%)	161
D, n (%)	30 (19.5%)	39 (25.3%)	85 (55.2%)	154
E, n (%)	3 (21.4%)	2 (14.3%)	9 (64.3%)	14
F, n (%)	37 (17.6%)	75 (35.7%)	98 (46.7%)	210
G, n (%)	31 (16.4%)	49 (25.9%)	109 (57.7%)	189
H, n (%)	122 (30.3%)	143 (35.5%)	138 (34.2%)	403
I, n (%)	108 (19.7%)	124 (22.6%)	317 (57.7%)	549
J, n (%)	85 (28.6%)	86 (29.0%)	126 (42.4%)	297

Abbreviations: ALPS: Amiodarone-Lidocaine-Placebo Study, CPR: cardiopulmonary resuscitation, EMS: emergency medical services, IQR: interquartile range, PEA: pulseless electrical activity, ROSC: return of spontaneous circulation, VT/VF: ventricular tachycardia/ventricular fibrillation.

Background

The administration of antiarrhythmic drugs during resuscitation of ventricular fibrillation (VF) or ventricular tachycardia (VT) out-of-hospital cardiac arrest (OHCA) follows the premise that modification of the arrhythmogenic myocardium can suppress recurrent VF episodes after initial return of spontaneous circulation (ROSC) [1]. In this sense, antiarrhythmic administration can be contextualized to the intermediate resuscitation outcome of *rearrest*, including the rhythm-specific subcategory of recurrent VF, previously associated with poor survival to hospital discharge and/or neurologic outcomes by our group and others [2–6]. The mechanism of antiarrhythmics in obviating recurrent VF or rearrest during resuscitation is conceptually complicated by the known effect of some antiarrhythmic drugs to increase the defibrillation threshold, an effect that should reduce the probability of successful defibrillation [7–9]. Even so, it was demonstrated almost two decades ago that both amiodarone and lidocaine can improve survival to hospital admission when administered for recurrent or refractory VF [10,11]. Later, the Resuscitation Outcomes Consortium (ROC) conducted the Amiodarone-Lidocaine-Placebo Study (ALPS), a large randomized controlled trial of amiodarone, lidocaine or placebo for treatment of recurrent or refractory VF [12]. In the general analysis, no significant differences were observed between treatment groups for the

survival to discharge or neurologic outcomes, although subgroup analyses showed heterogeneity of treatment effect based on witness status. Congruent with earlier studies, survival to hospital admission was greater among the antiarrhythmic treatment arms.

The ALPS trial provides a jumping off point for further investigation into the mechanisms and constraints by which antiarrhythmics fit into the resuscitation process, including their relationship to rearrest and their role in defibrillation. In the present study we sought to examine the intersection of these questions by considering not only the incidence and outcomes of rearrest in the ALPS trial, but also a measurable effect of the study drugs on the myocardium through analysis of the electrocardiogram (ECG) during resuscitation. We hypothesized that amiodarone and lidocaine would decrease the probability of rearrest occurrence compared to placebo and that their action would be demonstrable in ECG waveform analysis.

Methods

Primary clinical trial

We conducted this retrospective study under existing Institutional Review Board approved protocols. The population, design, and results of the primary analysis have been reported elsewhere [13], as have the