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Comparative Efficacy of Amiodarone and Lidocaine in Treating Cardiac Arrest Due to Ventricular Fibrillation and Pulseless Ventricular Tachycardia in Adults. A Literature Review

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ABSTRACT

Introduction

Sudden cardiac arrest (SCA) is a critical and lethal emergency, particularly in out-of-hospital settings, with shockable rhythms like ventricular fibrillation (VF) and pulseless ventricular tachycardia (VT) presenting significant challenges. Antiarrhythmic drugs, including amiodarone and lidocaine, are commonly used alongside defibrillation to stabilize cardiac rhythms. While amiodarone is the guideline-recommended choice, lidocaine serves as an alternative. Evidence from studies shows both drugs improve hospital admission rates, especially in bystander-witnessed cases, but their impact on survival to discharge and neurological outcomes remains uncertain. This review evaluates the comparative efficacy of these drugs to guide clinical practice and improve resuscitation outcomes.

Materials and methods

A thorough literature review was performed using electronic databases such as PubMed, Web of Science, Embase, and Google Scholar. The search strategy employed a combination of keywords, including "lidocaine," "amiodarone," "VF," "ventricular fibrillation," "pulseless ventricular tachycardia," "pVT" and "cardiac arrest." The search was restricted to English-language articles published from 1970 to 2024.

Aim of the study

The aim of this study is to systematically review and compare the efficacy of lidocaine and amiodarone in the treatment of cardiac arrest due to ventricular fibrillation and ventricular tachycardia in adults. This review seeks to evaluate the existing literature to determine the effectiveness and clinical outcomes associated with each medication.

Conclusions

The comparative analysis of amiodarone and lidocaine highlights their respective strengths and limitations in managing cardiac arrest, offering valuable insights for clinical practice. Amiodarone stands out as the preferred antiarrhythmic agent due to its significant efficacy in improving short-term outcomes, such as return of spontaneous circulation (ROSC) and survival to hospital admission. Its potential to enhance functional survival further reinforces its role, particularly when administered promptly during resuscitation efforts. In contrast, lidocaine remains a viable alternative, particularly in resource-limited settings or when contraindications to amiodarone exist. However, its limited impact on long-term survival and neurological recovery restricts its broader applicability.

Overall, amiodarone's efficacy and broader applicability position it as the first-line agent for shock-refractory ventricular fibrillation (VF) and pulseless ventricular tachycardia (pVT). Lidocaine serves as an important alternative in specific scenarios. Future research should aim to optimize antiarrhythmic protocols, improve long-term survival and neurological outcomes, and explore innovative approaches to resuscitation.

Key words: lidocaine, amiodarone, VF, ventricular fibrillation, pVT, pulseless ventricular tachycardia, cardiac arrest

1. Introduction

Sudden cardiac arrest remains a critical global health challenge, representing one of the most common and lethal emergencies in cardiovascular medicine. With annual incidences ranging from 320,000 to 700,000 in the United States and Europe, out-of-hospital cardiac arrest due to shockable rhythms—ventricular fibrillation (VF) and pulseless ventricular tachycardia (pVT)—is particularly concerning due to its high mortality and neurological morbidity rates. [1, 2] Despite significant advances in cardiopulmonary resuscitation and defibrillation techniques, long-term survival with favorable neurological outcomes remains disappointingly low. Among individuals admitted to intensive care units after return of spontaneous circulation (ROSC), fewer than half achieve meaningful neurological recovery.[1, 2]

In the context of resuscitating shockable rhythms, antiarrhythmic medications such as amiodarone and lidocaine are routinely employed as adjuncts to defibrillation, aiming to improve outcomes by stabilizing cardiac rhythms and preventing recurrent VF/VT episodes. While amiodarone is the guideline-recommended agent after failed defibrillation attempts, lidocaine is recognized as a suitable alternative. However, the clinical efficacy of these agents in improving survival to hospital discharge remains a subject of debate, and their comparative effects on overall survival and neurological outcomes warrant further investigation. [3–7]

This literature review critically examines and synthesizes evidence on the comparative efficacy of amiodarone and lidocaine in the management of OHCA caused by VF and VT in adults. By evaluating key randomized controlled trials, meta-analyses, and observational studies, this review aims to provide a comprehensive understanding of their role in resuscitation and inform clinical decision-making for optimizing patient outcomes.

2. Materials, Methods and Aim of the Study

A comprehensive literature review was performed using electronic databases such as PubMed, Web of Science, Embase, and Google Scholar. The search strategy incorporated a combination of keywords, including "lidocaine," "amiodarone," "ventricular fibrillation (VF)," "pulseless ventricular tachycardia (pVT)," and "cardiac arrest." Only English-language articles published from 1970 to 2024 were included. The primary aim of this study is to systematically review and compare the efficacy of lidocaine and amiodarone in the management of cardiac arrest due to ventricular fibrillation and ventricular tachycardia in adults. By synthesizing available evidence, this review provides valuable insights into the optimal use of lidocaine and amiodarone in resuscitation protocols and offers guidance for clinical decision-making in emergency and critical care settings.

3. Efficacy of Amiodarone in Cardiac Arrest

Amiodarone is a widely used antiarrhythmic agent, particularly in the management of shockable cardiac arrest rhythms, such as ventricular fibrillation (VF) and pulseless ventricular tachycardia (VT). Its introduction as part of advanced life support protocols has been a significant development in resuscitation medicine. This chapter examines the mechanisms, clinical evidence, and controversies surrounding the efficacy of amiodarone in the context of cardiac arrest. [1, 4, 8]

3.1 Pharmacological Properties and Mechanism of Action

Amiodarone is a diiodobenzofuran derivative, it is classified as a class III antiarrhythmic agent, though it also exhibits properties of other antiarrhythmic classes. Its primary mechanism of action involves blocking potassium channels (primarily IKr), which leads to prolongation of repolarization and action potential duration in both ventricular and atrial cardiomyocytes. This results in an extended refractory period, thereby suppressing ectopic and reentrant arrhythmias and causing QTc interval prolongation on the ECG.[8, 9]

Additionally, amiodarone partially blocks sodium channels (class I effect), which slows electrical impulse conduction within the heart, particularly in the ventricles, and calcium channels (class IV effect), which reduces activity in the atria and atrioventricular (AV) node, leading to a deceleration of conduction. Through these multi-faceted effects, amiodarone effectively controls various types of arrhythmias.[4, 8–10]

Amiodarone also acts as a noncompetitive antagonist of both beta- and alpha-adrenergic receptors, resulting in dilation of coronary and peripheral vessels and a reduction in blood pressure. This effect includes a beta-blocking component, producing negative inotropic, chronotropic, and dromotropic actions.[10]

After injection, the maximum effect is achieved within 15 minutes. After this time, distribution to tissues occurs, and there is a rapid decline in drug concentration in the plasma within 4 hours.[10]

3.2 Evidence Supporting Amiodarone Use in Cardiac Arrest

3.2.1 Clinical Trials

The efficacy of amiodarone in cardiac arrest was first highlighted in landmark trials, such as the Amiodarone in Out-of-Hospital Cardiac Arrest Trial (ARREST) and the Amiodarone versus Placebo in Resuscitation Trial (ALIVE). The ARREST trial demonstrated that patients receiving amiodarone had significantly higher rates of survival to hospital admission compared to placebo (44% vs. 34%, $p < 0.05$). Similarly, the ALIVE trial showed that amiodarone was superior to lidocaine in improving survival to hospital admission in cases of shock-refractory VF (22.8% vs. 12.0%, $p < 0.02$).
These studies established amiodarone as a preferred antiarrhythmic agent for shockable rhythms, leading to its inclusion in international resuscitation guidelines. [11, 12]

3.2.2 The ROC-ALPS Study

The Resuscitation Outcomes Consortium Amiodarone, Lidocaine, or Placebo Study (ROC-ALPS) provided further insights into the use of amiodarone. This large, multicenter

randomized controlled trial compared amiodarone, lidocaine, and placebo in out-of-hospital cardiac arrest (OHCA) cases. The primary endpoint was survival to hospital discharge. While amiodarone and lidocaine showed no significant difference in overall survival compared to placebo, both drugs improved survival to hospital discharge in bystander-witnessed arrests. This finding underscores the importance of early intervention and the context of cardiac arrest when evaluating the efficacy of antiarrhythmic agents. [13]

3.2.3 Meta-Analyses

A meta-analysis by Kudenchuk et al. (2014) synthesized evidence from several studies to assess the impact of amiodarone on outcomes in OHCA. The analysis confirmed that amiodarone increases the likelihood of ROSC and survival to hospital admission compared to placebo. However, the effect on survival to discharge and neurological outcomes remains less conclusive, necessitating further investigation. [13]

3.3 Factors Influencing Amiodarone Efficacy

3.3.1 Timing of Administration

The timing of amiodarone administration plays a crucial role in its efficacy. Delays in administration reduce its effectiveness, emphasizing the need for rapid drug delivery during resuscitation. Studies suggest that earlier administration, ideally within the first three defibrillation attempts, yields better outcomes. [8, 14][15]

3.3.2 Dosage and Formulation

The standard resuscitation dose of amiodarone is a 300 mg bolus, with an additional 150 mg if VF/VT persists. The use of newer formulations, such as Nexterone, which minimizes hemodynamic side effects, may improve the tolerability and overall success of amiodarone in cardiac arrest scenarios. [8, 14]

3.3.3 Patient Characteristics

Amiodarone's efficacy may vary based on patient factors such as the cause of cardiac arrest, underlying comorbidities, and the presence of bystander CPR. For example, its benefit is more pronounced in witnessed arrests with shockable rhythms, highlighting the heterogeneity of cardiac arrest populations.[8, 10, 14][16]

3.4 Challenges and Controversies

3.4.1 Lack of Impact on Long-Term Survival

While amiodarone improves intermediate outcomes, such as ROSC and hospital admission, its impact on long-term survival and neurological recovery remains uncertain. This limitation raises questions about its role in improving meaningful outcomes. [14, 17, 18]

3.4.2 Potential Adverse Effects

Amiodarone's side effect profile, including hypotension and bradycardia, may complicate resuscitation efforts. Balancing its benefits against these risks is a critical consideration in its use.[8, 9, 19]

3.5 Implications for Clinical Practice

Amiodarone remains a cornerstone of advanced life support for shockable rhythms in cardiac arrest. Its ability to improve short-term outcomes, such as ROSC and survival to hospital admission, justifies its use in resuscitation protocols. However, clinicians must recognize its limitations and consider individual patient characteristics when administering amiodarone. Future research should focus on refining its use to maximize benefits while minimizing risks. [14, 17]

3.6 Conclusion

Amiodarone plays a vital role in the management of VF and pulseless VT during cardiac arrest, demonstrating efficacy in achieving ROSC and improving survival to hospital admission. However, its impact on long-term survival and neurological outcomes remains uncertain. Ongoing research and clinical trials are essential to address these gaps and optimize the use of amiodarone in resuscitation efforts. In the interim, its judicious use, guided by current evidence and clinical judgment, is critical to improving outcomes in cardiac arrest patients.

4. Efficacy of Lidocaine in Cardiac Arrest

Lidocaine has been used extensively as an antiarrhythmic agent in the management of cardiac arrest, particularly for shockable rhythms such as ventricular fibrillation (VF) and pulseless ventricular tachycardia (VT). Its role in resuscitation has evolved over decades, shifting from a primary antiarrhythmic to an alternative option in cases where amiodarone is unavailable. This chapter explores the pharmacological basis, clinical evidence, and current challenges associated with lidocaine use in cardiac arrest.

4.1 Pharmacological Properties and Mechanism of Action

Lidocaine is a class IB antiarrhythmic drug that primarily acts by blocking fast sodium channels in cardiomyocytes, leading to a shortened action potential duration and accelerated repolarization. By binding to sodium channels in their open or inactivated states, it inhibits the influx of sodium ions into the cell, a mechanism particularly effective in ischemic or damaged tissues. This action shortens the refractory period in the ventricles, reducing the risk of ectopic beats and suppressing ventricular arrhythmias, especially under ischemic conditions, such as during acute myocardial infarction. [20, 21]

After intravenous administration, the antiarrhythmic effect of lidocaine begins rapidly. Peak plasma concentration occurs within 1–2 minutes. The effect of the bolus dose lasts for 10–20 minutes. After intravenous administration, the drug first quickly reaches highly perfused organs, followed by redistribution to skeletal muscles and adipose tissue. The half-life during the alpha distribution phase is approximately 6–9 minutes. [22]

4.2 Evidence Supporting Lidocaine Use in Cardiac Arrest

4.2.1 Early Observational Studies

Early observational studies and case series in the 1970s and 1980s established lidocaine as a mainstay in managing VF and VT during cardiac arrest. These studies demonstrated improved rates of return of spontaneous circulation (ROSC) and survival to hospital admission when lidocaine was administered. However, the absence of randomized controlled trials (RCTs) limited the ability to draw definitive conclusions regarding its impact on long-term survival and neurological outcomes. [20]

4.2.2 Randomized Controlled Trials

The comparative efficacy of lidocaine was first rigorously evaluated in trials such as the ALIVE study, which assessed amiodarone versus lidocaine. While amiodarone demonstrated

superior efficacy in achieving ROSC and survival to hospital admission, lidocaine remained effective in a substantial proportion of cases. Subsequent trials, including the ROC-ALPS study, evaluated lidocaine alongside amiodarone and placebo. ROC-ALPS found that lidocaine, similar to amiodarone, improved survival to hospital discharge in bystander-witnessed arrests, although no significant differences were observed in overall survival rates compared to placebo. [11–13]

These findings support lidocaine's continued utility as an alternative antiarrhythmic, particularly in resource-limited settings where amiodarone may not be available.

4.2.3 Meta-Analyses

A meta-analysis evaluated the efficacy of antiarrhythmic agents, including lidocaine, in the context of cardiac arrest. While lidocaine improved intermediate outcomes such as ROSC and survival to hospital admission, its effect on long-term survival and neurological outcomes was less pronounced. This underscores the need for further investigation into its role in optimizing meaningful recovery. [13, 23, 24]

4.3 Factors Influencing Lidocaine Efficacy

4.3.1 Timing of Administration

Similar to amiodarone, the timing of lidocaine administration is critical for its efficacy. Early administration, particularly after the failure of initial defibrillation attempts, enhances the likelihood of ROSC and survival. Delays in delivery may diminish its effectiveness, highlighting the importance of streamlined protocols during resuscitation. [14][15]

4.3.2 Dosage and Protocols

The standard dose of lidocaine during cardiac arrest is a bolus of 1–1.5 mg/kg, followed by additional doses if VF/VT persists. The cumulative dose should not exceed 3 mg/kg to minimize the risk of toxicity. Proper adherence to these protocols is essential for maximizing its benefits while minimizing adverse effects. [14, 20]

4.3.3 Patient Characteristics

Lidocaine's efficacy may vary based on patient-specific factors, including the etiology of cardiac arrest, comorbid conditions, and the presence of bystander CPR. For instance, in patients with ischemic cardiac arrest, lidocaine may be particularly effective due to its stabilizing effects on ischemic myocardial tissue. [20, 21] [16]

4.4 Challenges and Limitations

4.4.1 Lack of Definitive Evidence on Long-Term Survival

Although lidocaine improves short-term outcomes such as ROSC and hospital admission rates, its impact on survival to hospital discharge and neurological recovery is less certain. This limitation parallels the challenges observed with other antiarrhythmic agents, including amiodarone. [17, 25, 26]

4.4.3 Adverse Effects

Lidocaine's adverse effect profile, particularly central nervous system toxicity, presents a potential drawback. Symptoms such as seizures, confusion, and drowsiness may complicate post-resuscitation care, especially if cumulative doses exceed recommended limits.[20, 21]

4.5 Implications for Clinical Practice

Lidocaine continues to hold a valuable position as an alternative antiarrhythmic agent in cardiac arrest management. Its inclusion in resuscitation guidelines reflects its efficacy in improving short-term outcomes, particularly in bystander-witnessed arrests and settings where amiodarone is unavailable. Clinicians should carefully consider patient characteristics, timing, and dosage when administering lidocaine, balancing its benefits against potential risks. [1, 18, 27]

Ongoing education for emergency medical services (EMS) providers regarding the appropriate use of lidocaine is essential to ensure optimal outcomes. Furthermore, enhanced

systems of care, including rapid access to antiarrhythmic drugs and streamlined resuscitation protocols, can amplify its effectiveness.

4.6 Conclusion

Lidocaine remains a critical component of the resuscitation toolkit, offering a reliable alternative to amiodarone in the treatment of shockable rhythms during cardiac arrest. While it has demonstrated efficacy in improving intermediate outcomes such as ROSC and survival to hospital admission, its effect on long-term survival and neurological recovery requires further clarification. Continued research is essential to delineate its role relative to other antiarrhythmics and to optimize its use in diverse clinical scenarios. In the meantime, lidocaine serves as an effective and accessible option, particularly in resource-constrained environments.

5. Comparative Analysis

The use of antiarrhythmic drugs, particularly amiodarone and lidocaine, remains a cornerstone in managing ventricular fibrillation (VF) and pulseless ventricular tachycardia (pVT) during cardiac arrest. Despite their widespread application, their relative efficacy, timing of administration, and influence on long-term outcomes continue to be debated. This chapter provides a comprehensive comparative analysis based on recent evidence, including randomized controlled trials and meta-analyses, highlighting key findings and clinical implications.

5.1 Mechanism of Action and Pharmacodynamics

Amiodarone and lidocaine differ significantly in their mechanisms of action, pharmacokinetics, and systemic effects:

Amiodarone:

- Acts as a class III antiarrhythmic by prolonging repolarization through potassium channel blockade.
- Exhibits properties of other antiarrhythmic classes, including sodium channel blockade (class I) and calcium channel inhibition (class IV).
- Beta- and alpha-adrenergic blocking properties contribute to vasodilation and reduced myocardial oxygen demand but may induce hypotension and bradycardia during resuscitation.[9, 10, 24]

Lidocaine:

- A class IB antiarrhythmic that blocks sodium channels, shortening the action potential duration, particularly in ischemic tissue.
- Provides rapid onset of action with a shorter half-life than amiodarone, making it suitable for acute arrhythmia suppression. [20–22]

Table 2. Pharmacological Comparison

	Amiodarone	Lidocaine
Class	III (with I, II, IV properties)	IB
Onset of Action	15 minutes	1–2 minutes
Duration of Action	Hours to days	10–20 minutes
Key Adverse Effects	Hypotension, bradycardia	CNS toxicity (rare)

5.2 Timing of Administration: Critical Impact

Timing plays a pivotal role in the efficacy of both drugs. Data indicate that earlier administration yields significantly better outcomes:

- Amiodarone: When administered within eight minutes of ALS arrival, it significantly improves survival to discharge and functional outcomes. Delayed administration reduces its effectiveness, particularly beyond 20 minutes.
- Lidocaine: Timing effects are less pronounced, with minimal differences observed between early and late administration. This limits its utility in scenarios where delays in drug delivery are unavoidable.[15, 26][28, 29]

5.3 Survival Outcomes: Hospital Admission and Discharge

Numerous studies have evaluated the impact of amiodarone and lidocaine on survival rates. Data from the ROC-ALPS trial illustrate distinct differences between these agents:

1. Amiodarone:
- Improves rates of return of spontaneous circulation (ROSC) and survival to hospital admission. In shock-refractory cases, early administration of amiodarone increased survival to admission to 62.0% compared to 48.5% for placebo ($p < 0.001$).
- Enhances survival to hospital discharge in specific subgroups. In bystander-witnessed cardiac arrests, the survival rate was 37.1% compared to 28.0% for placebo ($p = 0.021$).
- Impact on functional survival (defined as a modified Rankin Scale score ≤ 3) reached 31.6% in the early administration group, compared to 23.3% for placebo ($p = 0.029$).

2. Lidocaine:
- Offers modest benefits in early stages, particularly for survival to admission (40.0% vs. 33.9% for placebo; $p = 0.023$).
- Does not consistently demonstrate significant improvement in survival to discharge or neurological outcomes compared to placebo.[30]

5.4 Neurological Outcomes

Amiodarone demonstrates a potential advantage in preserving neurological function, as reflected in functional survival rates (31.6% for early administration vs. 23.3% for placebo). Lidocaine has not shown a significant impact on neurological outcomes in most analyses.[31, 32]

5.5 Adverse Effects

Both agents carry distinct risk profiles:

- Amiodarone: Hypotension and bradycardia are common, potentially complicating hemodynamic stability during resuscitation.
- Lidocaine: Adverse effects are generally less frequent but may include CNS toxicity at high doses, such as seizures or confusion. [1, 8, 21, 22]

5.6 Clinical Implications and Recommendations

Current guidelines prioritize amiodarone over lidocaine for managing shock-refractory VF and pVT, reflecting its consistent performance in improving intermediate outcomes. Lidocaine remains a reasonable alternative in resource-limited settings or when contraindications to amiodarone exist.[32–34]

6. Conclusion

The comparative analysis of amiodarone and lidocaine reveals significant insights into their roles as antiarrhythmic agents in the management of shockable rhythms during cardiac arrest.

Both drugs are integral components of advanced life support protocols; however, their clinical applications and outcomes demonstrate important differences:

6.1. Efficacy in Survival Outcomes:

Amiodarone exhibits superior efficacy in achieving return of spontaneous circulation (ROSC) and survival to hospital admission compared to lidocaine and placebo. Its benefits are particularly evident when administered early, highlighting the importance of timely intervention. Lidocaine remains a viable alternative, showing benefits in improving short-term outcomes, but its effects on long-term survival and neurological recovery are less pronounced. [11, 14, 31, 34]

6.2. Impact on Neurological Outcomes:

While amiodarone shows some promise in preserving neurological function as reflected in improved functional survival rates, lidocaine's impact on neurological recovery remains limited. This distinction underscores the potential advantage of prioritizing amiodarone in resuscitation protocols, especially in scenarios where favorable neurological outcomes are critical.[3, 11, 14, 17, 18, 29, 33]

6.3. Safety Profiles and Practical Considerations:

Both drugs have distinct safety profiles that must be carefully considered. Amiodarone's risk of hypotension and bradycardia necessitates cautious use, particularly in hemodynamically unstable patients. Lidocaine, while generally well-tolerated, poses risks of central nervous system toxicity at higher doses. Clinicians must balance these risks against the potential benefits when selecting an antiarrhythmic agent.

Current evidence supports the guideline-recommended use of amiodarone as the first-line agent for shock-refractory ventricular fibrillation (VF) and pulseless ventricular tachycardia (pVT). Lidocaine remains a suitable alternative, particularly in resource-limited settings or when amiodarone is contraindicated. [11, 14, 31, 34]

7. Author's contributions

The authors confirm contribution to the paper as follows:
Conceptualization: Patryk Dryja
Methodology: Patryk Dryja
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Check: Patryk Dryja, Agata Boczar, Jakub Jarmłowicz, Sven Solisch
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Writing - review and editing: Patryk Dryja, Agata Boczar, Izabela Orzołek, Izabela Stawicka, Jakub Jarmołowicz
Visualization: Agata Boczar
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All authors have read and agreed with the published version of the manuscript.

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11. Data Availability Statement

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12. Conflicts of Interest

The authors declare no conflict of interest.

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