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AMIODARONE VERSUS LIDOCAINE FOR PEDIATRIC CARDIAC ARREST DUE TO VENTRICULAR ARRHYTHMIAS: A SYSTEMATIC REVIEW

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Abstract

Background: *Pediatric cardiac arrests are relatively uncommon but pose significant burdens. The management of pediatric cardiac arrest is unclear between amiodarone or lidocaine, necessitating further research to establish effective interventions.*

Aim: *to systematically review the effect and funtion of amiodarone and lidocaine, whether amiodarone is more recommended or vice versa.*
Methods: *this review conducted a thorough literature search comparing amiodarone and lidocaine for shock-refractory pVT/VF in children. Outcomes, including ROSC, termination of arrhythmia, and survival at discharge, were also evaluated.*

Results: *Out of 756 articles, only three met inclusion criteria comparing amiodarone and lidocaine for VT/VF. One adult study favored amiodarone for survival to hospital admission, but not discharge. Another study on pediatric cases showed lidocaine improved ROSC and 24-hour survival significantly. However, evidence quality was very low for both drugs, warranting further research. A small trial in adults favored amiodarone in stable VT, but its limited size and data quality pose limitations.*

Conclusion: *The findings of this systematic review proposes that either amiodarone or lidocaine could be considered for the treatment of pediatric shock-resistant VF/pVT.*

Keywords: *lidocaine, amiodarone, cardiac arrest*

INTRODUCTION

Cardiac arrests in pediatric admissions occur at a frequency of 0.7% to 3%, while in pediatric intensive care unit admissions, the rate is higher, ranging from 1.8% to 5.5%. These incidents impose substantial societal, familial, and economic burdens. Over the years, there has been progress in survival rates following in-hospital cardiac arrests, with an increase from 16% to 30% in recent years.[1] Pediatric cardiac arrests present unique challenges due to differences in etiology and outcomes compared to adult cases. The underlying physiology and epidemiology of cardiac arrest vary significantly between children and adults. In pediatric patients, cardiac arrest is often preceded by respiratory and circulatory insufficiency as underlying causes, while sudden cardiac death is more common in adults. This difference in etiology may result in children experiencing a more advanced state of acidosis, hypoxia, and metabolic deterioration at the time CPR is initiated, potentially impacting the effectiveness of resuscitation efforts. Furthermore, cardiac arrest events in pediatric populations are relatively rare, even in tertiary pediatric centers, and even rarer in non-pediatric emergency departments where the majority of pediatric patients are initially managed. This relative infrequency may lead to less optimal care delivery during CPR due to a lack of clinical experience with pediatric cases, potentially contributing to poorer outcomes in children receiving CPR during an ED visit.[2]

Pediatric cardiac arrest management necessitates a methodical and evidence-driven approach to enhance results. The International Liaison Committee on Resuscitation (ILCOR) serves as a global forum for achieving consensus on resuscitation science, collaborating with regional and national resuscitation councils like the American Heart Association (AHA) and the European Resuscitation Council. Over time, recommendations for managing pediatric cardiac arrest have evolved based on research findings. In the past, amiodarone was weakly recommended for pulseless ventricular tachycardia (pVT) and ventricular fibrillation (VF) in adults experiencing out-of-hospital cardiac arrest (OHCA). Similarly, the 2005 AHA Pediatric Advanced Life Support (PALS) guidelines supported the preference for amiodarone over lidocaine for pVT/VF based on an OHCA study involving adults. However, the available evidence for pediatric cardiac arrest management remains limited, necessitating further research to establish the most effective and safe interventions to improve outcomes in pediatric patients facing cardiac arrest. An in-depth understanding of the causes, mechanisms, and responses to interventions in pediatric cardiac arrest will facilitate the development of tailored guidelines for this distinct population, ultimately enhancing the delivery of high-quality care and increasing the likelihood of positive outcomes.[3,4]

Amiodarone and lidocaine have a different moechanism of action in managing pediatric cardiac arrest, specifically working on arrythmias. Amiodarone falls under the Vaughn-Williams III category due to its predominant influence on potassium channel inhibition. Nevertheless, it also exhibits traits of sodium channel blocking (class I), acts as a β-receptor antagonist (class II), and displays calcium channel blocking attributes (class IV). Moreover, it possesses various other antiarrhythmic properties not encompassed by this classification system. As a result, amiodarone's mechanism of action is intricate and multi-faceted, leading to its proven efficacy in managing a broad spectrum of arrhythmias.[5] While lidocaine works by blocking voltage-gated sodium channels, which are responsible for the initiation and propagation of action potentials in excitable cells such as neurons and cardiomyocytes. By blocking these channels, lidocaine can inhibit the generation and conduction of nerve impulses, which can lead to antiarrhythmic effects. Antiarrhythmic medications play dual roles within resuscitation protocols. Initially, as the duration of pulseless ventricular tachycardia (pVT) and ventricular fibrillation (VF) extends, the efficacy of defibrillation diminishes. Thus, these drugs are designed to reduce defibrillation thresholds and sustain normal sinus rhythm following defibrillation. Subsequently, after sinus rhythm has been restored, antiarrhythmic drugs aid in maintaining this rhythm and minimizing the likelihood of recurrent unstable ventricular rhythms.[6]

There is only a few recent review about the usage of amiodarone and lidocaine to manage the pediatric cardia arrest. Here, we aim to systematically review the effect and funtio of amiodarone and lidocaine, whether amiodarone is more recommended or vice versa.

Method

Search Strategy

The Pediatric Task Force of the International Liaison Committee on Resuscitation (ILCOR) conducted a thorough investigation during their 2015 update on resuscitation guideline. This systematic literature search was performed on PubMed, Cochrane, and Embased to identify relevant articles comparing the use of amiodarone and lidocaine in infants and children with shock-refractory pulseless ventricular tachycardia (pVT) or ventricular fibrillation (VF). The search utilized specific subject headings and keywords related to cardiac arrest, pVT/VF, and the drugs amiodarone and lidocaine, with a focus on pediatric populations. To maintain precision, letters, animal studies, comments, and case reports, were excluded from the search. The search was conducted on February 21, 2014, and no restrictions were applied regarding the publication date or language of the articles.

Table 1. Literature search strategy

Database	Keywords	Results
PubMed	"Heart Arrest" OR "cardiac arrest" OR "cardiovascular arrest" OR "pulseless electrical activity" OR "Ventricular Fibrillation" AND ("Amiodarone" OR "Lidocaine") AND ("Infant"OR "Child")	172
Cochrane Library	"Heart Arrest" OR "cardiac arrest" OR "cardiovascular arrest" OR "pulseless electrical activity" OR "Ventricular Fibrillation" AND ("Amiodarone" OR "Lidocaine") AND ("Infant" OR "Child")	310
Embased	"Heart Arrest" OR "cardiac arrest" OR "cardiovascular arrest" OR "pulseless electrical activity" OR "Ventricular Fibrillation" AND ("Amiodarone" OR "Lidocaine") AND ("Infant" OR "Child")	274

Eligibility Criteria

The selection criteria encompassed both retrospective and prospective observational studies or randomized controlled trials (RCTs). Case series without direct comparisons were excluded from consideration. The identified articles were then carefully assessed for their appropriateness in terms of population, intervention, comparison, and outcomes, following the PICO question framework. Since only one study met the initial criteria, supplementary searches were conducted to gather relevant studies involving adult patients.

Outcomes

The desired outcomes of interest included return of spontaneous circulation (ROSC), termination of arrhythmia, survival at discharge, recurrence of ventricular fibrillation (VF), and potential complications. The Cochrane Collaboration's tool for RCTs and the GRADE system for observational studies were employed to evaluate the retained articles. The GRADE method facilitated a systematic assessment of study design, quality, consistency, and the directness of evidence, allowing the grading of evidence for each outcome as high, moderate, low, or very low, considering various factors like bias, inconsistency, indirectness, imprecision, and publication bias.

Results

The search identified 756 articles, but only three studies met the inclusion criteria, comparing amiodarone to lidocaine for ventricular tachycardia (VT) or ventricular fibrillation (VF). Two studies were conducted on adults, and one on children. In one adult study, amiodarone showed a significant improvement in survival to hospital admission compared to lidocaine. However, there was no significant difference in survival to hospital discharge. The evidence for amiodarone's superiority was of very low quality. The study did not report data on VF recurrence or termination of arrhythmia, and complications were comparable between amiodarone and lidocaine groups, except for a higher incidence of asystole after defibrillation in the lidocaine group.

Valdes et al. studied pediatric in-hospital cardiac arrest cases with pulseless ventricular tachycardia (pVT) or ventricular fibrillation (VF). They analyzed data from the AHA's Get With the Guidelines-Resuscitation Registry (GWTG-R). The primary focus was on return of spontaneous circulation (ROSC), with secondary outcomes of 24-hour survival and survival to hospital discharge. Among the 889 patients, 19% received amiodarone, 33% received lidocaine, and 10% received both drugs. Lidocaine showed a statistically significant improvement in ROSC and 24-hour survival compared to amiodarone or no treatment. The evidence for preferring lidocaine over amiodarone was of very low quality due to limitations in the data. No significant difference in survival to hospital discharge was observed between the two drugs. The study suggested a preference for lidocaine use, but further research is needed to draw conclusive findings on other outcomes like VF recurrence, arrhythmia termination, and complications.

Somberg et al. conducted a double-blinded trial comparing amiodarone and lidocaine in adult patients with incessant ventricular tachycardia (VT) but a pulse. Amiodarone successfully terminated VT in 78% of patients, while lidocaine was successful in 27%. Survival at 24 hours was higher in the amiodarone group (39%) compared to the lidocaine group (9%). The study had limited patient recruitment with only 29 participants and did not address some important outcomes. Despite the preference for amiodarone in hemodynamically stable VT patients, the study's small size and limitations resulted in very low-quality data.

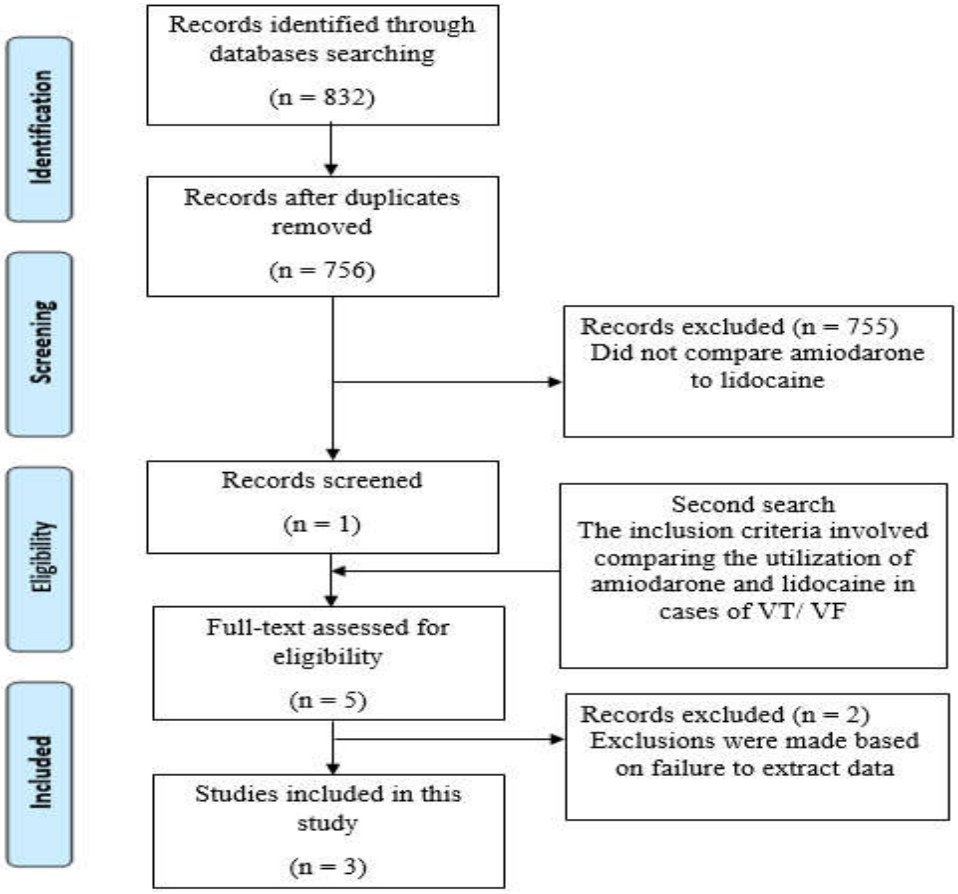

Figure 1. Selection flow diagram

Table 2. Summary of included studies

Source	Participants	ROSC (%)	Survival in 24h (%)	Survival to discharge (%)
Valdes et al[7]	Total = 889 Amio = 89 Lido = 213 Both = 82 Neither = 505	Amio = 39 (44) Lido = 136 (64) Both = 48 (59) Neither = 260 (51)	Amio = 27 (30) Lido = 100 (47) Both = 32 (39) Neither = 103 (20)	Amio = 15 (17) Lido = 54 (25) Both = 22 (27) Neither = 103 (20)
Somberg et al[8]	Total = 29 Amio = 18 Lido = 19	-	Amio = 7 (39) Lido = 1 (9)	-
Dorlan et al[9]	Total = 347 Amio = 180 Lido = 167	-	Amio = 41 (22.8) Lido = 20 (12)	Amio = 9(5) Lido = 5 (3)

Discussion

Limited studies compare amiodarone to lidocaine for cardiac resuscitation, with a focus on adults. This systematic review aim to make sure if any of choices whether amiodarone or lidocaine is superior compare to the other one. An observational study in pediatric cases favored lidocaine, while low-quality RCTs in adults favored amiodarone.[10] Due to the low quality and conflicting results, neither drug can be recommended as the first choice for pediatric resuscitation. Another large RCT in adults with out-of-hospital cardiac arrest showed no significant difference in survival between amiodarone, lidocaine, and placebo for shock-resistant pVT/VF.[11] Although the implications for pediatrics remain unclear, administering either amiodarone or lidocaine during pediatric resuscitation for shock-resistant pVT/VF seems reasonable.

Furthermore, the studies examined in this systematic revuew do not consider mechanistic information, which is crucial because the causes of cardiac arrest in pediatrics differ from those in adults. The applicability of the two RCTs conducted in adults to the pediatric population remains uncertain. Differences may exist in maintaining sinus rhythm after successful defibrillation or improving the rate of successful acute defibrillation (lowering defibrillation thresholds). Studies on implantable cardioverter-defibrillator testing suggest that lidocaine may increase the acute defibrillation threshold, while IV amiodarone may have no effect or decrease the threshold. Adult data on lidocaine and amiodarone effects may not be directly transferable to children due to varying causes of cardiac arrest. Adults often experience structural heart disease, leading to ongoing VF refractory to shocks, while children may lack such substrates, making the effectiveness of lidocaine or amiodarone in maintaining sinus rhythm uncertain in the pediatric population.[12]

The methodology utilized for the 2015 Consensus on Science with Treatment Recommendations by ILCOR was innovative. In an effort to employ the most effective methodological tools, ILCOR adopted GRADE based on the guidance of the Institute of Medicine of the National Academies. Developed over the past decade by health professionals, researchers, and guideline developers, this approach offers a transparent and rigorous process for guideline development. GRADE facilitates a more thorough examination of the literature and highlights areas that require further investigation in future studies. The stringent nature of this process is essential given the significance of these recommendations. [13]

This systematic review and consequent suggestion emphasize the necessity for additional investigation in this field. A preferable approach would involve a prospective RCT in pediatrics, comparing amiodarone to lidocaine, with a focus on longer-term outcomes like survival to hospital discharge and neurodevelopmental results. Further examination of arrest mechanisms, causes, drug dosages, administration methods, and defibrillation particulars would also contribute to enriching our understanding and enhancing care provision.

Conclusion

The findings of this systematic review proposes that either amiodarone or lidocaine could be considered for the treatment of pediatric shock-resistant VF/pVT. However, this recommendation is classified as weak, given the very low-quality evidence available to support it. Further research and evidence are required to establish more robust guidelines in this regard.

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