OPTIMIZING PEDIATRIC ANTIARRHYTHMIC THERAPY: A REVIEW OF EFFICACY AND SAFETY

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Abstract- **In light of differences in medication availability, regulatory approvals, and clinical expertise, tailored treatment plans are critical when managing pediatric arrhythmias. Certain drugs, like amiodarone, esmolol, and adenosine, have specific dosage recommendations, but other drugs, like digoxin or sotalol, don't. It is essential to compile and abide by published dosage recommendations for antiarrhythmic medications in children in order to reduce the risk of dosing errors and uncertainties. Healthcare institutions can ensure the safe and effective management of pediatric arrhythmias while taking into account the specific factors influencing drug administration and patient outcomes by creating center-specific protocols for antiarrhythmic drug therapy. There are few official guidelines and consensus documents regarding the treatment of pediatric arrhythmias; some drugs have standardized dosing recommendations, while others only possess broad directives. It is crucial to summarize published dosage recommendations for antiarrhythmic medications in children in order to address dosing uncertainties. Considering the vast differences in accessibility, legal authorization, and clinical background, each center should create its own unique protocols for pediatric antiarrhythmic medication therapy. For pediatric patients with arrhythmias, this method guarantees individualized and optimal treatment plans that account for differences in medication availability, regulatory clearance, and clinical knowledge.**

Keywords: **children; antiarrhythmic drugs; arrhythmia; electrophysiology; drug dosing.**

INTRODUCTION

Cardiac arrhythmias affect approximately 1 in 250 children, presenting recurrently and irrespective of structural heart disease, posing distinctive challenges for clinicians. Utilization of antiarrhythmic medications is widespread in both acute management and long-term therapy for pediatric arrhythmias. However, inadvertent ingestion of these medications by children, even in small doses, can be fatal, necessitating prompt recognition and intervention. Understanding the pharmacology and toxicities of antiarrhythmic medications is crucial for emergency department healthcare practitioners.This review aims to consolidate information on antiarrhythmics in pediatric patients, covering indications, pharmacology, and toxicological considerations. It encompasses standard dosing, available formulations, drug interactions, and recommendations for therapeutic monitoring. Additionally, a general approach to managing antiarrhythmic toxicities is proposed. Subsequent sections focus on commonly used antiarrhythmic agents categorized according to the Vaughan-Williams classification.

Pediatric arrhythmias primarily manifest as supraventricular tachycardias (SVTs), including atrioventricular reentry tachycardia (AVRT), atrioventricular nodal reentry tachycardia (AVNRT), and atrial tachycardia (AT). While atrial fibrillation (AF) and atrial flutter (AFL) are less prevalent in pediatric patients compared to adults, they may occur post-heart surgery or due to alcohol consumption. Ventricular tachycardia (VT) and ventricular fibrillation (VF) are rare in pediatric cases.Given the differing target arrhythmias compared to adults, antiarrhythmic drug (AAD) therapy in pediatric patients primarily involves beta-blockers and class I antiarrhythmics. Other agents like ivabradine are reserved for exceptional circumstances. However, recommendations regarding indications and dosage in pediatrics are largely based on expert consensus, with limited official guidelines available. In clinical practice, healthcare providers often rely on dosage recommendations from various sources, although gaps persist, particularly in comprehensive pediatric-specific information. This review aims to address this gap by providing a thorough overview of dosage recommendations for AADs in the pediatric population.

Classification of antiarrhythmic drug :

Class	Actions	Drugs
I	Sodium channel blockade	
IA	prolong repolarization	quinidine, procainamide, disopyramide
IB	shorten repolarization	lidocaine, mexiletine, tocainide, phenytoin
IC	little effect on repolarization	flecainide, encainide, propafenone
II	Beta-adrenergic blockade	propanolol, esmolol
III	Prolong repolarization potassium channel blockade	sotalol, amiodarone
IV	Calcium channel blockade	verapamil, diltiazem

Table No1

1.PROCAINAMIDE (CLASS IA)

Pediatric indications.

Procainamide is classified as a Class IA antiarrhythmic drug and is usually given intravenously as a bolus or continuous infusion. The oral version of procainamide, once used to treat heart arrhythmias, is no longer available in the United States. Procainamide is used for the rapid treatment of multimodal supraventricular tachycardia (SVT) and monomorphic ventricular tachycardia (VT). Additionally, procainamide effectively controls heart rate in postoperative junctional ectopic tachycardia, especially when used in conjunction with hypothermia.[1]

Mechanism of Action Procainamide works by binding to the internal sodium channel (Nav1.1) and preventing the rapid opening of this channel. 5) is encoded by SCN5A. This effect causes a decrease in sodium current (Ina), resulting in depolarization and slowing of conduction. As a result, the rise of phase 0 of the action potential in the atrium, ventricular muscle fibers and His-Purkinje system decreases. Nacetyl procainamide (NAPA), the main metabolite of procainamide, exerts its effects as a Class III antiarrhythmic drug by delaying repolarization. This helps in prolonging the working time and failure of cardiomyocytes. Notably, there genetic differences in the amount of NAPA acetylation and accumulation; patients exhibit the acetylation phenotype either rapidly or slowly.[2]

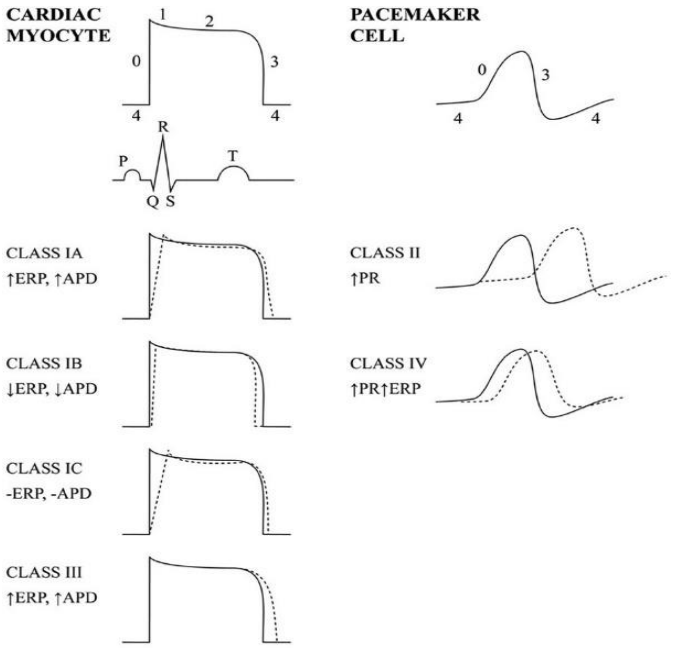
ADR

Conduction velocity slowing, widening of QRS complex, negative inotropic effect, hepatotoxicity, AFL with 1:1 AV conduction, bradyarrhythmia, sustained monomorphic VT.

Contraindication

(structural heart disease, ischemic heart disease), dose reduction during combination with warfarin or digoxin

Table No 2



2.LIDOCAINE (CLASS IB)

Pediatric Indications

Lidocaine is a type IB antiarrhythmic drug used as bolus or continuous injection in the treatment of ventricular arrhythmias. In pediatric support, amiodarone or lidocaine is recommended for the treatment of shock-refractory ventricular fibrillation or pulseless ventricular tachycardia. In the past, lidocaine was also used to treat cardiac arrest caused by digoxin overdose.[3]

Mechanism of action

Lidocaine generally binds to weak sodium channels, reduces late Ina, reduces the long-term action potential of His-Purkinje and ventricular muscle fibers. This often results in short run times and poor uptime. Lidocaine also reduces Ina, reduces the slope of phase 0, and reduces the slope of phase 4 (spontaneous depolarization), but does not apply to Class IA or Class IC antiarrhythmic drugs. Because lidocaine tends to bind to inactivated sodium channels in depolarizing cells, it is particularly effective in treating ventricular arrhythmias resulting from myocardial ischemia.[4]

ADR

Lidocaine may cause various side effects when used as a birth control method. CNS effects such as dizziness, confusion, drowsiness, and seizures may occur, especially when lidocaine is overdosed. Especially if lidocaine is taken too quickly or in excess, adverse reactions such as bradycardia, hypotension and even cardiac arrest may occur.

Contraindications

Lidocaine should not be used in children who are allergic to lidocaine or similar local anesthetics. There is also a risk of using lidocaine in children who have a slow heart rate, a heart attack, or high blood pressure because lidocaine may make the condition worse. Before giving lidocaine to children to treat heart problems, it is important to check their medical history to make sure it is safe.

3.FLECAINIDE (CLASS IC)

Pediatric Indications

Flecainide is a 1C antiarrhythmic drug widely used in the treatment of refractory supraventricular arrhythmias in children. It is important to maintain levels within a narrow range with a target trough level of 0.2 µg/mL and 1 µg/mL. Even a small amount (starting at 0.7 µg/mL) can be dangerous and cause a mortality rate of approximately 22.5%. The maximum recommended daily dose for pediatric patients is 200 mg/m2/day.[5]

Mechanism of Action

Flecainide works by specifically binding to fast internal sodium channels and blocking their open state, thereby causing cardiac arrest through depolarization of ventricular myofibers and the HisPurkinje system. This leads to prolonged activity and dysfunction of the atrial and ventricular muscles, as well as disturbances in the His-Purkinje system. Flecainide is use dependent, meaning that its sodium channel blocking effect increases as heart rate increases.[6]

Adverse Effects

Atrial flutter with 1:1 atrioventricular conduction, bradycardia, sustained monomorphic ventricular tachycardia, slowed conduction rate, widened QRS complex, negative and positive Inotropic effects, hepatotoxicity.

Contraindications

Include heart disease and ischemic heart disease. Drug interactions with CYP2D6 inhibitors (SSRI, amiodarone), synergistic hypotension when used with propranolol, need for dose reduction when used with digoxin or amiodarone, and glomerular filtration rate (GFR) less than 35 mL/min/1.73 m2.

4.PROPRANOLOL (CLASS II)

Pediatric Indications

Propranolol is an oral class II anticonvulsant drug commonly used to treat and prevent recurrence of supraventricular tachycardia (SVT) in infants and children. It is also used to treat the symptoms of children who experience palpitations due to failure of the ventricles. Additionally, propranolol may reduce the risk of heart attack in patients with heart disease such as long QT syndrome and catecholaminergic polymorphic ventricular tachycardia. In addition to its antiarrhythmic effects, propranolol is also used in the treatment of hypertension, infantile hemangioma, migraine prophylaxis and thyrotoxicosis in pediatric patients.[7]

Mechanism of Action

Propranolol is a non-selective beta-adrenergic blocker that affects 1 and 2 receptors equally. When it binds to α1 receptors on cardiomyocytes, it reduces calcium entering the cell via cyclic AMP. This leads to a decrease in automatic and slow activity in the tissue, resulting in a prolonged PR period. Additionally, propranolol has effects on sodium channels that may further increase its antiarrhythmic potential.[8]

Side Effects

Propranolol, when used as a birth control pill, can cause a number of heart problems, including slow heart rate, hypotension, and congestive heart failure, especially in children with heart disease. It may also cause bronchospasm or asthma in injured people. Additionally, some children may experience dizziness, fatigue, or sleep disturbances because

it affects the central nervous system. Monitoring for these side effects is important to ensure the safety of pediatric patients receiving propranolol for the treatment of cardiac arrhythmias.

Contraindications

Propranolol should not be used in children with a slow heart rate, heart failure, or high blood pressure because it may worsen the condition. Additionally, children with asthma or a history of asthma should not use it as it may cause breathing problems. Propranolol is not safe for children with heart failure or shock. Before giving propranolol to treat heart problems, doctors should carefully review a child's medical history to make sure the medication is safe for them.

5.SOTALOL (CLASS III)

Pediatric indications

Sotalol is a noncardiac, class III antiarrhythmic beta blocker. It can be given orally or by intravenous injection. Sotalol is often used to treat reentranttachyarrhythmias such as atrial flutter and intraatrialreentrant tachycardia, especially after surgery in patients with heart defects. Recently, sotalol injection has become an option to quickly stop rapid heart rate or reach a stable phase when starting sotalol therapy in pediatric patients.[9]

Mechanism of Action

Sotalol has d- and l-sotalol isomers, and l-sotalol has a strong beta-blocking effect. At lower doses, it works primarily as a beta-blocker, binding to alpha1- and alpha2-adrenergic receptors and slowing the activity of the atrioventricular node. At higher doses, sotalol inhibits the rapid effects of delayed rectifier potassium current (IKr), which is controlled by the KCHN2 gene. This causes prolonged conduction time and dysfunction of the atria, ventricles, and His-Purkinje system. Sotalol has shown dependence on repeated use, exhibiting more potent potassium channel blockade and prolonged activity in the lower heart.[10]

ADR

QT prolongation, TdP, bradycardia, adverse effects related to beta-blockade (fatigue, fatigue, dizziness) [11]

Contraindication

Half the dose for people with renal insufficiency (kidney disease) with poor function, When GFR <30 mL/min/1.73m2, reduce dose by half by 25%[12]

Antiarrhythmic Drug Dosing in Children

Guidelines, recommendations and information on the use of antiarrhythmic drugs. Dosagerecommendations vary by indication and data source [13]

Class 0 antiarrhythmic drug

Ivabradine is classified as a Class 0 antiarrhythmic drug (AAD) with hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blocking properties and is for oral use only. The recommended dose for children weighing 40 kg, the starting dose is 2.5 mg/kg twice daily, not to exceed 7.5 mg per dose. Ivabradine was approved by the FDA for the treatment of heart failure in2015, but it is not included in pediatric arrhythmia guidelines and its use in children is based on published data Future recommendations from further studies in pediatric patients may support the use of ivabradine in the treatmentof tachyarrhythmias in the general population.[14]

Class I antiarrhythmic drugs

Ajmaline is a Class Ia antiarrhythmic drug (AAD) with sodium-blocking properties derived from the roots of Rauvolfia serpentina (Indian snakeroot). It isusually placed initially in doses of 0.5 to 1 mg/kg. The maximum dose is 50 mg per dose or 8 mg/kg per day or 1,200 mg per day as a continuous injection, regardless of body weight. The initial dose for continuous injection is 0.5 to 1 mg/kg per hour, not to exceed 10 mg/minute. Additionally, the conclusion underscores the challenges in prescribing antiarrhythmic medications for children, including the use of unlicensed or off-label drugs, difficulties in obtaining prescriptions, and the need for close monitoring to prevent toxicity and manage side effects effectively.[15]

Drug	Procainamide	Lidocaine	Flecainide	Propranolol	Esmolol	Amiodarone	Sotalol
Vaughan	Class IA	Class IB	Class IC	Class II	Class II	Class III	Class III
Alternative names	Procan, Procanbid, Pronestyl, Pronestyl SR	Lidocaine hydrochloride, Lignocaine	Flecainide acetate, Tambocor	Propranolol hydrochloride, Inderal	Brevibloc Esmolol hydrochloride	Amiodarone Hydrochloride, Pacerone, Cordarone, Nexterone	Betapace, Betapace AF, Sorine, Sotalol hydrochloride, Sotylize

Dosing[a]	*IV loading*: 7–10 mg/kg in neonates and 10–15 mg/kg/day in children and adolescents (max 1000–1500 mg) given over 30 to 45 minutes. *IV continuous*: 20–80 mcg/kg/min (max 2 g/day)	*IV loading*: 1 mg/kg rapid bolus (may give second bolus if >15 min between initial bolus and start of infusion) *IV continuous*: 20–50 mcg/kg/min	*Oral initial*: 1–3 mg/kg/day or 50–100 mg/m2/day in 3 divided doses *Oral maintenance*: 3–6 mg/kg/day or 100–150 mg/m^2/day in 3 divided doses	*Oral*: 2–4 mg/kg/day in 3–4 divided doses	*IV bolus*: 100–500 mcg/kg over 1–2 min *IV continuous*: 100–500 mcg/kg/min	*Oral*: 10–15 mg/kg/day in 1–2 divided doses for 4–14 days followed by 5 mg/kg/day daily *IV loading*: 5 mg/kg over 60 min *IV continuous*: 5–15 mcg/kg/min	*Oral*: 30–60 mg/m^2/dose (max 320 mg/day) every 8 hours[b] *IV bolus*: 1 mg/kg over 1 hour (max 80 mg) *IV continuous*: 80–90% of calculated oral daily dose in 2–3 divided doses and administered over 3–5 hours
Therapeutic level	Combined procainamide and NAPA level trended for toxicity	1.5–5.0 mcg/mL	0.2–1.0 mcg/mL	Not routinely measured	Not routinely measured	Not routinely measured but effective at 1.0–2.5 mg/L (adults, plasma)	Not routinely measured
Oral preparations	N/A	N/A	Tablet liquid (EC)	Tablet (IR) Capsule (ER) Liquid	N/A	Tablet liquid (EC)	Tablet liquid

Table N0.3

Class 1A

Procainimide

Toxicity :

1.Cardiotoxicity: - Cardiotoxic effects are related to the levels of procainamide and/or NAPA in the blood. - Often occurs against the background of poor liver or kidney function. -Electrocardiographic findings include PR prolongation, QRS widening and QTc prolongation, which predispose to fibrillation flutter (TdP). - It may cause bradycardia and hypotension, mainly due to vasodilation. - Procainamide has a negative inotropic effect. -Procainamide has a more moderate effect on myocardial contractility than other intravenous antibiotics.

2.Immunotoxicity:- Oral administration of procaine amide may result in significant antinuclear antibody titers. - It may occur as a result of the treatment of lupus, which has symptoms such as joint pain, fever and rash.[18]

3.Hematology Toxicity:- A rare complication of oral administration of procaine amide. - Deficiency of blood, including pancytopenia (decrease in all types of blood cells) or agranulocytosis (decrease in the number of white blood cells called granulocytes). This classification provides detailed information on the toxicity of procainamide, including effects on the cardiovascular, immune and hematopoietic systems.[19]

Toxicologic treatment

General approach to the treatment of all antiarrhythmic toxicities. Sodium bicarbonate or lidocaine (Class IB) Rapid sodium channel blockade can reverse QRS narrowing. There are reports of hemodialysis being used in treatment. [20]

Class 1B

Lidocaine

1. Breathing in the lungs:- Acute lidocaine exposure may cause difficulty breathing and possibly lead to respiratory distress.
2. Cardiovascular effects: - Hypotension: Lidocaine toxicity may cause a decrease in blood pressure. - Myocardial depression: may reduce myocardial function. -Arrhythmias: Arrhythmias may occur, increasing the risk of arrhythmia. -Bradycardia risk: Caution is recommended as bradycardia may occur in patients with atrioventricular or intraventricular conduction.
3. Central Nervous System (CNS) Effects: - Fear: Patients will feel uncontrollable tremors. - Confusion: Mental illness and confusion may occur. - Convulsions: Involuntary muscle contractions may occur. - Visual changes: Lidocaine toxicity may cause visual changes. - Forgetfulness: The patient may forget. - Seizures: Acute toxicity may cause seizures. - CNS Depression: Overdose of lidocaine may cause CNS depression.
4. Onset:- CNS effects generally precede pulmonary effects that occur at higher levels.[21]

Toxicologic treatment

Management of lidocaine toxicity includes monitoring care and discontinuing lidocaine administration. Antiepileptic drugs should be given for long-lasting seizures. Hemodynamic support should be initiated as clinically indicated. When the drug is discontinued, toxic effects usually occur steadily but may be prolonged in patients with compromised liver or heart failure due to poor lidocaine clearance. Sodium bicarbonate and lipid emulsion are used early in resuscitation to prevent cardiotoxicity, and extracorporeal membrane oxygenation is used in severe or refractory cases. [22]

Class 1C

Flecainide

1.cardiovascular disease: Flecainide has proarrhythmic properties causing abnormalities such as PR delay, QRS prolongation, bundle branch block, and Brugada pattern on the electrocardiogram. These abnormalities can eventually lead to bradycardia, sinus arrest, or torsade de pointes (TdP). It can also cause myocardial failure, causing symptoms such as heart palpitations, chest pain and arrhythmia.
2.Musculoskeletal System: The negative inotropic effects of flecainide affect myocardial contractility, causing weakening of myocardial function and symptoms such as chest pain and arrhythmia.
3.Respiratory: Effects of flecainide toxicity include respiratory symptoms such as shortness of breath, which may indicate pneumonia.
4.Intestinal diseases: Patients may experience symptoms such as diarrhea, abdominal pain, nausea, vomiting, and constipation, and this may cause more complications in the treatment. 5.Nervous System: Flecainide toxicity may affect the central nervous system, causing symptoms such as dizziness, fatigue, blurred vision and seizures. These neurological symptoms pose a serious risk, especially in children.[23]

Toxicological Treatment

Initial treatment of flecainide toxicity in children is intravenous sodium bicarbonate at a dose of 1 mEq/kg over 1-2 minutes and repeated as necessary until QRS 100 msec is controlled. [24]

CLASS II

Propanolol

1.Cardiovascular: The primary cardiovascular side effect of propranolol toxicity is bradycardia, and severe overdose can cause hypotension, atrioventricular block, and heart failure. These heart diseases can cause serious illness and death.
2.Nervous System: Propranolol is more lipophilic than other beta-blockers and crosses the nerve-brain barrier, causing more severe neurotoxicity. Symptoms such as fatigue, convulsions and dizziness may occur, suggesting that the central nervous system is affected.
3.Respiratory: Bronchospasm is another side effect of propranolol toxicity that can cause respiratory distress in patients.
4.Gastrointestinal disease: Non-cardiac symptoms include diarrhea, which can cause pollution and electrolyte disturbances and lead to additional clinical presentation.
5.Metabolic System: Hypoglycemia is another complication of beta blocker toxicity and is especially important in young patients with low glycogen stores.[25]

Toxicological Treatment

Pretreatment of beta blocker toxicity includes stabilization. Administer isotonic intravenous fluids to control bradycardia and hypotension. Administer intravenous fluids and atropine if symptoms of bradycardia occur. Although there are limitations, the evidence supporting the effectiveness of glucagon is mainly as follows: Intravenous bolus and increasing continuous infusion alter cardiac output via cyclic AMP. Likewise, calcium settles into the bloodstream as calcium gluconate or calcium. Chlorination can be done to increase shrinkage. Recently, more insulin is being used for treatment. Beta Blocker and Calcium Channel Toxicity Theory Insulin increases muscle contraction and vasodilation and reduces insulin secretion. Against. Traditional methods include bolus insulin doses between 0.5 and 1.0. U/kg, followed by continuous injection and simultaneous administration of glucose. Fluids are given to maintain normal blood sugar levels. Finally, when other treatments are ineffective, lipoemulsion treatment may be considered. Even if it fails, the experience is limited to adults only. Pro-Propranolol may be more specific for lipid emulsion therapy. It is highly

lipophilic. If asymptomatic, the child can be discharged from the hospital after 6 hours of oral propranolol. To eat. Long-term drug therapy will be needed. Up to 24 hours monitoring.[26]

Class III

Sotalol

1.Cardiovascular: Bradycardia and Hypotension: Sotalol has been associated with bradycardia and hypotension, reflecting its negative chronotropic and positive inotropic effects, similar to other Class II and III antiarrhythmic drugs.
2.Arrhythmogenic Potential: Sotalol's dose-dependent QTc prolongation may cause proarrhythmias, including ventricular arrhythmias such as torsade de pointes (TdP), which may lead to cardiovascular instability.
3.Extracardiac Effects: Respiratory System: Sotalol may cause more severe respiratory symptoms such as shortness of breath by causing bronchospasm, especially in patients with respiratory diseases or asthma.
4.Time Toxicity: Sotalol toxicity usually occurs soon after initiation of treatment and is usually reported within the first 3 days of treatment. Therefore, it is recommended to start or adjust the dose of sotalol in hospitalized patients to monitor side effects and intervene in a timely manner.[27]

Toxicological Treatment

Management of sotalol toxicities, including TdP is often encouraged, with a focus on electrolyte optimization in the setting of QTc prolongation. Sotalol is not protein bound and hemodialysis can be used to lower sotalol plasma concentrations.[28]

CLASS IV

DILTIAZEM

1.cardiovascular diseases Bradycardia and Atrioventricular Block: Diltiazem overdose can cause bradycardia and atrioventricular block, affecting the function of the heart and possibly causing arrhythmias.
2.Hypotension and heart failure: An overdose of diltiazem may cause hypotension and, in severe cases, heart failure. Heart failure causes heart failure and poor circulation.
3.Heart disease Taking too much diltiazem might cause heart failure, a serious condition that occurs when the heart fails to meet the body's needs.
4.Stomach disease: Stomach pain: Diltiazem poisoning often occurs with diarrhea; This can lead to dehydration and electrolyte deficiency, worsening symptoms.
5.Metabolic System: Insulin Resistance and Hyperglycemia: Diltiazem can cause hyperglycemia by causing insulin resistance, which may increase the risk for diabetics or people with metabolic diseases. Lactic acidosis: Diltiazem toxicity secondary to psychogenic shock and hyperglycemia can lead to lactic acidosis, a serious metabolic disorder associated with tissue hypoperfusion and impairment of cellular respiration.[29]

Toxicological Treatment

Support is used in the treatment of bradycardia, atrioventricular block, hypotension and psychogenic shock . Evidence regarding the effectiveness of calcium supplements and high-dose insulin in reducing toxicity in patients varies but should be considered . The use of intravenous lipid emulsion in children with diltiazem overdose is limited to mixed reports of success, and patients are often considered refractory to treatment.[30]

Risk factor for developing Antiarrhythmics toxicity in children

1. Age: Children may be more affected due to differences in drug metabolism and elimination.
2. Body weight: Calculation of dosage is usually based on body weight, so accurate measurement is important to avoid undereating or overeating.
3. The following conditions: Children with conditions such as heart disease may have a higher risk of developing heart disease.
4. Combined drug use: Interaction with other drugs may increase the risk.
5. Genetic factors: Changes in drug-metabolizing enzymes or genetic factors may affect toxicity.
6. Improper Use: Improper dosing, administration or monitoring may increase risk.
7. Lack of monitoring: Regular monitoring of medications and heart functions is important for early diagnosis.
8. Slow elimination: Immature kidney or liver function may slow the elimination of the drug and increase the risk.[31]

TABLE 4 General management principles for antiarrhythmic toxicologic ingestions.[11]

Primary evaluation	Airway
Assess and maintain airway patency	
Breathing	
Assess breath sounds and ensure adequate tidal volumes with continuous pulse oximetry and end-tidal carbon dioxide monitoring	
Circulation	*Assess perfusion, blood pressure, and secure intravenous access*
Disability	*Assess level of consciousness in addition to pupillary size and reactivity*

Decontamination	Activated charcoal *Consider in patients with known ingestion within the first several hours of presentation. Patient must have a*

Diagnostics Continuous cardiorespiratory monitoring Serial electrocardiograms for diagnostics and evaluation of acute managementLaboratory studies including chemistries and serum drug concentrations

Therapeutics	Sodium bicarbonate Administer for QRS widening secondary to Class IA or IC toxicityHigh dose insulin and IV calcium Promote inotropy in Class II or Class IV toxicity Intravenous fat emulsion *Consider in seriously ill, deteriorating or refractory cases* Targeted management of arrhythmias *Magnesium for yorsades de pointes* Hemodialysis *Rarely used for due to large volumes of distribution, but discuss with a medical toxicologist if procainamide ingestion*

Sign and symptoms of Antiarrhythmics toxicity specific to children

1.Nausea and vomiting
2. Dizziness or dizziness
3. Fatigue or weakness
4. Confusion or mental changes
5. blindsight
6. Hallucination
7. Epileptic seizures
8. Irregular heartbeat (arrhythmia)
9. Hypotension
10. Difficulty breathing
11. Cyanosis (whitening of the skin or lips due to decreased oxygen)
12. severe heart attack

General principle of managing Antiarrhythmics toxicity in children

General principles for treating drug-resistant infections in children include prompt diagnosis, investigation, and appropriate treatment to prevent serious illness and death. This includes early detection of drug toxicity, understanding of guidelines, drug and toxicological evaluations of antiarrhythmic drugs used in the pediatric population, and use of methods to manage drug toxicity. Understanding antiarrhythmic drugs, their associated toxicities, and potential harms is crucial for effective treatment. In addition, individual treatment based on the specific characteristics of the patient and close monitoring of proarrhythmic effects are important components of antiarrhythmic drug management in children.[32]

Specific techniques and supportive measures

Initial and Stabilization Measures

1.Airway, Respiratory and Circulatory Support (ABC): Ensure your child's airway is open, measure breathing and monitor circulation.

2.Intravenous Access: Provide intravenous access for drug administration and fluid resuscitation. Monitoring ECG: Monitor the child's heart rate carefully for abnormalities.

Symptomatic bradycardia

1.Temporary pacemaker placement: Consider temporary pacemaker placement for symptomatic

2.bradycardia. Hypotension management: Use saline and vasopressors to treat hypotension.

3.Arrhythmias Class IB Drugs: You want to use Class IB antiarrhythmic drugs to treat arrhythmias.

Seizures Benzodiazepines: Use benzodiazepines to control seizures.

4.Gastrointestinal Decontamination Orogastric Lavage and Activated Charcoal:

If necessary, consider decontamination of the stomach with orogastric lavage and activated charcoal.

Specific Treatments

1.Glucagon: Consider glucagon, which has been shown to be effective in animal models.

2.Lidocaine-induced seizures: Treatment of lidocaine-induced seizures with benzodiazepines.

3.Intravenous Lipid Emulsions: Use intravenous lipid emulsions to treat severe cases of toxicity.

4.Extracorporeal Bypass: If cardiac arrest occurs due to lidocaine toxicity, extracorporeal bypass is required.[33]

Antidiote and treatment for Antiarrhythmics medication

1.Magnesium supplement: In severe cases of arrhythmia caused by antiarrhythmic drug toxicity, magnesium supplementation is important to stabilize the heart rhythm.
2.Intravenous sodium bicarbonate: In case of cardiotoxicity caused by some antiarrhythmic drugs, intravenous sodium bicarbonate can save lives, helping to alkalize the blood and preventing their effects.
3.Intravenous fluids and supportive care: Intravenous fluids and supportive care are important to manage drug toxicity, maintain fluid and electrolyte balance, and support body function.
4.Perform Advanced Cardiac Life Support (ACLS): In cases of severe drug-induced cardiac arrest or lifethreatening complications, ACLS measures should be taken, including cardiopulmonary resuscitation (CPR), defibrillation, and cardiac arrest breathing.
5.Continuous evaluation and re-evaluation: Regular monitoring of vital signs, heart rate, electrolytes, and a complete physical examination are important to detect problems early and treat them when necessary.[34]

FUTURE PERSPECTIVE:

In the future, the use of pediatric antiarrhythmic agents will likely continue as pharmacology advances and our understanding of cardiac electrophysiology in children increases. Depending on the genetics and characteristics of the patient, personalized treatment can be applied, or there may be different types of treatment that have fewer side effects and better results. Additionally, research will focus on developing new delivery systems to improve medication intake and adherence in pediatric patients. Overall, the outlook for progress in pediatrics is promising.[35]

CONCLUSION:

The conclusion drawn from the sources regarding pediatric antiarrhythmics and toxicity emphasizes the importance of careful prescribing and monitoring of antiarrhythmic medications in children. Antiarrhythmic drugs play a crucial role in managing arrhythmias in pediatric patients, but their use requires a deep understanding of each drug's unique pharmacological profile and potential toxic effects. It is highlighted that antiarrhythmic drugs have a narrow therapeutic index, and misprescribing can lead to inadequate control of arrhythmias or even proarrhythmic effects. The sources stress the need for individualized treatment considering factors like coexisting diseases, concurrent therapies, and metabolic variations. Additionally, the conclusion underscores the challenges in prescribing antiarrhythmic medications for children, including the use of unlicensed or off-label drugs, difficulties in obtaining prescriptions, and the need for close monitoring to prevent toxicity and manage side effects effectively.

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The authors have no conflict of interest to declare.

REFERENCES:

1. Mandapati R, Byrum CJ, Kavey REW, et al. Procainamide for rate control of postsurgical junctional tachycardia. Pediatr Cardiol. 2000;21(2):123-128. doi:10.1007/s002469910018
2. Walsh EP, Saul JP, Sholler GF, et al. Evaluation of a staged treatment protocol for rapid automatic junctional tachycardia after operation for congenital heart disease. J Am Coll Cardiol. 1997;29(5):1046-1053. doi:10.1016/S0735-1097(97)00040-5
3. Zamponi GW, Sui X, Codding PW, French RJ. Dual actions of pro- cainamide on batrachotoxin-activated sodium channels: open channel block and prevention of inactivation. Biophys J. 1993;65(6):2324-2334. doi:10.1016/S0006-3495(93)81291-8[6:56 pm, 17/03/2024
4. Mandapati R, Byrum CJ, Kavey REW, et al. Procainamide for rate control of postsurgical junctional tachycardia. Pediatr Cardiol. 2000;21(2):123-128. doi:10.1007/s002469910018
5. Walsh EP, Saul JP, Sholler GF, et al. Evaluation of a staged treatment protocol for rapid automatic junctional tachycardia after operation for congenital heart disease. J Am Coll Cardiol. 1997;29(5):1046-1053. doi:10.1016/S0735-1097(97)00040-5
6. Zamponi GW, Sui X, Codding PW, French RJ. Dual actions of pro- cainamide on batrachotoxin-activated sodium channels: open channel block and prevention of inactivation. Biophys J. 1993;65(6):2324- 2334. doi:10.1016/S0006-3495(93)81291-8
7. Zamponi GW, Sui X, Codding PW, French RJ. Dual actions of pro- cainamide on batrachotoxin-activated sodium channels: open channel block and prevention of inactivation. Biophys J. 1993;65(6):2324- 2334. doi:10.1016/S0006-3495(93)81291-8

8. Mackin C, DeWitt ES, Black KJ, et al. Intravenous amiodarone andsotalol impair contractility and cardiac output, but procainamide doesnot: a Langendorff study. J Cardiovasc Pharmacol Ther. 2019;24(3):288- 297. doi:10.1177/1074248418810811
9. Hanlon TM, Binkiewicz A, Feingold M, Necheles TF. ProcainamideHCl-induced Lupus Syndrome in a child with myotonia congenita.Am J Dis Child. 1967;113(4):491-493. doi:10.1001/archpedi.1967.02090190137019
10. Danielly J, DeJong R, Radke-Mitchell LC, Uprichard ACG.Procainamide-associated blood dyscrasias. Am J Cardiol.1994;74(11):1179-1180. doi:10.1016/0002-9149(94)90478-2
11. Low CL, Phelps KR, Bailie GR. Relative efficacy of haemoperfusion, haemodialysis and CAPD in the removal of procainamide and NAPAin a patient with severe procainamide toxicity. Nephrol Dial Transplant. 1996;11(5):881-884. doi:10.1093/oxfordjournals.ndt.a027421
12. Duff JP, Topjian A, Berg MD, et al. 2018 American Heart Asso-ciation focused update on pediatric advanced life support: an update to the American Heart Association Guidelines for cardiopul-monary resuscitation and emergency cardiovascular care. Circulation.2018;138:e731-e739. doi:10.1161/CIR.0000000000000612
13. Noessler, N.; Schweintzger, S.; Kurath-Koller, S. Holiday heart syndrome: An upcoming tachyarrhythmia in today's youth?Cardiol. Young 2021, 31, 1054–1056. [CrossRef] [PubMed]
14. Brugada, J.; Blom, N.; Sarquella-Brugada, G.; Blomstrom-Lundqvist, C.; Deanfield, J.; Janousek, J.; Abrams, D.; Bauersfeld, U.; Brugada, R.; Drago, F.; et al. Pharmacological and non-pharmacological therapy for arrhythmias in the pediatric population:EHRA and AEPC-Arrhythmia Working Group joint consensus statement. Europace 2013, 15, 1337–1382. [CrossRef] [PubMed]
15. Hernández-Madrid, A.; Paul, T.; Abrams, D.; Aziz, P.F.; Blom, N.A.; Chen, J.; Chessa, M.; Combes, N.; Dagres, N.; Diller, G.; et al.Arrhythmias in congenital heart disease: A position paper of the European Heart Rhythm Association (EHRA), Associationfor European Paediatric and Congenital Cardiology (AEPC), and the European Society of Cardiology (ESC) Working Group onGrown-up Congenital heart disease, endorsed by HRS, PACES, APHRS, and SOLAECE. Europace 2018, 20, 1719–1753. [CrossRef]
16. Hernández-Madrid, A.; Hocini, M.; Chen, J.; Potpara, T.; Pison, L.; Blomström-Lundqvist, C. How are arrhythmias managed inthe paediatric population in Europe? Results of the European Heart Rhythm survey. Europace 2014, 16, 1852–1856. [CrossRef]Balducci, V.; Credi, C.; Sacconi, L.; Romanelli, M.N.; Sartiani, L.; Cerbai, E. The HCN channel as a pharmacological target: Why,where, and how to block it. Prog. Biophys. Mol. Biol. 2021, 166, 173–181. [CrossRef] [PubMed]
17. Di Marco, G.M.; De Nigris, A.; Pepe, A.; Pagano, A.; Di Nardo, G.; Tipo, V. Ivabradine-Flecainide as Breakthrough DrugCombination for Congenital Junctional Ectopic Tachycardia: A Case Report and Literature Review. Pediatr. Rep. 2021, 13, 624–631.
18. Mehra P, Caiazzo A, Maloney P. Lidocaine toxicity. Anesth Prog. 1998;45(1):38-41.
19. Kunkel F, Rowland M, Scheinman MM. The electrophysiologic effectsof lidocaine in patients with intraventricular conduction defects.Circulation. 1974;49(5):894-899. doi:10.1161/01.CIR.49.5.894
20. Hoffman RS, Howland M, Lewin NA, Nelson LS, Goldfrank LR,eds. Goldfrank's Toxicologic Emergencies, 10e. McGraw Hill; 2015.Accessed November 07, 2022. https://accesspharmacy.mhmedical.com/content.aspx?bookid=1163&sectionid=64552562
21. Kannankeril PJ, Moore JP, Cerrone M, et al. Efficacy of flecainide inthe treatment of catecholaminergic polymorphic ventricular tachy-cardia a randomized clinical trial. JAMA Cardiol. 2017;2(7):759-766.doi:10.1001/jamacardio.2017.1320\
22. Price JF, Kertesz NJ, Snyder CS, Friedman RA, Fenrich AL. Flecainideand sotalol: a new combination therapy for refractory supraven-tricular tachycardia in children.
23. Moffett BS, Valdes SO, Lupo PJ, et al. Flecainide use in childrenwith cardiomyopathy or structural heart disease. Pediatr Cardiol.2015;36(1):146-150. doi:10.1007/s00246-014-0978-3
24. Echt DS, Liebson PR, Mitchell LB, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo: the cardiac arrhythmia suppression trial. N Engl J Med. 1991;324(12):781-788. doi:10.1056/NEJM199103213241201
25. Holmes B, Heel RC. Flecainide: a preliminary review of its pharmaco-dynamic properties and therapeutic efficacy. Drugs. 1985;29(1):1-33. doi:10.2165/00003495-198529010-00001
26. Follmer CH, Colatsky TJ. Block of delayed rectifier potassium current,I(K), by flecainide and E-4031 in cat ventricular myocytes. Circulation.1990;82(1):289-293. doi:10.1161/01.CIR.82.1.289
27. Tamargo J, Le Heuzey JY, Mabo P. Narrow therapeutic index drugs: aclinical pharmacological consideration to flecainide. Eur J Clin Pharma-col. 2015;71(5):549-567. doi:10.1007/s00228-015-1832-0
28. Brugada J, Boersma L, Kirchhof C, Allessie M. Proarrhythmic effects of flecainide. Experimental evidence for increased susceptibility to reen- trant arrhythmias. Circulation. 1991;84(4):1808-1818. doi:10.1161/01.CIR.84.4.1808

29. D'Alessandro LCA, Rieder MJ, Gloor J, Freeman D, Buffo-Sequiera I.Life-threatening flecainide intoxication in a young child secondary to medication error. Ann Pharmacother. 2009;43(9):1522-1527. doi:10. 1345/aph.1L549
30. Gardner Yelton SE, Leonard JB, De La Uz CM, Wadia RS, Barnes SS. Flecainide toxicity secondary to accidental overdose: a pediatric case report of two brothers. Case Rep Crit. 2021;2021:4-9. doi:10.1155/2021/6633859
31. Kakavand B, Di Sessa TG. Unusual amiodarone toxicity in a child. J Pediatr Pharmacol Ther. 2008 Apr;13(2):93-5. doi: 10.5863/1551-6776-13.2.93. PMID: 23055871; PMCID: PMC3462064.
32. saul JP, Scott WA, Brown S, Marantz P, Acevedo V, Etheridge SP, Perry JC, Triedman JK, Burriss SW, Cargo P, Graepel J, PhD, Koskelo EK, Wang R. A randomized, double-blind, antiarrhythmic drug trial. Circulation. 2005;112:3470–3477. for the Intravenous Amiodarone Pediatric Investigators: Intravenous Amiodarone for Incessant Tachyarrhythmias in Children. [PubMed] [Google Scholar]
33. Jacobs JM, Costa-Jussa FR. The pathology of amiodarone neurotoxicity. II. Peripheral neuropathy in man. Brain. 1985;108(Pt 3):753–769. [PubMed] [Google Scholar]
34. Laird WP, Snyder CS, Kertesz NJ. Use of intravenous amiodarone for postoperative junctional ectopic tachycardia in children. Pediatr Cardiol. 2003;24:133–137. et al. [PubMed] [Google Scholar]
35. Vignati G, Mauri L, Figini A. The use of propafenone in the treatment of tachyarrhythmias in children. Eur Heart J. 1993;14:546–550. [PubMed] [Google Scholar]