ECG Changes in Antiarrhythmic toxicity and their management in A & E and SCBU

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Homeless but everywhere

Based in Birmingham, UK
Causes

- Deliberate intake
- Error in Intake eg inadvertent duplication
- Non-compliance - breakthrough arrhythmia
- Dose variation with liquid preps
- Interaction with electrolytes, other drugs and systemic illness (including fever, absorption etc)
- Munchausen syndrome by proxy
- Presence of structural heart disease/underlying arrhythmia substrate counts
- Drugs may have not been prescribed for an arrhythmia eg Digoxin
Presentation

- Nausea/vomiting
- Palpitations
- Generally unwell due to BP drop and HR change
- Seizures
- Syncope
- Rarely sudden death
- For those with AICD - shocks
- Electro-mechanical dissociation
Advice

- Patients need to be aware when to contact and who to contact when symptoms arise and to ensure airway until help arrives in cases of syncope. Ask parents to bring all drugs being taken.

- Should be seen with ECG ASAP with cardiology input.

- Detailed history to include family dynamics.

- Always ask for drugs to be checked especially for new prescriptions - pharmacists are human and errors can be made esp with liquid preps, dose, frequency and storage.

- Young teens do take “recreational” drugs.
In A & E

- On arrival Triage according to presentation
- First Aid if required
- Monitor/ECG
- I.v access, first aid and ensuring staff are prepared for potential intervention
- Baseline bloods esp E’Lytes, drug levels, +/- toxicology
ECG Changes

- Slow HR
- AV conduction delay
- Intraventricular conduction delay
- Prolonged depolarisation +/- prominent U waves
- Irregular/fast rhythm/VT/VF
Frequent Culprits Cardiac

- Flecainide
- Propafenone
- B-Blockers
- Digoxin
- Quinidine/Disopyramide
- Amiodarone/Dronedarone
- Drug synergism eg Verapamil + B-Blocker
<table>
<thead>
<tr>
<th>Vaughan-Williams Class</th>
<th>Drug</th>
<th>ECG Changes</th>
<th>Channels</th>
<th>Receptors</th>
<th>Clinical Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Quinidine</td>
<td>A</td>
<td>Ca**</td>
<td>M</td>
<td>H, M</td>
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<td></td>
<td>Procainamide</td>
<td>B</td>
<td>Na</td>
<td>L</td>
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<td></td>
<td>Disopyramide</td>
<td></td>
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<td>M</td>
<td>M, M</td>
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<td>B</td>
<td>Lidocaine</td>
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<td></td>
<td>Mexiletine</td>
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<td>C</td>
<td>Propafenone</td>
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<td></td>
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<td>H, M</td>
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<td>M, M</td>
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<td>II</td>
<td>β-Adrenergic</td>
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<td>Ibutilide</td>
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<td></td>
<td>Dofetilide</td>
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**Antagonist relative potency**

- L = Low
- M = Moderate
- H = High

**Legend**

- △ = Agonist
- ■ = ECG Changes related to Ca** channel block
- ○ = ECG Changes related to Na+ channel block
- △ = ECG Changes related to K+ channel block

**Clinical Effects**

- Pro-Arrhy – Proarrhythmia potential
- Extra Cardiac – Extra-cardiac toxicity potential
- LV FX – Left ventricular function
- Heart Rate – Bradycardia potential

ACh – Acetylcholine
Ado – Adenosine
Frequent Culprits
Non-cardiac

- Tricyclic antidepressants
- Some anti-psychotics eg Carbamazepine/Lithium
- Some anti-histamines
- Sympathomimetic drugs
- Cocaine, Ecstasy, methadone
Beta blocker overdose
• Similar ECG changes are seen with other sodium-channel blocking agents.

• This ECG demonstrates QRS widening and positive R' wave in AVR consistent with sodium-channel blockade in a patient with flecainide poisoning.
Flecainide Toxicity
Impostors: Digoxin toxicity

- Digoxin is a drug commonly used to treat advanced CHF
- It has a small therapeutic index meaning it is easy to OD
- It can cause a depressed scooping ST segment, in addition to other cardiotoxic changes.
- Patients with dig tox will describe seeing a “yellow haze”

Digitalis Toxicity

Atrial tachycardia, 2:1 AV block
1. The P-wave axis is normal
2. The non-conducted P-wave hides in the T-wave
3. The conducted P-wave often has a long PR interval
4. The P-P interval may not be exactly regular

Box 9.1 Changes in Digitalis Toxicity
- S–T segment depression (including ‘j’ point depression)
- T wave inversion
- Sinus bradycardia
- Uniform or multiform ventricular extrasystoles
- Ventricular tachycardia, flutter, and fibrillation
- Paroxysmal atrial tachycardia
- Atrial flutter and fibrillation
- Sino-atrial block
- Bundle branch block
- First, second, and third degree AV block

Fig. 9.2  Diagrams of digitalis toxicity and digitalis effect. (A) Reverse check sign. Note the terminal positivity of the T wave. (B) Digitalis toxicity. Note that the terminal part of the T wave does not rise above the baseline. (C) Digitalis toxicity. Note that the terminal part of the T wave does not rise above the baseline. It can also be due to primary T wave abnormality because of coronary artery disease.
Dig Toxicity
Tricyclic OD
Tricyclic OD

Resolution with NaHCO3 + Hyperventilation
Hyperkalaemia with Ecstasy
Principles of Management

- Deal with immediate fallout from toxicity
- Remove, neutralise and encourage excretion of drug
- Treat arrhythmia and support the circulation
- Prevent recurrence
Management

• **First Aid first including airway/Oxygen, constant ECG monitor, i.v. access, supporting the circulation (mainly fluids +/- Noradrenaline), correcting acid/base, +/- ventilation, Bloods for E’lytes etc, toxicity screen. Temperature control and hydration. Alert ITU**

• **Detailed history + ECG**

• **In confirmed true OD, NG tube, stomach lavage, +/- activated charcoal, saline enema**

• **Atropin +/- Pacing for slow rates**

• **Rectify E’lytes e.g. replace K/Ca/Mg or Ca gluconate/Insulin/chelating agents for Hyper-K+**

• **May require hyperventilation to maintain low CO2 and hold acid/base stable in addition to NaHCO3. Sometimes dialysis for drug clearance and support.**

• **Consider LVAD in electro-mechanical dissociation or severe low CO - supports circulation & helps organs recover to metabolise drugs**

• **Time is a good healer - buy it!**
Specific

- Digoxin: Usually > 4mg dose. Digibind immune Fab if Serum level > 12.8 ng/ml 4-6 Hrs after intake or if > 19 anytime. Vial 38 mg will neutralise 0.5 mg of Digoxin

- Sympathomimetic drugs for B-Blocker overdose

- Sodium supplements may help with Ic drugs, Ca++/Mg++ for Ia

- Many a time DC is not effective or not sustained and occasionally makes the arrhythmia worse with haemodynamic consequences

- Occasionally other anti-arrhythmics
Post Event

- Pin down cause and assess if avoidable
- Counsel patient and family and involve named liaison nurse
- Initial clinic frequency and drug levels
- Consider implantable loop recorder
Post Event

- Pin down cause and assess if avoidable
- Counsel patient and family and involve named liaison nurse. Stress seriousness of event. Mortality > 20% compared to 1% for general OD
- Think of an alternative drug for arrhythmia
- Initial clinic frequency and drug levels
- Consider implantable loop recorder

Thank You
Digibind®
fragments d’anticorps spécifiques de la
digoxine [Fab (ovins)]
pour injection
ANTICORPS SPÉCIFIQUE
DE LA DIGOXINE
neutralise 0.5 mg de
digoxine ou de digitoxine
STÉRILE
POUR USAGE I.V.
SEULEMENT
GSK
GlaxoSmithKline
Flecainide is an increasingly used class 1C antiarrhythmic drug used for the management of both supra-ventricular and ventricular arrhythmias. It causes rate-dependent slowing of the rapid sodium channel slowing phase 0 of depolarization and in high doses
tricyclic
Fig. 2  QT prolongation showing electrolyte fluxes, action potentials and ECG phases 0–4 on the electrocardiogram

Electrolyte Flux

- Cell membrane
- Intracellular
- Extracellular
- Na⁺
- Ca²⁺
- K⁺

Cardiac Action Potential

- Phase 0: rapid depolarisation due to rapid sodium influx
- Phase 1: initial repolarisation due to potassium and chloride efflux
- Phase 2: the plateau where there is a balance of potassium efflux and calcium influx
- Phase 3: rapid repolarisation due to potassium efflux
- Phase 4: the resting membrane potential before the next depolarisation

ECG Complex

Repotted and adapted from WikiTox www.wikitox.org
Toxicologic Tachycardia

Wide QRS
- Group Ia and Ic antidysrythmics
- venlafaxine
- bupropion
- mirtazapine
- carbamazepine
- phenothiazines
- tricyclic antidepressants
- diphenhydramine

Narrow QRS
- cocaine
- sympathomimetics

Normal intervals
- Repeat if suspicion of toxicity, and consider acetaminophen, hypovolemia, CO, etc.

Legend
* Long QT
* Ischemia
Fast-Response Action Potential (e.g., ventricular myocyte)

ERP

mV

0

-50

-100

0

Ca++ in

Na+ in

K+ out

K+ out

Ventricular Action Potential

- Class IA: e.g., quinidine
  - Moderate Na+-channel blockade
  - ↑ ERP
- Class IB: e.g., lidocaine
  - Weak Na+-channel blockade
  - ↓ ERP
- Class IC: e.g., flecainide
  - Strong Na+-channel blockade
  - → ERP
Na\textsuperscript{+} Channel Blocker Toxicity resulting in delay of the phase 0 of depolarization

Prolongation of the QRS complex
Sodium channel blockade

Relationship Between Cardiac Action Potential and Ion Channel Currents

- $K^+$, $Cl^-$ (out)
- $I_{out}$ (transient outward)
- $Ca^{2+}$ (in), $K^+$ (out)
- $I_{Ca}$ ($Ca^{2+}$)
- $I_{K}$ ($K$ slow delayed rectifier)

$+52 \text{ mV}$

- $Na^+$ (in)
- $I_{NS}$ (rapid)

0 1 2 3 4

- $K^+$ (out)
- $I_{K}$ ($K$ slow delayed rectifier)
- $I_{K}$ ($K$ rapid delayed rectifier)
- $I_{K}$ ($K$ inward rectifier)

$-96 \text{ mV}$

200 ms
Early after depolarisation breaking threshold and leading to ectopic beat or development of torsades des pointes

Prolonged QT leading to early after depolarisation
The image depicts an electrophysiological waveform with the following key points:

- **Time Scale:** 200 ms
- **Voltage Levels:**
  - 0 V at 0 ms
  - +52 mV at 1 ms
  - -96 mV at 4 ms

**Key Events:***

- **0 to 1 ms:**
  - **Na⁺ (in)**
  - **Iₙa (rapid)**
  - **K⁺, Cl⁻ (out)**
  - **Ito₁,₂ (transient outward)**

- **1 to 2 ms:**
  - **Ca²⁺ (in), K⁺ (out)**
  - **Ica-L (Ca long)**
  - **IKS (K slow delayed rect.)**

- **2 to 3 ms:**
  - **K⁺ (out)**
  - **IKS (K slow delayed rect.)**
  - **IKR (K rapid delayed rect.)**
  - **IK₁ (inward rect.)**

- **3 to 4 ms:**
  - **K⁺**
  - **IK₁ (inward rect.)**

The waveform illustrates the dynamic changes in ion currents and voltage levels over time, typical in cardiac or neuronal electrophysiology.
Class III agents work K+ here
Class IV agents work Ca+ here
Class II agents Slow down the rise of the action potential
Class I agents work here