

## 1. Introduction and Who Guideline applies to

Trust wide

FOR STAFF Staff involved in paediatric and adult cardiology

PATIENTS Patients with suspected, but not confirmed, Brugada syndrome

## Background

Brugada syndrome is an autosomal dominant condition, which is associated with sudden death with no underlying structural heart disease. The proposed mechanism of action is a loss-of function mutation affecting the rapid inward sodium channel, which may lead to ventricular tachycardia, syncope, cardiac arrest and sudden death. The mean age of death for these patients is 41 years, and the only proven beneficial treatment is insertion of an implantable cardioverter-defibrillator (ICD). The prevalence in the general population is unknown, but it is more common in people of Asian or South East Asian origin – the incidence in people from Thailand, the Philippines and Japan is 0.5-1 per 1000. It is more common in men with an 8-10× higher prevalence compared to women.

## 2. Guideline Standards and Procedures

### Ajmaline challenge

Ajmaline is a Vaughn-Williams Class Ia antiarrhythmic agent, which acts by blocking the rapid inwards sodium channel. Ajmaline is used rather than other Class Ia agents as it has very potent activity and its electrophysiological effects only last for a few minutes after administration, making it suitable for day cases.

In patients with Brugada syndrome who do not have a diagnostic baseline ECG, Ajmaline exacerbates the loss-of-function of the sodium channels resulting in more pronounced ECG changes.

Ajmaline is not licensed in the UK, and it has to be requested on a named-patient basis under the direction of a consultant specialising in dysrhythmias.

Patients undergoing an Ajmaline challenge should be monitored closely due to the possibility of the drug causing various cardiac dysrhythmias.

## ECG

The diagnosis of Brugada syndrome is based upon the ECG. Patients with Brugada syndrome have one of several characteristic ECG patterns, as there is loss of the uniformity of the action potentials of the cardiac myocytes in the endocardium and epicardium. This manifests as ST segment abnormalities, seen best in leads V<sub>1-3</sub>, as detailed below:



- The type 1 “coved” ECG is defined as RBBB pattern with J-point (junction of the QRS complex with the ST segment) elevation of  $\geq 0.2$  mV with a slowly descending ST segment to a flat or negative T wave. This is diagnostic of Brugada syndrome.
- The type 2 “saddleback” ECG has  $\geq 0.2$  mV J point elevation with  $\geq 0.1$  mV of ST elevation and a positive or biphasic T wave. This can occur in healthy subjects.
- The type 3 ECG can be either “coved” or “saddleback” but with  $< 0.2$  mV J point elevation or  $< 1$  mV of ST elevation. This is commonly seen in healthy subjects.

The V<sub>1</sub> and V<sub>2</sub> leads should be positioned more superiorly (in the 2<sup>nd</sup> or 3<sup>rd</sup> intercostal spaces) to better see the characteristic ECG changes.

## Organisation

Unless there is an indication for an urgent test, Ajmaline challenges should be organised as an elective day case procedure. The availability of the following are pre-requisites for the performance of a test:

- For patients under 18 years old, the test should be performed in an HDU environment or in the catheter laboratory.
- Patients undergoing the test on PICU have to be officially admitted there.
- A cardiology doctor to supervise the test (must be up to date with adult or paediatric resuscitation, as appropriate, including the use of a defibrillator).
- A second person to aid with checking drugs, performing ECGs and who is able to help in the event of resuscitation being required.

- A bed space with an oxygen port, electrical sockets and cardiac monitoring (a defibrillator can be used for this).
- Equipment for intravenous access (including a sharps bin)
- A fully equipped resuscitation trolley, including resuscitation drugs and a defibrillator
- Isoprenaline should be available (this may work as an antidote to Ajmaline)
- Ajmaline should be made available by contacting the pharmacist in advance.

Given the necessary preparation, it would be beneficial to organise several Ajmaline challenges to be performed in a session.

## Patient education and consent

Patients should be advised that the test will involve them coming into hospital for several hours, and that they should not eat or drink for 4 hours beforehand.

They will have an intravenous cannula inserted and will receive several doses of a short-acting drug through this whilst ECGs are recorded.

Potential side-effects include a metallic taste when the drug is given, visual disturbances, flushing and rash, all of which usually disappear quickly when the drug wears off.

They should be made aware that there is a low risk (<1%) that Ajmaline may cause a rapid heart rate that may require other drugs to be used, or that an electric shock may be required to normalise the heart rhythm. A consultant will need to review the results; therefore the patient may not get them on the day of the test.

The patient or a parent / guardian with parental responsibility should sign a consent form before the test is performed. The form should contain the following:

- Name of procedure: Ajmaline challenge
- Intended benefits: To test for Brugada syndrome, and allow reassurance or further treatment depending on the result
- Frequent risks: Rash, flushing, metallic taste.
- Serious risks: <1% risk of abnormal heart rhythm requiring further treatment including cardioversion

## Contraindications

- Hypersensitivity to Ajmaline or one of the other ingredients in the IV solution
- 2nd and 3rd degree AV block
- History of Stokes-Adams attacks
- Manifest heart failure
- Prolonged corrected QT interval
- Intoxication with cardiac-acting glycosides
- Myasthenia gravis
- Hypertrophic cardiomyopathy
- Bradycardia (<50 beats/min)

- Within the first three months following myocardial infarction
- Left ventricular ejection fraction <35%

## Cautions

- Deranged liver function – check LFTs prior to test
- Renal impairment – check U&Es prior to test
- Sick sinus syndrome
- 1<sup>st</sup> degree AV block
- Hypotension (systolic BP <90mmHg)
- Impaired hepatic circulation

## Preparation

1. Prior to the challenge, all resuscitation equipment should be checked and resuscitation drug doses calculated and recorded.
2. The patient's weight should be measured and recorded.
3. A baseline ECG should be performed and reviewed.
  - If there is a type 1 Brugada pattern on the baseline ECG then the test is not indicated, as it will provide no further information.
  - If there is evidence of AV block on the ECG, the responsible consultant should be contacted before proceeding as the test may need to be performed in the catheter lab in case temporary pacing is required due to Ajmaline induced complete AV block.
  - Measure baseline PR interval, QRS duration and QTc
4. Obtain peripheral intravenous access – use a large vein and monitor the injection site closely.

## Performance

1. Ajmaline comes in a 5 mg/ml solution in 50 mg vials. It does not require dilution. Draw up 1 mg/kg (maximum dose = 50 mg) into a syringe
2. Attach 12 lead ECG to patient
3. Commence continuous cardiac monitoring (a defibrillator can be used for this)
4. Administer the Ajmaline in 0.25 mg/kg (maximum 10 mg) aliquots over 1 minute, every 2 Minutes - Maximum IV infusion rate = 10 mg/min
5. Record a 12 lead ECG one minute after each dose
6. Examine the ECG and cardiac monitor for any of the end points (see below)

## End points

The test should be stopped when any of the following conditions occur:

- The full 1 mg/kg dose has been given and no ECG changes have occurred (negative result)
- There is J point or ST segment elevation of  $\geq 0.2$  mV (2 mm) with coved ST elevation in more than one right precordial lead (positive result)
- There is QRS prolongation  $>30\%$  baseline
- Ventricular ectopic beats or ventricular tachycardia develop
- Sinus arrest or AV block develops

The patient should be closely monitored until the ECG has normalised and they are feeling well.

They can be discharged after 1 hour if they are feeling well.

The results should be sent to the responsible consultant for review.

**SAFETY** Very low risk ( $<1\%$ ) of developing ventricular dysrhythmia.

### **3. Education and Training**

None

### **4. Supporting References**

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4 Antzelevitch C, Brugada P, Borggrefe M, et al. Brugada Syndrome: Report of the Second Consensus Conference: Endorsed by the Heart Rhythm Society and the European Heart Rhythm Association. *Circulation* 2005;111:659–70.

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6 McMillan MR, Day TG, Bartsota M, et al. Feasibility and outcomes of ajmaline provocation testing for Brugada syndrome in children in a specialist paediatric inherited cardiovascular diseases centre. Open Heart 2014;1:e000023–3. doi:10.1136/openhrt-2013-000023

## **5. Key Words**

Ajmaline, Brugada, Cardiac arrest, ECG, Sudden death, Syncope, Ventricular tachycardia

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**The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs. As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.**

<b>CONTACT AND REVIEW DETAILS</b>	
<b>Guideline Lead (Name and Title)</b> Suhair Shebani – Paediatric Cardiologist	<b>Executive Lead:</b> Chief Medical officer
<b>REVIEW RECORD</b>	
<b>Description Of Changes (If Any)</b> <b>January 2022</b> Changed from Trust category C document to category B Scope clarified Administration of Ajmaline changed from 10mg(2ml) aliquots to 0.25 mg/kg (maximum 10 mg) aliquots over 1 minute, every 2 Minutes	