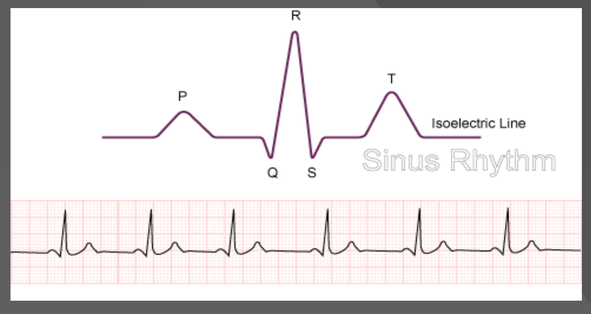
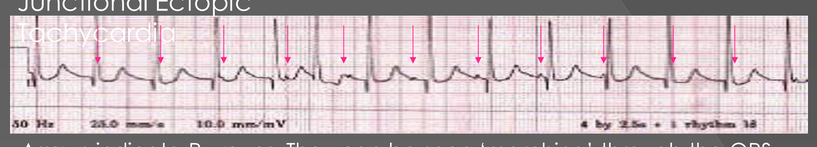
A case of refractory Junctional Ectopic Tachycardia (JET); thinking about alternative management or prevention.

Introduction: JET affects 1-15% of all post cardiac surgical patients and can be challenging to manage. It is a malignant tachycardia and it is associated with increased morbidity, prolonged mechanical ventilation as well as PICU and hospital length of stay (Sahu et al, 2018) . Post operative JET usually occurs within 72 hours of repair of congenital heart defects and can self-resolve within 8 days. It is thought to be attributed to ischaemia/infiltrative haemorrhage or injury by direct or indirect mechanical impact to the HIS bundle area (Till et al, 1992). It can be regular or irregular but does not involve a re-entry circuit. JET can present with a retrograde atrial conduction with 1:1 pattern or with atrioventricular dissociation with variable conduction.

Risk Factors for post-operative JET: Children less than 6 months old, Those undergoing repair for AV canal defects, Tetralogy of Fallot and Ventricular Septal Defects. JET is not exclusive to these defects and has been reported in patients who have had extra cardiac repairs such as BT shunts and completion of Fontan. Patients who have electrolyte imbalances, fever and use of inotropes and milrinone post-operatively are also at risk of developing JET. Those who have had a prolonged bypass time are also at risk.



Junctional Ectopic Tachycardia



Arrows indicate P waves. They can be seen 'marching' through the QRS complexes due to AV dissociation

Typical JET treatment flow diagram:

Suspicion of JET on monitoring:

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Exclude reversible causes:
- Tamponade
- Check electrolytes
- Check for evidence of Low Cardiac Output State (LCOS)

→ **Target:**
K^+ 4 to 5 mmols/L
iCa^{2+} >1.2mmols/L
Mg^{2+} >1.0mmols/L

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Perform:
- 12 lead ECG
- Atrial wire study

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Confirmation of JET?

→ No → Maintain vigilance and awareness of the possibility of the development of JET

↓ Yes

Inform PICU Consultant and Cardiologist:
- Ensure adequate analgesia/sedation used
- Cool to 35-36° (if ventilated)
- Reduce inotropes if possible (particularly if chronotropes such as Dopamine, Dobutamine and Adrenaline are in use)
- Monitor for evidence of LCOS
- Echocardiography to exclude a surgically redeemable cause and to assess heart function

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Ongoing JET?

→ No → Continue current treatment and monitor for recurrence of JET

↓ Yes

PICU consultant to inform Consultant Cardiologist and Cardiac Surgeon:
- HR <170 ?Trial atrial/DDD pacing

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Amiodarone (CAUTION= negative inotrope)
- Loading dose (if instructed) 5mg/kg over 1-4 hours
- Maintenance infusion of 5-15mcg/kg/min

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Further options:
- Paralyse and cool to 34°
- Bedside MDT
- ECLS

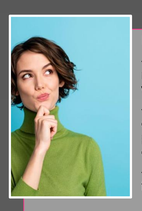
Though there is no expectation here for cooling to convert JET to SR, it does slow the JET rate to a more acceptable level which may allow for other therapies to restore AV synchrony and improve the cardiac output (Catton et al, 2020). If the patient is still in JET, then the treatment pathway needs to be escalated. Amiodarone is considered the 1st line anti-arrhythmic therapy and should be commenced following discussion with the consultant cardiologist, however care should be taken as the side effects of Amiodarone include: hypotension, bradycardia, AV block, nausea and vomiting, liver dysfunction (Saul et al, 2005).

Case study: A 5 month-old boy admitted to a cardiac PICU following uncomplicated Tetralogy of Fallot repair. He developed JET post operatively that was resistant to sedation, muscle relaxation, active cooling, pacing and Amiodarone. The patient progressed to a low cardiac output state despite maximal medical management, leading to cardiac arrest requiring cannulation to VA ECMO support. He remained in a junctional rhythm and required 7 days of IV Amiodarone at 10mcg/kg/min. He was successfully weaned and decannulated from ECMO on the third attempt. JET in the context of restrictive right ventricle physiology can have serious consequences. This case has demonstrated that refractory JET can contribute to unsuccessful weaning of ECMO support, prolonged ventilatory time and prolonged ITU and hospital length of stay.

On reflection of this case, a literature review was carried out to explore the evidence behind alternative strategies to manage JET. There is some suggestion that prophylaxis with Dexmedetomidine may have a role to play in reducing the incidence of post-operative JET. Another suggestion is the use of Ivabradine as a second line adjunct to Amiodarone when patients are refractory to it. There is a suggestion that when Amiodarone is commenced on patients who are already in a low cardiac output state, patients are particularly resistant to Amiodarone. Early consideration of second line adjuncts in patients with refractory JET, with evidence of low cardiac output, would benefit greatly if it resulted in earlier termination of the dysrhythmia. The use of prophylactic Dexmedetomidine or early use of Ivabradine as a second line adjunct may provide options that can be considered in patients at higher risk of refractory JET and associated low cardiac output state.

Prophylaxis with Dexmedetomidine.

Not only is Dexmedetomidine a good analgesic and sedative, it also has anxiety decreasing effects (Chrysostomou et al, 2006).

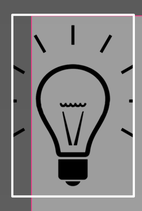


How does Dexmedetomidine work?

-Dexmedetomidine is a selective α-2 adrenoreceptor agonist which means it has limited action on the CNS without activating α-1 receptors with unwanted cardiovascular side effects (Chrysostomou et al, 2006).

-The stimulant effect that Dexmedetomidine has on the α-2 adrenoreceptors decreases the release of catecholamine which produces a sympatholytic action that causes negative dromotropic effects and chronotropic effects.

-Dexmedetomidine depresses both the sinus and atrioventricular nodal function through vagal stimulation (Chrysostomou et al, 2009).



A systematic review and meta-analysis of literature by Wang et al, 2021, suggests:

-Dexmedetomidine allows patients to come off bypass with a slower heart rate,

-JET incidence is lower in the Dexmedetomidine group compared to placebo group,

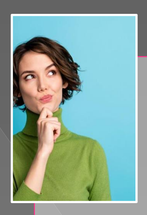
-The need for inotropes was lower in Dexmedetomidine group,

-Ventilation time, ICU and hospital length of stay was lower in Dexmedetomidine group in randomised controlled trials

-The results are statistically significant when compared with the placebo groups.

-Possible side effects of Dexmedetomidine include bradycardia and hypotension.

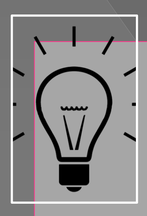
Treatment with Ivabradine:



-Ivabradine is a selective inhibitor of hyper-polarisation of cyclic neucleotide-gated channels.

-The selectivity of Ivabradine makes it an ideal candidate for pharmacology intervention as it directly targets the AV node and purkinje system which allows for remodelling of the arrhythmia at its origin.

-The major benefit is its haemodynamic profile; it has not effect on contractility, repolarisation or blood pressure.



-Ivabradine has been found to be effective as an adjunct to Amiodarone and as a singular agent (Kumar et al, 2017).

-Ivabradine works by blocking hyperpolarisation-activated cyclic neucleotide-gated channels at the Sinus and AV nodes (Lopez Fernandez et al, 2021).

-Heart rate reduction is achieved without modifying inotrpy, lusiotropy and intra-cardiac function (Patel et al, 2018).

-Its an oral formulation so early administration is necessary as absorption will be affected by LCOS (Sasikumar, 2021).

-A study by Arvind et al (2021) directly compared Ivabradine to Amiodarone in the time taken to convert patients to sinus rhythm and time taken until heart rate control was gained.

-Whilst minimal difference was found between both drugs for both conversion to SR and time taken to rate control, the data does suggest that Ivabradine's risk profile is superior to its alternatives.

In conclusion: When one takes into account the significant increased morbidity and mortality that is associated with JET, and the negative side effects that can be associated with parts of the management pathway, we must question whether the management pathway is the only option. Recent studies show that the use of dexmedetomidine pre-incision could have hugely beneficial effects for the patient in preventing JET and thereby reducing their ventilator days, and ITU and hospital length of stay. Other studies suggest that Ivabradine could be effective when used alone or in addition to Amiodarone when treating JET and that the patient would benefit from its haemodynamically neutral profile. Of course, further study is required for both of these methods when treating post operative JET in children. Both of these treatments have the potential to radically change the way patients are treated in the future.

References: Arvind B et al, *'Ivabradine versus Amiodarone in the management of post-operative junctional ectopic: a randomized, open-label, noninferiority study'*, J Am Coll Cardiol EP, 2021; 7, 1052-1060. Catton KG, Perterson JK. Junctional ectopic tachycardia: recognition and modern management strategies. Crit care nurse. 2020;40(1): 46-55. Chrysostomou, C. et al (2006) *'Use of Dexmedetomidine in Children After Cardiac and Thoracic Surgery'*, Paediatric Critical Care Medicine, vol 7, pages 126-131. Lopez Fernandez E, et al (2021) *'Uso de ivabradine en el tratamiento de la taquicardia ectopica de la union tras circugia cardiaca'*, An Pediatr (Barc), 95: 118-120. Patel PA et al, *'Effects of Ivabradine on haemodynamic and functional parameters in left ventriclular systolic dysfunction: A systematic review and meta-analysis'*, J Gen Intern Med, 2018; 33, 1561-70. Sahu MK, Das A, Siddarth B. Arrhythmias in children in early postoperative period after cardiac surgery. World J Ped Congen Heart Surg. 2018;9(1):38-46. Sasikumar N, Raman K.K and Seshadri B (2021) *'Diagnosis and Management of Junctional Ectopic Tachycardia in Children'*, Annals of Paediatric Cardiology, vol 14, pages 372-381. Till JA, Rowland E (1991) *'Atrial pacing as an adjunct to the management of post surgical HIS bundle tachycardia'*, British heart Journal, vol 66, pages 225-9. https://www.library.leicestershospitals.nhs.uk/PAGL/SharedDocuments/JunctionalEctopicTachycardia(JET)UHLChildrensIntensiveCareGuideline.pdf

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