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Adenosine in paediatric arrhythmias

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Adenosine is a valuable drug for diagnosis and treatment of tachycardia in infants and children. Recommended initial doses in most guidelines are too small to be effective. A dose of 100 or 150 microg/kg is preferred, with increments of 50–100 microg/kg if required.

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Introduction

After its introduction into clinical paediatric practice around twenty years ago, adenosine rapidly became the first line drug of choice for treatment of infants and children with sustained tachycardia. It is a very effective drug if used appropriately but the correct dosing has been widely misunderstood. It provides important diagnostic information as well as being therapeutically effective. This brief review will consider the correct use of adenosine in paediatric arrhythmias.

Adenosine is an endogenous purine nucleotide with potent anti-arrhythmic effects[1]. Its electrophysiological effects include slowing of atrioventricular (AV) node conduction and suppression of sinus node automaticity. It also shortens atrial refractoriness but has little effect on ventricular myocardium. Clinically the predominant effect is on the AV node and use is made of this in the diagnosis and treatment of tachycardia. The AV node is a right atrial structure and adenosine also has significant clinical effects on some atrial arrhythmias and may suppress the sinus node. Given in sinus rhythm it may cause sinus bradycardia or atrial bradycardia or atrioventricular block. A few rare types of ventricular tachycardia may also be suppressed by adenosine.

Adenosine is metabolised by red cells and its half life is very short[2]. Because of this, it has to be given by rapid bolus injection in a sufficient dose to reach the coronary circulation (the blood supply to the AV node) from a peripheral intravenous injection. Doses can be repeated with no cumulative effect.

Indications

Intravenous adenosine is the first line treatment for any sustained regular tachycardia in infancy or childhood, with either a normal or a wide QRS[3,4]. The main aim is termination of tachycardia but any change in the electrocardiogram (ECG), even if only transient, may give useful diagnostic information (Figures 1 and 2). Adenosine is not recommended for sustained *irregular* tachycardias, partly because the mechanism of the arrhythmia will already be apparent from analysis of the ECG and partly because there is the possibility of producing haemodynamic deterioration from acceleration of the ventricular rate (see below). Adenosine is not helpful in the treatment of intermittent tachycardias as its effect is so short lasting. It may occasionally be given in this situation if it is thought it might give diagnostic information.

Dosing

When the first clinical investigations of adenosine were performed in children in the 1980s, the appropriate dose was not known. Because of this,

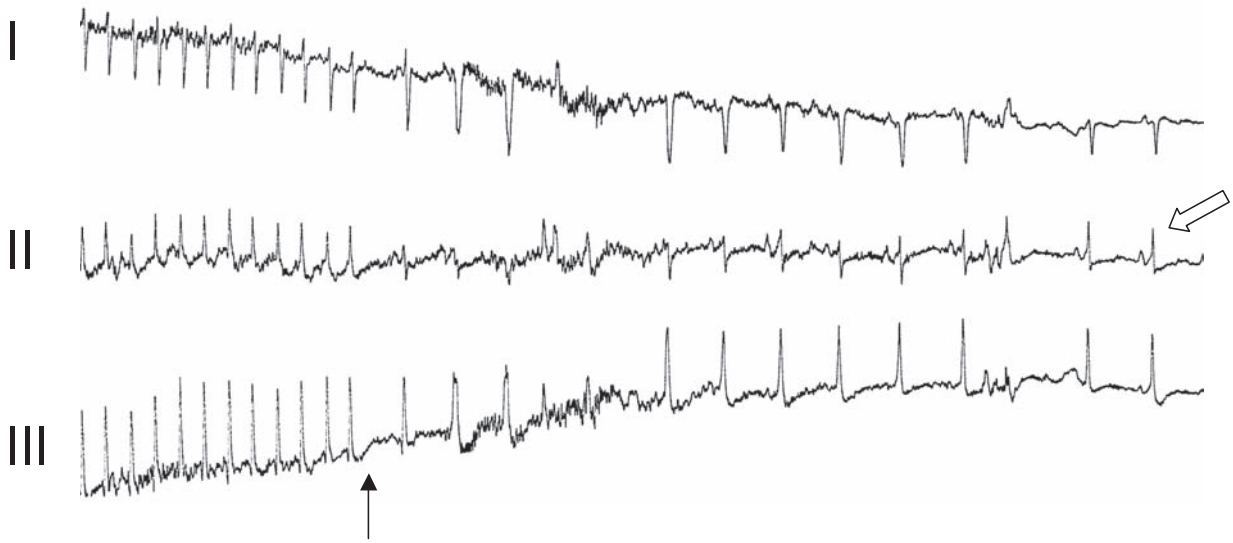

Figure 1 A three lead rhythm strip recorded during administration of adenosine to a neonate with sustained tachycardia. The ventricular rate is around 300/minute and the QRS is normal. Adenosine causes tachycardia to stop (arrow) and sinus rhythm resumes. The QRS is then wider and when the baseline disturbance settles there is clear evidence of a short PR interval and a delta wave, characteristic of Wolff-Parkinson-White syndrome (open arrow).

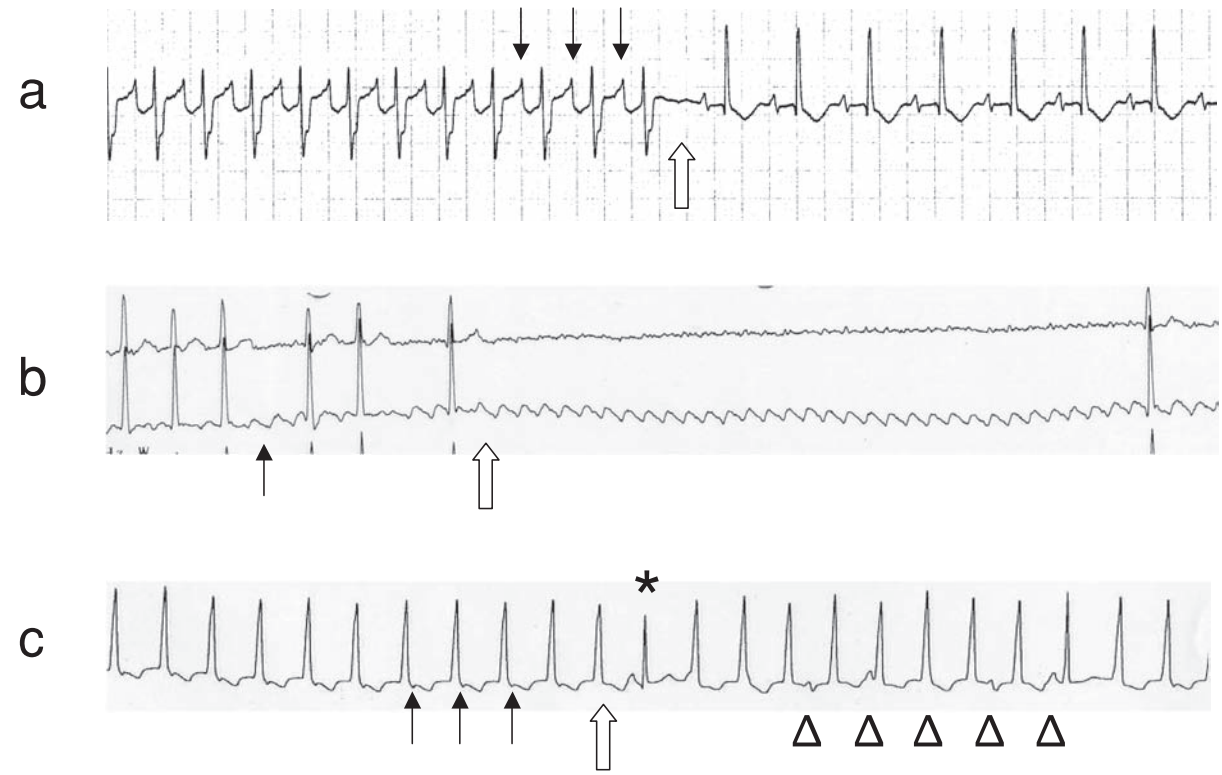

Figure 2 Some of the effects adenosine may have on sustained tachycardia.
(a) Tachycardia stops. The QRS here is wide and P waves are clearly visible (arrows). Adenosine causes retrograde AV block with a missing P wave (open arrow) and this breaks the re-entry pathway. Sinus rhythm resumes.
(b) Adenosine produces AV block but tachycardia continues. Atrial flutter waves are clearly visible in the lower lead. The atrial flutter is unaffected by the presence of AV block. This shows the advantage of a multi-channel rhythm strip as the diagnosis is less obvious on the upper lead.
(c) Adenosine produces retrograde ventriculo-atrial block but tachycardia continues. In this recording of tachycardia in a neonate the QRS is wide but the widening is subtle. There is a 1:1 AV (P-QRS) relationship with retrograde P waves (arrows). Adenosine produces retrograde block with a missing P wave (open arrow). This is followed by a sinus P wave which is conducted to the ventricles with a normal QRS – a capture beat (asterisk). Tachycardia continues unaffected but there is now clear evidence of dissociated P waves (arrow heads). The wide QRS tachycardia with ventriculo-atrial block proves the diagnosis of ventricular tachycardia.

early studies used a step-wise incremental dose strategy starting from 37.5 or 50 microg/kg with similar increments[5,6]. Unfortunately these experimental protocols have continued into present guidelines for dosing[7-9], despite many reports of the lack of efficacy of smaller doses[10-12]. The problem with recommending an ineffective dose is that parents and paediatricians lose confidence in what is a very effective medication. If the paediatrician finds that the first dose is not effective, it is often repeated before being increased, so two or three or more sub-therapeutic doses may be given.

Adenosine doses of 50 microg/kg are rarely effective and 100 microg/kg is also often ineffective, especially in infancy. A recent report by Dixon et al showed that around 35% of infants and around 80% of children respond to a dose of 150 microg/kg[12]. In earlier reports Sherwood et al. reported a 16% response to 50 microg/kg[10] and Losek et al showed a 22% efficacy for doses of up to 100 microg/kg[11].

The difference in effectiveness in infants and children may be explained by the difference in weight to body surface area ratio and there might be little difference if adenosine was prescribed and administered in mg/m² rather than microg/kg. Other possible explanations for the lower response in infants include smaller cannulae limiting the injection rate and the fact that babies tend to be more ill at presentation and may have prolonged circulation times.

Administration

The first dose of 100 or 150 microg/kg is given as a bolus via an intravenous cannula. Tachycardia will occasionally revert during cannula insertion. If the cannula does not have two injection ports it should be fitted with a three-way tap so the adenosine injection can be followed by a rapid flush of normal saline or dextrose. It is important to record the ECG during administration (preferably three leads – I, aVF and V1) as well as a 12 lead ECG before and afterwards. It is not adequate simply to observe the ECG on a monitor because termination of tachycardia, even for only one beat, will prove the efficacy of the drug and provide important diagnostic information.

If the first dose is ineffective, the second should be 50 or 100 microg/kg higher. Experimental data[13] and a case report[14] suggest that adenosine may also be effective if given by the intraosseous route.

Adverse effects

Side effects such as flushing, dyspnoea, or chest pain are relatively common but are fleeting and usually minor. It is worth warning older children of these before a dose is administered. Although warnings or contraindications to use in asthma are commonly given, there is no evidence that adenosine causes clinical problems in children with asthma and good evidence that it does not do so in adults[15]. No significant problems were encountered in reports on paediatric use of adenosine[5,10-12].

Transient bradycardia after termination of tachycardia with adenosine is common but significant proarrythmia is rare, especially in children. There are reports of various induced arrhythmias, mostly in the elderly on other drug treatment[16]. One situation to be aware of is the possibility of increasing AV conduction when giving adenosine to a patient with atrial flutter and 2:1 AV conduction. The sympathetic response to transient systemic vasodilation and mild hypotension induced by adenosine can increase AV conduction to 1:1. This may cause haemodynamic compromise and may be an indication for synchronised DC cardioversion. In adults, the clinical effects of adenosine may be enhanced in patients taking digoxin, verapamil or a beta-blocker and may be diminished by theophylline or caffeine[16].

Adenosine is also widely used during invasive investigation of arrhythmias in the electrophysiology laboratory using, for example, its effect on the AV node to unmask accessory pathways (which are mainly unaffected by adenosine)[17].

Clinical effects of adenosine

The clinical use of adenosine takes advantage of its dominant effect of slowing AV conduction. Many common types of supraventricular tachycardia involve re-entry through the AV node which is a fundamental part of the arrhythmia circuit[4]. Atrioventricular re-entry tachycardia via an accessory pathway is the commonest type of "supraventricular" tachycardia (SVT). The pathway is usually "concealed" in sinus rhythm (i.e. the ECG is normal) but may be overt, as in Wolff-Parkinson-White syndrome. Atrioventricular nodal re-entry tachycardia is another common variety of SVT in older children. It might be better termed atrio-nodal re-entry as the circuit involves the AV node and the adjacent low right atrium. Both these arrhythmias are reliably terminated by adenosine as they cannot continue in the presence of AV nodal block[17] (Figure 1).

The effect on atrial arrhythmias is less predictable. Adenosine will not terminate atrial flutter but does cause impairment of AV conduction to unmask the flutter. This can be a great help in diagnosis if

1:1 or 2:1 AV conduction makes precise diagnosis difficult (Figure 2). The effect on other atrial arrhythmias varies. Atrial ectopic tachycardia may be unmasked by showing 2:1 conduction but may also be transiently suppressed, making differential diagnosis from sinus tachycardia more difficult. Rarer re-entry tachycardias (such as permanent junctional reciprocating tachycardia or atrio-fascicular re-entry tachycardia etc) are usually terminated, if only transiently, but require specialist assessment. Adenosine rarely terminates ventricular tachycardia but careful analysis of the ECG during administration may identify production of retrograde block (Figure 2).

Adenosine in fetal tachycardias

Fetal tachycardias are usually managed by oral anti-arrhythmic drug administration to the mother. In unresponsive cases, direct fetal administration of anti-arrhythmic drugs is used. There are occasional case reports of fetal administration of adenosine[18,19]. Because reports will probably be written only in the event of success, there is no way of knowing at the moment how likely treatment is to be successful and what problems may be encountered.

Conclusion

Adenosine is a very effective drug in diagnosis and treatment of children with arrhythmias if used correctly. Recording an ECG before, during and after its administration gives very important clinical information. Guidelines for dosing need to be revised to recommend clinically effective doses.

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