Proarrhythmic effect of adenosine in a patient with atrial flutter

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Abstract
Adenosine has been proposed as a useful diagnostic agent in patients with narrow complex regular tachycardia of uncertain origin. Its effects are usually transient owing to its extremely short plasma half life and, as a consequence, it is thought to be safer than other drugs used in the acute treatment of such arrhythmias. However, adenosine had a proarrhythmic effect when administered to a patient in order to confirm the diagnosis of atrial flutter. As expected, a transient increase in atrioventricular block was seen but this was followed by a doubling of the ventricular rate and haemodynamic compromise requiring immediate DC cardioversion. It is postulated that the secondary catecholamine-mediated effects of adenosine were responsible for this phenomenon.

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Adenosine is an endogenous purine nucleoside that has recently been approved in the United Kingdom as a therapeutic agent for the termination of reentrant arrhythmias involving the atrioventricular node and also as a diagnostic agent in patients with regular arrhythmias of uncertain origin. It is given as a rapid intravenous bolus and gives rise to transient atrioventricular nodal block lasting a few seconds. The reported proarrhythmic effects of adenosine have been limited to bradycardias, bradycardia-induced torsades de pointes and atrial and ventricular extrasystoles of little haemodynamic consequence.

Case report
A 39 year old man was admitted to his local hospital complaining of palpitation and dizziness. He had been evaluated 5 years previously for Wolff-Parkinson-White syndrome at another hospital and electrophysiological study had shown an anterogradely conducting, “safe” accessory pathway. At that time he was reassured and discharged on no therapy. He had been free from further palpitation until the current episode. On arrival at his local hospital the electrocardiogram showed a narrow complex tachycardia with a ventricular rate averaging 140 beats per minute. There was no evidence of ventricular preexcitation. He was given intravenous amiodarone (400 mg) with no effect. Sinus rhythm was achieved after DC cardioversion and he was discharged on oral flecainide (200 mg twice a day). He presented again 48 hours later with further arrhythmias resistant to intravenous flecainide (130 mg over 10 minutes) and was then transferred to our hospital for further management. On arrival he was well perfused with tachycardia of 130 beats per minute. Though the electrocardiogram (fig 1A) was suggestive of atrial flutter with a 2:1 block it was thought that adenosine would help to distinguish this from an atrioventricular reentrant tachycardia associated with the known diagnosis of Wolff-Parkinson-White syndrome. Doses of 5, 10, and 15 mg had no effect. Fifteen seconds after administration of 20 mg adenosine a transient increase in atrioventricular block was observed (fig 1B), confirming the diagnosis of atrial flutter with 2:1 block. Immediately after the development of the increase in atrioventricular nodal block the patient sustained 1:1 atrioventricular conduction with a ventricular rate of 260 beats per minute (fig 2). This rhythm was sustained and associated with haemodynamic compromise, necessitating DC cardioversion. Sinus rhythm was restored.

Subsequent electrophysiology study confirmed the presence of a retrogradely conducting accessory atrioventricular connection, with earliest atrial activation (during ventricular pacing) in the roof of the coronary sinus os. Assessment of atrioventricular nodal refractoriness was limited by the achievement of atrial refractoriness (less than 200 ms after a drive cycle length of 600 ms).

Discussion
This case is the first report of a serious proarrhythmic effect of adenosine when given to a patient with atrial flutter. Administration of

Figure 1 Intravenous adenosine caused an initial increase in the degree of atrioventricular nodal conduction block during atrial flutter.
the atrioventricular nodal blocking agent was followed by a secondary enhancement of atrioventricular nodal conduction and a sudden doubling of the ventricular response to atrial activation, leading to severe haemodynamic embarrassment. This secondary effect is likely to be related to the activation of the sympathetic nervous system that has been shown to occur after administration of adenosine.2 Though the autonomic effects of adenosine are short-lived the onset of 1:1 conduction is likely to have further increased sympathetic stimulation, thereby preventing return to 2:1 atrioventricular nodal conduction. Previous reported experience of the use of adenosine in patients with atrial arrhythmias and 2:1 atrioventricular block is limited. Rankin and coworkers3 administered adenosine to 11 patients with atrial flutter and 2:1 block, and acceleration of ventricular rate was not reported. Haines and DiMarco4 reported no adverse effects when adenosine was administered to 14 patients with intra-atrial reentrant tachycardia, though the number of patients who received the drug in the presence of 2:1 atrioventricular nodal block was not stated. These studies together with the fact that a similar phenomenon was not seen when the agent was given to eight patients with atrial flutter and 2:1 conduction block through an accessory atrioventricular connection5 (where there are no counteracting effects of adenosine-induced conduction block) suggest that the effect of adenosine-induced sympathetic stimulation is likely to be small. The fact that in this case it was sufficient to allow 1:1 atrioventricular nodal conduction is likely to be related to a combination of a relatively slow flutter rate (because of previous antiarrhythmic therapy), an unusually short atrioventricular nodal refractory period in the baseline state, and the use of a relatively high dose of adenosine. Though the maximum single dose covered by the United Kingdom product licence for adenosine is 12 mg, it is not uncommon for higher doses to be required to cause atrioventricular nodal block in patients with narrow complex tachycardias.5 The unusual occurrence of a serious adenosine-induced acceleration of ventricular rate in this patient reinforces the recommendation that, as with all intravenous antiarrhythmic agents, continuous electrocardiographic monitoring and availability of DC cardioversion are required during administration of adenosine.5

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