Clinical Investigations

Use of Adenosine as a Diagnostic Tool for Dual Atrioventricular Nodal Pathways: Response of Control Patients to Incremental Doses of Adenosine

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Summary

Background: Adenosine at low doses preferentially blocks fast over slow pathway conduction in patients with dual atrioventricular (AV) nodal physiology and typical AV nodal reentrant tachycardia (AVNRT). During atrial pacing, this effect is manifested as an abrupt increase in the AH interval with low doses of adenosine. This demonstration of dual AV nodal physiology may be useful as a diagnostic tool during electrophysiologic studies in patients with supraventricular tachycardia who are not easily inducible, as clear demonstration of dual AV nodal pathways may indicate that AVNRT is a likely diagnosis and that further attempts at arrhythmia induction should be tailored in that direction. However, to be a useful test, adenosine should not cause an abrupt increase in AH interval in patients without dual AV nodal physiology.

Hypothesis: This study was designed to investigate the prevalence of dual AV nodal pathways with administration of adenosine in patients with no history suggestive of AVNRT.

Methods: Thirty-seven patients who had no prior history of AVNRT and were undergoing electrophysiologic study for standard indications were enrolled. Baseline Wenckebach cycle length (WCL) and AV nodal effective refractory periods were measured at atrial pacing cycle lengths of 400 and 600 ms. The atrium was then paced at WCL + 50 ms, and WCL + 100 ms, while incrementally larger doses of intravenous adenosine were administered until AV nodal block occurred.

Results: The mean ($\pm$ standard deviation) doses of adenosine required to cause AV nodal block while pacing at WCL + 50 ms and WCL + 100 ms were 7.1 ± 3.9 and 7.4 ± 4.5 mg, respectively. In 1 of 37 patients (2.7%, 95% confidence interval 0–8%), an abrupt prolongation of the AH interval was seen with the administration of adenosine during atrial pacing as well as during the atrial refractory period determination. In all other patients, no dual AV nodal physiology was demonstrated during the refractory period determination, and there were only gradual changes in the AH interval with atrial pacing during administration of adenosine.

Conclusion: Among patients with no history suggestive of AV nodal reentrant tachycardia, only 2.7% have clinically silent dual AV nodal pathways using this method. Incremental adenosine infusion during electrophysiologic study can be used as a highly specific diagnostic tool for patients with dual AV nodal pathways.

Key words: atrioventricular node, atrioventricular nodal reentrant tachycardia, adenosine

Introduction

Adenosine is an endogenous nucleoside that slows the sinus node (negative chronotropic effect) as well as impulse conduction through the atrioventricular (AV) node (negative dromotropic effect).¹ The depression of conduction through the AV node makes adenosine highly effective for the termination of supraventricular tachycardias using the AV node as part of the reentrant circuit.^{1, 2} We have previously demonstrated a functional difference in the response of the anterograde fast and slow AV nodal pathways to the effects of adenosine in patients with dual AV nodal pathways.³ We have shown that in 88% of patients with dual AV nodal pathways and typical AV nodal reentrant tachycardia (AVNRT), the anterograde fast pathway is more sensitive than the anterograde slow pathway to the effects of adenosine. In the presence of dual AV nodal pathways, low doses of adenosine will preferentially block fast pathway conduction.³ This differential effect is seen dur-

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ing the electrophysiology study as an abrupt increase in the AH interval during fixed rate atrial pacing with administration of adenosine, with induction of AVNRT in 56% of patients with dual AV nodal pathways. We have used this technique as a diagnostic tool to determine the presence of dual AV nodal pathways and AVNRT in patients with documented supraventricular tachycardia. However, to be useful as a diagnostic tool, the response to adenosine must be specific to patients with dual AV nodal pathways. The present study was designed to investigate the prevalence of apparent dual AV nodal pathways with administration of adenosine in patients with no history of AVNRT undergoing electrophysiologic studies.

Methods

All patients undergoing electrophysiologic study with no prior history suggestive of AVNRT were invited to participate in the study. The study was approved by the Institutional Review Board, and all patients gave informed consent. Patients were studied in the fasting state after all antiarrhythmic drugs had been discontinued for at least five half-lives. Three quadripolar catheters were inserted through sheaths in the femoral veins and advanced to the right ventricular apex, the high right atrium, and the His bundle position, respectively. In several patients, an electrode catheter in the coronary sinus was also employed.

Atrial pacing was performed at twice the diastolic threshold using a programmable stimulator (Bloom DTU 201, Bloom Associates, Narbeth, Pa., USA). Leads I, II, aVF, and V₁, and the intracardiac electrograms were recorded on an optical disk (Prucka Engineering, Inc., Houston, Tex., USA). Electrograms were filtered at 30 to 500 Hz. A baseline Wenckebach cycle length (WCL) as well as the AV nodal effective refractory period were measured at atrial pacing cycle lengths of 400 and 600 ms. Any abrupt increase in the AH interval during the atrial refractory period determination was recorded. The presence of dual AV nodal physiology was defined as a sudden increase of ≥ 50 ms in the AH interval for a 10 ms decrement in the A1-A2 coupling interval.⁴

In our previous study,³ the atrial pacing cycle length was determined by the fast pathway refractory period. Since by the design of the present study most patients were not expected to have dual AV nodal physiology, by definition we would not be able to determine a fast pathway refractory period. Thus, the atrium was paced at WCL + 50 ms and repeated at WCL + 100 ms in order to maximize the chances that dual AV nodal physiology could be unmasked by not pacing at a cycle length too short to permit both fast and slow pathway conduction. During atrial pacing at each cycle length, incremental doses of intravenous adenosine of 1, 2, 3, 4, 6, 9, 12, and 18 mg were administered at 5-min intervals until AV nodal block occurred. The longest AH interval was determined and any abrupt changes in the AH interval were noted at each dose.

Results are expressed as the mean $\pm$ standard deviation (SD) of the dose of adenosine required to cause AV nodal block while pacing at each cycle length. Patients demonstrat-

ing dual AV nodal physiology are expressed as a percentage of all those studied. The 95% confidence interval (CI) was calculated for the percentage of control patients with dual AV nodal physiology.

Results

In all, 37 patients (27 men, 10 women, mean age 63 ± 2 years) were enrolled in the study. The indications for electrophysiologic study were primarily syncope or ventricular arrhythmias. Two patients had Wolff-Parkinson-White syndrome and were studied after successful radiofrequency ablation of the accessory pathway (neither located in the slow pathway area), and one patient had typical atrial flutter and was studied prior to radiofrequency ablation. The mean ($\pm$ SD) doses of adenosine required to cause AV nodal block while pacing at WCL + 50 ms and WCL + 100 ms were 7.1 ± 3.9 and 7.4 ± 4.5 mg, respectively. Of interest, the mean dose of adenosine that caused AV block in the present study was comparable to the dose of adenosine that caused slow pathway block (7.2 ± 4.7 mg) in our previous study of patients with inducible AV nodal reentrant tachycardia (Table I).³

In 1 of the 37 patients (2.7%, 95% CI 0–8%), an abrupt prolongation of the AH interval was seen with the administration of adenosine during atrial pacing. This patient had a WCL of 350 ms, and pacing was performed at 390 and 440 ms. While pacing the atrium at 390 ms, the AH interval was 122 ms. With administration of 2 mg adenosine intravenously, there was an abrupt increase in the AH interval to 353 ms. When pacing the atrium at 440 ms, the maximum AH interval with 3 mg adenosine was 137 ms, while there was an abrupt increase in the AH interval to 270 ms from 118 ms with 4 mg adenosine. This patient also demonstrated dual AV nodal physiology during the atrial refractory period determination, as shown in Figure 1A. No AV nodal echoes were seen and AVNRT was not induced in this patient. In all the other patients studied, there were only gradual changes in the AH interval with the administration of adenosine during atrial pacing prior to AV block, and no dual AV nodal pathways were demonstrated during the refractory period determination (Figs. 1, 2).

TABLE I Dose of adenosine causing atrioventricular block

	Adenosine dose (mg $\pm$ SD)	
	Fast pathway	Slow pathway
Patients with dual AV nodal physiology (n = 16) ^a	2.7 ± 3.0^a	7.2 ± 4.7^a
	WCL + 50 ms	WCL + 100 ms
Present study (n = 37)	7.1 ± 3.9	7.4 ± 4.5

^a From Ref. No. 3.

Abbreviations: SD = standard deviation, AV = atrioventricular, WCL = Wenckebach cycle length.

FIG. 1 Intracardiac recordings from the single study patient found to have dual atrioventricular nodal physiology. (A) There is an abrupt increase in the AH interval from 118 to 258 ms during the atrial refractory period determination (A1A2: 400/320). (B) A similar abrupt increase in the AH interval from 172 to 243 ms is seen after the intravenous administration of 2 mg adenosine during atrial pacing at 390 ms (WCL + 50 ms). hRA = high right atrium, HIS pro, ds = proximal and distal His-bundle recordings, A = atrial signal.

Discussion

Because of its negative dromotropic effects, adenosine is frequently used for the termination of supraventricular tachycardias using the AV node as part of a reentrant circuit.^{1, 2} We have previously demonstrated a functional difference in the response of the anterograde fast and slow AV nodal pathways to the effects of adenosine in patients with dual AV nodal

pathways and inducible AV nodal reentrant tachycardia.³ We have been able to use this differential effect to initiate AVNRT in patients with known dual AV nodal physiology by administering incremental doses of adenosine during atrial pacing and to terminate the tachycardia by administering larger doses of adenosine. We found that 88% of patients with dual AV nodal pathways and inducible AVNRT have demonstrable dual AV nodal pathways with adenosine, and 56% of the patients developed sustained AVNRT with administration of adenosine.

In the present study, we have demonstrated that it is unusual to detect dual AV nodal physiology with adenosine during electrophysiologic study in patients in whom AVNRT is not suspected. To summarize our results, in the present study 36 of 37 patients without suspected AVNRT had a negative adenosine test, while 14 of 16 patients with inducible AVNRT had a positive adenosine test in our previous study.³ Thus, the sensitivity of the adenosine test is 88%, the specificity is 97%, the positive predictive value is 93%, and the negative predictive value is 95%. Thus, administration of adenosine during atrial pacing can be used as both a highly sensitive and specific test for the presence of dual AV nodal pathways. In patients in whom AVNRT is suspected but not inducible, the demonstration of dual AV nodal pathways when none are apparent with baseline testing may encourage further specific attempts to induce AVNRT. In patients without demonstrable dual AV nodal physiology either at baseline or with adenosine testing, it is likely that the patient has another diagnosis that should be pursued.

Belhassen *et al.*⁵ administered adenosine-5'-triphosphate (ATP) during sinus rhythm to patients with known AVNRT as well as to control patients. Similar to our findings, only 1 of 21 patients (5%) had evidence of dual AV nodal physiology with administration of adenosine in sinus rhythm, with an abrupt increase in the AH interval of 60 ms being observed. Signs of

FIG. 2 Representative recording of the effect of adenosine on atrioventricular (AV) conduction during atrial pacing at 460 ms in a subject not demonstrating dual AV nodal physiology at baseline. Block was achieved with the intravenous administration of 2 mg adenosine. The AH interval at the beginning of pacing increased gradually. The maximum AH interval is seen prior to AV block. From top to bottom are electrocardiographic leads I, II, aVF, and V₁. H = His bundle signal. Other abbreviations as in Figure 1.

dual AV nodal physiology were observed in 76% of patients with known AVNRT, suggesting that adenosine triphosphate (ATP) can also be used as a highly specific tool in the diagnosis of AVNRT by unmasking the presence of dual AV nodal pathways during sinus rhythm in patients with this diagnosis but rarely in patients without this tachyarrhythmia.

Belhassen *et al.*⁶ recently reported similar findings using ATP administered at the bedside to patients with inducible sustained AVNRT. Dual AV nodal physiology was found in 75% of patients by electrocardiographic (ECG) criteria and later in 85% by electrophysiologic criteria in the laboratory. They were also able to demonstrate the potential use of the ATP test as a postablation check for successful slow pathway ablation versus slow pathway modification. In this series, 1 of 31 control patients (3.2%) had dual AV nodal physiology with administration of ATP during sinus rhythm.

Tebbenjohanns *et al.*⁷ administered incremental doses of adenosine to 37 patients with symptoms suggestive of paroxysmal supraventricular tachycardia but no prior documentation to evaluate it as a means of testing at the bedside for the presence of dual AV nodal physiology, thus suggesting the diagnosis of AVNRT. Adenosine was administered during sinus rhythm until second degree or greater AV block was observed. The surface ECG was then evaluated for signs suggestive of dual AV nodal physiology. A sudden jump in PQ interval (≥ 50 ms) was seen in 13 (76%) of 17 patients with inducible AVNRT but in only 1 (5%) of 20 patients without inducible AVNRT.

For these findings to be of real use, it must be shown in a larger series of patients that the AV nodal response to adenosine is specific only to those patients with dual AV nodal physiology. In fact, it has been reported that up to 25% of patients without supraventricular tachycardia have dual AV nodal pathways in response to single atrial extrastimuli.⁸ However, the present study confirms the results of Tebbenjohanns *et al.* and demonstrates a methodology for testing for dual AV nodal pathways with adenosine in the electrophysiology laboratory. By pacing the atrium, changes in sinus cycle length are avoided that may make it more difficult to discern changes in the AH interval.

Limitations

Only a few patients studied had supraventricular tachycardia. It would be this group of patients (those undergoing diagnostic electrophysiologic studies for supraventricular tachycardia) in whom the response to adenosine would be most helpful in supporting or refuting a possible diagnosis of AVNRT. Thus, it would be worthwhile to confirm these results in a larger series of patients with non-AVNRT supraventricular tachycardia.

The adenosine test employed in this study is somewhat cumbersome, as two different pacing cycle lengths as well as incremental doses of adenosine were used. The method as described was developed to minimize any chance of missing dual AV nodal physiology if it could be demonstrated. In fact, one pacing cycle length would have been sufficient to demonstrate the results presented, as the one patient with dual AV nodal pathways showed the same abrupt increase in AH interval at both pacing cycle lengths tested. Likewise, all other patients were negative at both pacing cycle lengths. Whether one or two specific doses of adenosine could be used for testing to simplify the method remains to be determined.

Conclusion

At electrophysiologic study, administration of incremental doses of adenosine during atrial pacing rarely demonstrates dual AV nodal physiology in patients without AVNRT. Thus, this test can be used as a highly specific tool in the laboratory for detecting dual AV nodal pathways.

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