Effects of Adenosine Triphosphate on Wide QRS Tachycardia

Analysis in 18 Patients

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SUMMARY

A few studies have indicated that adenosine terminated triggered-activity idiopathic ventricular tachycardia, but all involved a small number of cases. The effects of adenosine triphosphate (ATP) on wide QRS tachycardia have thus not yet been completely clarified. This retrospective study was performed to evaluate the therapeutic and diagnostic utility of ATP in wide QRS tachycardia. A total of 18 patients with wide QRS tachycardia (QRS width > 120 msec, rate $\geq$ 150 beats/min) were evaluated. ATP, 20–40 mg, was administered intravenously. An electrophysiological study and treadmill stress test were performed in all patients to elucidate the mechanism of the tachycardia. ATP terminated tachycardia or induced atrio-ventricular block in all 6 patients who had supraventricular tachycardia, but it had no effect on pre-excited atrial fibrillation or pre-excited atrial flutter. Ventricular tachycardia was terminated by ATP in 5 of the 10 patients. In 4 of these 5 patients, the focus of the tachycardia was the right ventricular outflow tract. No entrainment phenomenon was demonstrated by electrophysiological study with induction of the tachycardia by stress test or isoproterenol infusion, suggesting the contribution of triggered activity to the tachycardia. In the remaining patient with complete right bundle branch block type tachycardia with right axis deviation, the mechanism of ventricular tachycardia could not be determined. In the 5 patients in whom ATP failed to terminate ventricular tachycardia, the reentry mechanism was suggested by the presence of entrainment phenomenon depicted on electrophysiological study. In summary, this study suggests that ATP terminates supraventricular wide QRS tachycardia and ventricular tachycardia due to triggered-activity, but that it has no effect on pre-excited atrial fibrillation or flutter or on ventricular tachycardia due to a reentry mechanism. These findings add to the mounting evidence regarding the therapeutic and diagnostic utility of ATP in wide QRS tachycardia. (*Jpn Heart J* 1996; 37: 463–470)

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BASIC studies^{1,2)} have revealed that adenosine P₁ receptors are located predominantly in the slow pathway of the sino-atrial and atrio-ventricular nodes. Adenosine triphosphate (ATP) is degraded to adenosine and couples to adenosine P₁ receptors, resulting in electrophysiological effects. Ventricular myocytes, however, have few adenosine P₁ receptors. These studies indicate that ATP affects supraventricular tachycardia. Indeed, it has even been reported to terminate supraventricular tachycardia.^{3,4)}

Based on these reports, ATP has been used in wide QRS tachycardia to distinguish supraventricular from ventricular tachycardia. In a recent report it was suggested that ATP terminates only supraventricular tachycardia, and could thus be used to distinguish supraventricular wide QRS tachycardia from ventricular tachycardia.⁵⁾

Other recent reports,^{6,7)} however, have indicated that some ventricular tachycardia may be terminated by adenosine. However, these studies dealt with a relatively small number of cases. The effects of adenosine on ventricular tachycardia are thus not yet completely clarified, nor are the effects of ATP on wide QRS tachycardia completely clear.

This retrospective study was performed to evaluate the therapeutic and diagnostic utility of ATP in wide QRS tachycardia. The results are discussed in comparison with those presented in previous reports.

PATIENTS AND METHODS

Patients: A total of 18 patients with wide QRS tachycardia were studied. Wide QRS tachycardia was defined as QRS duration > 120 msec with a rate of ≥ 150 beats/min.

Methods: *ATP administration and assessment of effects:* ATP was administered via the central vein at a dosage of up to 40 mg. ATP was regarded as being effective when termination of the tachycardia by ATP was observed at least twice without tachycardia occurring for at least 30 sec after termination.

Electrophysiological study: Tachycardia was induced by programmed electrical stimulation during routine electrophysiological study,⁸⁾ and the diagnosis was established according to conventional electrophysiological criteria.⁹⁾

Mechanism of ventricular tachycardia: The mechanism of ventricular tachycardia was regarded as reentry in patients with ventricular tachycardia, when the entrainment phenomenon was demonstrated electrophysiologically. The mechanism of ventricular tachycardia was regarded as triggered activity when all of the

following criteria were met: a reentry mechanism could be excluded; exercise stress test induced the tachycardia; and the induction of tachycardia was facilitated by isoproterenol infusion.

Other examinations: Two-dimensional echocardiography and coronary angiography were performed in all patients to examine them for organic heart diseases. When arrhythmogenic right ventricular dysplasia was suspected, right ventriculography was performed and endomyocardial biopsy samples were taken from the right ventricle.

RESULTS

Electrophysiological study: Electrophysiological study revealed that the wide QRS tachycardia was caused by supraventricular tachycardia in 8 patients and by ventricular tachycardia in 10 patients (Figure). Of the 8 patients with supraventricular wide QRS tachycardia, 2 had atrio-ventricular nodal reentry tachycardia, 3 had atrio-ventricular reentry tachycardia, and one each had atrial flutter without preexcitation, atrial fibrillation associated with Wolff-Parkinson-White syndrome, and atrial flutter with Wolff-Parkinson-White syndrome. In the 10 patients with ventricular tachycardia, the mechanism was thought to be triggered activity in 4 and reentry in 5. However, clinical ventricular tachycardia could not be induced during electrophysiological study in the one remaining patient in whom the mechanism of ventricular tachycardia could not be deter-

Figure Results of ATP administration during wide QRS tachycardia. SVT = supraventricular tachycardia; VT = ventricular tachycardia; AVNRT = atrioventricular nodal reentry tachycardia; AVRT = atrioventricular reentry tachycardia; Af = atrial fibrillation; AF = atrial flutter; WPW = Wolff-Parkinson-White syndrome.

Table. Patient Profiles and ATP Effects in Patients with Ventricular Tachycardia

Patient #	Age	Sex	Organic heart disease	ECG	VT morphology	VT rate	Perfect map	Exercise stress test	VT mechanism	ATP response
1	45	M	—	WNL	CLBBB, NAD	180/min	RVOT (Sep)	SVT	Triggered Activity	(+)
2	42	F	—	WNL	CLBBB, NAD	140/min	RVOT (FW)	NSVT	Triggered Activity	(+)
3	66	F	—	WNL	CLBBB, NAD	200/min	RVOT (FW)	SVT	Triggered Activity	(+)
4	22	F	—	WNL	CLBBB, NAD	150/min	RVOT (FW)	SVT	Triggered Activity	(+)
5	58	M	—	WNL	CLBBB, LAD	170/min	LV apical-inferior	Negative	Reentry	(—)
6	31	F	ARVD	inverted T (V ₁ , V ₂) LAD	CLBBB, NAD	150/min	RVOT	Negative	Reentry	(—)
7	60	M	ARVD	CRBBB	CLBBB, LAD	170/min	RVOT	Negative	Reentry	(—)
8	79	M	OMI	Af Q wave (II, III, aVF)	CRBBB, RAD	150/min	ND	Negative	ND	(+)
9	75	M	OMI	Q wave (V ₂ -V ₆)	CRBBB, LAD	150/min	ND	PVC	Reentry	(—)
10	70	M	OMI	inverted T (V ₄ -V ₆)	CRBBB, NAD	150/min	LV posterior	PVC	Reentry	(—)

ECG = electrocardiography; VT = ventricular tachycardia; ATP = adenosine triphosphate; M = male; F = female; WNL = within normal limits; CLBBB = complete left bundle branch block; CRBBB = complete right bundle branch block; NAD = no axis deviation; LAD = left axis deviation; RVOT = right ventricular outflow tract; LV = left ventricle; Sep = septum; FW = free wall; ND = not determined; SVT = sustained ventricular tachycardia; NSVT = non-sustained ventricular tachycardia; PVC = premature ventricular contraction; ARVD = arrhythmogenic right ventricular dysplasia; OMI = old myocardial infarction.

mined.

Effects of ATP: ATP did not cause any serious adverse effects such as shock, acceleration of tachycardia, or induction of ventricular fibrillation, in any patient. The effects of ATP administration on wide QRS tachycardia are shown in the Figure.

Supraventricular: ATP terminated supraventricular wide QRS tachycardia in the 2 patients with atrio-ventricular nodal reentry tachycardia and the 3 with atrio-ventricular reentry tachycardia. It had no effect on atrial fibrillation or atrial flutter with Wolff-Parkinson-White syndrome. In an atrial flutter patient with aberrant ventricular conduction, it attenuated the ventricular response, with the result that the mechanism of the tachycardia was clear.

Ventricular tachycardia: ATP terminated ventricular tachycardia in 5 of 10 patients (Table). In these 5 patients, the tachycardia was idiopathic ventricular tachycardia; it was of right ventricular outflow tract origin in 4 patients (Patients 1–4), and in one (Patient 8) it was ventricular tachycardia following myocardial infarction in which the QRS shape during tachycardia resembled complete right bundle branch block with right axis deviation. In the 4 former patients, entrainment was not demonstrated by electrophysiological study and the tachycardia

was induced by a treadmill stress test or by isoproterenol infusion. Therefore, the mechanism of ventricular tachycardia in these patients was thought to be triggered activity. In the one remaining patient, tachycardia with the complete right bundle branch block configuration of right axis deviation could not be induced and the mechanism underlying the tachycardia thus could not be determined.

ATP failed to terminate ventricular tachycardia in 5 patients (Patients 5–7, 9, and 10). Electrophysiological study demonstrated the entrainment phenomenon in all 5 of these patients, which suggested that reentry was the mechanism underlying ventricular tachycardia.

DISCUSSION

The findings of this retrospective study of the therapeutic and diagnostic utility of ATP in wide QRS tachycardia were that it terminated atrio-ventricular nodal reentry tachycardia, atrio-ventricular reentry tachycardia, and ventricular tachycardia due to triggered-activity mechanism with right ventricular outflow tract focus. In contrast, it did not have any effect on wide QRS tachycardia of pre-excited atrial flutter or of pre-excited atrial fibrillation, or on ventricular tachycardia due to a reentry mechanism.

Dose of adenosine triphosphate: We used 20–40 mg of ATP to determine its effect in terminating wide QRS tachycardia. When 20 mg were administered, the dose of ATP was 0.22–0.44 mg/kg. Studies^{3,4)} in which the effects of ATP on supraventricular tachycardia were examined have employed 5–20 mg of ATP. In another study,¹⁰⁾ 0.1–0.2 mg/kg of ATP was used to examine its effects on ventricular tachycardia. Since the dose used in the present study was even larger than that in these studies, the non-response to ATP was not due to the dose administered being too low.

Assessment of ATP effects: We defined ATP as being effective when termination of the tachycardia by ATP was observed at least twice without tachycardia occurring for at least 30 sec after termination. We used these criteria for the following reasons: Recurrent tachycardia may terminate spontaneously; the half-life of ATP in plasma is less than 10 sec;¹¹⁾ and the effects of adenosine, assessed by the induction of atrio-ventricular block, last 6–30 sec (average 13 sec).³⁾ We thus believe our methods of assessment of the effect of ATP in terminating wide QRS tachycardia to be quite reasonable.

Supraventricular tachycardia: As stated above, ATP terminated supraventricular tachycardia when it was atrio-ventricular nodal reentry tachycardia or atrio-ventricular reentry tachycardia, but it had no effect on pre-excited atrial flutter or atrial fibrillation. In one atrial flutter patient, adenosine triphosphate attenuated the ventricular response, with the result that the mechanism of the

tachycardia became clear. These observations for atrio-ventricular nodal reentry tachycardia, atrio-ventricular reentry tachycardia, and atrial fibrillation are consistent with previous reports.³⁻⁵⁾ Only one case has been reported in the literature in which pre-excited atrial flutter was terminated by ATP.¹²⁾ In the present study, ATP did not terminate pre-excited atrial flutter or pre-excited atrial fibrillation. Electrophysiological study has demonstrated that ATP does not have effects on the anterograde accessory pathway.⁴⁾ Although the mechanism responsible for the termination effects on pre-excited atrial flutter in the previously reported case was unclear, the lack of effect on the anterograde accessory pathway is probably the reason that ATP had no effect on pre-excited atrial flutter or pre-excited atrial fibrillation in the present study. It thus seems theoretically reasonable that ATP would have no effects on pre-excited atrial flutter or atrial fibrillation. Thus, ATP exerts an effect on wide QRS tachycardia when it is atrio-ventricular nodal reentry tachycardia or atrio-ventricular reentry tachycardia.

Ventricular tachycardia: ATP was effective in terminating the idiopathic ventricular tachycardia of right ventricular outflow tract focus with triggered-activity mechanism in all 4 patients in this study. Termination by adenosine of idiopathic triggered-activity ventricular tachycardia has been reported in only a small number of patients.^{6,12)} These investigators also found that adenosine had no effects on ventricular tachycardia with a reentry mechanism. Their findings are compatible with the present findings as to the effects of ATP on ventricular tachycardia.

It is unclear whether ATP has an effect on triggered-activity ventricular tachycardia with the focus in any area of the ventricle or only in those of right ventricular outflow tract origin. In this study, ATP was found to terminate triggered-activity ventricular tachycardia which had not only a right ventricular outflow free wall tract focus (Patients 2-4), but also a right ventricular outflow septum focus (Patient 1). Wilber et al⁷⁾ reported that ATP had effects on idiopathic ventricular tachycardia with a right ventricular outflow free wall tract focus but no effects on such ventricular tachycardia with a focus in the right ventricular outflow septum. However, in their patient with the focus in the right ventricular outflow septum, the tachycardia was not induced by stress test or isoproterenol infusion, whereas in our patient (Patient 1), the tachycardia fulfilled the criteria of triggered-activity ventricular tachycardia. In another patient in the present study (Patient 6) with ventricular tachycardia of right ventricular outflow tract origin, ATP did not terminate the tachycardia, as in Wilber's case, and the entrainment phenomenon was demonstrated. The diagnosis of arrhythmogenic right ventricular dysplasia was finally made based on right ventriculography and endomyocardial biopsy findings. It is possible that Wilber's patient may not have had idiopathic ventricular tachycardia due to triggered activity. Although the number of cases in both studies is small, the results of the present study suggest

that ATP exerts effects on all idiopathic triggered-activity ventricular tachycardia.

ATP terminated ventricular tachycardia of the complete right bundle branch block configuration with right axis deviation in one patient (Patient 8). To our knowledge, there have been only 2 patients described in the literature in whom ATP terminated ventricular tachycardia of the complete right bundle branch block configuration with right axis deviation.¹²⁾ Although the mechanism of ventricular tachycardia could not be determined in our patient with this configuration, triggered activity was determined as the mechanism of ventricular tachycardia in the patient studied by Griffith et al.¹²⁾ Both studies also suggest that ATP would have effects on all triggered-activity ventricular tachycardia.

The application of ATP did not provide any information for distinguishing supraventricular wide QRS tachycardia from ventricular tachycardia. However, the mechanism of ventricular tachycardia was suggested by the effect. Adenosine or adenosine-related agents have been used in wide QRS tachycardia to distinguish supraventricular from ventricular tachycardia. Our results indicate that ATP can be used to distinguish wide QRS tachycardia due to atrio-ventricular nodal reentry tachycardia, atrio-ventricular reentry tachycardia and triggered-activity ventricular tachycardia from pre-excited atrial flutter, atrial fibrillation, or ventricular tachycardia due to a reentry mechanism.

Limitations: There are two main limitations to this study. Because of the small number of patients examined, the results cannot be taken as conclusive. They represent, rather, further information on the therapeutic and diagnostic utility of ATP in wide QRS tachycardia. Moreover, this study did not elucidate the mechanism responsible for the effects of ATP in terminating the tachycardia, nor could the reason for the different effects of ATP in the various types of tachycardia be clarified.

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