Usefulness of Invasive and Non-invasive Electrophysiologic Studies in the Selection of Antiarrhythmic Drugs for the Patients with Paroxysmal Supraventricular Tachyarrhythmia

SHUTARO SATAKE, M.D*, KAZUMASA HIEJIMA, M.D*, YUKIO MOROI, M.D*
KENZO HIRAO, M.D*, ICHIRO KUBO, M.D*, FUMIO SUZUKI, M.D*
AND FUMIO SUZUKI, M.D**

A comparison of the effects of several antiarrhythmic agents was made in a study of 70 patients — 15 with manifest Wolff-Parkinson-White (WPW) syndrome, 17 with concealed WPW syndrome, 18 with AV nodal re-entrant tachycardia, 14 with paroxysmal atrial fibrillation and 6 with paroxysmal atrial flutter — employing intracardiac stimulation and esophageal pacing. For the termination of paroxysmal supraventricular tachycardia, intravenous administration of verapamil or aprindine was more effective than that of disopyramide or procainamide. In AV nodal re-entrant tachycardia, verapamil was the most effective for termination. In the manifest WPW syndrome, disopyramide or aprindine was indicated especially for patients with the accessory pathways of the short antegrade refractory period, because these drugs lengthened the refractory period of the accessory pathways.

For the purpose of converting atrial fibrillation or flutter to the sinus rhythm, type IA drugs such as disopyramide were indicated. However, verapamil was effective for slowing down the ventricular rate in atrial fibrillation or flutter except in cases of manifest WPW syndrome. A 6-month follow-up study showed that oral administration of verapamil was also useful for putting a stop to the attacks in 24 out of 32 patients with paroxysmal supraventricular tachycardia, while oral disopyramide prevented the recurrence of atrial fibrillation in only 4 of 10 patients.

RECENTLY, many antiarrhythmic agents have been produced, and their modes of action at the cellular level have become clear. But it has not been established clinically which agents are indicated for various types of paroxysmal supraventricular tachyarrhythmia (PSVTA). In ad-

dition, we have little data on whether long-term oral treatment with a drug is useful for reducing the recurrence of attacks. It may be due to the low frequency of the spontaneous attacks that treatment has not yet been established.

In this study, we repeatedly induced PSVTA using both invasive and non-invasive technique^{1,2} and compared the effectiveness of several agents in terminating tachycardia. We later followed up these patients, treating them with oral administrations of the effective drugs, and evaluated the results.

Key Words:

Esophageal pacing
Paroxysmal supraventricular tachyarrhythmia
His bundle electrogram
Antiarrhythmic drug
Non-invasive method

*First Department of Internal Medicine, School of Medicine, Tokyo Medical & Dental University

**Cardiovascular Department: Sohka City Hospital

Mailing address: Shutaro Satake, M.D., First Department of Internal Medicine, School of Medicine, Tokyo Medical & Dental University, Yushima, 1-5-45, Bunkyo-ku, Tokyo, Japan

TABLE I EFFECT OF INTRAVENOUS ANTIARRHYTHMIC AGENTS ON TERMINATION OF "PSVT"

	Verapamil	Disopyramide	Procainamide	Aprindine	P values					
					V vs D	D vs P	P vs A	V vs P	V vs A	A vs D
"PSVT"	46/50	22/34	7/12	16/17	< 0.01	NS	< 0.05	< 0.05	NS	< 0.05
AVNRT	18/18	10/14	2/3	4/5	< 0.05	NS	NS	< 0.05	NS	NS
CW	15/17	6/8	2/3	6/6	NS	NS	NS	NS	NS	NS
MW	13/15	6/12	3/6	6/6	< 0.05	NS	< 0.05	NS	NS	< 0.05

PSVT = paroxysmal supraventricular tachycardia; AVNRT = atrioventricular nodal reentrant tachycardia;
 CW = concealed W syndrome; MW = manifest W syndrome

Fig.1. Esophageal pacing method

The graph shows the threshold of the current (mean $\pm$ standard deviation) to excite the left atrium at a variable pulse duration in 10 patients.

MATERIALS AND METHODS

Eighty-one patients with PSVT induced by intracardiac pacing were studied. They were 41 males and 40 females, and were aged between 16 and 74 years.

After informed consent was obtained, bipolar or quadripolar electrodes were inserted through the femoral vein into the chambers of the heart for recording and stimulation.³ Standard ECG's leads (I, II and V₁) were recorded simultaneously with intracardiac recordings and programmed stimulation was performed in an atrium or a ventricle. By analysis of these data, the electrophysiologic mechanisms of PSVT were verified. Secondly, a catheter with hexapolar electrodes (11F) was inserted into the esophagus, recording intra-esophageal electrograms. It was positioned a few centimeters above the diaphragm, where the amplitude of the atrial electrogram was the highest. Esophageal pacing was carried out with a pair of electrodes, which excited the left atrium at the lowest current, using a constant-current stimulator with a variable pulse duration.

The acute effects of antiarrhythmic agents:

Induction and Termination of "PSVT" by Esophageal pacing

Fig.2. Induction and termination of "PSVT" by esophageal pacing in the patient with WPW syndrome. S = stimulation

verapamil (5–10 mg), disopyramide (50–100 mg) procainamide (300–500 mg), and aprindine (50–100 mg) were examined as follows: PSVTA was repeatedly induced by intracardiac and esophageal pacing, intravenous drugs were administered separately at sufficient wash-out interval, and a comparison of their effectiveness in terminating tachycardia was made. The refractory periods of the A-V conduction system were measured by extrastimulation method before and after administration of the drugs, and compared.

The patients with "PSVT" more than once a month, for which intravenous verapamil was effective on termination, were followed up, treating with oral verapamil (daily dosage, from 240 mg to 320 mg) for 6 months. If the patients had recurrent attacks, combination treatment with β -blocking agents (propranolol or indenolol, daily dosage, 30–60 mg) was employed.

The patients who had paroxysmal atrial fibrillation more than once a month, which was converted to sinus rhythm by intravenous disopyramide, were followed up with oral disopyramide (daily dosage, 400–600 mg) for 6 months.

RESULTS

The mechanisms of 81 PSVTA which were determined by the electrophysiological study were as follows⁴⁻⁷: 18 with manifest WPW syndrome (MWPW), 19 with concealed WPW syndrome (CWPW), 20 with AV nodal reentrant tachycardia (AVNRT), 16 with paroxysmal atrial fibrillation (Af) and 8 with paroxysmal

Fig.3. The mechanism of termination of "PSVT" in a patient with concealed WPW syndrome. In the middle panel verapamil caused A-V block, while in the lower panel, disopyramide caused V-A block. Eso = intra-esophageal electrogram; V = ventricular potential; A = atrial potential

Fig.4. Conversion of atrial fibrillation or atrial flutter to sinus rhythm by intravenous verapamil or disopyramide.

atrial flutter (AF).

In esophageal pacing, the threshold of current to excite the left atrium was decreased as the pulse duration was increased to 20 msec (Fig. 1). In 78 of 81 patients, the atrium was paced through the esophageal electrodes by a current between 10 mA and 25 mA, using a wide pulse duration from 10 msec to 20 msec, without discomfort except a burning sensation. In 70 of 78 patients, PSVTa was successfully induced by esophageal pacing. As illustrated in Fig. 2, "PSVT" was induced and terminated by esophageal pacing in the patients with MWPW. During esophageal pacing, a negative P wave was observed in leads II, III and aV_F, and a dome and dart P wave was recognized in lead V₁ just after a high deflection of pacing spike. These phenomena were compatible with left atrial pacing.

The details of PSVTa induced by esophageal pacing were as follows: 50 out of 57 patients with PSVT (15 of 18 with MWPW, 17 of 19 with CWPW, and 18 of 20 with AVNRT), 14 out of 16 with Af and 6 out of 8 with AF.

Effects of Antiarrhythmic Agents

A. The results of the acute effects of intravenous anti-arrhythmic agents can be summarized as follows:

1. PSVT (illustrated in Table I)

a) Verapamil terminated PSVT in 46 out of 50 patients (13 of 15 patients with MWPW, 15 of 17 with CWPW and 18 of 18 with AVNRT).

Fig.5. Measurement of the antegrade effective refractory period of an accessory pathway by esophageal extrastimulation before and after verapamil administration.

b) Disopyramide terminated PSVT in 22 out of 34 patients (6 of 12 with MWPW, 6 of 8 with CWPW and 10 of 14 with AVNRT).

Fig.6. Six months follow-up study with oral administration of verapamil in 30 patients with "PSVT".

Fig.7. Six months follow-up study with oral disopyramide in 10 patients with paroxysmal atrial fibrillation.

c) Procainamide terminated PSVT in 7 out of 12 patients (3 of 6 with MWPW and 2 of 3 with each of CWPW and AVNRT).

d) Aprindine terminated PSVT in 16 out of 17 patients (all of 6 with each of MWPW and CWPW and 4 of 5 with AVNRT).

As for the mechanism of termination, verapamil caused A-V block, while disopyramide, aprindine and procainamide caused V-A block in WPW syndrome. Figure 3 shows one of examples with CWPW.

2. Af or AF

a) Verapamil could not convert Af (16 cases) to the sinus rhythm or AF (7 cases) respectively, but suppressed the A-V conduction, resulting in a slowing of the ventricular rate in patients other than those with MWPW.

b) Disopyramide converted AF in 11 out of 14 patients to the sinus rhythm and AF in 4 out of 6 patients respectively. As illustrated in Fig. 4, Af was induced by rapid esophageal pacing and terminated by intravenous administration of disopyramide.

3. Effect on the Refractory Period of MWPW

Disopyramide prolonged the antegrade effective refractory period of the accessory pathways in 8 out of 12 patients with MWPW, procainamide did this in 4 of 6 patients and aprindine did the same in 5 of 6 patients. Verapamil, on the contrary, shortened it in 4 of 6 patients, as indicated in Fig. 5.

B. Effect of Oral Administration

In the 30 patients with attacks of PSVT more than once a month, intravenous verapamil was effective for termination of these attacks. The percentage of the patients without an attack of PSVT after oral treatment of verapamil is shown by table analysis in Fig. 6. During the first month, 13.3% of patients (4 out of 30) had recurrence of attacks, but the incidence of the recurrence declined as time passed. In a 6-month follow-up study, oral verapamil prevented attacks of PSVT in 22 out of 30 patients. In the 8 patients who had attacks, the combination of a β -blocker with verapamil reduced the incidence of attacks. Figure 7 shows the percentage of patients without attacks of Af after being treated with oral disopyramide during a 6-month follow-up. After the 6-month follow-up study, 60% of patients (6 out of 10) had recurrence.

DISCUSSION

Recent studies show that most PSVT is due to re-entry, and intracardiac stimulation with a recording technique is very useful for inducing PSVT and for analyzing its mechanisms^{4,5}. However, it cannot be used repeatedly on the same patient because it is an invasive method. We therefore tried inducing PSVT by a non-invasive technique. Our study showed that esophageal pacing using a wide pulse duration (10–20 msec) was effective in exciting the left atrium with a low current (10–20 mA), and induced PSVT with a high degree of success. The reason why a wide pulse duration was necessary may be that the electric capacity of the tissue between the esophagus and the left atrium needed to be saturated. The esophageal pacing method was valuable for comparing the effectiveness of several anti-arrhythmic agents in the same patients in terminating PSVT. As illustrated in Fig. 1, the efficacies of verapamil^{8,9} and aprindine¹⁰ are significantly higher than that of procainamide¹¹ and disopyramide¹² ($p < 0.05$). Verapamil should thus be considered as one of the first-choice drugs for PSVT, since it had minimal side effects. However, verapamil sometimes shortened the antegrade refractory period of the accessory pathway, as shown in Fig. 5, so that it should not be administered to the patients with short antegrade refractory period of the accessory pathway.

On the other hand, aprindine and disopyramide lengthened the antegrade effective refractory periods of the accessory pathways, and consequently are indicated for the patient with manifest WPW even if accompanied by an episode of pseudoventricular tachycardia in Af.

As illustrated in Fig. 4, class IA drugs¹³ such as disopyramide are applied to patients with atrial fibrillation or flutter for the purpose of conversion to the sinus rhythm, because of the ineffectiveness of verapamil. But verapamil, a so-called slow channel blocker, suppressed the AV node and brought about a slowing of the ventricular rate, except in cases of manifest WPW.

Oral administration of verapamil showed a markedly high and sustained antiarrhythmic

effect for the patient with PSVT, as shown in Fig. 6. For the patients with recurrent attacks, the combined use of a β -blocker with verapamil resulted in fewer attacks during the follow-up period. On the other hand, oral administration of disopyramide was less effective in preventing atrial fibrillation in contrast with verapamil for PSVT.

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