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Intravenous Verapamil for Reversal of Refractory Coronary Vasospasm and Cardiac Arrest

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불응성 관동맥 경련 및 심정지에 있어 Verapamil 정주의 치료 효과

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= 국문초록 =

관상동맥 경련은 심근 허혈의 병인론중 중요한 한 원인 기전이다. 관상동맥 경련이 합병증으로는 심경색, 심실 부정맥, 심차단, 그리고 때로는 급사 등이 있다. Ergonovine 혹은 Acetylcholine에 의해 유발된 관상동맥 경련은 흔히 설하, 정맥내 혹은 관상동맥내 nitroglycerin 주입에 의해 쉽게 풀려진다. 그러나 드물게 상당히 많은 양의 관상동맥내 nitroglycerin 양이 경련을 풀기 위해 필요하거나 응급 관상동맥 우회로 수술이 요구된다.

최근 저자들은 우측 관상동맥을 카테터삽입할 때 심한 자연 발생의 관상동맥 경련이 발생되어 설하, 관상동맥내 nitroglycerin과 설하 nifedipine으로 치료하였으나 반응이 없고 심실 세동과 심장 정지가 발생하여 심폐 소생술을 시행한 환자에서 정맥내 Verapamil의 주입으로 심전도와 혈액 저류주사 검사상으로 심근의 손상없이 경련을 성공적으로 푼 경험이 있어 보고하는 바이다.

KEY WORDS : Verapamil · Coronary artery spasm.

Introduction

Coronary vasospasm is an important etiologic mechanism in the pathogenesis of myocardial ischemia. It's consequences include acute myocardial infarction, ventricular arrhythmias, heart block, and, on occasion, sudden death[1,2].

The vasospasm induced by ergonovine or acetylcholine has usually been readily reversible by sublingual, intravenous nitroglycerin or intracoronary nitroglycerin[1].

But, sometimes high doses of intracoronary nitroglycerin are required to relieve spasm in rare cases emergent coronary artery bypass surgery is

indicated for refractory spasm[3].

In this report we describe a patient who developed severe spontaneous coronary spasm during engaging the coronary artery and failed to respond to sublingual, intracoronary nitoglycerin or sublingual nifedipine. The adminisration of intravenous verapamil resulted in successful reversal of spasm in a patient without adverse electrocardiographic effects.

Case Report

A 30 year old man was admitted on 2nd May in 1990 for evaluation of resting angina pectoris in the early morning of 11 months' duration. Chest pains were relieved by sublingual nitroglycerin. There was no chest pain on exercise. He had no previous history of diabetes mellitus, hyperlipidemia, cigarette smoking except mild hypertension. He completed 10 Mets of an exercise test(Bruce protocol) with no chest pain. He never took isosorbide and calcium channel blocker except sublingual nitroglycerin until an ergonovine provocation test was done. 12-lead electrocardiography(ECG) was normal during an episode of chest pain(Fig. 1).

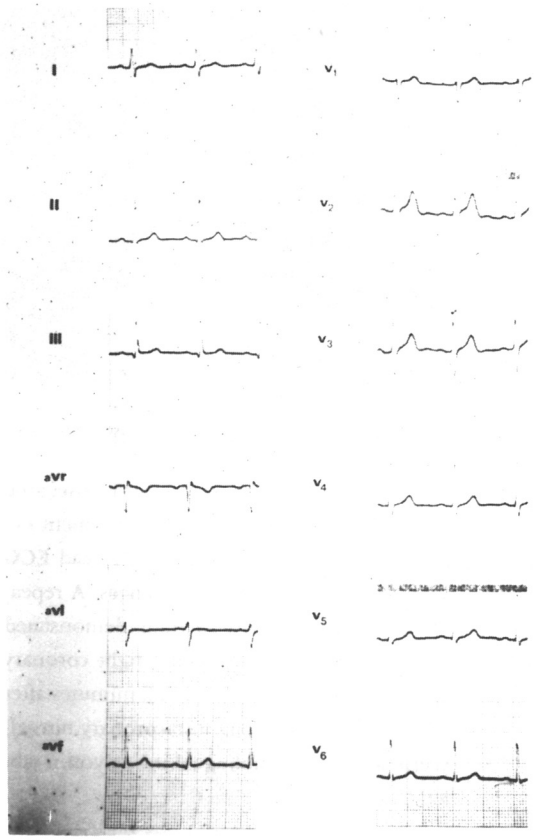


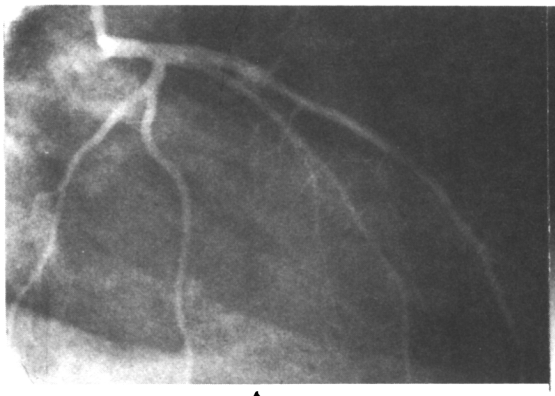
Fig. 1. 12-lead eiectrocardiography(ECG) was normal during an episode of chest pain. The ECGs were recorded at a sensitivity of 10 mm/mV at a paper speed of 25mm/sec.

Cardiac catheterization revealed normal hemodynamic status. A left ventriculogram was normal with an ejection fraction of 61 percent. Coronary arteriography performed using the Judkins technique showed no stenosis of the left(Fig. 2-4) and right coronary arteries. The patient was then givben according to a protocol with sequential ergonovine maleate doses of 0.05, 0.1 and 0.2mg administered intravenously at 5 minute intervals. Two minutes after the third dose(total 0.35mg) the patient experienced severe chest pain but 12-lead ECG showed no important ST-T changes. A repeated right coronary arteriogram demonstated 90 percent occlusions of the proximal right coronary artery that subsided within 2 minutes after administration of 200μg intracoronary nitroglycerin and 0.6mg sublingual nitroglycerin tablet (Fig. 2-B, C).

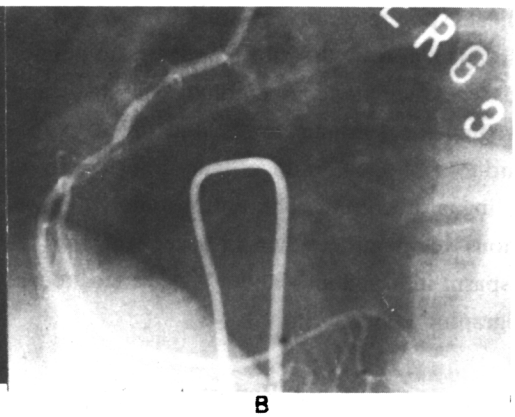
A diagnosis of variant angina was made, and the patient was discharged on treatment with isosorbide dinitrate 20mg t.i.d. and verapamil 80mg t.i.d.. The patient was free of chest pains with medication till 20th February in 1991.

The patient again began to feel light pains in the early morning and chest pains were relieved by sublingual nitroglycerin. But severity and frequency of chest pains were fewer than previously. 12-lead ECG showed no important ST-T changes during anginal attacks.

We were about to attempt to taper and discontinue medication therapy in him after ergonovine



A



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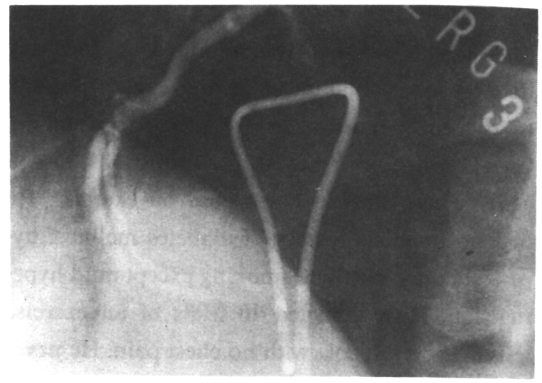

C

Fig. 2. A. Left cronary arteriography showed no stenosis.
B, C. Two minutes after the third dose(total 0.35mg) of ergonovine(ERG) the patient experienced severe chest pain but 12-lead ECG showed no important ST-T changes. A repeated right coronary arteriogram demonstated 90% stenosis of the proximal right coronary artery(B) that subsided within 2 mimutes after administration of 200μg intracoronary nitroglycerin and 0.6mg sublingual introglycerin tablet(C).

testing to detect spontaneous remissions of variant angina. The reason was that the patient remained asymptomatic during 10 months and coronary artery spasm was induced by ergonovine and there was no life-threatening arrhythmias during riant angina attacks.

Medication was discontinued and ergonovine testing was planned to perform 48 hours later. A second cardiac catheterization was performed on 7th March in 1991. The left ventriculogram was unchanged from the previous study. Left coronary arteriography demonstrated mild diffuse spasm of left anterior descending and circumflex coronary arteries(Fig. 3). The patient complained of light chest pain but 12-lead ECG showed no important ST-T changes compaired to a previous ECG. And so, we engaged right coronary artery.

Testing(Flushing) injection demonstrated spontaneous severe proximal right coronary artery spasm and aortic pressure damped from 160 mmHg to 80mmHg and the patient complained of severe substernal discomfort and 12-lead ECG revealed 2 to 3mm ST segment horizontal elevation in lead II, III, aVF and reciprocal changes in lead I, aVL(Fig. 4). We removed a catheter from coronary ostium and nitroglycerin, 0.6mg,

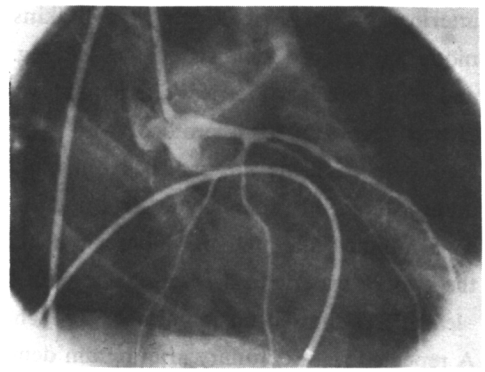

Fig. 3. Left coronary arteriography demonstrated mild diffuse spasm of the left anterior descending and circumflex coronary arteries.

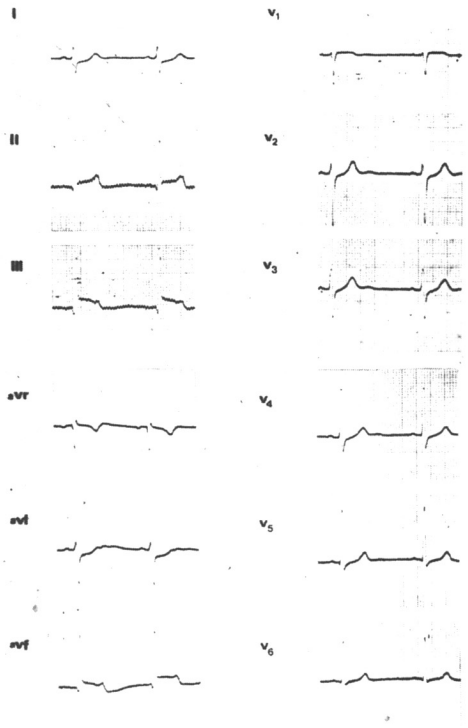

Fig. 4. 12-lead ECG revealed 2 to 3mm ST segment horizontal elevation in lead II, III, aVF and reciprocal changes in lead I, aVL. The ECGs were recorded at a sensitivity of 10mm/mV and at a paper speed of 25mm/sec.

was given sublingually and the dose repeated twice and nifedipine 10mg was given sublingually but the chest pain persisted, hypotension developed. An intracoronary nitroglycerin infusion, 200 μg, into the left coronary artery was immediately begun, but the systemic blood pressure rapidly decreased to 40mmHg. Ventricular fibrillation developed and electric cardioversion with 300 J was done(Fig. 5-A). But ventricular fibrillation persisted. And so 0.6mg sublingual nitroglycerin, two 10mg sublingual nifedipine and 200μg intracoronary nitroglycerin into the left coronary artery were given and electric cardioversion with 300 J three times was done again(Fig. 5-B). Frothy sputum produced and ausculation revealed crackles on both entire lung field and pupils were dilated. Femoral and radial pulses felt faint and the patient had a cardiopulmonary arrest. Cardiopulmonary resuscitation was initiated and 5mg

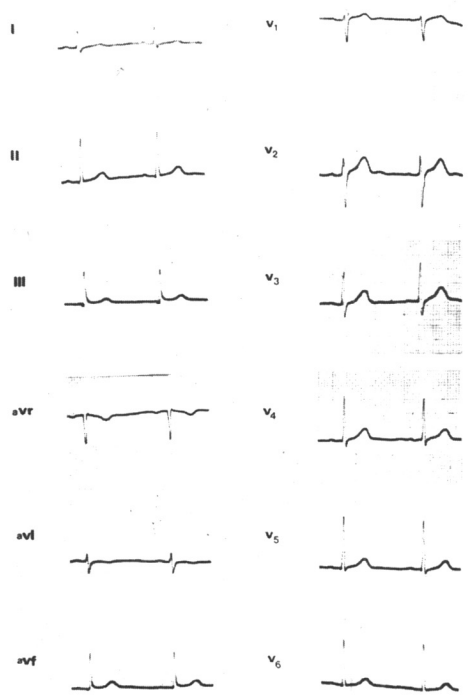

Fig. 6. A postarrest ECG showed no changes compared to a previous ECG(Fig. 1). The ECGs were recorded at a sensitivity of 10mm/mV and at a paper speed of 25mm/sec.

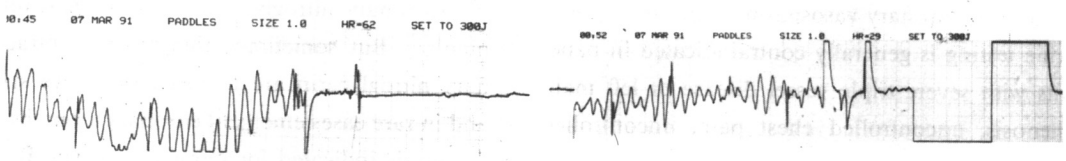

Fig. 5. A. Ventricular fibrillation developed and electric cardioversion with 300 J was done.
B. Electric carrdioversion with 300 J was done three times again.

verapamil was given intravenously.

The ST elevation gradually resolved and systemic arterial pressure increased. Light reflex returned normal and auscultation revealed no crackles. Approximately 30 minutes after the initial cardiac arrest the patinent regained normal sinus rhythm and blood pressure(130/90mmHg). A postarrest ECG showed no changes(Fig. 6) compaired to a previous ECG(Fig. 1). Further recovery was uneventful.

The patient remains symptomatic on medication with isosorbide 20mg t.i.d. and verapamil 120 mg t.i.d. and we added diltiazem 30mg t.i.d..

Discussion

Over the last 10 years, it has been clearly demonstrated that coronary arterial spasm could play a role in the various manifestations of ischemic heart disease. Coronary angiography is the only direct approach to the recognition of spasm during life.

The ergonovine maleate or acetylcholine test generally been accepted as a safe, sensitive, and specific maneuver for detecting coronary spasm, and has gained widespread use. Although ergonovine or acetylcholine testing are usually safe, a number of complications have been described. Major arrhythmias can be observed(ventricular tachycardia or fibrillation, complete atrioventricular block, atrial fibrillation, and asystole). These arrhythmias are ascribed to a myocardial ischemia caused by spontaneous or indued coronary artery spasm. Moreover, sudden deaths have been reported because of refractory ergonovine -induced coronary vasospasm[1]. And so, ergonovine testing is generally contraindicated in patients with severe triple vessel disease or left main stenosis, uncontrolled chest pain, uncontrolled ventricula arrhythmia and severe global left ventricular dysfunction[4].

Angina accompanied by objective evidence of myocardial ischemia almost always persists unless eliminated by treatment or myocardial infarction, becuase the underlying cause(severe coronary artery disease) persists. In contrast, variant angina is frequently characterized by spontaneous exacerbations and remissions[4].

Waters et al demonstrated that the ergonovine provocative test becomes negative during spontaneous remissions. Therefore, this test appears to be helpful not only in the diagnosis of spasm, but also in assessing the activity of the disease[5]. This may be important in deciding if medical therapy can be safely discontinued in asymptomatic patients. Waters et al also describe that they no longer do this routnely because angina does not recur in most patients and in patients without life-threatening arrhythmias during variant angina attacks, they usually begin to taper and discontinue treatment 6~12 months after angina disappears[4,6].

But, the pathophysiology of coronary artery spasm and the factors that induce remission remain obscure. Neither the onset nor remission of coronary spasm manifested an obvious relation to emotional stress, time of year, concurrent disease, alcohol consumption[5].

Therefore, it was suggested that because coronary spasm may recur even after a remission of 1 year or more, therapy should not be discontinued, especially in patients with a history of myocardial infarction, syncope or life-threatening arrhythmias due to spasm[4,5,6].

The spontaneous or ergonovine-induced vasospasm can be prevented and treated in most cases by the liberal use of sublingual, intravenous or intracoronary nitroglycerin, or sublingual nifedipine[1,3,7]. But, sometimes high doses of intracoronary nitroglycerin are required to relieve spasm and in rare cases emergent coronary artery bypass surgery is indicated for refractory spasm. But, in selected cases of severe spasm, intracoronary verapamil may be more effective than nitroglycerin

in the reversal of refractory spasm[3,7].

Verapamil restored endothelial dependent relaxation with acetylcholine comparable with relaxation observed in nonischemic segments, possibly by reducing calcium influx into the cell and thereby stabilizing cellular membranes. Johnson et al demonstrated verapamil's sbility to reduce anginal frequency, nitroglycerin usage, and electrocardiographic evidence of disease activity(assessed by transient episodes of ST segment deviation on ambulatory electrocardiographic monitoring)[8]. Previous studies have demeonstrated that verapamil alone is efficacious in patients with variant angina and suggest that it is especially beneficial when given to patients who remain symptomatic despite receiving long-acting nitrate preparations[4,5,8]. Intracoronary verapamil may be more beneficial than intravenous verapamil for a lesser systemic hemodyamic effect with a greater amount delivered to the coronary vascular bed.

But in rare occasions, when patients experience severe chest pain and suddenly sit-up, cry and acted-out or life-threatening conditions-ventricular fibrillation, electromechanical dissociation, asystole, cardiogenic shock and cardiac arrest happen to and don't respond to intracoronary nitroglycerin therapy and we cannot inject verapamil into the coronary artery, we suggest to try injecting verapamil intravenously.

Clinical Implications

Our case demonstrate that ergonovine-induced or spontaneous coronary artery spasm may be refractory to routine sublingual, intravenous, and even to intracoronary nitroglycerine or sublingual nifedipine. In such instances, the administration of verapamil by the intravenous route in repeated doses until angiographic and clinical evidence of myocardial ischemia is reversed may be crucial. Studies using intravenous verapamil need to be carried out to define efficarcy, safety and dosage needed to reverse vasospasm.

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