DIFFERENT RESPONSE OF LEFT VENTRICULAR DIMENSIONS TO NITROGLYCERIN IN PATIENTS WITH ARTIFICIAL PACEMAKER.
A POSSIBLE SIGNIFICANCE OF REFLEX TACHYCARDIA FOR THE REDUCTION OF LV CAVITY AFTER NITROGLYCERIN

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The effects of nitroglycerin (NTG) on cardiac function can be evaluated by echocardiography. In this paper, we discuss the effects of NTG on cardiac function in two groups of subjects, one with artificial pacemakers implanted with a fixed heart rate, and the other examined as the control group. Left ventricular dimension was obtained in the standard manner using the electronic sector scanning system of Toshiba SSH-11A. Left ventricular end-diastolic and end-systolic dimensions (Dd and Ds) were obtained in each case and the ejection fraction was calculated. After the sublingual administration of NTG (0.6 mg), the blood pressure decreased in both groups. The ventricular rate was fixed in the pacemaker group but increased significantly in the control group. Dd and Ds were found to decrease only in the control group. The ejection fraction showed an increase in the majority of the control group but remained unchanged in the pacemaker group. Heart rate change therefore may play a role in dimensional change and pumping function of heart after NTG.

In 1974, DeMaria et al. studied echocardiographically the effects of sublingual administration of nitroglycerin (NTG) on left ventricular function and reported that the end-diastolic dimension (Dd) and the end-systolic dimension (Ds) of the left ventricle decreased after administration of NTG. In our earlier work, a similar result was reported.

Preload (filling pressure), afterload (systemic blood pressure), heart rate and changes in the myocardial contractile force are thought to be associated with the reduction of the left ventricular dimension.

Since tachycardia (such as increasing pacing rate) is known to result in a fall of the preload and a reduction of the left ventricular dimension in experimental and clinical studies, the role of reflex tachycardia following NTG is to be studied for such change.

For this purpose, we administered NTG sublingually in a pacemaker-implanted group in which the heart rate was fixed (pacemaker group) and in a control group in which the heart rate could be variable. The changes of left ventricular dimensions and hemodynamics were then compared.

Key Words: Nitroglycerin Echocardiography Left ventricular dimension Reflex tachycardia

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SUBJECTS

The control group consisted of 10 patients (five men and five women). The age ranged from 13 to 58 years, averaging 43 years. Their diagnosis was hypertension in two cases, ischemic heart disease in one case, and post-commissurotomy of the mitral valve in one case. The remaining six cases showed no organic heart disease.

The experimental (pacemaker) group was made up of nine cases (seven men and two women). The age ranged from 64 to 81 years, averaging 72 years. Their diagnosis was complete atrioventricular block in eight cases and sick sinus syndrome in one case. All patients were under temporary or permanent right ventricular endocardial pacing.

METHODS

After a rest of 15 minutes, left ventricular echocardiograms, heart rate and blood pressure were obtained from the control group. Then the patients in both groups received sublingual administration of NTG (0.6 mg).

The left ventricular echocardiograms were recorded serially every minute for 10 minutes, while monitoring the heart rate and blood pressure.

The left ventricular echocardiograms were obtained by two-dimensional echocardiography (Toshiba SSH-11A). The paper speed of the strip chart (Honeywell Strip chart 1219) was set at 50 mm/sec for simultaneous phono-and electrocardiogram recordings.

Recording of echocardiograms was made from the left margin of the sternum in the 3rd or 4th intercostal space with the patient in a 45° left lateral position.

The left ventricular end-diastolic dimension (Dd) was measured at the top of the R wave on the electrocardiogram in the control group and at the S wave in the pacemaker group.

As to the left ventricular end-diastolic dimension (Ds), it was measured at the starting point of the second heart sound on the phonocardiogram. An average of 5 successive heart beats was used.

The left ventricular volume and ejection fraction (EF) were calculated by Pombo’s method.9

In the pacemaker group, the control heart rate was set at 70 beats/min. Cases that showed abnormal motion of the interventricular septum such as paradoxical movements were excluded.

In the control group, the blood pressure, Dd, Ds, left ventricular volume and ejection fraction were obtained at the time of the maximum heart rate increase and were compared with the control.
values before NTG.

In the pacemaker group, a comparative study was made at a time when the blood pressure was at the bottom following NTG. A statistical study was done by student t-test.

RESULTS

1) Serial changes after NTG administration.

Figure 1 illustrates the left ventricular echocardiogram before and after NTG administration in the control group. After the administration, Dd and Ds decreased with an increase in the heart rate and a fall in the blood pressure. The maximal increase in heart rate was found around 4 min after sublingual NTG and ranged from 3 to 5 min. In the pacemaker group, a fall in the blood pressure was seen after NTG, but Dd and Ds were as constant as the heart rate (Fig. 2).

2) Influence of NTG on heart rate.

In the control group, the heart rate showed a
Reflex Tachycardia and LV Dimension Following NTG

| TABLE I RESULTS OF HEMODYNAMIC AND LV DIMENSIONAL CHANGES FOLLOWING NTG |
|---------------------------------------------------------------|------------------|
| Control group                                                | Pacemaker group  |
| before            after            p-value | before           after            p-value |
| Heart rate (bpm)  | 70 ± 18 | 82 ± 19 | 0.01 | 71 ± 1 | 77 ± 1 | ns |
| SBP (mmHg)        | 135 ± 19 | 121 ± 13 | 0.01 | 133 ± 15 | 123 ± 15 | 0.05 |
| Dd (mm)           | 47 ± 5 | 41 ± 5 | 0.001 | 45 ± 4 | 44 ± 4 | ns |
| Ds (mm)           | 32 ± 6 | 26 ± 6 | 0.01 | 28 ± 8 | 28 ± 9 | ns |
| Ejection fraction (%) | 68 ± 7 | 73 ± 12 | ns | 71 ± 21 | 21 ± 20 | ns |

Dd and Ds = end-diastolic and end-systolic dimension of the left ventricle, respectively; LV = left ventricle; NTG = nitroglycerin; SBP = systemic blood pressure; SD = standard deviation; ns = non-significant

significant increase from 70 ± 18 bpm to 82 ± 19 bpm after administration of NTG (p < 0.001).
In the pacemaker group, it remained unchanged at 71 ± 1 bpm (Fig. 3, Left).

3) Influence of NTG on blood pressure.
The systolic pressure showed a significant fall after administration of NTG in both groups; from 135 ± 19 mmHg to 121 ± 13 mmHg in the control group and from 133 ± 15 mmHg to 123 ± 15 mmHg in the pacemaker group and these falls were significant (p < 0.01, p < 0.05) (Fig. 3, Right).

4) Influence of NTG on left ventricular dimension.
Following administration of NTG, Dd in the control group showed a significant decrease from 47 ± 5 mm to 41 ± 5 mm (p < 0.01) but no difference was observed in the pacemaker group (Fig. 4, Upper).
Ds in the control group showed a significant decrease from 32 ± 6 mm to 26 ± 6 mm (p < 0.01), but no significant change was observed in the pacemaker group as in the case of Dd (Fig. 4, Lower).

5) Influence of NTG on ejection fraction.
The ejection fraction (EF) rose slightly in 8 cases in the control group after administration of NTG, but no significant difference was observed on the whole. It remained unchanged in the pacemaker group (Table I).

DISCUSSION
The blood level of NTG after sublingual
administration was found to reach a peak within 2 to 3 minutes with a concomitant increase in heart rate and a fall in blood pressure. In this study, the peak of the heart rate or blood pressure fall was reached in 3 to 5 minutes in the control group.

In the pacemaker group, the peak fall in blood pressure was similarly reached at 3 to 5 minutes. The fall in the blood pressure was also significant as was the case with the control group (Table I). In the control group, a decrease in the left ventricular dimension (Dd and Ds) was observed after NTG and this change was at the maximum when the heart rate reached a peak. At that time, blood pressure was lower than the control level (Table I). Among several factors which may contribute to the reduction of heart volume, Vatner et al. have reported a decreased preload as the major cause for such change after NTG. The significant reduction in end-diastolic and end-systolic size was observed even after the arterial pressure returned to the control level in their study.

However, in the present study, the fall in the afterload and the increase in heart rate can be attributed to the reduced ventricular size in addition to the fall in preload in the control group. For a comparable fall in blood pressure, the group with pacemakers showed no reduction in heart size. If the decreased ventricular size was brought about by the fall in preload, such a finding could be expected in the pacing group, but no decrease in heart size was found. We need to specify the reason for it. First is a possible abnormal wall motion in the pacemaker group. In the present study, each patient showed almost normal interventricular wall motion (Fig. 2) and similar conclusions have been drawn in other papers. Secondary, a change in the direction of the ultrasonic beam might be involved after NTG. Therefore, we chose the beam direction very carefully using two-dimensional echocardiography to minimize any such possibility. Thirdly, in A-V blocked heart, the atrial contribution can be variable and the beat-to-beat volume change is too large to obtain accurate ventricular dimension. However, the longer successive measurements of the left ventricular dimension showed no significant difference from those obtained from the average of the 5 successive beats. The last possibility is that echocardiography is insensitive to ventricular dimension when the heart rate is changed by some intervention. In the patients with ventricular pacing or with atrial pacing, the increase in the pacing rate resulted in a significant fall in dimension and stroke volume. Echocardiography, therefore, can be used for such study.

For the constant ventricular size after NTG in the pacemaker group, several factors should be considered. Tachycardia, such as increasing the pacing rate causes a fall in the filling pressure, and the loss of reflex tachycardia in the pacing group may make the fall in preload smaller, even though the afterload falls in a similar manner. A less compliant ventricular wall in the pacemaker patients can explain the constant ventricular dimension after NTG for a given fall of preload but this is unproven.

At the present time, the detailed mechanism remains to be clarified.

CONCLUSION

1) Following sublingual administration of NTG, a significant decrease in Dd and Ds was observed with a fall in the blood pressure and a significant increase in the heart rate in the control group.

2) In the pacemaker group in which the heart rate was fixed before and after administration of NTG, the left ventricular dimension (Dd and Ds) remained unchanged despite a fall in the blood pressure seen after the administration.

3) These findings suggest that an increase in the heart rate may play a role in changes in the left ventricular dimension (Dd and Ds) following sublingual administration of NTG.

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