NON-INVASIVE RADIOCARDIOPHGRAPHIC ASSESSMENT OF THE EFFECTS OF PRAZOSIN IN CONGESTIVE HEART FAILURE

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To clarify the hemodynamic effects of prazosin in congestive heart failure, the changes of blood distribution were examined radiocardiographically in 9 patients. After obtaining control data, patients were given oral prazosin (5.9 ± 2.6 mg/day) for 3 weeks. Studies were repeated immediately before and one week after the cessation of the prazosin treatment.

Cardiac index (CI) and stroke index (SI) showed significant increases, and mean blood pressure (MBP) and peripheral vascular resistance significant decreases as compared with the control values. However, heart rate did not change significantly throughout the period of this study. After stopping prazosin, MBP, CI and SI returned to the control levels. Concerning the changes in blood distribution, total blood volume and body blood volume significantly increased during prazosin therapy. Pulmonary blood volume (PBV) had a tendency to increase, although the changes were not significant. In patients, in whom the PBV increased during prazosin treatment, diuretics had to be used concomitantly.

Our results show that prazosin is effective in the treatment of congestive heart failure and radiocardiography is a useful non-invasive procedure in assessing cardiac improvement and in designing the appropriate treatment.

The immediate beneficial hemodynamic and clinical effects of vasodilators in patients with congestive heart failure have been clearly established. Among the various vasodilating agents, nitroprusside has proved invaluable in the treatment of severe congestive heart failure. Its balanced effects on resistance and capacitance vessels permit an enhancement of cardiac output while simultaneously relieving pulmonary congestion. Among the systemic vasodilators nitroprusside has been used most widely in patients with severe congestive heart failure. However, despite its beneficial effects, the use of nitroprusside in the long-term management of heart failure appears to be impossible.

Oral, sublingual and topical vasodilators are all now employed in the management of congestive heart failure. Nitroglycerin and isosorbide dinitrate have been found to reduce left ventricular preload but usually fail to enhance cardiac output. Oral hydralazine substantially lowers systemic vascular resistance and thereby raises cardiac output, but when it is employed alone, its value is limited by its failure to reduce left ventricular filling pressure. To accomplish both impedance reduction with attendant augmentation of cardiac output and lowering of left

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468 Japanese Circulation Journal Vol. 46, May 1982
ventricular preload, it is necessary to combine hydralazine with a preload reduction agent. However, chronic hydralazine therapy may induce the systemic lupus erythematosus syndrome.

Recently, oral prazosin has been introduced as a useful agent in treating chronic heart failure, because its action is similar to that of nitroprusside. Acute beneficial effects of prazosin in heart failure are clear, but hemodynamic monitoring has been concerned with only the initial dose of the drug. Therefore, the ability of maintenance therapy to sustain preload and afterload reductions has not been demonstrated, and the chronic therapeutic effects of prazosin remains unclear.

As a non-invasive method to evaluate the cardiac state, an echocardiogram is most often employed. However, this method causes various problems when dealing with patients with coronary artery disease. This institute has developed a radiocardiographic method which is non-invasive.

In the present study, the authors have evaluated prazosin-induced hemodynamic changes and blood distribution in patients with congestive heart failure employing radiocardiographic method over a 4-week period.

MATERIALS AND METHODS

Patient Population

Table I shows the patient population studied. Nine patients, 8 men and one woman with a mean age of 48 years (range: 42 to 60 years) with congestive heart failure were studied. All but one (Patient 5) had a normal sinus rhythm.

Hemodynamic Measurements

After obtaining informed consent from all patients, cardiac output (CO) and blood distribution were measured radiocardiographically according to the analog simulation method, which was reported previously. Heart rate (HR, beats/min) was obtained from a continuously recorded electrocardiogram. Arterial pressure was measured by sphygmomanometer with the mean arterial pressure (MAP, mmHg) derived from the formula: MAP = D + (S−D)/3, where S is the peak systolic pressure and D the end-diastolic pressure. Other parameters were calculated as follows: cardiac index (CI) (L/min/m²) = CO/BSA (BSA = body surface area in square meters); stroke index (SI, ml/m²) = CI/HR, and peripheral vascular resistance (PVR, dynes·sec·cm⁻⁵·m²) = MBP × 80/CI.

Experimental procedure

Studies were performed over a 4-week-period in 9 patients. After obtaining baseline RCG values (PZ-c), each patient was given 5.9 ± 2.6 mg of prazosin per day for 3 weeks and measurements were taken at the end of the third week (PZ-on). Then prazosin administration was stopped and the same studies were performed one week later (PZ-off).

Statistical Analysis

Data were analyzed by the paired t-test. A p value less than 0.05 was considered significant. Values are presented as mean ± SD.

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<th>Patient No.</th>
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Abbreviations: NYHA = New York Heart Association functional class, CCM = congestive cardiomyopathy, MI = myocardial infarction, MSR = mitral stenosis and regurgitation, AR = aortic regurgitation, NSR = normal sinus rhythm, AF = atrial fibrillation, M = male, F = female

Japanese Circulation Journal Vol. 46, May 1982
TABLE II  EFFECTS OF PRAZOSIN ON HEMODYNAMIC CHANGES

<table>
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<th>Patient No.</th>
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Abbreviations: MBP = mean blood pressure (mmHg), HR = heart rate (beats/min), CI = cardiac index (L/min/m²), SI = stroke index (ml/m²), PVR = peripheral vascular resistance (dynes-sec-cm⁻²·m²) *: p < 0.05, **: p < 0.005, ***: p < 0.001, ns = not significant. PZ-c = controls, PZ-on = 3 weeks after prazosin therapy, PZ-off = one week after the cessation of prazosin.

Fig.1. Effect of prazosin on blood distribution.

RESULTS

After 3 weeks of prazosin therapy, symptoms of congestive heart failure were relieved. In some cases, however, in which pulmonary blood volume increased significantly, combined administration of diuretics was necessary to manage pulmonary congestion. Body weight did not change significantly during the study: PZ-c: 57 ± 10 kg, PZ-on: 57 ± 9, PZ-off: 59 ± 9.

Effects of Prazosin on Hemodynamic Parameters

Table II shows the effects of prazosin on hemodynamic parameters. After 3 weeks, the control low CI and SI of 1.79 ± 0.46 L/min/m² and 24.1 ± 9.6 ml/m² were increased significantly to 2.89 ± 0.75 and 40.2 ± 14.3, and one week after stopping prazosin, these parameters were reduced to 2.09 ± 0.67 and 29.4 ± 11.0. MBP and PVR were decreased significantly from the control levels of 93 ± 11 mmHg and 4450 ± 1490.

Japanese Circulation Journal  Vol. 46, May 1982
Prazosin Therapy in Congestive Heart Failure

dynes-sec-cm$^{-5}$-m$^2$ to 86 ± 10 and 2490 ± 610. One week after the cessation, MBP and PVR increased to 91 ± 15 and 3930 ± 1720. HR remained unchanged throughout the study.

Effects of Prazosin on Blood Distribution

Figure 1 shows the changes in blood distribution during the study. Total blood volume (TBV) and body blood volume (BBV) significantly increased during prazosin therapy: PZ-c: 2830 ± 640 ml/m$^2$, 1910 ± 351 ml/m$^2$, PZ-on: 2980 ± 760, 2020 ± 380 and PZ-off: 2600 ± 340, 1920 ± 240. Pulmonary blood volume (PBV) tended to increase by prazosin administration and decreased after its cessation, although the changes were not significant: PZ-c: 279 ± 78 ml/m$^2$, PZ-on: 294 ± 49 and PZ-off: 269 ± 65.

DISCUSSION

Subjects in this study were patients with chronic ventricular dysfunction. The exercise tolerance of all subjects was severely reduced. Even in patients with congestive heart failure being unresponsive to digitalis and diuretic treatments, prazosin effectively lowered MBP and improved clinical symptoms. Our patients tolerated prazosin without side effects or tachyphylaxis as reported previously.

Previous studies of prazosin therapy in congestive heart failure have all been conducted by a single dose administration after 3 weeks of PZ administration, CI and SI showed significant increases when compared to corresponding control values, and one week after its cessation they returned to the control levels. Thus, therapy over a 3-week period proved as effective as that of a single administration. Awan et al. reported sustained clinical improvement in severe congestive heart failure with the prazosin maintenance therapy. However, they evaluated ventricular function by echocardiography and exercise testing only. Unfortunately, echocardiography is of limited value in evaluating left ventricular function in ischemic heart disease. Patients with this disease may have an abnormal regional wall motion which is not detected echocardiographically. In these cases, echocardiographic evaluations of left ventricular performance and volume may be misleading.

In the present study, blood distribution changes were examined radiocardiographically. TBV and BBV increased significantly after administration of prazosin. This may be due to the fluid retention effect of prazosin. PBV tended to increase as long as prazosin was administered and fell after discontinuation. Nitroprusside reduces partial pressure of oxygen in arterial blood (PaO$_2$) in left ventricular failure, and this change is partially explained by the pulmonary vascular effects of this drug. Prazosin has been reported to have effects hemodynamically similar to nitroprusside. In some cases in the present study, PaO$_2$ reductions were documented, and in these cases, increases in PBV by prazosin were found (unpublished data). Thus, there may be a relationship between increased PBV and decreased PaO$_2$.

Empirically, a concomitant use of diuretics is necessary during the prazosin treatment in some patients with congestive heart failure. The present results suggest that this is due to an obvious fluid retention effect of prazosin in pulmonary as well as systemic circulation.

In conclusion, oral prazosin therapy was very effective in our 9 patients, and radiocardiographic evaluation of cardiac function seemed to be useful in the long-term management of patients. The long-term study of prazosin-therapy for more than one month in patients with congestive heart failure are now under investigation in our institute.

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REFERENCES


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