A study of the use of prazosin in hypertensive patients in Korea

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Summary

1. The effects of prazosin administered alone or in combination were studied in thirty patients between August 1974 and March 1975.

2. All patients had previously received treatment for hypertension with other agents, for from 2 months to 10 years. All thirty patients had refractory hypertension which had not responded satisfactorily to other treatment.

3. Patients were treated initially with prazosin; polythiazide, or polythiazide plus tolamolol, were added when necessary.

4. A satisfactory blood pressure response to prazosin alone, or prazosin in dual or triple combination therapy, occurred in all thirty patients.

5. Prazosin was well tolerated.

Key words: peripheral vasodilator, polythiazide, prazosin, refractory hypertension, tolamolol, triple therapy.

Introduction

Prazosin, a quinazoline derivative, is a new oral anti-hypertensive agent with a peripheral mode of action involving direct relaxation of arteriolar smooth muscle and sympathetic blockade occurring without receptor occupancy and of a type not previously described. Laboratory (Scriabine, Constantine, Hess & McShane, 1968) and human (Kincaid-Smith, Fang & Laver, 1973; Stokes & Weber, 1974; Bolli & Simpson, 1974; Turner, Watson & Peel, 1975) studies have indicated prazosin is effective both on its own and when used in combination with other agents. The aim of this study was to assess in hypertensive Korean patients, the response of prazosin administered alone, the response on addition of a thiazide diuretic in those patients whose blood pressure had not returned to a satisfactory level with prazosin alone, and the response on the addition of a β-adrenoreceptor-blocking agent in those patients whose blood pressure had not returned to a satisfactory level with the combination of prazosin and thiazide.

Methods

Thirty patients with moderate or severe hypertension were selected for study at the Busan National University Hospital, Korea, between August 1974 and March 1975. All patients had previously received treatment for hypertension; the range of duration of previous treatment was from 2 months to 10 years; all patients had been referred because of failure to obtain satisfactory blood pressure control with other therapy. The patients were studied for up to 6 months; there were fifteen males and fifteen females; ages ranged from 17 to 68 years; twenty-five of the patients were in the fourth, fifth or sixth decades. On admission to the study all previous anti-hypertensive therapy was suspended and each patient was observed during a wash-out period of no less than 2 weeks. At the end of this period blood pressures in supine and standing positions were measured, and recorded (pretreatment value); prazosin therapy was begun with each patient receiving 2 mg three times daily; immediately before commencing therapy patients were advised of the side effects which are known to occur with anti-hypertensive therapy. Patients were examined after 1 week and supine and standing blood pressures were again recorded; in those patients whose standing systolic blood pressure had fallen to less than 150 mmHg or whose standing...
diastolic blood pressure had fallen less than 90 mmHg response was regarded as satisfactory and treatment with prazosin (2 mg three times daily) was continued unchanged throughout the rest of the trial; in the remainder, prazosin was continued at a dose of either 2 or 5 mg three times daily, and polythiazide 1 mg three times daily and potassium chloride added. At the end of the second week those patients receiving combination therapy whose response was then satisfactory continued with the combination throughout the rest of the trial; in the remainder a β-adrenoreceptor-blocking agent, tolanmolol, was added at a dose of 50–100 mg three times daily, and the triple regime continued throughout the rest of the trial. At each examination blood pressures were measured in both supine and standing positions after the patient had rested for at least 30 min. A record was made of all side effects of which each patient complained.

For assessment of results the patients were divided into three groups; those who received prazosin alone, those who received prazosin and polythiazide, and those who received prazosin, polythiazide and tolanmolol. For each group the mean pretreatment blood pressures measured in supine and standing positions were compared with those measured at the end of the trial; the differences were subjected to statistical analysis to determine their significance. The differences between supine and standing systolic and diastolic blood pressures on treatment were calculated for each of the three groups.

**Results**

All thirty patients responded satisfactorily to treatment. Six patients responded satisfactorily to prazosin alone. In this group the supine systolic blood pressures before and after treatment were 185 ± 16 and 150 ± 12 mmHg respectively; the supine diastolic pressures were 106 ± 5 and 90 ± 3 mmHg respectively. The standing systolic blood pressures before and after treatment were 173 ± 13 and 134 ± 4 mmHg respectively, the standing diastolic pressures 102 ± 5 mmHg and 81 ± 6 mmHg respectively. All differences were significant (P < 0.005). Seventeen patients responded satisfactorily to the combination of prazosin and polythiazide. In this group the supine systolic blood pressures before and after treatment were 197 ± 26 and 148 ± 16 mmHg respectively; the supine diastolic pressures before and after treatment were 121 ± 13 and 92 ± 6 mmHg respectively. The standing systolic blood pressures before and after treatment were 188 ± 27 and 137 ± 16 mmHg respectively; the standing diastolic

![Fig. 1. Effect of drugs on blood pressure in patients undergoing treatment with prazosin alone and in combination. Open columns: before treatment; cross-hatched columns: after treatment.](image-url)
pressures before and after treatment were 110 ± 14 and 85 ± 5 mmHg respectively. All differences were significant (P < 0.005). The remaining seven patients responded satisfactorily to the combination of prazosin, polythiazide and a β-receptor-blocking agent (tolamolol). In this group the supine systolic blood pressures before and after treatment were 230 ± 25 and 181 ± 6 mmHg respectively; the supine diastolic pressures before and after treatment were 138 ± 15 and 93 ± 6 mmHg respectively. The standing systolic blood pressures before and after treatment were 224 ± 24 and 151 ± 9 mmHg respectively; the standing diastolic pressures before and after treatment were 136 ± 12 and 75 ± 4 respectively. All differences were significant (P < 0.005).

In the six patients who received prazosin alone mean differences on treatment between supine and standing systolic and diastolic blood pressures were 16 and 9 mmHg respectively; in the seventeen patients who responded to prazosin plus polythiazide 11 and 7 mmHg respectively; and in the seven patients who responded to prazosin, polythiazide and tolamolol 30 and 20 mmHg respectively. The data are summarized in Fig. 1.

There was a total of thirty complaints of side effects from eight patients; there were five complaints of headache, five of palpitations, five of malaise, five of oedema, five of drowsiness and five of fatigue. In each case the side effect was mild in severity and of short duration; no side effect lasted for more than 3 days. Twenty-two of the thirty patients studied did not complain of side effects.

Discussion

There is a high incidence of hypertensive cardiovascular disease in Korea (Park, 1974); hypertension is often refractory to drug treatment and there is a high incidence of deaths due to complicating cerebrovascular catastrophes.

The rationale for the use of peripheral vasodilator drugs in the management of hypertension has been recognized for many years (Koch-Weser, 1974; Kincaid-Smith, MacDonald, Hua, Laver & Fang, 1975) but the high incidence of severe side effects, mainly resulting from the associated increase in reflex sympathetic activity, had resulted in their failure to be used extensively in clinical medicine. These side effects can now largely be overcome by adding a β-receptor-blocking agent in combination therapy. The efficacy of this combination can be improved, and any tendency to fluid accumulation reduced by the addition to the regime of a thiazide diuretic.

Prazosin is a new peripheral vasodilator with a dual mode of action not previously described; it acts directly on the arteriolar smooth muscle causing relaxation and arteriolar vasodilatation and also produces α-receptor blockade without occupancy of the receptor sites (Scriabine et al., 1968). This unique mode of action has allowed prazosin to be used both on its own as well as in combination in the treatment of hypertension. In this study of thirty patients with moderate or severe hypertension refractory to other therapy a satisfactory response was achieved with prazosin in every patient; six patients responded to prazosin alone, seventeen to prazosin plus polythiazide, and six to triple therapy of prazosin plus polythiazide plus the β-receptor blocker tolamolol; the mean pretreatment blood pressures were lowest in the group responding to prazosin alone and highest in the group requiring triple therapy. Prazosin was well tolerated and only eight of thirty patients complained of mild side effects, which were of short duration in each case. In this study prazosin, used alone or in combination, was highly effective in controlling moderate and severe hypertension, refractory previously to other drug therapy. These results with prazosin confirm those of other workers (Kincaid-Smith et al., 1973; Stokes & Weber, 1974; Bolli & Simpson, 1974; Kincaid-Smith et al., 1975; Turner et al., 1975).

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References


