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A modified isometric test to evaluate blood pressure control with once-daily slow-release verapamil

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Abstract **Blood pressure at rest is not predictive of round-the-clock values. Blood pressure should therefore be measured during effort to evaluate hypertension and its response to treatment. The effect of sustained-release verapamil (240 mg taken once a day) on blood pressure at rest and during isometric effort was therefore investigated. Overall, verapamil reduced blood pressure significantly in 41 of 45 hypertensive patients: the mean systolic blood pressure at rest (± SD) fell from 151 ± 35 mmHg to 137 ± 13 mmHg ($P < 0,001$) and the diastolic blood pressure from 97 ± 21 mmHg to 83 ± 7 mmHg ($P < 0,001$), while the systolic blood pressure during isometric effort fell from 186 ± 23 mmHg to 156 ± 13 mmHg ($P < 0,001$) and the diastolic blood pressure from 118 ± 14 mmHg to 95 ± 8 mmHg ($P < 0,001$). The simple, inexpensive handgrip method described is cost-effective and strongly recommended as an integral part of the evaluation of hypertensive patients. The combination of a drug to which compliance is good and a simple method of blood pressure evaluation should result in improved effectiveness of treatment in the long term.**

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Adequate control of blood pressure in hypertensive patients reduces the morbidity and mortality associated with this condition.[1,2] This can be achieved by a variety of medications. However, appropriate methods to evaluate the antihypertensive effectiveness of these drugs are required. Blood pressure measurement at rest may be of limited value, since it does not reflect the fluctuations occurring during everyday physical and mental stress.[3] Measurement of the mean 24-hour blood pressure with an ambulatory blood pressure Holter monitor is probably the best method available, but it is expensive and can only be used in a small number of patients. A simple, robust, inexpensive handgrip enabling blood pressure to be measured during exercise has been described.[4] This is a convenient way to monitor medical therapy, identifies latent and borderline hypertension and is more practical and less expensive than an isotonic stress test. Verapamil, a calcium antagonist, has been shown to lower systolic and diastolic blood pressure during rest[5,6] and isotonic effort[7] when administered in doses ranging from 240 mg/d to 480 mg/d. The present study evaluated the efficacy of sustained-release verapamil (240 mg, taken once a day) in mild-to-moderate hypertension, using a validated handgrip protocol.[4]

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Patients and methods

Forty-five patients (38 male, 7 female, mean age (± SD) 52 ± 9 years) were included in the study. All had mild-to-moderate hypertension (World Health Organisation class I-II), with a mean blood pressure at rest of 151 ± 35 mmHg systolic and 97 ± 21 mmHg diastolic. Twenty-nine patients were unresponsive to various drug combinations as judged by diastolic blood pressures which remained above 100 mmHg at rest, while 16 had not received any prior medical therapy. Four patients had coronary artery disease, treated with nitrates and aspirin, and 5 were non-insulin-dependent diabetics.

Isometric handgrip stress test

The protocol of isometric (static) handgrip testing has been described previously[4] and correlates well with the widely used isotonic (dynamic) stress test. A hand-dynamometer (Preston Co. (D 704607 Pat.)) was used and the contraction intensity was monitored on a digital display to determine all the handgrip measurements. Subjects were seated in a comfortable position and were instructed to avoid the Valsalva manoeuvre during the handgrip test. Maximal voluntary contraction (MVC) was calculated from the mean value of 3 maximal measurements.

The handgrip was performed for 90 seconds at 30% of the patient's own MVC. Blood pressure was measured on the opposite side to the arm the patient chose to grip with.

Blood pressure was measured using the same calibrated mercury manometer (cuff 13 cm wide and 20 cm long) for all patients. The systolic blood pressure was recorded according to Korotkoff phase I and the diastolic blood pressure according to Korotkoff phase V (disappearance of sounds). All the tests were performed by the same physician.

Design

On entry to the study, all patients taking antihypertensive medication were told to stop doing so for 1 week. Blood pressure was then measured at baseline (no treatment), 7 (±1) hours after the initial dose of 240 mg sustained-release verapamil (which was taken each morning) (acute response), and 1 week later, 22 (±1,5) hours after the last dose (chronic response). These measurement intervals were based upon pharmacological data.[8-10] Three blood pressure measurements were made on each occasion in the sitting and standing positions and at the end of the isometric handgrip test.

Statistical evaluation

All data are presented as mean ± SD. Student's two-tailed paired *t*-test was used.

Results

Four patients (9%) were excluded from the study because higher doses of verapamil or additional medication were required to control their blood pressure. The results for the remaining 41 are presented in Table I and Fig. 1.

TABLE I.
Blood pressure (mmHg) and heart rate (/min) before and after treatment*

	Sitting			Standing			Handgrip		
	Systolic	Diastolic	Heart rate	Systolic	Diastolic	Heart rate	Systolic	Diastolic	Heart rate
No treatment	151 ± 35	97 ± 21	73	159 ± 18	106 ± 9	75	186 ± 23	118 ± 14	92
Verapamil									
7 h after 1st dose	137 ± 13	83 ± 8	70	136 ± 14	90 ± 10	74	158 ± 18	95 ± 7	93
22 h after last dose	137 ± 13	83 ± 7	75	139 ± 13	88 ± 8	77	156 ± 13	95 ± 8	95

*41 patients.

Statistically significant reductions in systolic and diastolic blood pressures were shown after the first and last doses of verapamil in all three blood pressure measurements.

There were no significant differences between the first (7 hours after the initial dose of verapamil) and second (22 hours after the last dose, after 1 week of treatment) blood pressure measurements. Blood pressures in the sitting and standing position were similar, but both sitting and standing measurements differed significantly from blood pressure during the handgrip test ($P < 0{,}001$) (Table I and Fig. 1). The greatest reductions in systolic and diastolic blood pressures were demonstrated during the handgrip test; diastolic pressure was reduced to a greater extent than systolic blood pressure during all the measurements ($P < 0{,}001$). A slight but not significant slowing of the heart rate was also observed.

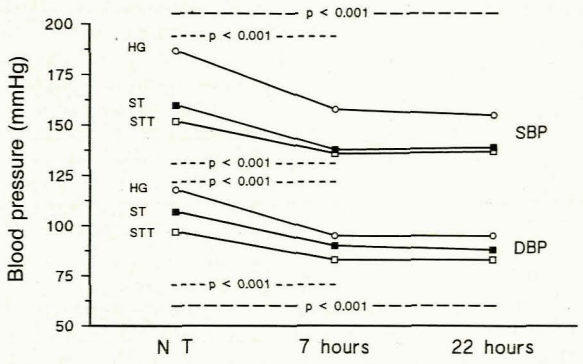

FIG. 1.
Systolic and diastolic blood pressures (SBP and DBP) in the sitting (STT) and standing (ST) positions and during the handgrip effort test (HG) (NT = no treatment; 7 hours = 7 hours after 1st dose of verapamil; 22 hours = 22 hours after the last dose of verapamil, 1 week later).

Adverse effects were minimal in this patient group. Two patients had transient palpitations, 2 complained of headaches, and 3 had slight facial flushing during the first 3 days.

Discussion

A large number of antihypertensive agents have recently become available, but antihypertensive efficacy has been examined almost exclusively at rest. Since daily activities involve isometric effort (lifting and supporting weights) and have an important influence on blood pressure, it is essential to evaluate blood pressure response to isometric effort. This test can reveal high blood pressure that might otherwise not be detected.

Only a few studies have evaluated the effect of antihypertensive agents during physical stress (isotonic and isometric).[7,10-14] To the best of our knowledge no other study has recommended isometric stress testing[4] as an evaluation technique in hypertension. This protocol could be beneficial not only for screening but also for long-term follow-up. We previously showed an excellent correlation between maximal isotonic exercise on a treadmill and isometric handgrip exercise. Measurement of the diagnostic value showed 98% sensitivity, 78% specificity and 90% positive predictive value.[4]

Many studies suggest that verapamil is effective in reducing raised blood pressure at rest, on its own or in combination with other drugs.[3] A long-acting verapamil preparation was shown to control mild-to-moderate hypertension effectively, both at rest and during isometric effort, with minimal adverse effects. The beneficial antihypertensive effect of the drug was the same at 7 and at 22 hours after drug administration. Interestingly, the maximal effect of verapamil was achieved during isometric exercise, and it was slightly more effective in lowering the diastolic blood pressure (Table I, Fig.1).

These results suggest that the handgrip isometric test could play an important role in the evaluation of antihypertensive treatment. It is simple and can be widely used on a large number of patients. Other authors[14] have used the handgrip test to evaluate patients with hypertension and the effect of antihypertensive drugs.[15] However, the application of the handgrip or isometric test (which might be better termed the 'isotonic-equivalent method') in the evaluation of antihypertensive therapy has not been reported to date.

In conclusion, the combination of monotherapy for hypertension[8] and a simple method (handgrip) of blood pressure evaluation could improve the effectiveness of treatment in the long term and thus lower morbidity and mortality. It appears to be the most cost-effective and reliable method currently available for the evaluation and follow-up of hypertensive patients,[16] and it has also been shown to be useful in the evaluation of various antihypertensive drugs.[17]

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