Within-Visit Blood Pressure Changes in Outpatient Clinic

To the Editor:

Epidemiological blood pressure (BP) surveys suggest that BP determinations are often subject to considerable within-visit variation. For this reason, a memorandum from a WHO/ISH meeting published in 1983 stressed that BP should be measured at least three times over a period of at least 3 minutes at each visit and the lowest reading should be recorded. The same committee has now recommended that two or more measurements should be taken over the same interval and the mean value should be used. The scientific basis for this slight change in the recommendation has not been fully explained. The present study was performed to obtain information on the magnitude and time course of the variability in casual BP measurements recorded for individual patients during routine clinical practice that would be useful in determining the desirable number of BP readings in outpatient clinic settings.

Patients with a history of hypertension (systolic BP ≥ 160 mm Hg or diastolic BP ≥ 90 mm Hg, or both) were recruited consecutively from our outpatient clinic. The study subjects consisted of 63 patients (38 men and 25 women) aged 63 ± 11 (SD) years, 46 of whom were undergoing antihypertensive therapy. Seventy-eight percent of patients had end-organ damage, as evidenced by Grade II and III retinopathy or left ventricular hypertrophy, or both.

BP and heart rate (HR) were recorded in the sitting position by nurses using an automatic blood pressure recorder (Model BP103-N; Nippon Kohrin, Komaki, Japan) throughout to eliminate observer error. This device determines the systolic, mean, and diastolic BPs based on an orderly sequence of oscillations in cuff pressure. The device was set to inflate automatically every minute. Each patient had four consecutive BP measurements at each visit, and the examination was repeated four times in an identical manner at 2- or 4-week intervals.

Figure 1 shows the mean differences between the individual values and the average of four serial readings at each visit for a total of 252 (63 patients x 4 visits) BP and HR measurements. They were significantly different from each other when tested by one-way analysis of variance (\(p < 0.0001\)). As seen in Figure 1, systolic, mean, and diastolic BP levels progressively decreased during multiple readings. The mean value of the fourth reading was lower than that of the first by 4.3, 2.3, and 1.9 mm Hg, respectively. The differences between the mean values of the first two readings and those of the last two readings were statistically significant, while the differences between each of the last two readings were not significant. For systolic and mean, but not diastolic, BP the differences between each of the first two readings were also insignificant. Finally, the HR obtained in the first reading was significantly higher than that of successive readings. The mean value of the second reading was lower than that of the first one by 2.5 beats/min.

Thus, we may conclude that at least three, rather than two, BP readings over a short interval in an outpatient clinic practice are desirable, since even duplicate readings might lead to overestimated BP values. This conclusion is in accordance with 1983 WHO/ISH...
guidelines. It cannot be inferred from the present study, however, which value — the average, the highest, or the lowest — of the serial readings should be used as the value for the visit.

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Hydrochlorothiazide augments the antihypertensive effect of enalapril.

Enalapril tends to reverse the potassium loss often associated with hydrochlorothiazide.

Highly effective in adults, regardless of age or race.*

This fixed-dose combination is not indicated for initial therapy. Patients already receiving a diuretic when enalapril is initiated or given a diuretic and enalapril simultaneously can develop symptomatic hypotension. In the initial titration of the individual entities, it is important, if possible, to stop the diuretic for several days before starting enalapril or, if this is not possible, to begin enalapril at a low initial dose (2.5 mg; see DOSAGE AND ADMINISTRATION). This fixed-dose combination is not suitable for titration but may be substituted for the individual components if the titrated doses are the same as those in the combination.

VASERETIC, containing 10 mg enalapril maleate and 25 mg hydrochlorothiazide, is contraindicated in patients who are hypersensitive to any component of this product. Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

Evaluation of the hypertensive patient should always include assessment of renal function.

*Although enalapril was antihypertensive in all races studied, black hypertensive patients (usually a low-renin hypertensive population) had a smaller average response to enalapril maleate monotherapy than non-black patients. In contrast, hydrochlorothiazide was more effective in black patients than enalapril. Concomitant administration of enalapril maleate and hydrochlorothiazide was equally effective in black and non-black patients.
Once-A-Day
(Enalapril Maleate-Hydrochlorothiazide/MSD)

This fixed-dose combination is not indicated for initial therapy. Patients who are already on enalapril maleate and hydrochlorothiazide therapy should be changed to the fixed-dose combination after an adequate period of therapy with enalapril maleate and hydrochlorothiazide to ensure that clinical response has been adequate. The patient's weight should be considered when adjusting the dosage of hydrochlorothiazide. The diuretic component is contraindicated in patients who are hypersensitive to thiazide diuretics. Patients who are hypersensitive to sulfa drugs may also have an increased incidence of hypersensitivity reactions to hydrochlorothiazide, but the incidence has not been documented.

**Possible adverse reactions**

- **Cardiovascular System:** Edema, hypotension
- **Central Nervous System:** Fatigue, dizziness, headache, vertigo
- **Gastrointestinal System:** Nausea, vomiting, constipation, diarrhea
- **Nephrological System:** Proteinuria, hematuria, uric acidosis
- **Endocrine System:** Hyperglycemia, hyperuricemia, hypokalemia, hypernatremia
- **Hematological System:** Anemia, leukopenia, increased eosinophils
- **Skin:** Rash, pruritus, photosensitivity

**Precautions for use**

- **Cautions:** Patients with a history of hypersensitivity to sulfa drugs, thiazides, or other diuretics should be monitored closely during treatment with this product. The use of hydrochlorothiazide in patients with concurrent diuretic therapy should be carefully considered due to the potential for increased kaliuresis and hypotension.

**Contraindications**

- **Hypersensitivity to sulfa drugs, thiazides, or other diuretics
- **Hyperkalemia
- **Hypotension
- **Hypovolemia
- **Renal failure
- **Severe hepatic disease
- **Severe gastrointestinal disturbances
- **Severe fluid and electrolyte disturbances
- **Severe anemia
- **Severe insulin-dependent diabetes mellitus
- **Severe porphyria
- **Severe systemic lupus erythematosus
- **Severe dermatologic conditions
- **Severe wound healing

**Warnings**

- **Hypotension:** Patients with a history of hypotension or pronounced decreases in blood pressure should be monitored closely during treatment with this product. The use of hydrochlorothiazide in patients with concurrent diuretic therapy should be carefully considered due to the potential for increased kaliuresis and hypotension.

**Precautions**

- **Diabetic patients:** Hyperglycemia may occur in diabetic patients; therefore, blood glucose should be monitored closely during treatment with this product.

**Adverse reactions**

- **Edema:** Edema may occur in patients with renal impairment, congestive heart failure, or hepatic cirrhosis. Edema may be controlled by the concomitant use of a thiazide diuretic, particularly if the hydrochlorothiazide component is increased. Edema may be more frequent in patients with impaired renal function or hepatic cirrhosis.

**Dosage and administration**

- **Adults:** Initially, 2.5 mg enalapril maleate and 25 mg hydrochlorothiazide once daily. The dosage may be increased at 1- to 2-week intervals as necessary. The maximum daily dose is 10 mg enalapril maleate and 50 mg hydrochlorothiazide.

**Overdosage**

- **Signs and symptoms:** Hypotension, edema, nausea, vomiting, tachycardia, flushing, dizziness, headache, and diaphoresis.

**Treatment**

- **Supportive measures:** Cessation of further drug administration, administration of diuretics, and maintenance of electrolyte balance with particular attention to potassium should be carried out. If necessary, hemodialysis or peritoneal dialysis may be required.

**Interactions**

- **Antihypertensives:** Use with caution, the antihypertensive action may be increased.

**Pregnancy category C**

**Lactation**

- **Breastfeeding:** Hydrochlorothiazide is excreted in breast milk. The decision to breastfeed should be made considering the potential benefit to the infant and the potential risk of the drug to the infant.

**Pregnancy category C**

- **Lactation:** Hydrochlorothiazide may be excreted in breast milk. The decision to breastfeed should be made considering the potential benefit to the infant and the potential risk of the drug to the infant.

**Potentially relevant,-
may be acidified with stomach contents if gastric delay is present or after prolonged therapy. Monitor adequacy of oral intake of fluids and electrolytes, particularly in the elderly or patients with impaired renal function. Some patients may require increased attention to fluid and electrolyte balance during treatment with this product.

**Hydrochlorothiazide**

- **Hypokalemia:** Hypokalemia may occur with other diuretics and may be accentuated by concurrent use of potassium-depleting drugs. K^+ supplements or potassium-sparing diuretics or aldosterone antagonists may be required. Potassium-sparing drugs may be inadequate in some patients. Potassium-sparing diuretics or aldosterone antagonists may be required in some patients with severe diuretic therapy with hydrochlorothiazide.

**Drug interactions**

- **Thiazide diuretics:** Use with caution, the antihypertensive action may be increased.

**Lithium**

- **Lithium:** Use with caution, lithium levels should be monitored closely during treatment with this product.

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Within-visit blood pressure changes in outpatient clinic.
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