Hypertension

Letter to the Editor

Effect of Verapamil on Catecholamine Secretion by Human Pheochromocytoma

To THE EDITOR:

The pivotal role played by calcium in the regulation of many hormonal secretions, including catecholamine (CA) release from chromaffin tissue, is well known. Data on the in vivo effects of Ca\(^{2+}\) channel blockers on the secretion of human chromaffin cells are scanty and difficult to obtain because of the action exerted by these drugs at different sites in the cardiovascular and sympathoadrenal system, where reflex mechanisms are easily activated. In 1983, Serfas et al.\(^1\) reported that nifedipine therapy caused a decline in urinary norepinephrine (NE) levels in a patient affected by hypertrophic cardiomyopathy and a NE-secreting pheochromocytoma.

To evaluate whether a Ca\(^{2+}\) channel blocker modulates blood pressure in patients with pheochromocytoma through an inhibition of CA secretion, we studied, in a single-blind randomized manner, the effects of intravenous verapamil infusion in four patients with pheochromocytoma. Each patient gave her or his informed consent. Myocardial insufficiency and conduction defects were excluded in each patient.

Verapamil (Isoptin) was diluted in a 0.9% NaCl solution to a final volume of 100 ml and a concentration of 0.075 mg/kg body weight. Placebo and verapamil infusion were performed on separate days at a rate of 6.6 ml/min for 15 minutes using a microdrip apparatus. Each infusion was begun at 0800 after at least 30 minutes of quiet recumbency. Plasma samples for CA measurement were drawn before and 5, 10, 20, 30, and 40 minutes after the beginning of placebo or verapamil infusion. Samples were drawn in vacutainers containing 100 \(\mu\)l of a solution of ethylene glycol bis(\(\beta\)-aminoethyl ether)-\(N,N',N''N''\)-tetraacetic acid (90 mg/ml) and glutathione (60 mg/ml), put immediately in an ice-water bath, centrifuged at 0 to 4°C, and stored at \(-25^\circ\)C until assayed.

Plasma CAs were assayed by a radioenzymatic method previously described,\(^3\) using the CAT-A-Kit (Upjohn Diagnostics, Kalamazoo, MI, USA). The limits of the assay sensitivity were 20 pg/ml for NE and 15 pg/ml for epinephrine. The between-assay coefficients of variation were 10% for NE and 7.5% for epinephrine. Blood pressure was measured with a Riva-Rocci sphygmomanometer. Mean arterial pressure was calculated as diastolic pressure plus one third of the pulse pressure. Statistical analysis was performed using Student’s \(t\) test for paired data (placebo vs verapamil).

Saline and verapamil infusion caused no side effects in any of the patients. Saline administration did not cause significant changes in heart rate or mean arterial pressure (Figure 1). Compared with placebo infusion, verapamil infusion did not affect heart rate but caused a significant fall in mean arterial pressure at 15 (\(p<0.025\)) and 20 minutes (\(p<0.005\); see Figure 1).

Although plasma CA levels showed great intraindividual and interindividual variability, verapamil infusion did not cause changes in plasma NE (Figure 2) or epinephrine levels (Figure 3) that significantly differed from those induced by saline infusion.

The results of our study confirm the hypotensive effect of Ca\(^{2+}\) channel blockade on the high blood pressure of patients affected by pheochromocytoma\(^2,4\) but do not support the hypothesis of an inhibition of

![Figure 1. Effect of placebo and verapamil infusions on mean arterial pressure (MAP) in four patients with pheochromocytoma. Values are means ± SEM. Single (\(p<0.025\)) and double (\(p<0.005\)) asterisks indicate significant difference between treatments.]
CA secretion by tumoral tissue in vivo. Nevertheless, an inhibitory action of Ca\(^{2+}\) channel blockers on pheochromocytoma secretion might become evident if larger doses of the drugs are given. The specific mechanism by which Ca\(^{2+}\) channel blockers induce their hypotensive effect in patients with pheochromocytoma cannot be ascertained by the present data, and more complex pharmacological studies are needed.

References

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Errata

The editors regret that the following acknowledgment was inadvertently omitted from the article by Given et al., “Prostaglandin E\(_2\) Analogue Elicits Renal and Hormonal Compensatory Mechanisms in Human Hypertension,” published in the June issue of Hypertension (8: 489–496, 1986). We are grateful to Dr. Thomas F. Ferris for acting as guest editor in the evaluation of this manuscript.

The names of three of the authors of the following article were omitted from the table of contents of the July 1986 issue. All authors’ names are correctly listed on the title page of the article.

Synthetic Atrial Natriuretic Factor Does Not Dilate Resistance-sized Arteries
George Osol, William Halpern, Belay Tesfamariam, Kengo Nakayama, Don Weinberg

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