L-Arginine and Salt Sensitivity

P.	Paolo	Coruzzi
G.	Gianluigi	Mossini

Istituto di Semeiotica Medica, Università di Parma, Italia

Paolo Coruzzi, Institute of Semeiotica Medica, University of Parma, Via Gramsci 14, I-43100 Parma (Italy)

Dear Sir,

A significant hypotensive role of L-arginine, a precursor of endothelium-derived nitric oxide (NO), has been demonstrated in both normal and hypertensive subjects [1, 2]. Recent data have been accumulated suggesting that, in Dahl rats, an increased dietary salt load resulted in increased activity of the NO system in salt-resistant (SR) but not in salt-sensitive (SS) rats. Thus, it was concluded that the development of SS hypertension may be secondary to an inability to enhance NO synthesis in response to increased dietary salt load [3]. In support of these results, the same authors also reported that long-term supplementation with endothelium-derived NO precursor L-arginine prevents the development of hypertension in genetically SS rats fed a high-salt diet.

We hypothesized that if a defect in NO production exists in SS hypertensive subjects given a high-salt diet, there should be a greater hypotensive response during L-arginine administration in these subjects with respect to that obtained in SR hypertensive patients. The study, approved by the local ethical committee, was done in 14 essential hypertensive patients (8 males) aged 20-52 years, classified as SS (n = 7) or SR (n = 7) subjects who gave informed consent. In agreement with previously described and well-reproducible results [4, 5], salt sensitivity was defined as a significant drop in mean arterial pressure (MAP) of 10% or greater, calculated as the difference between the average of 25 readings (from 8.00 to 10.00 h at 5-min intervals) under the high-salt (220 mmol/day for a week) and the low-salt (30 mmol/day for a week) periods; a change in blood pressure of 5% or less, including those subjects with a rise in pressure, was defined as an SR response.

Antihypertensive agents were withdrawn 14 days before the experiment.

At the end of the high-salt period, after an overnight fast and with the patients in the supine position, L-arginine was infused at 9.00 h into the left cubital vein at a dose of 8 mg/kg/min for 30 min. We used L-arginine monochloride (Damon Pharmaceuticals, Naples, Italy), which contains 30 g L-arginine monochloride in 100 ml sterile distilled water (pH 4.5-6.5). Blood pressure was recorded every 2 min with an automated monitor (SpaceLabs, Inc. Redmond, Wash., USA) on the upper right arm.

With respect to the baseline period (20 min), the infusion of L-arginine caused a rapid onset of hypotension in both groups: systolic, diastolic pressures and MAP (from 110 ± 4 to 104 ± 4 in SS and from 109 ± 4 to 104 ± 4 mm Hg in SR patients; mean $\pm$ SEM, paired t test, $p < 0.005$) were reduced, and this significant decrease persisted throughout the recovery period (20 min), after cessation of the infusion.

On the other hand, no significant correlation was found between the percent drop in MAP during the low-salt diet (salt sensitivity test) and the percent blood pressure reduction obtained in the 14 essential hypertensives during L-arginine infusion (Pearson's correlation coefficient, $r = 0.127$, $p < 0.66$).

Our results do not confirm previous data showing a selective hypotensive effect of L-arginine infusion in SS but not in SR rats [3]. In this human study, L-arginine administration was able to induce a similar blood pressure reduction in SS and in SR patients (mean decrease in MAP of 5 and 4.7%, respectively).

The documented hypotensive effect of L-arginine in both hypertensive groups may suggest that the defect in NO production does not selectively belong to SS human hypertension; this defect, corrected when hypertension is reversed [6], may presumably be secondary to a diminished production of endothelium-derived NO due to chronic hypertension per se [3, 6].

References

Petros AJ, Hewlett AM, Bogle RG, Pearson JD: L-Arginine-induced hypotension. *Lancet* 1991; 337:1044-1045.

Nakaki T, Hishikawa K, Suzuki H, Saruta T, Kato R: L-Arginine-induced hypotension. *Lancet* 1990;336:696.

Chen PY, Sanders PW: L-Arginine abrogates salt-sensitive hypertension in Dahl/Rapp rats. *J Clin Invest* 1991;88:1559-1567.

Weinberger MH, Fineberg NS: Sodium and volume sensitivity of blood pressure: Age and pressure change over time. *Hypertension* 1991; 18:67-71.

Sullivan JM: Salt sensitivity: Definition, conception, methodology, and long-term issues. *Hypertension* 1991;17(suppl I):I-61-I-68.

Luscher TF, Raij L, Vanhoutte PM: Endothelium-dependent responses in normotensive and hypertensive Dahl rats. *Hypertension* 1987;9:157-163.

KAIUEH

E-Mail karger@karger.ch Fax + 41 61 306 12 34

©1996 S. Karger AG, Basel 0028-2766/96/0722-0335\$8.00/0