Central Hypervolemia Does Not Invariably Modulate Calcium Excretion in Essential Hypertension

P.	Paolo	Coruzzi
G.	Gianluigi	Mossini

Institute of Semeiotica, University of Parma, Italy

Paolo Coruzzi, MD, Istituto di Semeiotica Medica, Università degli Studi di Parma, Via A. Gramsci, 14, I-43100 Parma (Italy)

Dear Sir,

It has been frequently suggested that an increased intake and excretion of sodium is a likely explanation for the increased urinary calcium excretion in essential hypertension [1], because calcium excretion has been demonstrated to correlate closely with sodium excretion in a number of experimental and clinical situations. More recently, MacGregor and Cappuccio [2] suggested that the increase in calcium excretion with increasing salt intake is not a direct effect of the increase in urinary sodium on tubular calcium excretion, but is secondary to an increase in 'central blood volume' induced by sodium retention. A hypothesis was consequently formulated linking central blood volume expansion to hypercalciuria, kidney stones and bone demineralization in essential hypertension.

Water immersion to the neck (WI) induces a marked isotonic-isooncotic central volume expansion without resorting to exogenous fluid infusion; hemodynamic and humoral [3] effects are similar to those obtained during intravenous short-term iso-tonic saline administration. By this maneuver, we were able to evaluate the actual role of central volume expansion per se in mediating the calciuretic event previously found in essential hypertensives during specific changes by either oral salt intake or saline administration. Our data permit a better analysis of the nonspecific (volume-induced) changes in urinary calcium excretion of hypertensive humans [4]. WI studies were performed in 41 essential hypertensive subjects; they consumed a controlled diet containing 180 mmol sodium/day and 25 mmol calcium/day. As previously described by Epstein et al. [5], WI-induced central hypervolemia identified two distinct populations with a markedly different natriuretic response. Twenty-nine patients exhibited a significant diuretic response ($p < 0.001$) and either appropriate or exaggerated natriuresis (from 121 ± 11 to 330 ± 24 $\mu\text{mol}/\text{min}$, $p < 0.001$). In the same hypertensive group ($n = 29$) a significant increase of urinary calcium excretion was found during WI (from 5.7 ± 0.5 to 10 ± 1.3 $\mu\text{Eq}/\text{min}$, $p < 0.05$). A marked suppression of PRA (from 1.4 ± 0.2 to 0.8 ± 0.1 $\text{ng}/\text{ml}/\text{h}$, $p < 0.001$) and plasma aldosterone (from 24 ± 3 to 11 ± 2 ng/dl , $p < 0.001$) and a significant increase of atrial natriuretic peptide (ANP) plasma levels (from 30 ± 4 to 62 ± 7 pg/ml , $p < 0.001$) were observed in these subjects at the end of WI.

In the remaining 12 hypertensives, WI produced a significant diuretic response ($p < 0.001$) but a sluggish or barely discernible increase ($p = \text{NS}$) in urinary sodium excretion (inappropriate response). The hypertensive subjects ($n = 12$) in whom WI failed to induce an appropriate natriuretic response exhibited a significant reduction of urinary calcium excretion during WI with respect to preimmersion levels (from 6.7 ± 0.7 to 4.4 ± 0.6 $\mu\text{Eq}/\text{min}$, $p < 0.003$). A

significant suppression of PRA (from 1.5 ± 0.4 to 0.7 ± 0.2 ng/ml/h, $p < 0.001$) and plasma aldosterone (from 27 ± 5 to 11 ± 2 ng/dl, $p < 0.001$) and a significant increase of plasma ANP (from 27 ± 6 to 50 ± 9 pg/ml, $p <$

KARGER

E-Mail karger@karger.ch Fax + 41 61 306 12 34 <http://www.karger.ch>

© 1997 S. Karger AG, Basel 0028-2766/97/0753-0368\$12.00/0

This article is also accessible online at: <http://BioMedNet.com/karger>

2.5

Fig. 1. Relation between urinary sodium and urinary calcium excretion expressed as WI/control period (CP) ratio in 41 essential hypertensive subjects.

-1.0

2.0

-0.5

0.5 1.0 1.5

log($\frac{Na}{WI} \frac{Na}{CP}$)

0.01) were also found during WI in this hypertensive group.

Finally, a highly positive correlation ($r = 0.81$, $p < 0.001$) between urinary sodium and calcium excretion was detected during WI in the whole hypertensive population (fig. 1). The quite identical increase in urine flow (i.e. ADH suppression), in ANP plasma levels and the significant suppression of PRA-aldosterone system in both hypertensive groups may strongly suggest a similar degree of central hypervolemia attained during WI. On the other hand, a significant increase in urinary calcium excretion was found only in those hypertensive patients showing either an appropriate or exaggerated natriuretic response.

Our data suggest that central volume expansion per se does not invariably control calcium excretion; sodium handling appears to play a pivotal role in modulating calcium excretion during central volume expansion.

References

Kaplan NM, Meese RB: The calcium deficiency hypothesis of hypertension: A critique. *Ann Intern Med* 1986;105:947-955.

MacGregor GA, Cappuccio FP: The kidney and essential hypertension: A link to osteoporosis? *J Hypertens* 1993;11:781-785.

Coruzzi P, Musiari L, Biggi A, Ravanetti C, Vallisa D, Montanari A, Novarini A: Role of renal hemodynamics in the exaggerated natri-uresis of essential hypertension. *Kidney Int* 1988;33:875-880.

Coruzzi P, Biggi A, Musiari L, Ceriati R, Mosconi GL, Guerra A, Novarini A: Calcium and sodium handling during volume expansion in essential hypertension. *Metabolism* 1993;42: 1331-1335.

Epstein M, Loutzenhiser R, Levinson R: Spectrum of deranged sodium homeostasis in essential hypertension. *Hypertension* 1986;8:422-432.

Central Hypervolemia Does Not Invariably Modulate Calcium Excretion in Essential Hypertension

Nephron 1997;75:368-369