REVISTA ESPAÑOLA DE FISIOLOGIA, 36, 237-242. 1980

The Effect of Orthostatism, Passive Tilting and Recumbent Exercise on Renin Release

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(Received on May 14, 1979)

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Three postural tests, orthostatism, passive tilting and recumbent exercise, were applied to fourteen normal volunteers. Orthostatism and tilting produce a significant increase in plasma renin activity (PRA) and plasma renin concentration (PRC), without changes in plasma renin substrate concentration (PSC). Recumbent exercise induces an inhibition of PRA and PRC and does not changes PSC. The present study seems to suggest that sympathetic activity and intravascular blood volume could play an important role in the responses of the renin-angiotensin system to postural changes.

Recently, it has been demonstrated (1, 3, 16, 18) that orthostatism produces an increase in plasma renin activity (PRA) and plasma renin concentration (PRC) without changes in plasma renin substrate concentration (PSC). However, the mechanisms through which the assuming of an upright position stimulates the renin secretion are not clear. Orthostatism results in a blood volume depletion (12, 14) and an increase in sympathetic activity (5), and there is disagreement as to whether the response of the reninangiotensin system to orthostatism is related to changes in intravascular volume, changes in renal function, or to a direct effect of the nervous system on renin secretion (6, 10, 13, 15).

In the present study, three tests have been employed: orthostatism, passive tilting and recumbent exercise, in order to obtain further information about the mechanism of renin release in postural change under physiological conditions.

Materials and Methods

Materials. The investigation was carried out on fourteen healthy human volunteers, 7 males and 7 females, ages ranging from 20 to 30, without diet control. The females were between the 7th and 12th day of their menstrual cycle and had never used oral contraceptives.

Three functional tests: orthostatism, passive tilting and recumbent exercise, were applied to all subjects. The basal level was obtained for each subject in

each test in the following way: on the testing day the subjects awoke at 8 a.m. and without having eaten breakfast came to the laboratory. At 9 a.m. the volunteers lay on a bed during one hour in absolute repose and at the end of this period the basal level was obtained.

In the orthostatism the subjects were allowed to deambulate during three hours. In the passive tilting each of the fourteen subjects was placed on a tilt table tilted at 80-85° during three hours in absolute repose. For the recumbent exercise, each subject alternated 15 min of arm and leg movements with 15 min of rest during three hours.

Sample collections. Urine and blood samples were taken at the end of the basal period and at the end of the corresponding test.

Blood samples were divided in two aliquots of 10 ml each. One, with EDTA-Na_2 as an anticoagulant and angiotensinases inhibitor, was centrifuged at 4° C during 10 min at 3,000 r.p.m. The plasma obtained was then frozen to —20° C until the PRA, PRC and PSC were determined.

The other 10 ml blood aliquot was centrifuged at 3,000 r.p.m. and the resulting serum was used for creatinine and osmolarity determination.

Creatinine and vanil-mandelic acid excretion were determined in the urine samples collected.

Methods. Plasma renin activity (PRA) was determined by radioimmunoassay of angiotensin I generated during two hours of plasma incubation at 37° C and expressed as ng/ml/h (7).

Renin and renin substrate concentrations (PRC and PSC respectively) were calculated by the simple kinetic method previously described (2).

Osmolarity was measured in a Medical Inst., 3 Lx model osmometer. Endogenous creatinine clearance was determined by the method of LYNCH (9), and urinary vanil-mandelic excretion was measured by the GLITOW method (4).

Statistical analysis. All results were expressed as mean + S.E.M. Correlations were calculated by using multiple regression analysis. Statistical evaluation was performed using the Student's «t» test.

Results

Plasma renin activity (PRA) and plasma renin concentration (PRC) show a significant increase in orthostatism (fig. 1) and tilting (fig. 2) ($p < 0.001$), without significant variations in plasma renin substrate concentration (PSC) (fig. 1 and 2).

Endogenous creatinine clearance shows a significant decrease in orthostatism (fig. 1) and tilting (fig. 2) ($p < 0.01$) compared with basal values, urinary vanil-mandelic excretion is increased in orthostatism (fig. 1) ($p < 0.01$), while no changes were found in tilting (fig. 2).

As can be seen in fig. 3, the recumbent

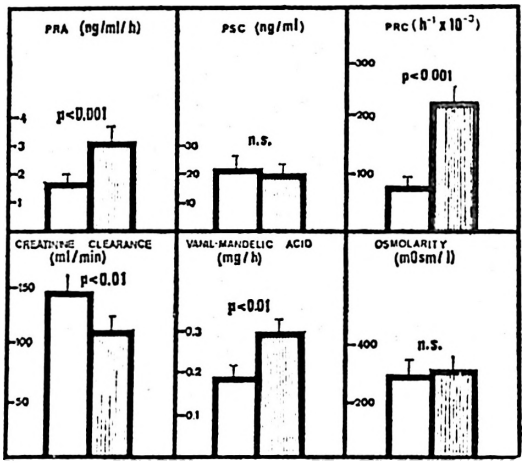

Fig. 1. *Effects of orthostatism on PRA, PRC, PSC, endogenous creatinine clearance, urinary vanil-mandelic excretion and plasma osmolarity.*
Open bars: basal values. Shaded bars: stimulated values.

exercise induces a significant decrease in PRA ($p < 0.001$) and PRC ($p < 0.01$) without significant variations in PSC.

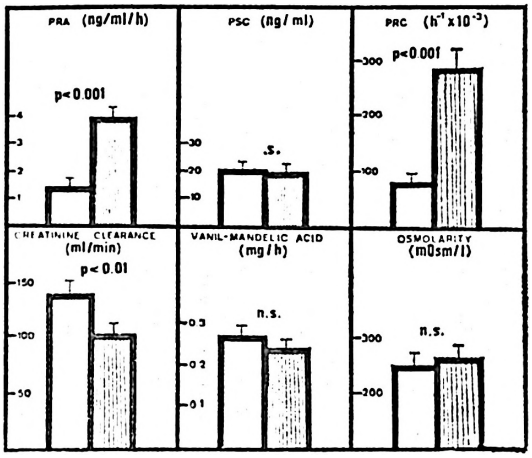

Fig. 2. *Effects of passive tilting on PRA, PRC, PSC, endogenous creatinine clearance, urinary vanil-mandelic excretion and plasma osmolarity.*
Open bars: basal values. Shaded bars: stimulated values.

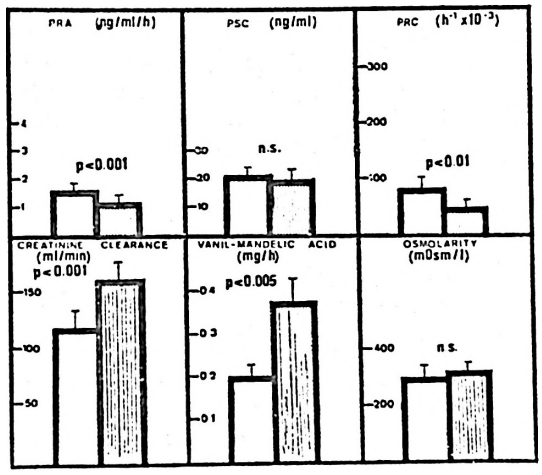

Fig. 3. *Effects of recumbent exercise on PRA, PRC, PSC, endogenous creatinine clearance, urinary vanil-mandelic excretion and plasma osmolarity.*
Open bars: basal values. Shaded bars: stimulated values.

Moreover, in this test, endogenous creatinine clearance and urinary vanil-mandelic excretion were increased significantly ($p < 0.001$ and $p < 0.005$ respectively). The rise in urinary excretion of vanil-mandelic acid is not due to an increase in the glomerular filtration rate, since in recumbent exercise the renal depuration of vanil-mandelic acid was greater than the creatinine clearance.

There were no changes of osmolarity in any of the tests used in the present study (fig. 1, 2 and 3).

Discussion

Orthostatism induces a significant increase in PRA and PRC without changes in PSC (fig. 1). The actual mechanism of these acute changes are not yet clear. Acute changes in «effective» blood volume due to pooling of blood in the lower extremities (3, 12, 14) could produce a significant depression of renal arterial perfusion or stimulate the autonomic nervous system. The blood volume depletion could result in a renal creatinine clearance decreased in this test (fig. 1), which seems to be due exclusively to postural change since in the tilting test we have found a similar fall in creatinine clearance (fig. 2). This volume depletion could increase the renin secretion in two forms: in stimulating the presoreceptor placed on afferent arteriole (17) or in decreasing the sodium load to macula densa (20).

The increase in urinary vanil-mandelic excretion after orthostatism (fig. 1) could be due to an elevation in catecholamine release. However, COHEN *et al.* (3) suggest that the catecholamine release is secondary to postural change, while KOZLOWSKI *et al.* (8) suggest that this elevation is due to exercise. The present results show that this elevation in catecholamines seems to be due to exercise and not to postural change. Indeed, in the tilting test we did

not find changes in urinary vanil-mandelic excretion from control values (fig. 2), while in recumbent exercise it shows a significant increase ($p < 0.005$) (fig. 3). Then, it can be assumed that if the increase in vanil-mandelic excretion is secondary to catecholamine release, which could also explain the increase in renin release induced by orthostatism (19).

In passive tilting a raise in PRA and PRC without changes in PSC was found (fig. 2). The increase in PRC must be secondary to volume depletion since in this test the glomerular filtration rate decreases, as is shown by the significant fall in renal creatinine clearance (3, 21) (fig. 2).

In the test of recumbent exercise, PRA and PRC decrease significantly, and do not show modifications in PSC (fig. 3). COHEN *et al.* (3), who performed this test on seven subjects offered inconsistent results: three subjects exhibited a raise in PRA; three did not show any changes, and only one showed an inhibition in PRA. The present work found a significant inhibition in PRA and PRC in thirteen out of the fourteen subjects who undertook the test. It is quite difficult to explain from the present results the striking effects of recumbent exercise on PRA and PRC. The inhibition on renin release might be due to a raise in renal perfusion pressure (21) which could induce the elevation in endogenous creatinine clearance found in this test (fig. 3) but the increase in vanil-mandelic excretion must also be taken into account for it could well stimulate renin secretion (fig. 3).

It has been suggested (11) that in orthostatism the variations in renin release could be due to hemoconcentration. However, since the present tests do not show any osmolarity changes, this effect must be discarded as a factor in renin secretion (fig. 1, 2 and 3).

Thus, the present study demonstrates that acute changes in posture are associated with closely correlated changes in PRA and PRC. To varying degrees, sympathetic activity and intravascular blood volume play a role in the responses of these parameters to postural variations.

Resumen

En 14 individuos normales se han realizado tres pruebas posturales: ortostatismo, inclinación y ejercicio en supino. Las dos primeras pruebas producen un aumento significativo en la actividad plasmática de renina (APR) y en la concentración plasmática de renina (CPR) sin cambios en la concentración plasmática de sustrato (CPS). La prueba de ejercicio en supino induce una inhibición de APR y CPR, sin cambios en CPS. De los resultados del presente trabajo se desprende que la actividad simpática y el volumen intravascular pueden tener un papel importante en la respuesta del sistema renina-angiotensina al cambio postural.

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