**Gadolinium Effect of Experimental Orthostatic Hypotension**

Zarco Olvera G.,
Pastelín Hernández G.

Departamento de Farmacología,
Instituto Nacional de Cardiología "Ignacio Chávez",
Tlalpan, México D.F., México.

**ABSTRACT**

**Introduction:** Gadolinium is a lanthanide that blocks stretch-activated ion channels (SAIC's) within the vascular endothelium. Stimulation of such SAIC's increases nitric oxide release, therefore, vasodilation is observed.

**Objective:** Investigate how can gadolinium administration modify arterial pressure and cardiac frequency in a experimental orthostatic hypotension model.

**Materials and methods:** Six mongrel dogs (18 ± 2 kg) were anesthesized with sodium pentobarbital (35 mg/kg, i.v.). The animal was artificially ventilated with a positive pressure pump. The dog was placed in dorsal decubitus at a special table, were inclination angles were varied (20, 40, 60 and 90°). Gadolinium was administrated at 5 mg/kg, i.v., after control inclination changes. Arterial pressure was recorded with a quimiograph. DII electrocardiogram was registered using a VR-6 polygraph. Left intraventricular pressure and dP/dt were also recorded by placing a femoral catheter. Results: Mean arterial pressure prior to gadolinium administration was 93 mmHg at 0°, 89 mmHg at 20°, 79 mmHg at 40°, 75 mmHg at 60° and 65° mmHg at 90°. After gadolinium administration, mean arterial pressure values were 80, 75, 73, 73 and 45 mmHg, respectively. Therefore, gadolinium does not induce changes in arterial pressure as previously induced by postural changes in our experimental model.

**Conclusion:** Gadolinium administration, after a change in position, does not statistically decreases arterial pressure. By such, SAIC's stimulation does not play a key role in the experimental orthostatic hypotension.

**INTRODUCTON**

Orthostatic hypotension is characterized by a decrease in systolic pressure greater than 20 mmHg or more than 10 mmHg in diastolic pressure by sudden changes in position from clinostatism to orthostatism. This decrease is commonly observed in the elderly and it's frequently accompanied with sudden heart attack [1-3].

For the latter to happen, a distension of the heart vessels should occur and it's probably due to a smooth muscle relaxation within these vessels, generated by blood flow. These signals regulate the vascular endothelium and, in turn, facilitate the release of endothelium-derived vasoactive substances such as prostaceline (PI2), adenosine (ADO), nitric oxide (NO), endothelins, ATP, histamine, among others. Additionally, activation of K+ and Ca2+ - selective channels as well as stretch-activated ion channels takes place.

NO is generally regarded as an endogenous vasodilator and is a chemical component in humans, animals, plants, etc. Within the vessels, is a transmitting molecule, synthesized in the endothelial cells and act on adjacent smooth muscle cells in order to keep vasodilation and blood flow. L -arginine is NO precursor, a
process in which nitric oxide synthase (NOS) actively participates. NOS have at least two isoforms: one located in the vascular endothelium and neurons, which has been labeled as the constitutive isoform, acting in short periods, which leads to vasodilation. The so-called inducible isoform is found in macrophages, synthesizing NO in large quantities during a long period of time so bacteria and parasites could be destroyed.

Constitutive NOS isoform is inactive in the endothelium until a rise in Ca\(^{2+}\) concentration is observed. In the endothelial cells, agonists such as acetylcholine, ADP, bradikinine, or stress can act as stimuli that lead to increases in intracellular Ca\(^{2+}\). Calmodulin, a Ca\(^{2+}\) -fixing protein, binds to Ca\(^{2+}\) and a Ca\(^{2+}\)-calmoduline complex is formed. Once it has done so, this complex activates inducible NOS isoform, which arises NO concentrations until Ca\(^{2+}\) is depleted. At the smooth muscle, NO can activate an enzyme known as soluble guanylyl cyclase (sGC), converting by so GTP to cGMP.

All the previously describe functions are Ca\(^{2+}\) - dependent, whose intracellular Ca\(^{2+}\) concentration is flow-triggered. One possibility for this increase is the activation of stretch-activated ion channels, which are located on the cell membrane of the vascular endothelium, being these channels affected by shear-stress [4].

Gadolinium (Gd) is a metallic element (lanthanide) than in its oxidation 3+ state is a non-selective blocker of stretch-activated ion channels [5,6].

If stretch-activated ion channels have a significant role in postural hypotension mechanisms, gadolinium administration will block the hemodynamic effects produced by sudden changes from orthostatism to clinostatism.

MATERIALS AND METHODS
For this study, we employed six mongrel dogs (18 ± 2 kg), with no sex preference, anesthetized until surgical anesthesia was achieved (sodium pentobarbital, 33 mg/kg, i.v.). We performed a tracheotomy to place a ventilation cannula (tidal volume 30 mL/kg). The femoral vein was cannulated to administrate an isotonic saline solution (ISS). The animal was placed on dorsal decubitus on a special table, in which position was changed by varying inclination angles (20, 40, 60 and 90°, respectively). ECG on DII, left intraventricular pressure and dp/dt were recorded on a VR-6 polygraph. On a quimiograph, we recorded arterial pressure. Gadolinium (III) chloride as continuously infused.

Results are expressed as mean ± MES. Statistically significance was assessed using one-way ANOVA followed by Student's \(t\)-test. P values less than 0.05 were considered as statistically different.

RESULTS
Our results showed that mean arterial pressure (MAP) was 90 mmHg at 20°, 88 mmHg at 40°, 79 mmHg at 60° and 65 mmHg at 90°. These changes are more evident on the first 30 seconds, and recovery is observed. Cardiac frequency tends to be increased, although with no statistically significantly differences.

Gadolinium administration did not modify the observed changes on MAP induced in our model by postural changes.

CONCLUSIONS
Gadolinium administration, at a sudden position change, did not significantly modify MAP decrease on our experimental model of orthostatic hypotension.

FIGURES CAPTIONS
**Figure 1:** Effect of sudden position changes on arterial pressure. Value represents mean ± MES; N=6; P<0.05

**Figure 2:** Effect of sudden position change from clinostatism to orthostatism on left intraventricular pressure. Value represents mean ± MES; N=6; P<0.05

**Figure 3:** Effect of sudden position change from clinostatism to orthostatism on mechanic systole duration. Value represents mean ± MES.
BIBLIOGRAPHY


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