IS RED CELL ACETYLCHOLINESTERASE RELATED WITH ARTERIAL HYPERTENSION?

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In addition to the suggestive involvement of the noradrenergic system, there is substantial evidence that blood pressure regulation in the man and some other mammals (e.g. cat, dog and rat) is dependent on the cholinergic activity. Many experimental and some clinical studies have demonstrated that the stimulation of the central cholinergic system by direct receptor agonists or acetylcholinesterase (AChE) inhibitors, mediates a rise in arterial pressure (Fig. 1).

According with these findings (still questionable), the activation of the cholinergic system might play a role in the pathogenesis of essential hypertension (EH) as well as in SHR, apparently via increased peripheral sympathetic activity. Meanwhile, other studies have claimed to a suppressed parasympathetic activity in the SHR and humans with essential hypertension.

The AChE activity might be interpreted as an index of the parasympathetic innervation if it were more specific than observed; the AChE activity is identified in regions containing pacemaking and conducting tissues and, also, in red blood cells and other non-neural tissues. Nevertheless, pharmacologic and kinetic studies in all molecular forms of AChE have identified a remarkable similarity in their enzymatic sites. Beyond this, a high level of homology is shown between the AChE from human erythrocytes and neuromuscular junctions.

Although the presence of AChE activity in non-neural regions seems to be a factor hardly involved in the pathogenic mechanisms of hypertension, a very significant elevation in red cell AChE activity has been detected by us in humans with essential hypertension. This observation was not confirmed by others, being the discrepancy with our results attributed to differences in technical methodologies or the patients studied. Recently, we could reaffirm an increase in AChE activity in hemoglobin-free membranes from hypertensive patients without evidence of renal insufficiency.

Acetylcholinesterase from human erythrocytes is a membrane bound enzyme with still obscure function. Among other mechanisms, there is increasing evidence that AChE might be involved in sodium exchanges across the erythrocyte and other cell membranes. However, if the increase on red cell AChE activity is related to the well known altered cation transport in patients with EH is still a matter to further studies.

Furthermore, it might be conjectured that erythrocyte AChE activity is dependent on cell membrane alterations, consequent to the external or internal effect of some released factor, or viewed as reflection of a localized change in lipid-protein interactions in EH.

Acetylcholinesterase is a lipid-glycoprotein complex molecule with an asymmetrical orientation on the outer surface of the erythrocytes; the allosteric properties of the enzyme depend on the fatty acid composition of the red cell membrane. Any change in the membrane lipid composition, as such as a modification in the transmembrane potential, might interfere with the hydrophilic environment and the enzymatic activity of acetylcholinesterase. These facts would confirm that red cell AChE sensitivity probes the dynamics of the membrane integrity and its dependence on the membrane fluidity. No data are yet available to steadily confirm or deny these possibilities in what concerns the increased activity of AChE in red cells of EH patients.

Figure 1: Cholinergic mechanisms in primary hypertension
REFERENCES


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