

New trends in hypertension research

Maria Dorobantu

M.D, PhD, FESC, FACC
Editor-in-Chief of the Journal of Clinical Hypertension

Through its complex pathogenic interactions with risk factors for atherosclerosis or other diseases such as chronic kidney disease, diabetes mellitus and also through its cerebral, cardiac and renal complications, hypertension offers the most complex model of basic and clinical research.

As a consequence, numerous research communities dedicate their activity to unravel the pathogenic mechanisms involved in the appearance and progression of this disease.

When discussing pathogeny, risk factors for hypertension or its complications, the latest research has turned to genetic analysis to identify predisposing phenotypes for hypertension and its complications or, even further, to transcriptomics, the study of transmission of genetic information through mRNA, to proteomics or metabolomics in trying to understand the mechanisms through which the processes generated by genetic information are finalized. Perhaps this type of in-depth exploration is only at its very beginning.

Another broad research field in the study of hypertension is represented by the vascular endothelium, a vast organ fairly ignored in the past.

Moreover, researchers have a special interest in discovering new antihypertensive molecules in order to obtain the ideal therapeutic agent (efficient, without adverse effects and cost-effective). Despite being far from reaching the ideal, considerable efforts are made to obtain molecules with new mechanisms of action (*e.g.* prorenin blockers, AT₂ receptors activators) and there is even contemplation of a vaccine against angiotensin I and II. The study of such molecules is still in its laboratory phase or at the most in the first phase of clinical trials.

However, there is apparently higher success obtained through the combination of certain molecules with known pharmacological mechanisms such as neutral

endopeptidases (NEP) dual inhibitors with renin-angiotensin system inhibitors. The association of NEP dual inhibitors with ACE inhibitors although efficient, is not recommended due to the high risk of angioedema. The combination of NEP dual inhibitors with AT₁ receptor blockers (sartans) seems to be overall more successful. Therefore, the combination of valsartan with sacubitril seems particularly efficient without notable adverse reactions, including in the treatment of heart failure (the PARADIGM study).

Certainly, initial expectations are not always validated, but in research questioning the truth of the moment can lead to new ideas.

Positive and sometimes negative results in relation to the proposed objectives are published in prestigious journals of hypertension, cardiology, biology, nephrology, which are currently present worldwide in significant numbers. Why would there be any need for one more? The answer is the concept that the scientific committee proposes in this new publication – “Journal of Hypertension Research” – which is dedicated exclusively to basic and clinical research articles. Therefore, its structure (editorials, expert reviews, original articles etc.) offers a means of expression to all specialists involved in arterial hypertension as an interface in-between specialities (cardiology, internal medicine, nephrology, diabetology, pediatrics, endocrinology etc.).

We hope that our scientific message will encourage further research and publishing.

References

1. Ruilope LM, Dukat A, Böhm M, *et al.* Blood-pressure reduction with LCZ696, a novel, dual-acting inhibitor of the angiotensin II receptor and neprilysin: a randomized, double-blind, placebo-controlled, active comparator study. *Lancet* 2010; DOI:10.1016/S0140-6736(09)61966-8.

2. Laurent S, Schlaich M, Esler M. New drugs, procedures, and devices for hypertension. *Lancet*. 2012 Aug 11;380(9841):591-600.
3. Seed A, Kuc RE, Maguire JJ, Hillier C, Johnston F, Essers H, de Voogd HJ, McMurray J, Davenport AP. The dual endothelin converting enzyme/neutral endopeptidase inhibitor SLV-306 (daglutril), inhibits systemic conversion of big endothelin-1 in humans. *Life Sci*. 2012 Oct 15;91(13-14):743-8. Epub 2012 Mar 28.
4. James PA, Oparil S, Carter B.L. *et al.* - Evidence-Based Guideline for the Management of High Blood Pressure in Adults Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8), AMA. 2014;311(5):507-520.
5. O'Donnell CJ, Nabel EG. Genomics of cardiovascular disease. *N Engl J Med*. 2011 Dec 1;365(22):2098-109.