0428
Binding mechanism of pharmacological inhibitors and antihypertensive food peptides to human somatic angiotensin I-converting enzyme (ACE)
Gabrielle Zeder-Lutz (1), Faïza Zidane (2), Kaddidja Legrani (2), Annie Dary (2), Laurent Miclo (2), Danièle Altshu (1), Céline Calcir-Kiefer (2)

Angiotensin I-converting enzyme (ACE), which is a key enzyme of the renin-angiotensin system, is one of target for antihypertensive molecules. Indeed, ACE is well known for its involvement in hypertension which is the main risk factor involved in the development of cardiovascular and kidney diseases and is a major cause of morbidity and mortality. Currently, many pharmacological ACE inhibitors (captopril, lisinopril...) are used for hypertension treatment, but their administration over a long period is associated with some undesirable side effects. Furthermore, there are many publications dealing with antihypertensive peptides from food proteins. ACE-inhibitory peptides, generated by hydrolysis of food proteins, may be a natural alternative to prevent hypertension appearance. However, among the bioactive peptides published in the literature as ACE inhibitors, a very small number really displays an antihypertensive activity in vivo in animals. Moreover, their mechanism of action at the molecular level is still misunderstood. The objective of our work was to characterize the molecular interactions between ACE and some peptides described as ACE-inhibitors, which have or not a true antihypertensive activity in vivo. For this purpose, a methodology already developed in our teams was employed (Zidane et al., 2013). It is based on the use, for the first time, of Biacore® technology (SPR). This real time technology provides some important molecular information such as the rate constants of association and dissociation, the stoichiometry and the site of the interaction on ACE. In our study, the direct interaction between ACE and inhibitors (without substrate or ligand) showed dissociation constants (Kd) of the same order of magnitude as IC50. Moreover, the formed ACE-inhibitor complexes are unstable. Given these results, it is difficult to attribute significant antihypertensive effect demonstrated in vivo for these peptides (for example IPP, VPP) to the only ACE inhibition.

0273
Beneficial effect of sequential nephron blockade on central pressure and large artery remodeling in resistant hypertension
Helene Beaussier (1), Marie Briet (2), Michael Frank (3), Guillaume Bobrie (3), Severine Peyrard (4), Pierre François Plouin (3), Stephane Laurent (5), Michel Azizi (2), Pierre Boutouyrie (5)

Objective: We have previously shown that combined renin-angiotensin system blockade (RB) was less effective than sequential-nephron blockade (SNB) for controlling BP in resistant hypertension (RH). Whether this is accompanied with an improvement in the mechanical properties of large arteries is unknown.

Design and Method: Pts with daytime ambulatory SBP/DBP (dASBP/dADBP) >135 and/or 85 mmHg, despite 4 week with irbesartan (Irb)+HCTZ-amlodipine, were randomised to SNB (n=82) or RB (n=82) for 12 weeks. Central pulse pressure (CPP) and carotid-femoral pulse wave velocity (PWV) were measured by aplanat tonometry. High-resolution echotracking system (Walltrack®) was used to measure carotid artery diameter (Dcca), wall thickness (WT), circumpart wall stress (CWS), and stiffness. All parameters were measured at baseline and week 12.

Results: Baseline clinical characteristics did not differ between groups. dASBP decreased more in SNB (–19±12 mmHg) vs RB (–8±13 mmHg, p<0.01) and CPP (–19±12 mmHg) vs RB (–8±13 mmHg, p<0.001) after adjustment on baseline CPP and deltaMeanBP. CCA stiffness and PWV decreased similarly in both groups. Dcca decreased more in SNB (–5±2.0 kPa) vs RB (–2.0±1.5 kPa, p=0.001).

Conclusions: In RH pts, a tit strategy based on SNB improved CPP to a greater extent than a RB strategy. This may lead to a better target organ damage prevention and CV outcome. SNB improved CWS. Whether this effect is due aldosterone blockade or sodium depletion remains to be investigated.

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Effect of nebivolol treatment during pregnancy on the genital circulation, fetal and postnatal development in the wistar rat
Kassem Alotaama (1), Yassine Mallem (1), Eric Betti (2), Jean-Claude Desfontis (1)
(1) ONIRIS, UPS5304, Nantes, France – (2) ONIRIS, Unité d’Anatomie Comparée, Nantes, France

Introduction: This study was designed to evaluate the effect of nebivolol (vs. bisoprolol) on the genital circulation, fetal growth and postnatal development in wistar rat.

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