TREATMENT TARGET IN HYPERTENSION

SACUBITRIL/VALSARTAN IMPROVES SEXUAL FUNCTION AND FIBROSIS OF THE CLITORAL AND VAGINAL TISSUES IN FEMALE SPONTANEOUSLY HYPERTENSIVE RATS

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Objective: Female sexual dysfunction is common in hypertension. The effects of sacubitril/valsartan (SAC/VAL) as a potential therapy for hypertension and heart failure have not been studied in relation to sexual function and genital fibrosis in female spontaneously hypertensive rats (SHRs). To evaluate the effect of SAC/VAL on sexual function and genital fibrosis in female SHRs.

Design and method: Thirty female SHRs were administered VAL (30 mg/kg/day), SAC/VAL (60 mg/kg/day) or saline. Ten normotensive female Wistar-Kyoto (WKY) rats were included in the control group. We assessed estrous cyclicity and sexual behavior in the female rats. In addition, the morphology of clitoral and vaginal tissues was evaluated by histological analyses. Western blotting and enzyme-linked immunosorbent assays were used to assess the levels of fibrotic markers in vaginal and clitoral tissues. Furthermore, the protein levels of phosphatase and tensin homolog deleted from chromosome 10 (PTEN), phosphoinositide-3-kinase (PI3K) and AKT expression were measured by western blotting. We investigated the effect of SAC/VAL on the fibrosis of vaginal and clitoral tissues, estrus cyclicity and sexual behavior, including sexual receptivity (lordosis quotient and intensity), plus the number of proceptive and aggressive events.

Results: SAC/VAL treatment improved hypertension-induced sexual dysfunction, exhibited as a prolonged estrus phase, increased receptivity and proceptive events, and decreased aggressive events, compared to those of VAL treatment and control SHRs without treatments. In addition, SAC/VAL-treated SHRs had lower levels of fibrotic markers than the levels of VAL-treated SHRs or SHRs without treatment. Moreover, SAC/VAL decreased p-PTEN expression and increased p-PI3K and p-AKT expression at the protein level compared to those in VAL treatment alone.

Conclusions: SAC/VAL treatment is superior to VAL treatment in attenuating sexual dysfunction and fibrosis of vaginal and clitoral tissues, which may be related to the PTEN/PI3K/AKT pathway.

VASCULAR STIFFNESS AS AN TARGET OF OPTIMAL ANTIHYPERTENSIVE THERAPY

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Objective: To evaluate the 24-hour blood pressure (BP) control and the effect of the triple fixed combination (TFC) amlodipine / indapamide / perindopril on the arterial stiffness parameters according to 24-hour blood pressure monitoring (ABPM) data in patients with uncontrolled hypertension (HTN).

Design and method: The study involved 78 patients with insufficient BP control, against the background of various combination therapy. All patients received TFC amlodipine / indapamide / perindopril. The patient’s condition was assessed during 4 observation visits: visit 1 - inclusion, visit 2 - 4 weeks, visit 3 - 12 weeks, visit 4 - 24 weeks observation. At each visit, the achievement of the target BP level < 130/80 mmHg was assessed, as well as the effect of therapy on the parameters of arterial stiffness (pulse wave velocity (PWV), pulse pressure (PP), augmentation index (Aix), arterial stiffness index (ASI)) and central aortic pressure parameters (systolic aortic pressure (SBP), central pulse pressure (PP)) according to ABPM.

Results: In subjects with HTN with insufficient antihypertensive therapy the initial office BP was 160.8 ± 10.3/95.5 ± 9.1 mmHg. After 24 weeks of therapy with a TFC there was a significant decrease in blood pressure to 121.3 ± 5.5 / 73.6 ± 4.2 mmHg (p < 0.001). According to ABPM data, mean values of daily BP significantly (p < 0.001) decreased from 153.9 ± 9.04 / 8.38 ± 9.18 to 120.3 ± 4.7 / 73.4 ± 4.7 mm Hg. Data analysis showed a decrease PWVao (11.39 ± 1.32 m/s vs 9.98 ± 0.91 m/s, p < 0.05) as well as ASI (174 (138, 253) vs 139 (107.196) mmHg; p < 0.001) and Aix -29.9 (-41,12) vs -33,7 (-53, 9) p < 0.05. There was a statistically significant decrease in the parameters the central pressure in the aorta (Fig.1).

Conclusions: In patients with HTN and previous ineffective antihypertensive therapy the FTC amlodipine / indapamide / perindopril provided high antihypertensive effectiveness. Parameters of vascular stiffness can serve as criteria for quality control of blood pressure and can be used to assess the effectiveness of antihypertensive therapy.

APPROPRIATENESS OF CARDIOVASCULAR PREVENTIVE MEDICATION IN OLDER PEOPLE: A QUALITATIVE RAM-STUDY

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Objective: In clinical practice and science, there is debate for which older adults the benefits of cardiovascular preventive medications (CPM) still outweigh the risks in older age. Therefore, we aimed to assess how various clinical characteristics influence the judgment of appropriateness of CPM (i.e. antihypertensive treatment) in older adults.

Design and method: With the RAND/ University of California at Los Angeles appropriateness Method (RAM) the appropriateness of CPM for adults = > 75 year was assessed with regard to clinical characteristics (cardiovascular history, complexity of health problems, age, side-effects and life expectancy). A multidisciplinary panel (n = 14 panelists) received an up to date overview of the literature, and judged the appropriateness of starting and stopping cholesterol lowering medication, antihypertensives, and platelet aggregation inhibitors, on 1- to 9 point Likert scales (1 = extremely inappropriate; 9 = extremely appropriate), for various clinical scenarios. There were two rating rounds, with one face-to-face discussion in between. The appropriateness judgments were based on the median panel rating and level of disagreement.

Results: The panelists emphasized the importance of the individual context of the patient for appropriateness of CPM. They judged that in general, a history of atherosclerotic cardiovascular disease (ASCVD) strongly adds to the appropriateness of CPM, while increasing complexity of health problems, presence of hindering or severe side-effects, and life expectancy < 1 year all contribute to the inappropriateness of CPM. Age had only minor influence on the appropriateness judgments. The appropriateness judgments were different for the three types of CPM. The literature, time-to-benefit, remaining life-expectancy, number needed to treat, and quality of life, were major themes in the panel discussions. The considerations to stop CPM were different from the considerations not to start CPM.

Conclusions: Next to the patients’ individual context, which was considered decisive in the final decision to start or stop CPM, there were general trends of how...