Klippel-Feil syndrome is clinically characterized by a short neck, low posterior hairline and limited neck movement.

Conclusions: The present study provides sufficient evidence that KFS is caused by a mutation in the MEOX1 and GDF3,GDF6 genes. This issue which has a scientific and clinical interest require an interdisciplinary approach that will ensure efficient planning of resources with involving of a performance type of management aimed to improve the situation in this category of patients as soon as possible.

Key words: cranio-vertebral anomalies, variability

285. ALDOSTERONE SYNTHASE GENE CYPIIB2 -344C/T POLYMORPHISM AND GENDER ASPECTS OF ANTIHYPERTENSIVE TREATMENT EFFICACY

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Background. There is growing evidence that high interindividual variability in response to blood-lowering medications is partially explained by genetic factors. Multiple genes, encoding blood pressure-regulating drug receptors and receptor response mechanisms are Associated with different results in achieving target BP values under antihypertensive treatment. Despite some consistent research, showing that various genetic single-nucleotide polymorphisms (SNP) may affect antihypertensive treatment efficacy, study results in this field continue to be conflicting and provide disparate results [1]. Aldosterone is the key mineralocorticoid rennin-angiotensin-aldosteron system (RAAS) hormone, affecting distal nephron to regulate sodium resorption, excretion of potassium, and intravascular volume. So the associations between aldosterone synthase gene polymorphism and hypertension would thus be of significant interest. Studies about the potential role of aldosterone synthase gene CYP11B2 (-344T/C) polymorphism and primary hypertension demonstrated controversial results. Some results indicate that -344T/C polymorphism has an impact on hypertensive target organ damage and the response to antihypertensive drugs [2 YP41.B2 (-344T/C) gene. For example, studies have polymorphism is Associated with the antihypertensive response to diuretics and RAAS-inhibitors [5 □7]. Due to small study samples and controversial results, even in conditions of one population, it remains unclear, whether CYP11B2 -344T/C single-nucleotide polymorphism (SNP) affects antihypertensive treatment response and long-term treatment outcomes.

Gender-related aspects of hypertension is a research field based on physiological tendency of men to have higher BP values during the whole lifespan, regardless of race or ethnicity. Men also tend to have more modifiable risk factors, such as excessive alcohol consumption, smoking, poor diet, sedentary lifestyle, etc. [8] Highlighting mechanisms, underlying sex differences in hypertension may lead to development of tailored therapeutic strategies, adaptive to specific gender-related variables, thus improving treatment outcomes [9 □10].

Aim. Current study aimed to evaluate gender aspects of interindividual response to antihypertensive treatment along with the role of SNP CYPIIB2 -344C/T in achieving target BP levels.

Patients and methods. 93 patients with primary hypertension, 33 men (35.5%) and 60 women (64.5%) were enrolled into the study. Such gender proportion does not demonstrate any preference for enrolling women, making the studied group peculiar. Patients with secondary hypertension and documented first line antihypertensive treatment intolerance were not included into the study. All patients underwent standard clinical evaluation. Classical cardiovascular risk factors were assessed: family history of hypertension (FHH), history of premature cardiovascular events (CVEs) (defined as an event at the age ≤55 years of age in men and ≤60 years in women), smoking status, alcohol consumption, diet, daily sedentary time. Documented anamnesis of polycystic ovary syndrome (PCOS), gestational hypertension, preeclampsia and eclampsia, surgical menopause and hypertension in menopause were assessed in women. Concomitant clinical conditions, such as obesity, type 2 diabetes mellitus were also taken into consideration.

SNP CYPIIB2 -344C/T was assessed with polymerase chain reaction restricition fragment length polymorphism method (PCR-RLFP). Genetic material was obtained with buccal swab after obtaining patient's informed consent. Epithelial cell deoxyribonucleic acid (DNA) extraction was performed with modified method, using Chelex solution [11]. Concentration and purity of a DNA-sample was assessed with spectrophotometry (Nanophotometr, Implen), after aliquot withdrawal directly from the vial with DNA solution. CYP11B2 (-344C/T) allelic variants were determined with PCR-RFLP. Amplification was performed with CFX96-amplifier (BIO-RAD, USA) in 20 μL buffer («Fermentas», Lithuania) and 100 nm of each oligonucleotide primer, 100 □150 ng DN
stained with ethidium bromide, applying electrophoresis visualized under UV-light. Products of amplification were identified with DNA molecular mass marker pUC19: Msp1.

Obtained data was statistically processed with the use of STATISTICA 10.0 software (StatSoft, USA). Frequency data were analyzed by Fisher exact p method, two-tailed. P values $p<0,05$ were considered statistically significant.

Figure 1. End-stage PCR RFLP products, electrophoresis in agarose gel.

M – DNA molecular mass marker, tracks numbered 1-15 represent corresponding DNA samples.

Results. Approximately one third (11; 33,3%) of men enrolled into the study controlled BP effectively under the treatment. Proportion of women with proper BP control was significantly higher (p=0,03), more than half of women (34; 56,7%) had proper office BP levels. Groups of men and women were comparable between each other according to the mean quantity of prescribed medications, type of combination, administered in order to reduce BP. Remarkably, equally men and women, who did not reach target BP levels, have had family history of early CVEs (p=0,034; p=0,007, correspondingly). Women with lack of proper BP control had significantly higher rate of concomitant type 2 diabetes mellitus, than women with target BP levels under antihypertensive treatment.

Table 1.

Risk factors	Rate among women with BP≥135/85 mm Hg (n=32)	Rate among men with BP≥135/85 mm Hg (n=23)	P
FAH, %	90,6	91,3	1
FH of premature CVE, %	37,5	39,1	1
Smoking, %	18,8	86,9	**0,001**
Excessive alcohol intake, %	0	43,5	**0,001**
Sedentary lifestyle, %	46,9	39,1	0,59
Excessive salt intake, %	50	65,2	0,28
Excessive intake of saturated and trans-fats, %	75	82,6	0,28
Obesity, %	71,9	56,5	0,26
Type 2 diabetes mellitus, %	46,9	39,1	0,59

Comparing subgroups of men and women with inadequate response to antihypertensive therapy by major cardiovascular risk factors showed that men with poor BP control have had some statistically significant differences with women, not achieving target BP levels. Men have had a current status of smoker significantly along with the excessive alcohol intake more often, than women (p=0,001; p=0,001, correspondingly).

Genotyping demonstrated, that the men were CYPIIB2 -344C/T CC-genotype carriers less often, then women (p=0,03), while differences between gender groups regarding heterozygous genotype and TT-genotype were insignificant (see Table 2).

Table 2.

CYPIIB2 -344C/T haplotype	Female hypertensive patients (n=60)	Male hypertensive patients (n=33)	P, two-tailed, Fisher method
CC, %	28,3	9,1	0,03
CT, %	27; 45	21; 63,6	0,08
TT, %	16; 26,7	9; 27,3	0,95

Analyzing women's cardiovascular risk factors, that can have an implication in hypertension course and outcomes no statistically significant differences were found between women who properly controlled BP under treatment and those, who did not achieve BP goals. Women with CC-genotype of CYPIIB2 gene demonstrated high rates of hypertension occurrence during the menopause (see Table 3).

Table 3.

Risk factors	Women with CC-genotype (n=17)	Women with TT-genotype (n=16)	P, two-tailed, Fisher method
PCOS	1 (5,9%)	1 (6,3%)	1
Gestational hypertension	5 (29,4%)	3 (18,8%)	0,688
History of preeclampsia and/or eclampsia	1 (5,9%)	1 (6,3%)	1
Surgical menopause	1 (5,9%)	1 (6,3%)	1
Hypertension in menopause	11 (64,7%)	4 (25%)	**0,037**

Conclusions. Thus, study results showed that proportion of men, tending to control BP levels under prescribed treatment was lower than in women. Traditional cardiovascular risk factors analysis showed an association between family history of premature cardiovascular events and improper BP control in both men and women, receiving adequate and comparable antihypertensive treatment. Comparison for the rate of cardiovascular risk factors within gender subgroups, experiencing inadequate BP control under treatment demonstrated high rates of current smokers and alcohol abuse in males. Gender groups demonstrated statistically significant difference in C-monozygous genotype rate, representing men to be T-allele carriers more often than women. Carrying CYPIIB2 -344C/T CC-genotype was a factor, Associated with high rate of hypertension during the menopause, pointing towards special attention for women with certain gene-environmental interaction, regarding BP control and cardiovascular prevention.

Keywords: aldosterone synthase gene CYPIIB2 -344C/T polymorphism, antihypertensive treatment, classic modifiable and non-modifiable risk factors, gender.