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PREVALENCE OF MTHFR GENES MUTATIONS IN RESISTANT HYPERHOMOCYSTEINEMIA

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Objectives: To evaluate the prevalence of MTHFR genes mutations in resistant hyperhomocysteinemia.

Material and method: N = 33 patients with moderate-high CV risk and c linica &biochemical criteria for resistant hyperhomocysteinemia (RH) cosented to genetic screening by the use of molecular genetic testing; 24 males (72.7%): 53.8 ± 17.2 yrs; BMI: 29.1 ± 4.4 Kg/m2; 9 females (27.3%): 62.7 ± 20.3 yrs. BMI: 28.5 ± 6.5 Kg/m2. Smokers 18.2%; Hyperglycemia 48.5%. Hypertension 66.7%. Clinical atherosclerosis (including coronary heart disease) in 33.3%.; venous thrombosis history in 9.1%. Subjects with type 1 diabetes, LADA, folic acid and/or vitamin B12 deficiency, and chronic renal failure were excluded. RH deined by: Hy > 16 uM/L (normal values in local laboratory: < 12) after 6 months of treatment with 5 mg of folic acid and 150 mg of vitamin B6 or a dose of 1000 gammas of injected vit B12 every 2 or 3 months. Plasma Homocysteine: IMX Abbott. Statistical analysis: Continuous variables described as mean ± SD.

Results: N = 20 (60.6%) were homozygous; n = 10 (30.3%) heterozygous for MTHFR C667T mutation. Only 3 subjects (9.1%) were non carriers. 29/33 (87.9%) showed at least one Cardiovascular Risk Factor (CVRF) associated. In our study, homozygous prevalence was higher than expected in the general population (60.6% vs 15- 25%), whereas heterozygous prevalence was slightly lower than estimated in Caucasian population (30.3% vs 45%). Clinical atherosclerosis (including coronary heart disease) is more prevalent than venous thrombosis history (33.3% vs 9.1%).

Discussion: The role of the homocysteine (Hcy) as a cardiovascular risk factor has been questioned for a long time but according to recent data from MESA study and NHANES study, patients with elevated Hcy levels show an increased risk not only for blood clots in the veins, but also for heart attack and stroke. MTHFR C667T is an autosomal recessive mutation within the MTHFR gene that results in the production of a thermolabile enzyme with decreased activity for methylating homocysteine. This mutation involves a single nucleotide substitution of thymidine for cytosine at nucleotide position 667 of the MTHFR gene. Carriers of this mutation are associated with elevated levels of homocysteine in plasma, which, in turn, increases the risk of arterial disease and venous thrombosis. The prevalence of the MTHFR C667T mutation in the general population is estimated to be 15-25% of homozygosity. Heterozygosity has a reported incidence of approximately 45% in the Caucasian population. This genotype, however, is not reported to significantly increase homocysteine levels. Is controversial whether the genetic study aids to the initial management

of hyperhomocysteinemia but do we know the prevalence of mutations MTHFR genes in the treated population and resistant to the therapy?

Conclusions: Our work is the irst one to study the prevalence of mutations in RH. The resistant hyperhomocysteinemia is mostly accompanied by a gen alteration. Hyperhomocysteinemia is not a trivial alteration and the present study emphasizes the relevance of genetic testing at least in patients wi thresistant hyperhomocysteinemia. Further studies should be designed speciically to meet the proper handling of drugs and doses for this situation, especially in subjects at high cardiovascular risk. When no genetic testing is available, the evaluation of a short-term response to treatment could be a good alternative.