Category :**Brain: Cerebral resuscitation/postanoxic**

A171 - *HTR1A C(-1019)G polymorphism contributes to neurological impairment in a cohort of neuro-ICU patients*

V Pisarev [1] ; A Chumachenko [2] ; I Redkin [2] ; V Zakharchenko [2] ; A Kalov [2] ; M Petrova [2]

[1]Federal Research and Clinical Center of Intensive Care medicine and Rehabilitology, V.A.Negovsky Institute of General Reanimatology, Moscow, Russian Federation , [2]Federal Research and Clinical Center of Intensive Care medicine and Rehabilitology, Moscow, Russian Federation

Introduction:

The 1A receptor HTR1A is one of the most abundant serotonin receptors in the brain and immune cells that contribute to stress, anxiety, aggression, cognition, and immune responses [1-2]. Single nucleotide polymorphism (SNP) *HTR1A* C(-1019)G (rs6295) site is located in promoter area and affects *HTR1A* gene transcription[1]. Allele G associates with depression, post-traumatic mental disorders, and resistance to antipsychotic drugs [1]. Altered expression of the *HTR1A* gene associates with increased oxidation due to a deficient anti-oxidation mechanism [3]. Our study aimed to investigate whether the *HTR1A* SNP links to neurological impairment and circulating oxidized DNA (oxDNA) in patients re-admitted to a neuro ICU.

Methods:

Study cohort included 240 neuro ICU patients (median age 54 years, range 18-88 years) with consequences of trauma, anoxic brain injury, stroke, brain tumor. *HTR1A* rs6295 polymorphism was studied using an *HTR1A* specific oligonucleotide tetra primer set, PCR, and gel electrophoresis. Oxidized DNA (oxDNA) concentration in plasma was determined with antibodies to 8-oxo-2'-deoxyguanosine and membrane immunoassay.

Results:

On day 1, Nihss scores (but not Glasgow or SOFA scales) revealed differences between patients with CC genotype vs. G carriers: medians 8(6.5;12.5) vs. 13(9.2;18.0), respectively (P=0.012, Mann-Whitney). Increased oxDNA values were associated with CC genotypes: odds ratio (OR) 2.213, 95%CI%: 1.201-4.077, P=0.016 (Fisher test), n=240. This association was significant only in a cohort of patients with no pneumonia (OR 2.991, 95%CI%: 1.170-7.645, P=0.036, n=92).

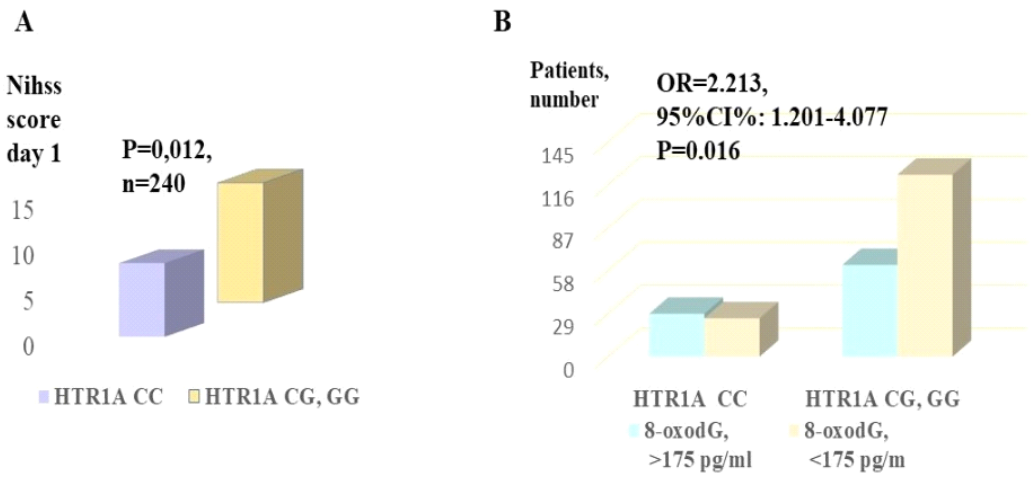
Conclusion:

The results link enhanced neurologic impairment and decreased oxDNA in circulation in the cohort of carriers of *HTR1A* G resistant to a lung infection that may stem from the dual effect of the mutant gene in neural and immune cells.

References:

1.Soga T. et al. Frontiers in Genetics 11: 601868, 2021. 2. Liu Y. et al. Eur J Cancer 114:8-24, 2019. 3. Mössner R et al. . J Neural Transm (Vienna), 109(5-6):557-65,2002.

Image :



HTR1A polymorphism impacts NIHSS scores and circulating oxidized DNA in plasma