Under the Auspices of
International Headache Society

GLOBAL MIGRAINE & PAIN SUMMIT
4th MENA Meeting & 2nd Turkish African Meeting of Headache and Pain Management
October 28-30, 2020 Virtual Congress

OP 19 Sulfotransferase Inhibitors in the Pathophysiology of Migraine

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Background: Certain constituents in migraine food triggers and non-steroidal anti-inflammatory drugs(NSAIDs) inhibit sulfotransferases (SULTs)that detoxify drugs/chemicals and play role in the metabolism of neurotransmitters. We hypothesized that SULT1A inhibition is a common mechanism by which food triggers and NSAIDs modulate migraine susceptibility, in a way that to explain food triggers of migraine attacks and medication overuse(MO) headache. Our goal was to investigate SULT1A1 involvement in MO and migraine triggers and to observe how cortical excitability and behavior is altered in MO after exposure to a trigger.

Methods: Hesperidin was used as SULT1A inhibitor found in orange juice, a migraine trigger and mefenamic acid(NSAID), another SULT1A inhibitor, was used to induce MO in rats. The groups were; 1) Hesperidin(ip) or its vehicle-DMSO(ip) 2) Chronic(4 weeks) mefenamic acid(ip) or its vehicle(ip) 3) Chronic mefenamic acid+hesperidin(ip) or DMSO(ip). CSD susceptibility was evaluated and behavioral testing was performed. SULT1A1 enzyme activity was measured in brain samples.

Results: Single-dose of hesperidin neither changed CSD susceptibility nor resulted in any behavioral change. Chronic mefenamic acid exposure resulted in increased CSD susceptibility, mechanical-thermal hypersensitivity, increased head shake-grooming and decreased locomotion. Hesperidin administration after chronic mefenamic acid exposure resulted in increased CSD susceptibility and mechanical-thermal hypersensitivity and decreased locomotion. SULT1A1 enzyme activity was lower in mefenamic acid group and mefenamic acid+hesperidin group compared to their vehicles.

Conclusion: Mefenamic acid and hesperidin have synergistic effect in modulating CSD susceptibility and pain behavior. SULT1A inhibition may be the common mechanism by which food triggers and NSAIDs modulate migraine susceptibility.

Acknowledgement: DV was supported by a Fellowship from the International Headache Society.