Alpha1 MZ Foundation - Information & Research

News & Research Update

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Dear Subscribers,

We noticed that not all Alpha1 patients with the Z mutation are aware yet of the impact that NSAID medication like Ibuprofen may have on your MZ or ZZ liver and, as such, on your health.

NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) are widely used, and you can get most of them just over the counter without a prescription from your physician.

NSAIDs block a specific enzyme called cyclooxygenase (or COX) that the body uses to make prostaglandins. By reducing the production of prostaglandins, NSAIDs help relieve fever discomfort and reduce inflammation and the associated pain.
(The cyclooxygenases (COX) are enzymes that have a role in the activation of inflammatory pathways (e.g., Nuclear Factor (NF)-κB) that lead to the release of prostaglandins, chemokines, cytokines and ROS)

Examples of common NSAIDs are ibuprofen, naproxen, diclofenac, celecoxib, mefenamic acid, etoricoxib, and indomethacin. (they are sold under different brand names)
You are most likely familiar with them because they account for approximately 5–10% of all medications prescribed yearly. (~ 20 billion dollars/year)
NSAIDs come in pills for oral use but also in gels for use on the skin, which, by the way, has the same effect on the Alpha1 liver because it enters the bloodstream.

Not all Alpha1 MZ patients will be affected, similar to the fact that not all Alpha1 MZ patients will develop liver issues over time. This depends on variants in autophagy genes MTMR12 and FAM134A, which we discussed in our May 18 weekly (see link below).
https://www.alpha1mz.org/_files/ugd/ce6f88_b548577da93e409c9263b0aa2b2ec221.pdf

However, for the ~15% of MZs (and ZZs) who are liver-affected, it is crucial to understand the impact of NSAIDs on your Alpha1 liver because it can have a significant impact on your liver and, as such, on your life!! (Personal experience here…)

In easy-to-understand language, an NSAID accelerates the effect of the Alpha1 Z mutation in the liver. So, there will be significantly more polymerization in the liver cells and significantly more liver inflammation/damage.
In one particular case, applying a gel containing Diclofenac three times in 24 hours caused severe liver issues, which will take the liver months to recover.

So, the bottom line is, when you are one of ~15% MZ patients who are affected, please take good care of your liver and be aware that NSAIDs can severely harm your liver (either in pills or gels)

Below is a part of a somewhat older research paper from 2006 that investigated the effect of NSAID on an Alpha1 Z liver in mice models. They reported:

"Results showed that administration of indomethacin (NSAID) to PiZ mice resulted in increased hepatic injury, indicated by increased hepatocellular proliferation and increased activation of caspase 9. This indomethacin-induced injury was associated with activation of IL-6–STAT3 signaling,

increased expression of Alpha1-AT mRNA, and greater accumulation of mutant polymerized, Alpha1-ATZ protein in livers of indomethacin-treated PiZ mice.
In conclusion, NSAID administration can significantly potentiate the liver injury associated with Alpha1-ATZ hepatic accumulation; NSAIDs may be especially injurious to patients with Alpha1-AT deficiency, possibly by increasing the expression and accumulation of the hepatotoxic mutant protein.
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Link to the paper https://aasldpubs.onlinelibrary.wiley.com/doi/10.1002/hep.21326

And, like always, enjoy the ride !!

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