Dynamic Chiropractic

HEALTH & WELLNESS / LIFESTYLE

NSAIDs -- The Unintended Consequences

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We have forgotten. Prior to 1938, the year penicillin was synthesized, there was a very small pharmacy industry. Contrast this with 1997, where the pharmacy companies' stocks are almost universally a good investment, and their advertisements appear in all forms of the media.

We have also forgotten the many examples of the pharmacy industry's wares causing unintended consequences. Remember the stories of diethylstilbestrol (DES) and cancer and reproductive tract defects, swine flu vaccine and Guillain-Barre syndrome, or aspirin and Reyes syndrome?

Another story of unintended consequences associated with drugs is currently unfolding. The class of drugs is familiar to all of us: non-steroidal anti-inflammatory drugs (NSAIDs). Much has been written with regards to NSAIDs and their caustic effects on the gastrointestinal tract.[1-7] Toxicity and the extant of damage caused tends to vary widely when comparing the many NSAIDs; they are not all equal. The unintended consequences of NSAIDs are not limited to the GI tract: this is just the most widely written about and experienced side effect.

Researchers estimate that 8-10% of the overall incidence of end-stage renal disease (ESRD) is attributable to acetaminophen. The risk was dose dependent with measurable increases of risk beginning at 105-365 pills per year or greater than 1,000 pills per lifetime. Aspirin did not increase the risk of ESRD, however, other NSAIDs (non-aspirin, non-acetaminophen) sharply increased ESRD risk in persons who consumed 5,000 or more pills during their lifetime.[8] These are doses easily achieved with over-the-counter products. Only recently have negative side effects on the central nervous system been appreciated. Cases of aseptic meningitis, psychosis, and cognitive dysfunction have been reported.[9] These side effects are more commonly seen in the elderly.

A mechanism of action of NSAIDs is to inhibit prostaglandin synthesis. Prostaglandins are involved in pain and inflammation mechanisms, but this is not their only function. Prostaglandins are also involved in thermoregulation and melatonin synthesis.[10] This directly impacts body temperature, sleep, and may affect circadian rhythm.

A recent double blind study found that normal circadian decrease in body temperature during the nighttime hours was attenuated by the administration of aspirin or ibuprofen.[11] Daytime body temperature was not affected by these same NSAIDs. In addition, melatonin was suppressed by the administration of these NSAIDs during the nighttime hours. This confirmed earlier reports of suppression of melatonin synthesis10 and alteration of normal sleep patterns in healthy individuals.[12,13] These effects were not found in all study subjects; there were wide variations.

Gastrointestinal damage, kidney damage, cognitive disturbances, alteration of sleep and circadian rhythms -- all are unintended consequences directly attributable to NSAIDs. But wait ... there's more.

The first-line treatment for osteoarthritis, from the medical perspective, is NSAIDs. These drugs are recommended for chronic use either as an over-the-counter or prescription item. Here is the

sad irony. Human articular cartilage is continually remodelled during growth and development and during adult life. The remodelling involves, in part, the synthesis of glycosaminoglycans (GAG), the principal macromolecule of the extracellular matrix. Normal synthesis and breakdown of these molecules is mediated by chondrocytes.[14-16] Changes in the metabolic activity of these cells has been postulated to be a factor in the development of cartilage lesions characteristic of osteoarthritis.[17-19] If the synthesis of GAG is reduced, this may eventually lead to deterioration, which is part of the osteoarthritic process. Conversely, the ability to accelerate the synthesis of GAG should aid in repair and regeneration.

A study of the effect on GAG synthesis in human articular cartilage using NSAIDs was undertaken (this was an in vitro experiment).[20] The following table rates the various NSAIDs as to those that stimulate GAG synthesis, have no significant effect, and those that have significant inhibitory effects.

NSAID (generic name)	NSAID (trade name)	effect on GAG synthesis
aceclofenac	(European drug)	stimulate
tenidap	Enable	stimulate
tolmetin	Tolectin	stimulate
diclofenac	Voltaren	neutral
piroxicam	Feldene	neutral
tiaprofenic acid	(European drug)	neutral
aspirin	* * *	neutral
naproxen	Naprosyn, Aleve	inhibition
ibuprofen	Advil, Motrin	inhibition
indomethacin	Indocin	inhibition

These distinct categories discount the individual variabilities that were present. For example:

1. When considering aceclofenac, 35 cartilage samples showed stimulation of GAG synthesis, none showed inhibition.

2. When considering diclofenac, two samples showed increased GAG synthesis, 27 showed some degree of inhibition.

3. When considering naproxen, 27 samples showed significant inhibition, none showed stimulation of GAG synthesis.

The weaknesses of the above study include the fact that it was done in vitro (it is too invasive to contemplate measuring GAG synthesis in vivo with current testing techniques) and the measurements were taken over only seven days. To the researchers' credit, this was the best study to date looking at this crucial issue. How ironic that use of several of the above listed NSAIDs, if prescribed for an osteoarthritic patient, would inhibit GAG synthesis, thereby hastening the decline of the articular cartilage -- an iatrogenic worsening of the degenerative process.

Given the damage wrought by the class of non-steroidal anti-inflammatory drugs, it is astounding how large an audience they have captured. Documented side effects to the gastrointestinal tract, liver, kidneys, central nervous system, endocrine system, and articular cartilage should strike a

note of warning to all. Yet, NSAIDs are the most frequently prescribed medications worldwide.[21] Remarkably, some chiropractors recommend these drugs, even for chronic use. Perhaps, in addition to your favorite NSAID, the use of alcohol and cigarettes should be considered.

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NOVEMBER 1997