The Truth About the Dangers of COX-2 Inhibitors
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As MOST READERS ARE AWARE, VIOXX WAS RECALLED FROM THE marketplace in late September of 2004. It was discovered that a significant number of patients taking Vioxx suffered from heart attacks or strokes.

A total of three COX-2 inhibitors have been in the marketplace. These drugs are sometimes referred to as “coxibs,” celecoxib (Celebrex), rofecoxib (Vioxx), and valdecoxib (Bextra). Celebrex and Bextra are still in use. COX is the acronym for cyclo-oxygenase. In 1990, researchers discovered that there were two distinct COX enzymes, and referred to them as COX-1 and COX-2. More recently, it has been proposed that there is even a COX-3 enzyme.

The difference between COX-1 and COX-2 is generally straightforward. COX-1 is a constitutively expressed enzyme; in other words, it is involved in normal homeostatic functions such as gastric protection, hemostasis, and normal renal function. In contrast, COX-2 is not normally expressed and not involved in tissue homeostasis; instead, its activity is induced after tissue injury.

Confusion about regular NSAID’s and COX-2 inhibitors

A substantial area of confusion revolves around the notion that COX-2 is an inflammatory enzyme; it is not. COX-2 is an enzyme that is induced by tissue injury. The subsequent pro- or anti-inflammatory outcome depends on the pro- or anti-inflammatory nature of the fatty acids in the cell membrane. COX-2 can act on three different cell membrane fatty acids, including arachidonic acid (AA), dihomo-gamma-linolenic acid (DGLA), and eicosapentaenoic acid (EPA).

If COX-2 acts on AA, the outcome will be the synthesis of pro-inflammatory eicosanoids, known as prostaglandin E2 (PGE2) and thromboxane A2 (TXA2). PGE2 sensitizes nociceptors and promotes inflammation. TXA2 causes local vasoconstriction and platelet aggregation. Anti-inflammatory drugs like ibuprofen and Celebrex are taken to block the production of these pro-inflammatory eicosanoids.

If COX-2 acts on DGLA, the outcome will be the synthesis of non-nociceptive/inflammatory PGE1 and non-vasoconstricting/aggregating TXA1. These non-inflammatory eicosanoids do not cause pain and inflammation.

If COX-2 acts on EPA, the outcome will be the synthesis of non-nociceptive/inflammatory PGE3 and non-vasoconstricting/aggregating TXA3. Again, the outcome of these non-inflammatory eicosanoids will be a reduction of pain and inflammation.

Clearly, the inflammatory potential of our tissues depends on the inflammatory potential of the fatty acids in our cell membranes. Pharmacology articles and pathology texts do not make this distinction, which is why many of us are led to believe that COX-2 enzymes are inherently inflammatory.

Cell membrane fatty acids and inflammation

Almost all DC’s learned about essential fatty acids (EFA’s) in biochemistry or nutrition class while going to chiropractic college. EFA’s are the special fatty acids we must get from our diets, as we cannot synthesize them ourselves. The two EFA’s include linoleic acid (LA), an omega-6 (n-6) fatty acid, and α-linolenic acid (ALA), an omega-3 (n-3) fatty acid. Linoleic acid is converted into DGLA and then into AA (also n-6), whereas, α-linolenic acid is converted into EPA (also n-3).

The ratio of LA:ALA, or our n-6:n-3 dietary ratio is supposed to be about 1:1; at least below 4:1 is the goal. With an LA:ALA ratio of 4:1 or less, the outcome will be the modulation and control of excessive immune responses and inflammation. This is because a dietary ratio of below 4:1 insures that there will be an even distribution of AA, DGLA, and EPA into cell membranes, which then leads to the synthesis of more anti-inflammatory eicosanoids compared to pro-inflammatory.

Not surprisingly, the average American has an n-6:n-3 ratio of 20:1 or greater, which means that we are eating 20 or more n-6 fatty acids for every single n-3 fatty acid. This leads to a significant increase in the synthesis of AA and its related pro-inflammatory eicosanoids, and is a main reason why Americans medicate with excessive amounts of ibuprofen.
Celebrex and other anti-inflammatory drugs.

We, literally, eat ourselves into a state of inflammation and pain, and then have to take medications as a counteractive measure. The excessive inflammation created by n6 fatty acids is also thought to be the driving force behind the development of cancer, heart disease, stroke, and other inflammatory diseases.1

Diet and supplements to increase cell membrane n-3 fatty acids

An n6:n3 ratio of 4:1 or better is found in fruits, vegetables, grass fed animal products, wild game, and specially fed n-3 chicken eggs. Accordingly, these foods can be referred to as anti-inflammatory.

In contrast, all grains have a ratio of 20:1 or greater and grain-fed animals have ratios above 4:1, and so should be referred to as pro-inflammatory foods. Most packaged goods are prepared with oils that have n-6:n-3 ratios greater than 4:1, such as safflower, sunflower, and corn oil. Margarine is almost purely an omega-6 fatty acid. Additionally, margarine has been chemically altered by the partial hydrogenation process, which increases the inflammatory potential of margarine.

At this point, it should be clear that the COX-2 is really not the problem; the issue is our excessive consumption of n-6 fatty acids, which increases the level of pro-inflammatory AA in cell membranes. The COX-2 enzyme merely acts on the pro-inflammatory fatty acids that we eat.

According to the U.S Department of Agriculture and Jean Carper's book, Your Miracle Brain, flax seed oil has the best ratio of omega-6 to omega-3 of all the cooking oils. In some studies, flax seed oil also helped relieve manic depression.

Research suggests that most people would do well to take n-3 fatty acid supplements to get a boost in the anti-inflammatory direction. EPA/DHA is the most common n-3 fatty acid supplement. Patients should take 1-3 grams per day, levels which are extremely safe for nearly everyone save for patients taking strong anti-coagulants, such as coumadin. 

References

Dr. Seaman is the Clinical Chiropractic Consultant for Anabolic Laboratories, one of the first supplement manufacturers to service the chiropractic profession. He is on the faculty of Palmer College of Chiropractic Florida and on the postgraduate faculties of several other chiropractic colleges, providing nutrition seminars that focus on the needs of the chiropractic patient. Dr. Seaman believes that chiropractors should be thinking like chiropractors, while providing nutritional recommendations. Doctors and patients who follow his programs report improved feelings of well-being, weight loss, dramatic increases in energy, and significant pain reduction. Dr. Seaman can be reached by e-mail at docseaman@mac.com.

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