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Meta-analysis study on fish oil effectiveness is fatally flawed

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One of the events in the food industry you never want to see is the making of sausage where sometimes good cuts of meat are combined with items you would never want to eat.

The same is true of meta-analysis studies in medical research. Meta-analysis means that you take a lot of different studies (some good, some not so good) using different patient populations, different inclusion criteria, different protocols, and different outcome criteria and mix them together to get a conclusion that often demonstrates a non-result. The best example of this is the recent study in the Journal of the American Medical Association that combined a wide number of studies using fish oil supplements to come up with the conclusion that omega-3 fatty acids have no benefit (1). So let's take a look at this study in a little more detail.

First, it is always useful to look at the investigators. In this case, the authors are from Greece (not exactly a hotspot of high-quality clinical research since Aristotle), and to my knowledge none of them has been involved in any actual cardiovascular intervention studies in the past, let alone any work with omega-3 fatty acids. (I believe a little background is a good foundation to build from, but then call me crazy.)

Second, the average dose used in these studies was 1.5 grams of omega-3 fatty acids per day. Surprisingly, the American Heart Association recommends more than double this dose to reduce triglycerides, a known risk factor for heart disease (apparently not in Greece since the authors ignored this fact). This would indicate the authors were making conclusions based on placebo doses of omega-3 fatty acids. Usually a placebo dose gives placebo effects, which was confirmed in their meta-analysis. Furthermore, just giving a dose of anything is meaningless unless it is reducing a measureable clinical parameter in the blood that has a relationship to the disease condition being studied. For example, if I gave a statin dose that reduced LDL cholesterol levels from 250 mg/dl to 245 mg/dl, I wouldn't expect any therapeutic benefits unless I gave enough statin drug to reduce the LDL cholesterol level to less than 130 mg/dl, if not much lower.

So what is a good dose of omega-3 fatty acids? As I have already mentioned, the American Heart Association recommends 3.4 grams of EPA and DHA per day to lower triglyceride levels. However, I believe a better marker is the amount of omega-3 fatty acids needed to reduce the AA/EPA ratio to the levels found in the Japanese population, which has the lowest levels of cardiovascular events in the world. Recent studies with healthy Americans indicate that would take between 5 and 7.5 grams of EPA and DHA per day (2). Again, this indicates that the dose of omega-3 fatty acids in this meta-analysis was providing a placebo dose.

Third, another problem with meta-analysis is conflicting protocols. In this study, almost half the patients came from two just studies: The GISSI study and the JELIS study. The GISSI study (more than 11,000 patients) indicated that omega-3 fatty acid supplementation on the foundation of a Mediterranean diet could reduce sudden cardiovascular death rate by 45% versus a placebo and reduced overall cardiovascular death by 20% (3). This study was criticized because the care that all groups were receiving didn't include statins (since they were not yet approved). After all, the thinking for a typical cardiologist is that there is no reason to use omega-3 fatty acids if you can simply give a statin drug instead.

That faulty thinking was addressed by the JELIS study in which all the patients (about 18,000) were getting statins (4). Unlike the GISSI study, the AA/EPA ratio was measured in these patients. The initial AA/EPA ratio was 1.6 (a level requiring Americans to take about 5 to 7.5 grams of omega-3 fatty acids per day just to reach that starting point), and then even more EPA was added to the active group. After 4 ½ years, those Japanese patients getting the statins and extra fish oil had another 20% reduction in cardiovascular events over and above those getting the statins and an equivalent amount of supplemented olive oil. The take-home lesson from the JELIS study was that any physician who didn't prescribe supplemental omega-3 fatty acids along with statins was simply practicing bad medicine.

Meta-analysis studies are supposed to make up for potential shortcomings in small clinical trials (like the ones used to approve virtually all pharmaceutical drugs). In the hands of unqualified researchers who have little understanding of the field or compound being studied, a meta-analysis can become an instrument for the mass confusion generated by this recent article in the Journal of American Medical Association.

The bottom line is that you need adequate doses of natural compounds to generate a therapeutic effect. The levels of these doses of natural compounds will always be far greater than with drugs, but also with far fewer side-effects. If you give a placebo dose of a natural compound, then expect a placebo result. But please don't try to pass off such an obvious result as "science".

References

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