

## Scientists suspect omega-3 fatty acids could slow acute wound healing

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A recent study shows that popular fish oil supplements have an effect on the healing process of small, acute wounds in human skin. But whether that effect is detrimental, as researchers initially suspected, remains a mystery.

The omega-3 fatty acids found in fish oils are widely considered to benefit cardiovascular health and other diseases related to chronic inflammation because of their anti-inflammatory properties. But insufficient inflammation during the initial stage of wound healing may delay the advancement of later stages.

In the study, blister wounds on the arms of people taking fish oil supplements were compared to the wounds of people taking a placebo. The wounds healed in about the same amount of time – but at the local cellular level, something unexpected happened. The levels of proteins associated with initiating and sustaining inflammation were higher in the blister fluid in people who had taken the active fish oil supplements. The researchers had expected those proteins to be lowered by the increased systemic presence of omega-3 fatty acids in the blood.

"That finding was hard to explain," said Jodi McDaniel, lead author of the study and an assistant professor of nursing at Ohio State University. "These proteins may have other functions that we don't yet fully understand. And our results also suggested there could be a difference between men and women in the amount of inflammatory proteins that are produced, because on average, women had lower levels of one of the

proteins."

If the polyunsaturated fatty acids in the fish oils do indeed delay acute wound healing, then they probably should be discontinued for awhile by patients scheduled for surgery, McDaniel said. They appear to have enough of an effect that patients should at least inform their doctors if they're taking a fish oil supplement, she added.

But there could still be a bright side to the supplements' ability to alter those proteins and other molecular substances that control inflammation locally. Fish oil's systemic anti-inflammatory power, which has been illustrated in previous studies, still might assist in the healing of chronic wounds at the local level. Chronic wounds are essentially stuck in an inflammatory stage that slows or prevents transition to the later stages needed for complete healing. That mechanism needs to be explored further, McDaniel said.

"There's so much information out there now about omega-3s and they clearly have lots of potential," McDaniel said. "We're just trying to figure out how to evaluate what they do and how to advise people to take these supplements. Our goal isn't to stop supplement use but to fill in the picture of what conditions they help and what they might hurt."

The research is published in a recent issue of the journal *Wound Repair and Regeneration*.

Study participants were divided into two groups of 15 healthy adults each. One group took a placebo, and the other took an active supplement containing 1.6 grams of eicosapentaenoic acid (EPA) and 1.1 grams of docosahexaenoic acid (DHA) daily for four weeks. EPA and DHA are the polyunsaturated fatty acids obtained primarily from fish oil that serve as the basis of most standard omega-3 supplements.

Previous research has suggested that these fatty acids affect the production of proteins called proinflammatory cytokines, which signal biological processes during the inflammatory stage of wound healing. The primary cytokines in the process are interleukin-1 beta (IL-1b), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-a).

But research had not yet addressed how the interaction between fatty acids and these cytokines might affect human wounds.

McDaniel and colleagues expected to find that research participants taking the fish oil supplements – and therefore being affected by their anti-inflammatory properties – would have significantly lower levels of the cytokines in their blister wounds during the initial stage of inflammation, resulting in a slower healing process.

Instead, the group taking the fish oil had significantly higher levels of IL-1b in their blister wounds than did the placebo group 24 hours after the wounds were created. The active group also had higher levels of IL-6 and TNF-a cytokines in their blisters over time than did the placebo group, but those differences in levels were not significant. The blisters took an average of 10.7 days to completely heal in the active supplement group and an average of 9.8 days in the placebo group, but the difference was not significant.

The results suggest that the function of these cytokines still isn't completely understood, McDaniel said. And the scientists were also surprised to find that gender appeared to make a difference in cytokine production. Men were more likely than women among the active supplement group to have higher levels of the IL-1b cytokine in their wounds. McDaniel said that some studies have suggested that estrogen plays a role in inhibiting the production of this particular protein during the inflammatory stage of wound healing, but more research is needed.

McDaniel and colleagues are following up with a similar study in which they are adding a low-dose aspirin to both the fish oil supplement and placebo groups. Some research has shown that aspirin can facilitate the anti-inflammatory properties of omega-3 fatty acids, and low-dose aspirin is commonly included in the medication regimen of patients with cardiovascular disease.

The researchers also will look at different biological markers in blister wounds to see if the combination of fish oil and aspirin produces compounds that function as what McDaniel called "stop and go switches" in controlling inflammation.

"If we find that the fish oil can work in an anti-inflammatory fashion at the local level of wound sites, we would consider moving on to the chronic wound population," McDaniel said. "Even if we find that there are times when omega-3 fatty acids should not be taken in advance of creating an acute wound, such as in elective surgery, we still have high hopes that fish oil might be beneficial for chronic wounds in certain situations."

Source: Ohio State University

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