LETTER TO THE EDITOR

Reply to “Letter to the Editor: Determining the potential effects of oxidized fish oils in pregnant women requires a more systematic approach”

Benjamin B. Albert,1 José G. B. Derraik,1 Mark H. Vickers,1 Manohar L. Garg,2 David Cameron-Smith,1 Paul L. Hofman,1 and Wayne S Cutfield1

1Liggins Institute, University of Auckland, Auckland, New Zealand; and 2Nutraceuticals Research Group, School of Biomedical Sciences and Pharmacy, University of Newcastle, Callaghan, New South Wales, Australia

REPLY: We welcome the acknowledgment from members of the marine oil industry that further studies are necessary to establish the potential harm posed by consumption of oxidized fish oils during pregnancy. This will require dose-response studies in animals and the identification of the harmful compounds to accurately quantify the risk, which we had already planned to perform. However, a number of the claims and implications made by Rice et al. are incorrect or misleading.

It was implied by their letter that fish oils sold at retail are not significantly oxidized because: 1) there are steps taken during production that attempt to prevent oxidation, and 2) industry have agreed to a maximum peroxide value of 5 meq/kg in marine oils. However, omega-3-rich oils purchased at retail are frequently oxidized above 5 meq/kg. Studies worldwide from Europe (7), North America (2, 5), Africa (4), and Oceania (1) showed that 17–93% of products exceeded this limit, with 12–50% exceeding 10 meq/kg. Four of these studies identified fish oil products sold at retail with peroxide values exceeding 30 meq/kg (1, 2, 4, 7). Therefore, the level of oxidation in our oil was not dramatically higher than that of some retail products. Rice and colleagues have also criticized the use of artificial oxidizing conditions in our study, when in fact this was the only way to achieve a precise level of oxidation in the trial oil.

To clarify, the aim of our study was to examine differences in biological effects between the consumption of unoxidized and oxidized fish oils during pregnancy. The finding of major neonatal mortality was unexpected. The extent to which this harm can be extrapolated to humans in association with ingestion of oxidized retail oils remains unknown.

Finally, Rice et al. implied that the effects of n-3 polyunsaturated fatty acids (PUFAs) on gestational length are so strong and well established that their recommendation for women not to take fish oil supplements and instead consume oily fish during pregnancy could dramatically increase the rate of preterm birth. This is not only factually incorrect but also a distraction from the actual results of our study. There are serious flaws in the systematic review cited by Rice et al. (3). It contains obvious errors including differences in results between the abstract and body of the paper, and the extraordinary claim that fish oil prolonged gestation by 2 wk. This conclusion is at odds with the markedly smaller differences in gestational length in the individual randomized-controlled trials included in this systematic review. Importantly, that study contrasts with another recent and more inclusive systematic review that showed no effect of n-3 PUFAs supplementation on the rate of preterm birth (6).

Given the ease at which oils rich in n-3 PUFAs oxidize, it is important that the health effects of oxidized oils are investigated by scientists independent of industry. Our study used a high dose of a highly oxidized fish oil exposing the rats to a larger peroxide dose (relative to body size) than women would be exposed to when taking fish oil supplements. If there had been no harmful effects, this would have been immensely reassuring. However, we identified significant harm, which provides important proof-of-concept that oxidation is important to the effects of fish oil during pregnancy. It is difficult to know whether there is an important risk in human pregnancy. Our next step will be to better estimate the potential risks by performing dose-response studies in line with Organisation for Economic Co-operation and Development (OECD) guidelines for the determination of developmental toxicity. Until there is better safety data for oxidized fish oil or until retail supplements are invariably unoxidized, we continue to encourage women who are pregnant to gain their n-3 PUFAs through consumption of fish and not fish oil supplements.

REFERENCES

1. Albert BB, Derraik JGB, Cameron-Smith D, Hofman PL, Tumanov S, Villas-Boas SG, Garg ML, Cutfield WS. Fish oil supplements in New Zealand are highly oxidised and do not meet label content of n-3 PUFA. Sci Rep 5: 7928, 2015. doi: 10.1038/srep07928.