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Review

To sea or not to sea: Benefits and risks of gestational fish consumption

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A B S T R A C T

Prenatal nutritional status and the gestational environmental milieu have increasingly been identified as major determinants of long-term morbidity and mortality for the developing child. While omega-3 fatty acids – found abundantly in fish – are required for normal fetal development as well as for optimal maternal outcome, recent public health warnings to limit some types of seafood intake because of potential contamination with chemical toxicants have resulted in a dilemma for prenatal educators and maternity care providers. This paper reviews the benefits and harms of gestational seafood consumption and provides practical recommendations to address this important public health dilemma.

Contents

1. Introduction

There is considerable discussion going on in the medical literature about the risks and benefits of eating seafood during pregnancy [1]. While officials cognizant of the potential impact of gestational toxicants may recommend seafood restriction, some nutritional researchers have raised concern about the harm of insufficient ingestion. In this paper, pros and cons of gestational seafood consumption will be explored and specific recommendations will be provided for consideration.

There have been numerous studies which suggest significant benefit from fish ingestion during pregnancy, due in great measure to intake of essential lipids called omega-3 fatty acids (ω3FAs). Required lipids or 'essential fatty acids' (EFAs) refer to obligatory fats the body cannot manufacture and must be consumed to meet physiological demand. There are two types of EFAs – ω3FAs and omega-6 fatty acids (ω6FAs) – which are fundamental to normal human physiology. Both types of EFAs are metabolized by the same enzymes and their intake ratio has been found to have significant health implications [2]. Sufficient amounts of docosahexaenoic acid

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(DHA), a type of ω3FA and arachidonic acid (AA), a type of ω6FA, are required for proper intra-uterine development [3]. With fetal EFA sufficiency entirely dependent on maternal intake and transfer, it is estimated that in the third trimester the fetus accrues about 70 mg/day of DHA [3,4] and a comparable amount of AA [5]. While ω6FAs are abundantly found in the typical Western diet, DHA is found in only a few foods – particularly in seafood – which are consumed sparingly by much of the North American and European populations. DHA can also be produced to some extent through maternal conversion of another omega-3 fatty acid – alpha linolenic acid (ALA) – present in selected non-marine foods such as walnuts and flaxseed. As this conversion to DHA is variable and dependent on enzymatic availability as well as functionality of metabolic conversion mechanisms, recommendations to secure gestational DHA requirements generally focus on direct ingestion of seafood.

As ω3FAs are essential components of the human brain and are involved in fetal insulin regulation, growth and development, blood vessel formation and CNS maturation [6–9] it is important to maintain gestational sufficiency. With biochemical and metabolic individuality in each person, as well as limited available laboratory testing for EFA status in most clinical settings, it is difficult to quantify pre-existing maternal DHA levels and to determine specific individual requirements. Average intake of about 200–300 mg per day of DHA has been recommended in general to supply the ω3FA needs of mother and child [10]—a requirement that many women fail to meet by diet alone [11,12]. Increasing numbers of individuals consume minimal fish because of dietary preference or in response to public health warnings about toxicant contamination of seafood [13]. One study, for example, reported a significant decline in fish consumption in response to a national mercury advisory [13]. Accordingly, some pregnant women have deficient ω3FA intake with potential sequelae for themselves and their offspring [13]. Various authors in the medical literature have explored this issue and have endeavored to find a sustainable solution to this public health concern.

2. Potential benefits of gestational omega-3 fatty acid consumption

In pregnancy, ω3FAs are involved in various maternal and fetal functions including placental formation, maternal homeostasis, fetal neurological development, and other processes critical to normal gestational progress as well as to pediatric and maternal health. Inadequate ω3FA consumption, for example, may increase the likelihood of early labor [14]—a prospective cohort study recently confirmed that women who avoided seafood had a 7.1% incidence of preterm birth compared to a 1.9% risk for women eating fish once weekly [15]. A recent study also demonstrated that pregnant women with low levels of ω3FAs were 7.6 times more likely to develop preeclampsia [16].

A large study recently found that about 1 in 7 new mothers experienced depression during at least one phase of pregnancy: 8.7%, 6.9%, and 10.4% of the women had a record of depression right before, during, or after pregnancy [17]. Recent results from a randomized, double-blind, placebo-controlled study involving pregnant women with major depressive disorder suggest that gestational supplementation with ω3FAs exerts significant therapeutic benefit [18]. While mood disorders in general have been linked in many cases with EFA status [19,20], postpartum mood difficulties in particular appear to be associated with levels of ω3FAs: lower DHA content in mother's milk has been correlated with elevated postpartum depression rates [21]. Although cultural factors may be involved, it is interesting that postpartal depression incidence is about 12% in North America where seafood intake is limited compared to about 2% in Japan where fish consumption is high [21].

As well as preferred pregnancy outcomes, there is abundant literature suggesting general health benefits to women who consume adequate ω3FAs including a diminished risk of various afflictions such as breast cancer [22], osteoporosis [23], heart disease [24], arthritic problems [25], psychiatric illness [20], and Alzheimer's disease [26].

The benefits of gestational seafood consumption also appear to extend to the developing child. Gestational fish intake with adequacy of maternal ω3FAs during pregnancy and lactation has been associated with less allergic disease [27], improved eye and hand co-ordination [28], enhanced cognitive and behavioral functioning [9,29], improved sleep behavior [30], and diminished risk of metabolic afflictions such as type-1 diabetes in the offspring [31]. Reduced rates of cerebral palsy [32] and improved intelligence quotients measured at four years of age [33] attest to the potential long-term benefits for offspring of mothers ingesting marine source ω3FAs in pregnancy and lactation. Recent study suggests that ample intake should be commenced prior to conception to secure adequate gestational EFA physiology as existing stores in maternal adipose tissue appear to be relevant for proper fetal development [34].

In review, ω3FAs are essential components of the human brain and are required for normal fetal development as well as maternal health during and after gestation. There is abundant evidence in the medical literature which links adequate gestational fatty acid status with maternal and fetal advantage. With noteworthy benefit suggested by numerous studies, various authors disagree with regulatory bodies that admonish pregnant women to limit fish intake [35].

3. Potential harm associated with gestational seafood consumption

Juxtaposed with the many benefits of consuming seafood in pregnancy is the concern about potential teratogenic effects resulting from aquatic contamination by myriad toxicants including dioxins, PCBs, heavy metals such as mercury, and pharmaceutical residues including synthetic estrogens [36–39]. Industrial waste, agricultural runoff and domestic sewage have tainted the aquatic system with diverse chemical agents which proceed to contaminate fish. The World Health Organization, for example, has recently identified seafood as a leading source of mercury exposure [40]. As a result, various articles in the medical literature and some public health agencies including the U.S. Food and Drug administration have issued recommendations over the last few years to limit some gestational seafood intake because of potential toxicity [41,42]. Is the concern about toxic exposure sufficient to warrant seafood restriction in pregnancy?

Numerous publications confirm that in utero pollution by vertical transmission is an increasing dilemma with unknown long-term sequelae. In 2005, a study of newborn cord blood samples taken by the American Red Cross found that the average sample contained 287 toxicants including heavy metals, various pesticide residues, gasoline by-products and flame retardants [43]. Various studies have linked certain gestational chemical exposures with assorted subsequent pediatric afflictions including neurological problems [44], respiratory dysfunction [45], allergic disease [46], genital abnormalities [47,48], as well as behavioral and psychiatric disorders [49,50]. There has also been recent research to suggest that prenatal exposure to certain endocrine disrupting compounds has the potential to affect psychosexual indices [51–53]. Furthermore, animal studies have found that toxic exposures may affect the epigenome, with alterations persisting through subsequent generations [54].

There are two issues of particular concern when considering prenatal toxicant exposure: (a) toxicant induction times and (b) prenatal vulnerability. Like the DES tragedy that insidiously affected so many offspring [55], the adverse sequelae of most toxicants is not apparent at birth and ultimate impact is not immediately recognized. Many toxic agents have long induction times and their impact may not be realized for years to come. A study reported in the *Journal of Epidemiology and Community Health*, for example, suggests that prenatal toxic exposures account for a high percentage of lethal pediatric cancers—few of which are apparent at birth [56]. Furthermore, with limited understanding of the impact of contemporary exposures on biochemically unique genomes, research is not yet able to conclusively identify all the long-term sequelae of the expanding repertoire of present-day toxicants on developing individuals [57]. The enduring impact of multiple toxicant synergism in pregnancy is also an issue that is only beginning to be discussed in obstetrical circles [58].

The next issue of concern is that developing children in utero are not miniature adults and safe levels for mothers do not necessarily coincide with safety in the fetus [59–61]. A recent study found that mercury levels, for example, were higher in the offspring than in fish-consuming mothers [41]. Fetal vulnerability is significantly greater for many reasons: the fetal liver is immature and unable to efficiently detoxify contaminants; low levels of fetal binding proteins result in high unbound fractions of bioactive toxicants; excretion pathways are undeveloped and excreted urinary pollutants are recycled into the nose and mouth in amniotic fluid; the blood–brain barrier is immature and more permeable; and, compared to mother, there is higher toxicant concentrations by weight in the fetus which may impact rapidly developing fetal organs—all factors which mark the prenatal period as a time of unique propensity for untoward effects [58].

Some contend that apparently minor exposures as might occur with gestational seafood consumption are not significant or clinically relevant to the fetus. Persistent chemical pollutants may bioaccumulate, however, and have the potential to reach levels where teratogenic impact is possible. At levels measuring in parts per trillion and parts per billion, inherent hormones such as insulin and estradiol are bioactive on fetal cells and tissues; exposure to some toxic chemicals also appears to have bioactive impact at seemingly minuscule levels [62]. Accordingly, at this time it is not possible to ascertain the final outcome of many prenatal exposures and it would be premature and dangerous to conclude that gestational exposure to low levels of existing and newly emerging chemical toxicants are without long-term impact.

4. Quo vadis

The dichotomous nature of this 'nutrition versus toxicology' issue can be found in recent publications. While Hibbeln and colleagues conclude that reduced maternal fish consumption might result in more harm than good [63], Grandjean and Landrigan highlight the serious impact of myriad neurotoxicants on the developing human brain [64]. A recent publication in the *Journal of Pediatrics* illustrates the dilemma as well as the importance of securing gestational DHA sufficiency [65]. This paper reports on a study performed in the Inuit community of Artic Quebec and found, as expected, that preferred cord levels of DHA were associated with better visual, cognitive, and motor development in offspring, even after controlling for contaminant exposure to lead, mercury and PCBs [65]. The challenge with the study, however, is that potential long-term sequelae of toxicant exposure from consuming contaminated fish are not necessarily recognized in the first year of life and thus have not been factored into reported outcomes. While the research confirms the benefits of DHA, the limited time frame of the study precludes assessment of potential long-term sequelae of toxicants, including adverse outcomes from persistent pollutants. With uncertainty about the long-term safety of eating contaminated seafood in pregnancy, how should maternity care providers proceed?

The practical outcome of this unresolved issue is that many prenatal educators and maternity care providers are not addressing this important concern with their pregnant patients, much to the detriment of many women and their offspring. Accordingly it behooves the medical community to develop and disseminate guidelines and recommendations that are effective and safe for reproductive aged women considering childbearing. A few suggestions are provided for consideration.

In general, physicians dealing with women of childbearing age must become increasingly cognizant of potential toxicants in pregnancy and acquire the necessary skills to proactively educate in strategies of precautionary avoidance. Increasing recognition of the serious sequelae of adverse exposures combined with the ubiquitous problem of chemical toxicants has led to the emergence of the burgeoning field of environmental medicine and comprehensive training in preconception as well as prenatal care [66]. Some departments (such as Obstetrics and Gynecology at University of California San Francisco and the Ontario College of Family Physicians) have begun environmental medicine training in their residency portfolio and certain clinical journals have published series on human exposure medicine as well as preconception strategies to optimize maternal–fetal outcome [67,68].

Regarding fish intake in pregnancy, it is clear that ω3FA sufficiency is necessary for fetal development and maternal health. Accordingly, the uncertainty about the long-term impact of various seafood contaminants must be balanced with the need to fulfill nutritional requirements. In response to this challenge, numerous suggestions and approaches have been discussed [69–73]. Some authors recommend eating smaller fish which are lower on the food chain and have less contaminants than bigger fish. Other suggestions include limiting fish intake during pregnancy (e.g., 340 g per week), avoiding consumption of particular species (e.g., predator fish such as shark), and staying away from fish caught in waters deemed to be particularly polluted. Citing potential differences in toxicant concentrations between varying types of seafood such as shellfish, shrimp and assorted fish, some suggest that selective intake might preclude adverse exposure. Each of these suggested options, however, is based on the presumption of long-term safety for offspring when exposure levels are maintained within currently acceptable reference limits—a construct that remains unproven scientifically [57].

In public health, contemporary reference levels for various toxicant chemicals represent the predicted daily human exposure dose alleged to be able to occur without deleterious effects during a lifetime. Many chemical agents are new, however, with incomplete recognition of the totality of adverse effects—accordingly, adequate testing on most agents has never been performed. In addition, reference levels are generally determined by animal experiments—animal testing for safety levels may not be relevant for humans as experimental animals frequently possess inherent detoxification mechanisms not found in people [74]. Furthermore, the existing safety levels frequently reflect one-time exposure and do not consider fetal bioaccumulation, repeated exposure, pre-existing maternal toxicant load, genomic variance in toxicant response, and multiple toxicant synergism. Although probabilistic estimates of fetal toxicant levels based on maternal intake are currently being explored for some xenobiotic exposures [75], most fetal contaminants have not yet been sufficiently studied and long-term impact remains uncertain.

Another recommended approach to minimize exposure while assuring nutrients is to avoid seafood intake and to routinely supplement with fish oil in pregnancy. Recent evidence, however, raises concern about routine gestational supplementation with fish oil products such as cod liver oil containing abundant ω3FAs. Although many reports elucidate benefit, there have been a few recent studies which fail to confirm benefit or suggest harm as a result of gestational supplementation with fish oil [76,77]. For example, in contrast to various studies showing improved blood pressure control in pregnancy, a recent observational study with high dose cod liver oil demonstrated increased risk of gestational hypertension [77].

A major confounder in this research and some other interventional studies, however, is that regular cod oil from the liver of fish (the major organ of detoxification) is generally contaminated with the range of toxicants including heavy metals [72] found in the tissues of the source fish. Accordingly, consumers of fish products may also experience high levels of various toxicants which may independently or synergistically affect physiological processes and influence metabolic outcomes. It is recognized, for example, that methyl mercury – a common aquatic contaminant – can induce hypertension in animals [78] and may account for some adverse outcomes in consumers of regular fish oil. Furthermore, as it is documented that some toxicants may impair or modify absorption, utilization and metabolism of nutrients such as vitamin D [79], adverse sequelae and lack of impact in some studies may represent confounding by toxicant accumulation.

As some mothers-to-be appear to be deficient in required DHA and avoid gestational seafood intake because of warnings about toxicant exposure [13], what advice can be given to assure that pregnant women and their offspring safely obtain these required nutrients? The provision of *purified* fish oil containing sufficient ω3FAs may provide the benefits without the attendant harms of toxicant contaminant products. Through a process of distillation and independent toxicology testing, both ω3FA sufficiency and uncontaminated nutrients can be secured. Purified fish oil is readily available and supplementation should be explored as a potential strategy to meet maternal and fetal DHA requirements in pregnancy. In addition to supplementary purified fish oil, regular intake of plant source ALA will provide substrate for maternal endogenous production of some DHA. For those individuals wishing to follow a vegan or vegetarian lifestyle, it is possible to obtain organically produced DHA from oil derived from microalgae—the source of DHA in aquatic ecosystems [80].

5. Concluding thoughts

In review, recent medical literature has confirmed that the environment of the first 38 weeks of life in the confines of the mother's womb is a major determinant of subsequent morbidity and mortality, and may profoundly influence physical and intellectual well-being for the remainder of life. While ω3FAs – found abundantly in fish – are a recognized determinant of obstetric outcome and an absolute requisite for normal fetal development, recent public health admonitions to restrict seafood intake because of potential teratogenesis from aquatic contaminants have resulted in a quandary for prenatal educators and maternity care providers. At this point in history, routine gestational supplementation with purified fish oil or microalgae oil in addition to regular ALA intake should be studied as a potential means to secure the benefits without the risks: adequate nutrition without toxicant exposure. In the long term, however, the issue of ubiquitous environmental contamination and its impact on human health needs to be comprehensively explored and addressed by the medical community and society at large.

Conflicts of interest

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