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ROLE OF OMEGA 3 FATTY ACIDS DURING PREGNANCY AND LACTATION

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ABSTRACT

Adequate consumption of Omega-3 fatty acids are essential during pregnancy because they play an important role in the development of fetal brain and retina. The rate of growth remains high during the first year of life. Omega-3 is converted inside the body into longer chain polyunsaturated fatty acids docosahexanoic acid (DHA) and eicosapentaenoic acid (EPA). DHA and EPA are primarily derived from fish and algae. DHA is essential for the growth and functional development of the brain in infants. DHA is also required for the maintenance of normal brain function in adults. The inclusion of adequate amount of DHA in the diet improved learning ability, whereas deficiencies of DHA are associated with deficits in learning. DHA is readily taken up by the brain in preference to other fatty acids. The turnover of DHA in the brain is very fast, more so than is generally realized. The visual acuity of healthy, full-term, formula-fed infants is increased when their formula includes DHA. However, health professionals and the general public in Malaysia may not be aware about the importance, sources or the quantities required for these essential fat components in foods. This review discusses the benefits of omega-3 consumption with particular emphasis during pregnancy and the first year of life. This review will also attempt to discuss sources of omega-3 fatty acids in Malaysia with the aim to achieve the recommended nutrient intakes for omega-3 fatty acids.

***Keywords**:Omega 3 fatty acids, Lactation in Pregnancy, Sources of Omega-3 FA*

INTRODUCTION

Dietary fats and oils are often misunderstood for being portrayed as bad for health. Fat is an essential component of the diet (Burr and Burr, 1929). Rats on a fat-free diet do not grow or reproduce. The essential fatty acids are the critical components of fat (Holman, 1968). Essential fatty acids include linoleic acid and its omega-6 derivative, arachidonic acid and alpha-linolenic acid and its omega-3 derivative, docosahexaenoic acid. The active components in both series are the longer chain acids such as arachidonic acid and DHA. These are produced by desaturation and elongation or obtained from the diet. A high ratio of linoleic acid to alpha linolenic acid causes a depletion of the longer chain omega-3 fatty acids, including DHA, by competing with the enzymes necessary for desaturation and elongation.

Presently, most population of the world had a higher intake of omega-6 as compared to omega-3.The present ratio in Malaysia is 10 and in the US is greater than 10, causing a deficiency of the omega-3 fatty acids. The excess of omega-6 fatty acids stimulates the formation of arachidonic acid, the fatty acid precursor of prostaglandins and other eicosanoids that are involved in inflammation. Although some arachidonic acid is essential, the present high ratio may be responsible for the increased incidence of arthritis and other chronic inflammatory diseases. Much evidence supports the conclusion that an increased intake of linoleic acid and an elevated ratio of omega-6 to omega-3 fatty acids is a major risk factor for western-type cancers, thrombotic diseases, apoplexy, allergic hyper reactivity, and other diseases. Anti-inflammatory drugs are effective and are extensively used for such diseases (Okuyama, 1997).

PRESENT SCENARIO

Based on this evidence, the Japan Society for Lipid Nutrition recommended that the ratio of omega-6 to omega-3 fatty acids should be less than 4:1 for healthy adults and less than 2:1 for the prevention of the chronic diseases of the elderly. The World Health Organization (FAO/WHO, 1993) and others (The British Nutrition Foundation, 1992) are now recommending a ratio of 3:1 to 4:1 for omega-6 to omega-3 fattyacids. Flaxseed oil is rich in essential fatty acid whilst fish and other seafood containing long-chain omega-3 polyunsaturated fatty acids (PUFA) are essential nutrients. The most biologically active omega-3 fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Both have been shown to have multiple beneficial effects, including improvement of the childhood development when ingested during pregnancy (Jensen, 2006).

Fetal brain growth is accelerated during the second half of the pregnancy, and the rate of growth remains high during the first year of life with continued growth for the next several years. It is likely that, during pregnancy, omega-3 requirements increase over normal to support fetal growth, particularly for the brain and eyes. Data from animal studies showed that deprivation of omega-3 fatty acids during pregnancy is associated with visual and behavioral deficits that cannot be reversed with post-natal supplementation (Nesheim and Yaktine, 2007). Based upon these reasons, it is important that adequate intake of omega-3 fatty acids should be consumed throughout pregnancy (Jensen, 2006).The use of nutraceuticals in Malaysia was higher among Chinese women in comparison to other ethnic groups' i.e Malay and Indians. In general it was found that women were more likely to use nutraceuticals for sliming purpose, while men used it for improving the body function (Khan, Hassali and Mohammad Al-Haddad, 2011).

But little is known about the knowledge of the Malaysian regarding omega-3, the safety and benefits of omega-3 especially its use in pregnancy. Thus the present review attempts to provide the consumers and health care providers the proper information on the benefits of omega-3. The safety concerns as well as the process of consumption of an adequate amount of omega-3 fatty acids during pregnancy will be addressed in the present study.

WHAT ARE OMEGA-3 FATTY ACIDS?

Essential fatty acids are lipids that cannot be synthesized within the body and must be ingested through the diet or from supplements (Bell, *et al.*, 1997). Two families of essential fatty acids, omega-3 and omega-6 are required for physiologic functions including oxygen transport, energy storage, cell membrane function, regulation of inflammation and cell proliferation.

Humans can synthesize many other fatty acids, such as saturated and monounsaturated fatty acids, but are incapable of making fats with the first double bond at the omega-3 and omega-6 position. These polyunsaturated fatty acids are required for normal growth and maturation of many organ systems, most importantly the brain and eye (Innis and Friesen, 2008).

The parent fatty acid for omega-3 is alpha-linolenic (ALA) acid and for omega-6 the parent fatty acid is linoleic acid (LA). LA is converted to the biologically active omega-6 fatty acid, arachidonic acid (AA), which is involved in cell-signaling pathways and functions as a precursor for pro-inflammatory eicosanoids. ALA is converted to the biologically active omega-3 fatty acid, EPA, which, inturn, is converted to the omega-3 fatty acid, DHA. DHA is the critical component of cell membranes in the brain and retina, where it is involved in visual and neural function as well as neurotransmitter metabolism (Innis and Friesen, 2008). The accumulation of DHA begins in utero and is derived predominantly through placental transfer. Ultimately, fetal DHA concentrations are determined by maternal diet as the human body is not efficient at converting ALA to DHA.

Diets that are balanced for both omega-6 and omega-3 may cause less inflammation and immuno suppression. But unfortunately, the Malaysian diet is lopsided with too many omega-6s and too few omega-3s, which may lead to a pro-inflammatory milieu. This may increase the risk of chronic diseases such as cardiovascular disease, type 2 diabetes, and osteoarthritis (Simopoulos, Leaf, and Salem, 1999).

UTILITY OF OMEGA-3 DURING PREGNANCY AND FIRST YEAR OF LIFE:

Omega-3 Fatty Acids: Effect on the Pregnancy and on the Fetus

Consumption of omega-3 fatty acid during pregnancy either in the diet or via supplements is associated with improved developmental outcomes in children (Oken and Bellinger, 2008; Hibbeln *et al.*, 2007; Helland *et al.*, 2003; Makrides *et al.*, 2010). Various tests such as problem solving and language development were used to assess developmental outcomes among infants whose mothers were supplemented with fish oil compared with those who were not. A higher maternal fish consumption during pregnancy resulted in higher novelty preference on visual recognition memory and higher scores of verbal intelligence (Oken and Bellinger, 2008).

Children born to mothers who reported no seafood intake had the greatest risk of adverse or suboptimal outcomes. These included testing in the lowest quartile for verbal and performance IQ at 8 years of age, behavioral problems at age 7 years, and poor scores on early development tests evaluating fine motor skills, social skills, and communication skills (Hibbeln *et al.*, 2007). They also noted that for those women with high maternal seafood intake during pregnancy is less likely to have a child with these suboptimal outcomes. There was, however, no difference in children born to women who ate more than 340 g per week of seafood than children born to women who ate less than that amount of seafood.

This finding is supported by a randomized, double-blind study conducted in women who were supplemented with either cod liver oil or placebo during pregnancy and lactation (Helland *et al.*, 2003). The children born to the mothers supplemented with cod liver oil had a 4% point advantage in scores on the Kaufman Assessment Battery for Children (K-ABC). A more recent randomized, controlled trial that followed infants up to age 18 months, however, found no difference in cognitive and language scores between offspring of women supplemented with fish oil during pregnancy and those who received placebo (Makrides *et al.*, 2010; DOM InO Investigative Team, 2010).

OMEGA-3 FATTY ACID AND LACTATION

Adequate supplies of arachidonic acid and DHA are needed for brain growth and functional development of infants (Dyerberg *et al.*, 1995). Both neural integrity and function can be permanently disturbed by deficits of omega-6 and omega-3 essential fatty acids during fetal and neonatal development (Innis, 1994; Anderson, 1994). The levels of DHA in mother's milk vary considerably and are dependent on the diet of the mother. Intake of linoleic acid and alpha linolenic acid derivative from vegetable oils, the precursor to arachidonic acid and DHA, did not increase the levels of arachidonic acid and DHA. It is thus necessary to supplement the mother's diet with preformed long-chain polyunsaturated fatty acids (Ratnayake and Hollywood, 1997). In one study it was shown that consumption of herring or menhaden oil by lactating women significantly increased the levels of DHA in human milk within 6 h with maximum levels at 24 h (Francois *et al.*, 1998).

Jensen (2006) reported that lactating women who received 200 mg of DHA per day for 4 months had infants who performed significantly better on the Bayley Psychomotor Development Index after 30 months compared with women who received a vegetable oil supplement. Fish oil supplementation taken during pregnancy and lactation also resulted in a decreased risk of infant allergies (Furuhjelm *et al.*, 2009). It would appear that omega-3 also played an important role in the mental development of infants when taken by lactating mothers.

A few studies in animals have shown that pretreatment with DHA as well as treatment with DHA reduced the degree of functional deficits after a hypoxia ischemic injury (Berman *et al.*, 2010; Zhang *et al.*, 2010). This finding is important as hypoxic ischemic injury in births may lead to cases of cerebral palsy (Graham *et al.*, 2008; Wu *et al.*, 2004). This is promising and future studies may focus on the long term effects of hypoxic ischemic encephalopathy.

Preclinical and clinical studies have indicated that omega-3 fatty acid taken during pregnancy and lactation is important for fetal brain development and the child's subsequent neuro development. Omega-3 fatty acid deprivation during pregnancy is also shown to be associated with impaired developmental and behavior scores.

Premature Birth and ratio of omega-6 to omega-3 fatty acids:

Premature labour is still the leading cause of neonatal morbidity and mortality in Malaysia and also globally. The pathophysiology of premature birth is largely a mystery. Risk factors such as the role of diet and medication needs more research.

Maintaining the correct plasma ratio of omega-6 : omega-3 is essential for maintenance of wellness. A high ratio of omega-6 to omega-3 fatty acids will result in increased pro-inflammatory eicosanoid production (i.e. prostaglandin E2 [PGE2] and prostaglandin F2 (PGF2). These metabolites have been associated with the initiation of labour and preterm labour. Including more EPA in the diet may lead to a reduction in the production of pro-inflammatory eicosanoids and increased production of prostacyclin (PGI2), which may promote myometrial relaxation (Fig.1). Omega-3 fatty acids inhibit the production of prostaglandins PGE2 and PGF2, and may thereby inhibit the parturition process (Olsen, 2004; Roman *et al.*, 2006).

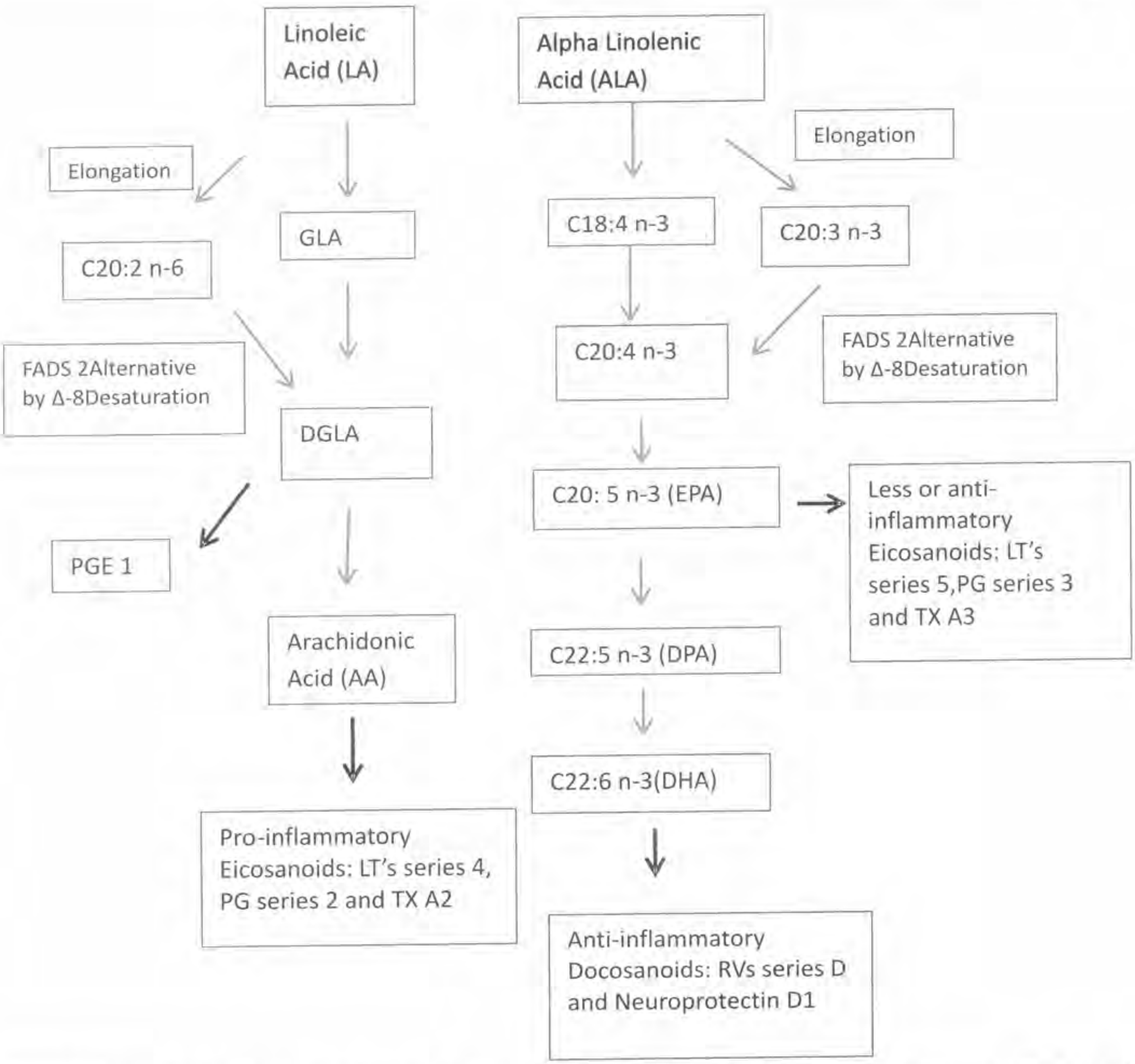

Figure 1: Scheme showing metabolism of essential fatty acids (EFAs). Dietary EFAs linoleic acid (LA) is converted to ã-linolenic acid (GLA), dihomo-GLA (DGLA) and arachidonic acid (AA). á-linolenic acid (ALA) is converted to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). DGLA forms precursor to 1 series of prostaglandins (PGs), AA is the precursor of 2 series of PGs and thromboxanes (TXs) and 4 series leukotrienes (LTs). EPA is the precursor of 3 series PGs, TXs and 5 series LTs. In general, most of the PGs, TXs and LTs have pro-inflammatory actions. But, some such as PGE1, PGI2 and PGI3 show anti-inflammatory properties and have vasodilator and platelet anti-aggregatory actions. In addition, AA, EPA and DHA give rise to anti-inflammatory compounds lipoxins, resolvins and protectins.

Historically, the study on the possibility of dietary supplementation of omega-3 fatty acids in the prevention of preterm birth originated from studies conducted in the Faroe Islands. Compared to the dietary intake in Denmark, the population of the Faroe Islands has a higher intake of marine foods, and babies born to these women have higher birth weights (about 200 g) at full term. In fact, birth weights of babies from the Faroe Islands are higher than those in 33 other countries (Olsen and Joensen, 1985).

However, a number of randomized, controlled trials have attempted to validate these findings, but with variable results. Four randomized, controlled trials have demonstrated either a reduction in the rate of preterm birth or an increase in the average length of gestation (Smuts *et al*., 2003; Coletta, Bell and Roman, 2010)

On the other hand, an equal number of trials have found no impact of fish oil or omega-3 fatty acid supplementation on the rate of preterm birth or length of gestation (Bulstra-Ramakers, Huisjes and Visser, 1995; Helland, Saugstad and Smith *et al*., 2001; Ramakrishman *et al*., 2010).

Since the effect of omega-3 fatty acid on the length of gestation is not conclusive, its supplementation cannot be recommended for the sole purpose of prolong ingestation or reducing the risk of preterm birth. However, the amount of omega-3 fatty acids derived from the recommended amount of seafood intake or daily supplementation to optimize fetal brain development may have the added benefit of reducing the risk of preterm birth in high-risk populations especially women with a history of preterm birth or women with low baseline omega-3 fatty acid intake.

REQUIREMENT OF OMEGA 3 FATTY ACID

PREGNANCY

Additional requirement for dietary fat during pregnancy is needed to provide maternal fat storage during the early trimester, and subsequent uterine growth, preparative development of the mammary glands, the expansion of blood volume, and placental and foetal growth in the second and third trimesters (FAO/WHO, 1994). The Recommended Nutrient Intakes (RNI) in pregnancy (2nd trimester) for Malaysiais 54-82 g/day and Pregnancy(3rd trimester) is 57-85 g/day (NCCFN, 2005).

LACTATION (1-6 MONTHS)

Most Malaysian women breast fed their child and breast milk is the preferred source of nutrition for infants in this age group. Human milk provides 50-60% of its energy as lipid in which about 5% energy is EFA (LA + ALA) with 1% energy as long-chain polyunsaturated fatty acids (LCPUFA)(FAO/WHO, 1994).

During lactation, it has been estimated that about 3-5g of EFA are secreted in average of 850 ml milk produced per day; part of this amount will be as long chain-PUFA. The EFA requirements during lactation are recommended at 2-4% energy above basic EFA requirements, making the total requirement as 5-7% energy (FAO/WHO, 1977). This physiological condition during lactation probably represented human's highest requirement for dietary LA. The RNI for lactating women is 58 - 86 g/day (1st 6 months) (NCCFN, 2005).

During weaning, the fat component is able to provide 30-40% of the dietary energy (FAO/WHO, 1994). This means that complementary foods used during the weaning period should include adequate amounts of fats and oils as the breast milk component of the diet declines. The RNI is 31 - 37 g/day (0 - 5 months) and 21 - 28 g/day (6 - 11 months) (NCCFN ,2005).

OMEGA-6/OMEGA-3 FATTY ACID (FA) BALANCE

The omega-6 FA in the diet consists of mainly LA and its metabolite, arachidonic acid (AA), while the omega-3 FA comprises ALA, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Currently, the omega-6/omega-3 FA ratio of the typical Malaysian diet is about 3.5/0.35, i.e. 10 (Ng, 1995), while in the diets of western populations this ratio is much higher, i.e. 15-20.

FAO/WHO (1994) recommends an omega-6/omega-3 FA ratio of 5-10. Both the absolute amounts of omega-6 and omega-3 FA, as well as their ratio are important nutritional considerations. Increasing the intake of omega-3 poses a serious challenge and any excess intake of LA (>7% energy) would make achieving the recommended omega-6/omega-3 FA ratio even more difficult.

The omega-3 fatty acid intake of the average Malaysian is currently low and correcting this imbalance by increasing the intake of EFA and DHA requires substantial changes in dietary habits.

There are a number of ways that we can remedy this, namely:

(1) Eating more fish and vegetables such as beans, dhall and tofu

(2) Usage of cooking oil that is a blend of palm olein + an omega-3rich vegetable oil (eg. canola, soybean)

(3) Use edible oil in salads

(4) Include omega-3 enriched eggs into diet and

(5) Take daily supplements of DHA

FOOD SOURCES FOR OMEGA-3 FATTY ACIDS

Fetal development is dependent on many essential nutrients including DHA and EPA. EPA can only be obtained from dietary sources (Koletzko *et al*., 2008). The richest sources of these omega-3 fatty acids are marine sources, such as fish (especially deep-sea type), other seafoods (EPA + DHA), fish oil supplements and Omega-3 enriched eggs (EPA + DHA)(NCCFN, 2005).

Potential sources of omega-3 fatty acid content of Malaysian fish (Table 1), vegetable oils (Table 2) and meat and eggs and vegetables (Table 3).

Table 1: Potential sources of omega-3 in selected fish and seafood (Ng, 2006)

Fish and seafoods	Omega-3 (mg) content in 55 gm serving
Jelawat	350
Tuna	170
Sardines	165
Perch (Siakap)	130
Crab	175
Shrimp	135
Eel (Belut)	95
Anchovy	25
Haruan	20
Tilapia	20
Carp ("Lee koh")	15

Among the fishes Tenualosatoli (Terubok), Rastrelligerkanagurta (Kembung) Stolephorusbaganensis (Bilis), Pangasius hypothalamus (Patin), Clariasmacrocephalus (Keli) and Channastriatus (Haruan) showed a considerable amount of saturated and unsaturated fatty acids (Muhamad and Mohamad, 2012).

Other sources of omega-3 fatty acids such as Flaxseed oil, perilla oil (50-60% ALA), Canola oil, grape seed oil (11% ALA), Soybean oil (8% ALA) and Pulses (eg. beans, dhall), certain nuts/seeds (eg. walnut, linseed) vegetable oils contain ALA that needs to be converted to the active form which is the longer-chain EPA and DHA (Table 2).However, this conversion is a slow and inefficient process as only 5 to 7 % of ingested ALA is converted into omega-3 LC-PUFAs.

Table 2: Potential sources of ALA in selected edible oils (Ng, 2006).

Edible Oils	ALA (mg) content in 6 gm serving
Flaxseed oil	2640
Perilla oil	2400
Cod liver oil	1170
Canola oil	600
Walnut oil	560
Soybean oil	400
Palm oil	30

Table 3: Potential sources ofomega-3 in selected meat,eggs and vegetables (Ng, 2006).

Meat and Eggs	Serving	Omega-3 (mg)
Egg (hen, omega-3 enriched) Egg (hen, regular) Beef Chicken	1 egg (50 g) 1 egg (50 g) 55 g 55 g	300 50 60 50
Vegetables		
Soyabean milk Soyabean curd "tau-hoo" Soyabean curd: "fucok" Soyabean sprout ("taugeh") Legumes (beans, peas) Green leafy vegetables	1 pkt (250 ml) 1/2 pc (76 g) 1 sheet (28 g) 1/2 cup (52 g) 1/2 cup (98 g) 1/2 cup (60 g)	400 276 126 77 75 50

SAFETY CONCERNS

The maximum tolerated dose for omega-3 fatty acid is 0.3 g/kg/day and a 70 kg patient can consume up to 21g/day. Dose limiting toxicity in the case of gastrointestinal disease, mainly diarrhea is recommended (Burns, *et al*., 1999). To optimize pregnancy outcomes and fetal health, consensus guidelines have been recommended for pregnant women to consume at least 200 mg of DHA per day (Koletzko *et al*., 2008). A woman can achieve this threshold by consuming 1 to 2 servings of seafood per week, the dietary intake consistent with the current US Food and Drug Administration (FDA) and Environmental Protection Agency (EPA) advisory. But seafood can also contain organic mercury and other harmful toxins (eg, polychlorinated biphenyls [PCBs]), which could be harmful to the growing fetus (Ser and Watanabe, 2012).

Mercury is a reactive heavy metal emitted from both natural and human sources. Although inorganic mercury is poorly absorbed and does not readily cross tissue barriers, methylmercury is a known neurotoxin and accumulates in aquatic food chains with levels depending on the predatory nature and lifespan of the species. Larger, longer-living predators like swordfish, king mackerel, shark, and tilefish—have higher tissue concentrations than smaller, shortlived species (eg. salmon, pollock).

As methylmercury crosses the placenta, fetal exposure correlates directly with maternal ingestion. A positive correlation between maternal seafood consumption and neurotoxicity in exposed fetuses was first noted in women exposed to the industrially polluted Minimata Bay in Japan in the 1950s (Mozaffarian and Rimm, 2006).

In Malaysia, the average fish consumption is 180.19 + 11.34g/day/person with higher fish consumption in rural communities compared with the urban communities. More than half of the Malaysian population (59.30%) in this study exceeded the safe limit of 1 ppm total hair mercury concentration, as recommended by the U.S. Environmental Protection Agency (USEPA) (TengkuHanidza *et al.*, 2010).

The Malaysian public should be educated about the risks and benefits of fish consumption. The benefit of eating small fish outweighs the risk of mercury exposure. According to Knobeloch *et al.* (2007), children and women of child bearing age should be limited to 6 ounce meal or 3 ounce meals per week. They suggested that fish such as northern pike and bass contain moderate mercury level, therefore should be limited to one meal per month. For big predatory fish, such as swordfish and shark, these should be avoided. Model simulation performed by Cohen *et al.* (2005) showed that women of child bearing age can reduce MeHg exposure but maintain comparable n-3 PUFAs by changing their fish consumption pattern from consuming fish with high (>0.6 ìg/g) or medium (0.14-0.6 ìg/g) MeHg concentration to fish with low (<0.13 ìg/g) MeHg.

CONCLUSION

Omega-3 fatty acids are essential for life and must be obtained from dietary means, either from seafood or fish oil capsules. It is likely that, during pregnancy, omega-3 requirements increase over normal requirements to support fetal growth, particularly the brain and eyes. Pregnant women can limit the effects of contaminants on their fetus by limiting fish intake to 2 servings per week and by avoiding larger predatory fish that tend to be higher in mercury concentration. Consumption of higher amount of fish may pose a risk of mercury toxicity, although the absolute risk is small. Alternate sources of DHA include fish oil capsules, which provide variable amounts of DHA (ranging from 150-1200 mg/d), and are low in contaminants such as mercury and other harmful compounds like PCBs. Many prenatal vitamins contain up to 200 to 300 mg of DHA. DHA-enriched eggs are another source of omega-3 fatty acids and may contain up to 300 mg of DHA per egg. Prospective studies in pregnant women who consumed the recommended fish intake or received supplements of fish oil generally demonstrate a beneficial effect on neuro developmental outcomes of offspring (Coletta, Bell and Roman, 2010).

The use of omega-3 acid supplementation solely for the purpose of reducing the risk of preterm birth is not recommended due to lack of clinical data. Lactating women did not benefit from intake of LA and ALA, as they were not found to increase DHA levels in breast milk. Thus lactating women need supplementation with preformed DHA. An intake of 200 mg of DHA per day by lactating women is sufficient to ensure improved neurodevelopment outcomes in the child. Malaysians ratio of omega-6 to omega-3 is high and need to be improved. In order to reduce the ratio from 10 to 4 or lower require a significant change in dietary habits.

In general, DHA foods are beneficial because DHA is essential for brain functioning. The inclusion of plentiful DHA in the diet improves learning ability and the development of the brain. DHA is good for the eyes and is helpful in recovery from certain visual dysfunctions. DHA has been reported to prevent and treat senile dementia. DHA has a positive effect on diseases such as hypertension, arthritis, atherosclerosis, depression, diabetes mellitus, myocardial infarction, thrombosis, heart disease, and some cancers. Thus the consumption of omega-3 acid or its precursor is beneficial for pregnant mother and every individual for the eradication of various diseases and motor development.

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