

Effect of Omega 3 Fatty Acids in Reducing Risk of Preterm Labour

Benish Khanzada¹, Saba Mansoor¹, Tehmina Rehman¹, Shahzad Naeem^{2*}

¹Department of Obstetrics & Gynecology, Qims, Fc Hospital Quetta, Pakistan

²Department of Obstetrics & Gynecology, Riphah International University, Islamabad, Pakistan

*Corresponding author: Shahzad Naeem, Assistant Profesor Department of Obstetrics & Gynecology, Riphah International University, Islamabad, Pakistan, Tel: 03335491914; E-mail: shahzadflyer@yahoo.com

Recieved date: March 21, 2018; Accepted date: March 29, 2018; Published date: March 31, 2018

Copyright: © 2018 Khanzada B, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Objective: To compare effect of Omega 3 fatty acid supplementation versus no supplementation in high risk pregnant females from 20 weeks gestation in terms of frequency of preterm delivery.

Methods: We conducted a prospective randomized controlled clinical trial in department of Obstetrics and Gynecology and, Railway Teaching Hospital Islamic International Medical College Trust, from January 2015 to Jan 2017. Women with a history of prior spontaneous singleton preterm birth and a current singleton gestation were divided into two groups A and B by computer generated random numbers. Omega 3 fatty acid supplementation was given to group A patients from 20 weeks to 36 weeks gestation and patients in group B was received no such treatment. Frequency of preterm delivery was compared among patients of both groups.

Results: A total of 500 women with singleton pregnancy with history of one or more preterm deliveries were included, and none was lost to follow up. The mean duration of pregnancy at delivery between the omega3 supplemented and control groups [38.2 (SD, 0.6) weeks and 36.6 (SD, 0.9) weeks, P<0.0001 respectively] was statistically different. The data were also analyzed for birth weight and statistically significant difference of the weights were found in the two groups [3.2 (SD, 0.233) and 2.8 (SD, 0.259) controls P <0.0001].

Conclusion: In this study we found that gestational age and birth weight, both are significantly improved with oral administered omeg-3 in high risk pregnancy when compared with controls.

Keywords: Omega 3 fatty acid; Pregnancy; Preterm Delivery

Introduction

Preterm delivery defines as birth that occurs before 37 weeks of gestation [1]. It complicates about 5-18% of pregnancies and is the single most important determinant of adverse infant outcomes, by increasing neonatal morbidity and mortality and late pathologic sequelae [2].

Maternal nutrition, particularly micronutrients involved in one carbon metabolism (folic acid, vitamin B12 and docosahexaenoic acid) have a major impact on foetus development and determination of epigenesis [3]. Several possible mechanisms have been proposed but it may be important to have a testable mechanistic hypothesis that can explain the possible common mechanism of preterm births around the globe [4]. A series of studies in pregnancy complications have well established the role of omega 3 fatty acids especially docosahexaenoic acid. In one carbon metabolic pathway membrane phospholipids are major methyl group acceptors and reduced docosahexaenoic acid levels may result in diversion of methyl groups towards deoxyribonucleic acid resulting in DNA methylation. So it is proposed that altered maternal micronutrients, increased homocysteine and oxidative stress levels that cause epigenetic modifications may be one of the mechanisms that contribute to preterm birth and poor fetal outcome [5,6].

Lower maternal erythrocyte docosahexaenoic acid concentration in pregnant women delivering preterm, suggest that increased oxidative stress may be responsible for decreased docosahexaenoic acid levels. This may alter the uterotonic factors like prostaglandins leading to premature triggering of labour. A single previous preterm delivery increases the risk of preterm delivery in subsequent pregnancy fourfold compared with a previous term delivery [7,8].

The purpose of this study is to explore the effect of Omega 3 fatty acids in reducing risk of preterm delivery so that Omega 3 fatty acid supplementation may be recommended in future for management of such patients.

Methodology

This prospective randomized controlled clinical trial is carried out in department of Obstetrics and Gynaecology of IIMCT-Railway Hospital Rawalpindi between Jan 2015 and Sep 2017. A total of 500 patients with singleton pregnancy and history of preterm delivery in previous pregnancy were included in this study through Consecutive non probability sampling. We excluded patients who had a non-viable fetus (before or after randomization), a history of placental abruption, bleeding episode in current pregnancy, use of prostaglandin inhibitors, multiple pregnancy, allergy to fish, regular intake of fish oil, a positive cervical swab for bacterial vaginosis infections, major fetal abnormalities. Gestational age was calculated based on the ultrasound scan performed in the first trimester of pregnancy and if not available between 16-18 weeks of gestation. We obtained written informed

consent from each patient by explaining to the patient the risks and benefits of the study, use of data for research and publication and details of medication and investigations required. The study was approved by the Local Ethics Committee of the "IIMCT-Railway Hospital Rawalpindi". Patients were divided into two groups A and B by computer generated random numbers. Omega 3 fatty acid supplementation was given to group A patients from 20 weeks to 36 weeks gestation and patients in group B was received no such treatment. Relevant entries for each patient were made in already prepared Performa, Confidentiality of the patient record were maintained and kept by the researcher. Patients' contact numbers were kept in record in order to avoid loss of follow up and followed until delivery. All data was analyzed by using SPSS version 17. Mean \pm Standard Deviation was calculated for quantitative variable like age, BMI, gestational age at the time of presentation and delivery. Frequencies and proportions were calculated for qualitative variables like preterm delivery. Chi-square test was used to compare between two groups. P value <0.05 was significant.

Results

For this study a total of 500 patients had the eligibility criteria were enrolled. As shown in table 1, there were no significant differences in

	Omega 3	N	Mean	Std. Deviation	Std. Error Mean
Preterm delivery	Yes	250	1.2	0.40684	0.07428
	No	250	1.8	0.40684	0.07428
Gestation age at delivery	Yes	250	38.2333	0.68699	0.12543
	No	250	36.6533	0.93578	0.17085
Weight of baby	Yes	250	3.2533	0.23302	0.04254
	No	250	2.8667	0.25909	0.0473

Table 2: Gestational Age and Weight of Baby.

Discussion

In our study we established that length of pregnancy and birth weight both were significantly improved with oral administered Omega 3 fatty acid in high risk pregnancy when compared with controls. Several randomized controlled trials and studies demonstrate that omega 3 supplementation seem to have a tocolytic effect that delay the onset of labor and reducing recurrence risk of preterm delivery [3]. Both maternal and fetal levels of omega-3 fatty acids are correlated to maternal intake, due to significant trans placental transportation. A proposed mechanism of action of omega-3 fatty acids reducing the risk of spontaneous preterm birth and therefore low birth weight is by altering the balance of prostaglandins PGE2 and PGF2 α and prostacyclin (PGI2). Increased intake of omega-3 fatty acids reduces the hepatic synthesis of omega-6 fatty acids which are precursors of PGE2 and PGF2 α . That cause myometrium contractility and cervical ripening. Their beneficial effect could also be attributed to their influence on the eicosanoids environment in favor of PGI2, which causes uterine relaxation [9,10] Another possible effect on the duration of pregnancy could be linked to antiarrhythmic activity exerted by omega 3 derivatives on the heart through Ca²⁺ channels that causes disorganization of the electrical myometrial activity, which could result in a delay in the onset of uterine contractions at regular interval and

baseline characteristics of omega 3 supplemented and control group. As shown in table 2, the mean duration of pregnancy at delivery between the treatment and control groups [38.2 (SD, 0.6) weeks and 36.6 (SD, 0.9) weeks, P<0.0001, respectively] was statistically different. There were a significant statistical birth weights difference in the two groups [3.2 (SD, 0.233) and 2.8 (SD, 0.259) controls P <0.0001, respectively] as shown in table 2.

	Cases (N=250)	Controls (N=250)	P
Maternal age (years)	32.6 \pm 4.6	32.2 \pm 4.8	0.81
BMI (Kg/m ²)	23.0 \pm 2.9	23.2 \pm 3.4	0.84
Cesarean Section	57.10%	47.60%	0.54
Previous preterm delivery	59.10%	52.40%	0.66
Shortening of cervix	73.60%	76.20%	0.37

Table 1: Baseline characteristics of enrolled patients.

delaying labor [10,11] In our study, at time of delivery, mean age of gestation between omega 3 supplemented group and not supplemented groups [38.2 (SD,0.6) weeks and 36.6 (SD,0.9) weeks respectively, P<0.0001] that is statistically significant. This finding is in agreement with Claudio Giorlandino whose study showed that the length of pregnancy and birth weight both significantly improved in high risk pregnancy where DHA administered when compared with controls but in his study they administered DHA vaginally instead of orally [12]. Same results have shown in a study conducted by Szajewska H, et al. [10] whose study analysis indicate that increase in duration of pregnancy by an average of 1.6d, at time of birth, in pregnancies where n_3 LC-PUFA supplementation was given during pregnancy. In RCT conducted by Koletzko, et al. [13] that shows significantly greater increase in duration of pregnancy (2.77 days) and significantly greater birth weight (97g; 95% CI: 8,186g) supplementation with fish oil supplemented pregnancies than control subjects.13 A studies conducted by Oken E, et al. [14], did not confirm these findings. Available results from RCTs involving women at high risk of preterm birth indicate that Omega-3 fatty acids supplementation during pregnancy are effective in preventing preterm delivery and has a small effect of prolonging gestation [15,16]. Whereas study by Meher A, et al. [17] and Zhou SJ, et al. [18] shows that Omega-3 fatty acid supplementation during pregnancy was not associated with prevention

of preterm birth, pre-eclampsia, IUGR or increasing birth weight in women with high-risk pregnancies. In our study, we found a statically significant difference of the birth weights in the two groups [3.2 (SD, 0.233) and 2.8 (SD, 0.259) controls $P < 0.0001$]. Overall, the findings agree with the randomized trials showing that consumption of fish oil in pregnancy can increase birth weight by prolonging gestation and reduce the risk of recurrence of preterm delivery [19,20,21]. These conclusions are based on limited available evidence, further studies with larger numbers of subjects are needed to examine that omega3 supplementation can prevent preterm birth and its consequences by prolonging pregnancy and increasing birth weight.

Conclusion

From the results of this study, it can be concluded that DHA administered during pregnancy, significantly improves both the length of pregnancy and birth weight in high risk pregnancies when compared to controls. Some evidence exists that improving maternal DHA status through supplements is vital since maternal DHA levels are correlated with fetal DHA status and also represent enhanced DHA stores to support lactation with small increment in the duration of pregnancy, early infant growth and cognitive development. So further research is needed in order to evaluate the use of Omega 3 supplementation during pregnancy.

References

1. World Health Organization: WHO Recommendations on Interventions to Improve Preterm Birth Outcomes. Geneva, WHO, 2015.
2. Grieger JA, Grzeskowiak LE, Clifton VL (2014) Preconception dietary patterns in human pregnancies are associated with preterm delivery. *J NUTR* 144: 1075-1080.
3. Dhobale M, Joshi S (2012) Altered maternal micronutrients (folic acid, vitamin B12) and omega 3 fatty acids through oxidative stress may reduce neurotrophic factors in preterm pregnancy. *J Matern Fetal Neonatal Med* 25: 317-323.
4. Imhoff-Kunsch B, Briggs V, Goldenberg T, Ramakrishnan U (2012) Effect of n-3 Long-chain Polyunsaturated Fatty Acid Intake during Pregnancy on Maternal, Infant, and Child Health Outcomes: A Systematic Review. *Paediatric and perinatal epidemiology* 26: 91-107.
5. Calabuig-Navarro V, Puchowicz M, Glazebrook P, Haghiac M, Minium J, et al. (2016) Effect of ω -3 supplementation on placental lipid metabolism in overweight and obese women. *Am J Clin Nutr* 103: 1064-1072.
6. Starling P, Charlton K, McMahon AT, Lucas C (2015) Fish intake during pregnancy and foetal neurodevelopment-A systematic review of the evidence. *Nutrients* 7-14.
7. Dhobale MV, Wadhvani N, Mehendale SS, Pisal HR, Joshi SR (2011) Reduced levels of placental long chain polyunsaturated fatty acids in preterm deliveries. *Prostaglandins, Leukotrienes and Essential Fatty Acids* 85: 149-153.
8. Larqué E, Gil-Sánchez A, Prieto-Sánchez MT, Koletzko B (2012) Omega 3 fatty acids, gestation and pregnancy outcomes. *Br J Nutr* 107: S77-84.
9. Mozurkewich EL, Klemens C (2012) Omega-3 fatty acids and pregnancy: current implications for practice. *Curr Opin Obstet Gynecol* 24: 72-77.
10. Szajewska H, Horvath A, Koletzko B (2006) Effect of n-3 long-chain polyunsaturated fatty acid supplementation of women with low-risk pregnancies on pregnancy outcomes and growth measures at birth: a meta-analysis of randomized controlled trials. *Am J Clin Nutr* 83: 1337-1344.
11. Harris MA, Reece MS, McGregor JA, Wilson JW, Burke SM, et al. (2015) The effect of omega-3 docosahexaenoic acid supplementation on gestational length: randomized trial of supplementation compared to nutrition education for increasing n-3 intake from foods. *Biomed Res Int* 2015 1-8.
12. Giorlandino C, Giannarelli D (2013) Effect of vaginally administered DHA fatty acids on pregnancy outcome in high risk pregnancies for preterm delivery: a double blinded randomised controlled trial. *J Prenat Med* 7: 42.
13. Koletzko B (2005) Early nutrition and its later consequences: new opportunities. In *Early Nutrition and its Later Consequences: New Opportunities*. Springer Netherlands 1-12.
14. Oken E, Kleinman KP, Olsen SF, Rich-Edwards JW, Gillman M (2004) Associations of seafood and elongated n-3 fatty acid intake with fetal growth and length of gestation: results from a US pregnancy cohort. *Am J Epidemiol* 160: 774-783.
15. Leventakou V, Roumeliotaki T, Martinez D, Barros H, Brantsaeter AL, et al. (2014) Fish intake during pregnancy, fetal growth, and gestational length in 19 European birth cohort studies. *Am J Clin Nutr* 99: 506-516.
16. Kar S, Wong M, Rogozinska E, Thangaratinam S (2001) Effects of omega-3 fatty acids in prevention of early preterm delivery: a systematic review and meta-analysis of randomized studies. *Eur J Obstet Gynecol Reprod Biol* 198: 40-46.
17. Meher A, Randhir K, Mehendale S, Wagh G, Joshi S (2016) Maternal fatty acids and their association with birth outcome: a prospective study. *PLoS one* 11: e0147359.
18. Zhou SJ, Yelland L, McPhee AJ, Quinlivan J, Gibson RA, et al. (2012) Fish-oil supplementation in pregnancy does not reduce the risk of gestational diabetes or preeclampsia. *Am J Clin Nutr* 95: 1378-1384.
19. Le Donne M, Alibrandi A, Vita R, Zanghi D, Triolo O, et al. (2016) Does eating oily fish improve gestational and neonatal outcomes? Findings from a Sicilian study. *Women Birth* 29: e50-57.
20. Akerele OA, Chema SK (2016) A Balance of Omega-3 and Omega-6 Polyunsaturated Fatty Acids is Important in Pregnancy. *J Nutr* 5: 23-33.
21. Grieger JA, Clifton VL (2014) A review of the impact of dietary intakes in human pregnancy on infant birthweight. *Nutrients* 7: 153-178.