Effect of Omega–3 Supplementation on Hormone Profile in Women with Poly Cystic Ovarian Syndrome

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Abstract
Poly Cystic Ovarian Syndrome (PCOS) affects women in their reproductive ages, and is a hormonal disorder usually marked by high levels of androgen hormones. Approximately 2.2% - 26 percent of Indian women suffer from PCOS. Dietary modifications and exercise normalize the androgen levels and thus improve reproduction, hence are effective treatments for PCOS management. Omega-3 Fatty acid supplementation (i.e. fish oil capsule) are important in the management of PCOS. The present study aimed at assessing the impact of fish oil capsule supplementation on serum LH, FSH and Testosterone levels of women with PCOS. For the present study, forty women between the ages of 18-40 years, having PCOS were selected using purposive sampling technique. Blood samples were taken and analysed for the parameters to be studied, before and after 3 months of supplementation. BMI of the respondents was also assessed prior to and after intervention. The results of the study reveal a significant decrease (at 0.01%) in the mean serum LH levels. A statistically non-significant reduction in the mean Testosterone and mean FSH levels of the respondents was observed. Supplementing the two Fish Oil capsules per day for a period of 90 days resulted in an improved serum LH level.

Key words: PCOS, Hormone profile, LH, FSH, Testosterone, Omega-3 Fatty Acids, fish oil

1. Introduction:
Poly Cystic Ovarian Syndrome (PCOS), was first reported in 1935 by Stein and Leventhal, and is now prevalent as the commonest female endocrine disorder (Baptiste et al, 2010) causing anovulatory infertility, affecting up to 15% of women in the US and up to 33% in UK (Fakhoury et al, 2012, Taher et al, 2012, Ganie and Karla, 2011). Around 2.2% to 26% of the Indian women have been reported to have this disorder (Nidhi et al., 2011). The causes implicated for PCOS are multifactorial. Raised levels of androgens & insulin, chronic inflammation, genetic & environmental factors as well as obesity, contribute to the pathogenesis of this disorder (Kelly et al 2013; Goodarzi et al 2011; Diamanti et al 2009 and Arslanian & Witchel, 2002). Idiopathic hirsutism and oligomenorrhea are commonly reported in women with polycystic ovaries (Adamas et al 1986). These are accompanied by other symptoms which include irregular menstruation, acne (Alemzadeh et al 2010; Hassa et al 2006) alopecia, miscarriage (Eid et al., 2005) and obesity which is an important contributing factor for PCOS (Setji et al 2007). Research shows that 35-50% of women with multiple ovarian cysts are obese. A high rate of hirsuitism and anovulation is observed in obese women as compared to non-obese women with ovarian cysts (Pettigrew et al., 1997). Metabolic syndrome in US women with PCOS is commonly reported by 33%–50% of women, as compared to 12% in a similarly aged general population (Glueck et al, 2003). Becoming pregnant may be difficult for women with ovarian cysts as they have high levels of serum testosterone. These high testosterone levels may bring about the symptomatology of PCOS and also affect organs like brain, liver, pancreas, muscle and fat ( NIH, 2012) Apart from the raised serum androgens, PCOS induced other endocrine abnormalities may be increased levels of Luteinizing Hormone (LH), altered levels of FSH, raised LH/FSH ratios and hyperinsulinemia. An increased risk of NIDDM, gestational diabetes, stroke, raised blood lipid
levels, coronary artery disease and endometrial carcinoma are associated with PCOS (Eid et al 2005).

Dietary modifications and exercise improves the androgen levels, reproductive function, hence are effective treatments for the management of PCOS (Moran et al. 2004). Research shows that a 5-10% loss in body weight in overweight PCOS women by restriction of energy, reduces hyperinsulinemia, lowers the raised androgen levels (Hoeger et al., 2006), brings about menstrual cycle regularity (Crosignani et al., 2003), and decreases the risk of heart diseases (Moran et al., 2003). Along with weight loss, achieving the desirable levels of circulating insulin concentrations exerts many benefits (Norman et al., 2002). Supplementation of the diet with Omega-3 Fatty acids is important in the management of PCOS. Fish oil exerts antiatherogenic and anti-inflammatory effects. Dietary Polyunsaturated Fatty Acids (PUFA) also have been proven to have a beneficial effect on glycemic and lipidemic profile (Ebbesson et al 2005). Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA) alter metabolic parameters positively & this can be due to the increase in adiponectin production (Kartz et al 2008). Mehendale et al (2009) reported reduced EPA (plasma) and erythrocyte DHA levels in infertile women with the control group and postulated that omega-3 fatty acids help in managing the female infertility. Cussons et al (2009) reported that there was a beneficial effect of omega-3 fatty acid supplementation on cardio-metabolic risk factors in PCOS patients.

2. Objective

The objective behind conducting the present study was to study the impact of fish oil capsules on Leutinising Hormone (LH), Follicle Stimulating Hormone (FSH) and Testosterone levels of women with PCOS.

3. Materials and Methods

For the present study, forty women with polycystic ovarian syndrome, were selected using purposive sampling technique from a hospital in Jaipur, India. The selection of the respondents was done as per the inclusion criteria. They were given 2 capsules of fish oil per day (each containing 300 mg fish oil) for an intervention period of 90 days. Blood samples were analysed for the parameters under study, at baseline and after 90 days of supplementation.

Table 4.1: Mean Difference (from pre to post intervention) in Hormone Profile and Body Mass Index of subject on fish oil capsule supplementation

| S.No | Variable     | Mean Difference (From pre to post intervention) |
|------|--------------|--------------------------------------------------|
| 1    | Testosterone (ng/dl) | ↓3.52 ns                                          |
| 2    | LH (mIU/ml)  | ↓1.96**                                             |
| 3    | FSH (mIU/ml) | ↓0.15 ns                                              |
| 4    | Weight (kg)  | ↓0.18 ns                                              |
| 5    | BMI          | ↓0.06 ns                                              |

NS = Non-significant; ** p<0.01
A statistically non-significant reduction was observed in the difference of mean values (the difference in the values of means from pre intervention to post intervention) of Body Mass Index (BMI) of the subjects (Table 4.1; Figure 4.2)

5. Discussion

Research indicates that PCOS has started affecting younger girls nowadays, thus bringing about a need to generate awareness about PCOS among young females (Bronstein et al., 2011).

PCOS is a common condition (Kauffman et al, 2008; Azziz et al, 2004) which makes a woman more prone to problems related to reproduction like infertility, cancer of the endometrium, delayed menopause (Navaratnarajah et al, 2008; Balen et al, 1995). They also have elevated chances of metabolic alterations, like insulin resistance, adult onset diabetes, elevated lipid levels and diseases of the heart (Christakou et al, 2008; Talbott et al, 2004). Ovulation is enhanced by increased levels of omega-3 fatty acids which are alpha-linolenic, EPA and DHA. Supplementing the diet with omega 3 fatty acids and consuming food sources rich in these fatty acids may be beneficial in glucose clearance, insulin sensitivity, reducing fat deposition, promoting heart health, promoting ovulation & correcting depression (Bramon,2005) and also in improving the hormone profile by altering the LH levels & thereby decreasing the testosterone concentration (Forouhia et al, 2015; Nadjarzadeh et al, 2013). LH helps in androgen production by theca cells, whereas aromatization of these androgens to oestradiol by granulosa cells is done by FSH (Bart et al, 1997).

The findings of the present study show a significant reduction in the mean levels of Luteinizing Hormone after fish oil capsule supplementation and this may prove beneficial for the treatment of PCOS. A similar study reported a decline in the serum LH as well as testosterone levels and simultaneously, a significant increase in sex hormone binding globulin after supplementation with omega 3 fatty acids over a period of 6 months (Oner and Murderris et al 2013).

In a meta-analysis it was concluded that Omega-3 supplements containing EPA and DHA were of help in achieving statistically significant reductions in testosterone levels of PCOS women (Forouhia et al, 2015)

Supplementation with 3 capsules of omega-3 (each containing 180 mg EPA and 120 mg DHA) daily for 2 months, resulted in a decrease in mean LH along with a significant change in LH/FSH ratio between groups in the omega-3 group, but no change in FSH (Nadjarzadeh et al 2015). In yet another study, no significant changes in concentrations of estrogen, LH, or FSH after fish oil capsule supplementation were reported (Phelan et al. 2011).

Obesity worsens PCOS. Research shows that in women with PCOS, fish oil supplementation at a dosage of 3.5 g/day for 6 weeks did not alter the body weight, BMI and Waist Circumference (WC) significantly, as compared to control group (Vargas et al, 2011). On the other hand, in a study conducted by Silva et al. (2013) BMI, WC and WHR were reduced after fish oil supplementation in women with type 2 diabetes. Khani et al (2017); Mohammadi et al (2012) and Hajianfer et al (2011) show that BMI in omega-3 fatty acid group was reduced significantly after intervention in comparison to the control group.

One gm of EPA/DHA daily in addition to consuming fish at least twice per week benefits Coronary heart disease patients, as per the recommendations of The American Heart Association (AHA), that also recommends taking a supplement of 2 to 4 gm which may be beneficial in decreasing raised Tg levels. It has been reported that consumption of foods with anti-inflammatory
properties improves androgenic profile (Liepa et al, 2008).

From the results of the present study it can be concluded that fish oil capsule supplementation exerts a favourable effect on the hormone profile of women with PCOS.

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