OPEN ACCESS
Scholars International Journal of Obstetrics and Gynecology
Abbreviated Key Title: Sch Int J Obstet Gynec
ISSN 2616-8235 (Print) |ISSN 2617-3492 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article

Effect of Levocarnitine on Physical and Biochemical Parameters in Patients with Polycystic Ovary Syndrome

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DOI: 10.36348/sijog.2023.v06i07.006 | **Received:** 21.04.2023 | **Accepted:** 31.05.2023 | **Published:** 26.07.2023

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a common disorder in women of reproductive age closely related to insulin resistance, obesity, dyslipidaemia and long term diseases including diabetes and cardiovascular disease. The management of PCOS may be challenging on account of the comorbidities associated with the disease. ***Objective:*** The objective of the study was to evaluate the effect of Levocarnitine supplementation on physical and biochemical parameters in polycystic ovary syndrome. ***Methods:*** This randomized controlled study was conducted in the Department of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University, Dhaka from January 2021 to December 2021. Total 78 diagnosed cases of PCOS were selected for medication and were included in this study. Eligible women who gave their informed consent were allocated into either Group A (Levocarnitine) or Group B (Placebo) on the basis of computer generated table. Group A received Levocarnitine and Group B received Placebo for 12 weeks. Then pretreatment and post treatment physical parameters including BMI, waist circumference and biochemical parameters including cholesterol, triglyceride, LDL, HDL, fasting plasma glucose, fasting insulin, HOMA-IR were assessed. ***Results:*** Treatment with levocarnitine significantly reduced BMI (-6.00±0.00 vs -0.45±0.07) waist circumference (-4.88±2.85 vs -0.77±0.30) compared with the placebo. In Levocarnitine group, total cholesterol (-38.15±7.33 vs -0.79±27.00 mg/dl), serum triglycerides (-60.00±53.33 vs. -0.33±9.59 mg/d) and LDL (-23.49±1.81 vs. -0.41±0.07 mg/dl) were significantly reduced and HDL level was significantly increased (4.23±1.62 vs 0.41±0.49 mg/dl) compared with the placebo group. Moreover, compared with the placebo, levocarnitine led to a significant reduction of fasting plasma glucose, fasting insulin and HOMA-IR (-0.49±0.95 vs. 0.09± 0.29). ***Conclusion:*** In conclusion, levocarnitine administration led to an improvement in physical parameters including BMI, waist circumference as well as biochemical factors including cholesterol, triglyceride, LDL, HDL. Insulin resistance was significantly reduced in post treatment patients of Levocarnitine. In contrast, although physical and biochemical parameters improved in the placebo group, the change was not significant.

Keywords: Polycystic ovary syndrome (PCOS), Insulin resistance, Obesity, Dyslipidaemia, Diabetes, Cardiovascular.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder that affects 6-10% women of reproductive age [1, 2]. About 40% of PCOS patients suffer from infertility due to ovulatory dysfunction [3]. Several hormonal disorders involved in PCOS include abnormal gonadotropin secretion (elevated luteinizing hormone, depressed FSH), altered LH-FSH ratio (2 or more), elevated androgen and prolactin and insulin resistance. Overall prevalence of insulin resistance in PCOS is 30-35%. Obesity has been described in 50-65% and hyperinsulinaemia affects more than 80% of them. Insulin resistance is also associated with elevated triglyceride and decreased HDL cholesterol. Signs and symptoms of PCOS may comprise of acne, hirsutism, obesity or abdominal fat, alopecia, acanthosis nigricans and irregular menstrual cycle. Women with PCOS are at higher risk of developing obesity, insulin resistance, infertility, type 2 diabetes mellitus, cardiovascular disease, endometrial cancer and psychological disorders like depression and anxiety. Exact pathogenesis of PCOS remains unknown. Researchers believe that genetics, intrauterine androgen exposure, prenatal nutrition, environment, lifestyle and obesity are all risk factors. Some risk factors like prenatal environment and genetics cannot be changed. However, lifestyle factors including diet, physical activity and obesity may play a role in disease progression and are modifiable. Main treatment of PCOS is dependent on the signs and symptoms. For anovulatory infertile PCOS women, treatment modalities are dietary and lifestyle modification, insulin sensitizers, oral ovulation induction, gonadotropin and laparoscopic ovarian drilling. Current recommendation includes weight loss even as low as 5% restores normal menstruation and improves ovulation. Insulin sensitizer drugs like (Metformin, Myoinositol) are well established drugs that decrease insulin resistance and may increase ovulation rate in PCOS. Metformin may facilitate weight loss primarily by suppressing appetite, however the overall effect is modest and inconsistent. But it has no direct effect on body weight reduction and dyslipidaemia. Metformin has several side effects like GI upset and causes abnormal liver function by producing lactic acidosis. More research may be needed for searching another drug that may overcome these side effects. By applying current knowledge, it can be suggested that Levocarnitine, has a role in reduction of BMI, hyperinsulinaemia and dyslipidaemia in PCOS. Carnitine is a quaternary amino acid synthesized in the body from lysine and methionine. It is used as a micronutrient. L-Carnitine (active form) plays important role in glucose metabolism and oxidative stress. It also stabilizes the mitochondrial membranes and prevent cell apoptosis [4]. Some authors drew attention to the role of carnitine in the treatment of insulin resistance and dyslipidaemia in PCOS. Levocarnitine has fat burning action. It utilizes fat by transfer of long chain fatty acid into mitochondria as acylcarnitine ester for subsequent β-oxidation and produce energy. It acts as a scavenger by binding with acyl residues which are derived from the intermediary metabolism of amino acid. Levocarnitine improves insulin resistance by cellular glucose uptake (skeletal muscle) from plasma and it also increases sensitivity of pancreatic β cell to glucose and decreases gluconeogenesis in liver. Against this backround, randomized controlled trial was conducted to evaluate the effect of Levocarnitine on physical and biochemical parameters in PCOS.

OBJECTIVES

General objective:

The general objective of the study was to evaluate the effects of Levocarnitine supplementation on physical and biochemical parameters in PCOS.

Specific objectives:

- To see the effects of Levocarnitine on physical parameters including BMI and waist circumference.
- To see the effects of Levocarnitine on biochemical parameters including lipid profile, fasting plasma glucose, fasting insulin and HOMA-IR.
- To evaluate the effects of Placebo on physical and biochemical parameters.
- To compare the effects between Levocarnitine and placebo groups.

MATERIALS AND METHODS

This was a randomized controlled study, conducted in the Department of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from January 2021 to December 2021 A total of 78 diagnosed cases of PCOS patients were selected for medication study population,

Inclusion criteria:

- Diagnosed case of PCOS patients according to Rotterdam criteria.
- Age 18 to 40 years.
- Primary or secondary infertility.
- BMI >27 kg/m2 to 32 kg/m2.
- HOMA-IR >1.7 [5]

Exclusion criteria:

- Endocrine disorder (Diabetes mellitus, Thyroid disorder, hyperprolactinoma)
- Medical co morbidity (Hypertension, Kidney disease).
- History of taking insulin sensitizer metformin and myoinositol in last 3 months.
- History of taking antidepressant and anticoagulant drug.

Study procedure

Total 78 diagnosed cases of PCOS participants were enrolled after all eligible criteria was confirmed. After full explanation of the study procedure, informed written consent was taken. Data was collected by interview, physical examination and laboratory investigation using questionnaire containing all the variables of interest. Randomization was done by a computer generated random table. Women who gave their informed consent were randomized to Levocarnitine or placebo. Eligible subjects were randomized in the ratio of 1:1 to 330 mg Levocarnitine orally two times daily after a meal in group A (39 participants) or to similar regimen of placebo in group B (39 participants). Study medications were encapsulated so that Levocarnitine and placebo appeared to be identical. All participants and trained staff at infertility clinic were blinded to treatment allocation during the whole study period. Allocation concealment was done using closed opaque envelopes. The participants were asked to return the medication container after 12 weeks.

Procedure of collecting data:

A detailed history and examination were obtained. Participants were 18 to 40 years of age, BMI > 27kg/m^2 to 32 Kg/m^2. Primary or secondary infertility were included in this study. Physical examination including BMI, waist circumference, hirsutism, acanthosis nigricans, acne and base line investigations including FSH, LH, TSH, AMH were measured. Pretreatment fasting plasma glucose, fasting insulin, HOMA-IR and lipid profile were observed. Data were collected in a structured case report form which were filled as per the available records and laboratory results. The patient was briefed in details regarding the objective, rationality and potential benefits of the study. Participants were counselled regarding the drugs and unexpected side effects. Eligible women who gave their informed consent were allocated into either Group A (Levocarnitine) or Group B (Placebo). Group A was treated with Levocarnitine 330 mg two times daily for 12 weeks and group B was treated with placebo for the same duration. All participants were asked to take daily 500-1000 calorie deficit diet and perform 150 minute's exercise per week for 12 weeks. They were instructed not to take any medications during the study procedure except after consulting the physician. There were two hospital visits during the dosing period, first being the initial visit when the participants were recruited for the study. One week later, a telephone interview was conducted to review the side effects and arrange an early appointment if needed. Telephone interviews were conducted again in the next month from the administration of drug. After 12 weeks of treatment, both groups were advised for follow up visits to check BMI and waist circumference and repeat biochemical assay for fasting glucose, fasting insulin, HOMA-IR and serum lipid profile. Laboratory investigations were conducted in the department of Biochemistry at BSMMU. For every subject, separate data collection sheets were prepared. Data were collected from the patients on different visits. Cumulative data were subjected to analysis.

Procedure of data analysis:

Statistical analysis was carried out by using SPSS version 26.0. Quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency and percentage. Chi-Square test was performed to compare qualitative data. Paired Student's t test was performed to compare quantitative data within the groups and unpaired Student's t test was performed to compare quantitative data between two groups. A probability (p) value of <0.05 was considered statistically significant and p> 0.05 was considered non-significant.

Ethical implications

Written approval was taken from the concerned authority in the department with due procedure. The aims of the study along with its procedure, alternative diagnostic methods, risk and benefits were explained in detail to the patient in an easy and understandable language. Privacy, anonymity and confidentiality were maintained during the procedure. It was assured that the procedure was helpful for the physician and the patients in making rational approach regarding the management of the case. Ethical clearance was taken from the local Ethical committee to perform study and investigation.

RESULTS

A total of 78 diagnosed cases of PCOS patients with infertility were included in this study. Among them 39 patients received levocarnitine (Group A) & 39 patients received placebo (Group B). After 12 weeks follow up period, 1 patient dropped out from group A and 2 patients from group B.

Table 1: Socio demographic characteristics of study population, (N=78)

Variable	Group A (Levocarnitine) (n=39)		Group B (Placebo) (n=39)		p value
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)	
Age (In years)					
18-24 yrs.	10	25.6%	12	30.7%	0.660^{ns}
25-30 yrs.	7	17.9%	9	23.1%	

Variable	Group A (Levocarnitine) (n=39)		Group B (Placebo) (n=39)		p value
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)	
31-40 yrs.	22	56.5%	18	46.2%	
Educational status					
Illiterate	4	10.3%	6	15.4%	0.531^{ns}
Primary	5	12.8%	7	17.9%	
SSC	11	28.2%	10	25.6%	
≥HSC	19	48.7%	16	41.1%	
Occupation					
House wife	19	48.7%	17	43.6%	0.792^{ns}
Business	6	15.4%	10	25.6%	
Service	14	35.9%	12	30.8%	
Socioeconomic status					
Lower Class	7	17.9%	9	23.1%	0.660^{ns}
Middle Class	22	56.4%	18	46.2%	
Upper Class	10	25.7%	12	30.7%	

Table 1 showed that majority patients belonged to age group 31-40 years in both groups. Mean age was found 23.2±2.3 years in group A and 23.6±2.1 years in group B. Most of the patients were educated HSC and above, housewife and came from middle class family in both groups. No significant difference was observed in age, educational status, occupational status, and socioeconomic condition between two groups.

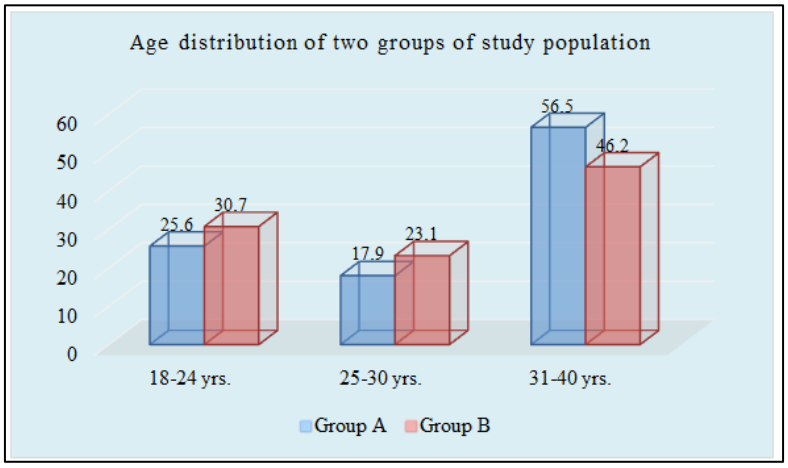

Figure I: Age distribution two group of study population, (N=78)

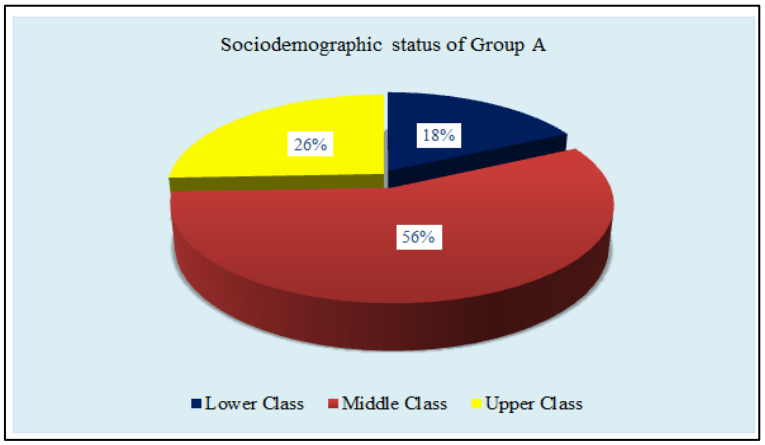

Figure II: Sociodemographic status of Group A, (n=39)

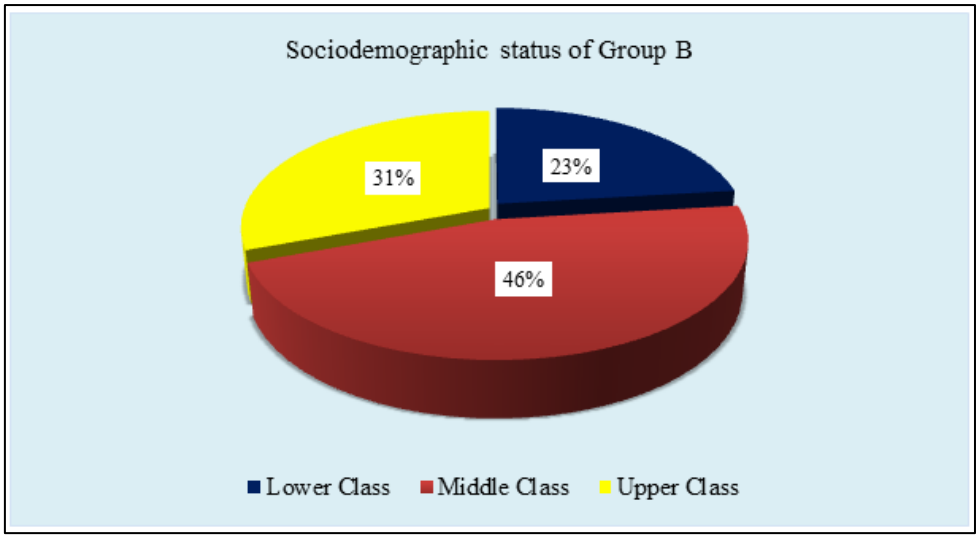

Figure III: Sociodemographic status of Group B, (n=39)

Table 2: Distribution of study population according to infertility, (N=78)

Variables	Group A (Levocarnitine) (n=39)		Group B (Placebo) (n=39)		p value
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)	
Types					
Primary	21	53.8	18	46.2	0.497^{ns}
Secondary	18	46.2	21	53.8	
Duration					
<5 years	12	30.8	18	46.2	0.163 ^{ns}
≥5 years	27	69.2	21	53.8	
Mean ±SD	5.46 ±1.73		5.57 ±1.97		

Table 2 showed that primary infertility was 21(53.8%) and 18(46.2%) and secondary infertility 18(46.2%) and 21(53.8%) in levocarnitine and placebo groups. Duration of infertility was <5 years in 12(30.8%) and 18(46.2%) cases and ≥5 years in 27 (69.2%) and cases 21(53.8%). No significant difference was observed in types and duration of infertility of both groups.

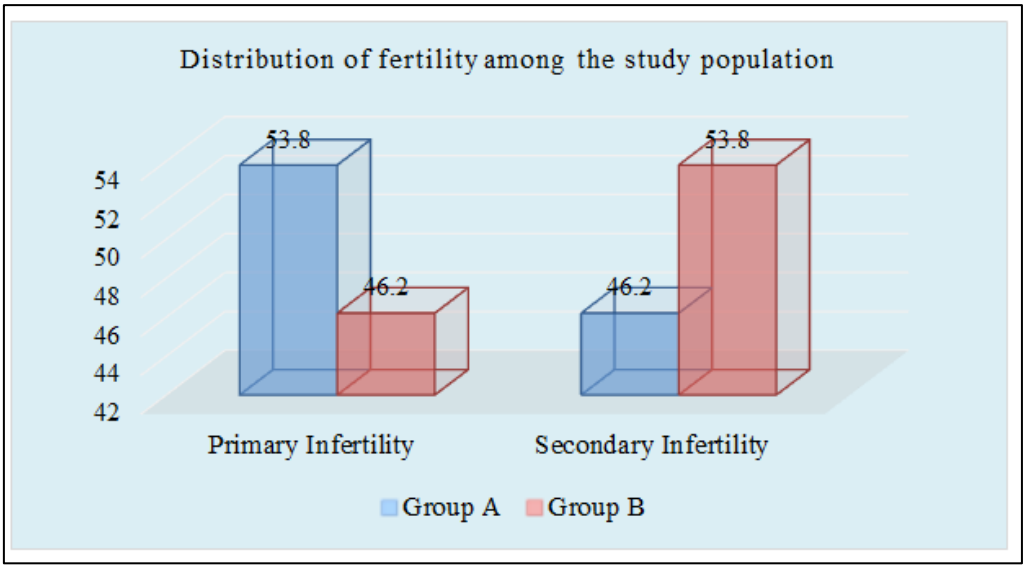

Figure IV: Group wise fertility distribution of study population. (N=78)

Table 3: Distribution of study patients by clinical characteristics, (N=78)

Clinical presentations	Group A (Levocarnitine) (n=39)		Group B Placebo (n=39)		p value
	n	%	n	%	
Oligomenorrhoea	39	100.0	39	100.0	1.000^{ns}
Acanthosis nigricans	27	69.2	21	53.8	0.163^{ns}
Hirsutism	27	69.2	24	61.5	0.478^{ns}

Hirsutism using modified Ferriman-Gallwey score ≥8

Table 3 showed that all patients had oligomenorrhoea in both groups. Acanthosis nigricans was found 27(69.4%) in group A and 18(46.2%) in group B (Placebo). Hirsutism was found 27(69.2%) in group A and 24(61.5%) in group B. The difference was not statistically significant (p>0.05) between two groups.

Table 4: Distribution of study patient by laboratory parameters and TVS of study population in two groups, (N=78)

Investigations	Group A (Levocarnitine) (n=39)	Group B (Placebo) (n=39)	P value
	Mean ±SD	Mean ±SD	
Serum LH (µIU/mL)	6.5±2.0	6.3±0.6	0.560^{ns}
Serum FSH (µIU/mL)	5.5±0.5	5.3±0.5	0.736^{ns}
TSH (µIU/mL)	2.4±0.6	2.1±0.6	0.094^{ns}
AMH (ng/mL)	6.2±2.2	6.1±2.7	0.84^{ns}
TVS PCO	39(100.0%)	39(100.0%)	

Table 4 showed that at baseline, mean serum LH, FSH, TSH and AMH were not statistically significant (p>0.05) between two groups. All patients had bilateral PCOS in both groups.

Table 5: Comparison of pretreatment physical and biochemical parameters between two groups, (N=78)

Baseline parameters	Group A (Levocarnitine) (n=39)	Group B (Placebo) (n=39)	P value
	Mean ±SD	Mean ±SD	
BMI	32.05±2.81	31.67±3.16	0.105^{ns}
Waist circumference	102.53±6.99	103.10±7.69	0.302^{ns}
Total Cholesterol (mg/dl)	226.04±55.30	227.14±60.23	0.487^{ns}
Triglyceride (mg/dl)	207.07±119.43	205.50±111.84	0.187^{ns}
LDL (mg/dl)	217.95±22.72	212.23±26.72	0.181^{ns}
HDL (mg/dl)	40.64±6.29	40.85±5.85	0.439^{ns}
Fasting glucose (mmol/L)	6.25±0.02	6.56±0.80	0.340^{ns}
Fasting Insulin (µIu/ml)	15.5±5.9	13.9±4.6	0.130^{ns}
Homa-IR	3.6±1.5	3.2±1.1	0.929^{ns}

Table 5 showed that the baseline BMI, waist circumference, total cholesterol, triglyceride, LDL, HDL, fasting plasma glucose, fasting insulin and HOMA-IR were not statistically significant (p>0.05) between two groups.

Table-6: Pre-treatment and post-treatment of physical parameters in group A, (n=39)

Parameters	Pre treatment (n=39)	Post treatment (n=38)	p value
	Mean ±SD)	Mean ±SD)	
BMI (Kg/m2)	32.05±2.81	26.05±2.81	0.014^{s}
WC (cm)	102.53±6.99	97.65±9.84	<0.001^{s}

Table 6 showed that in post treatment, group A, BMI (32.05±2.81 vs 26.05±2.81kg/m^2) and waist circumference (102.53±6.99 vs 97.65±9.84 cm) were significantly (p<0.05) reduced than pretreatment.

Table 7: Pre-treatment and post-treatment of biochemical parameters in group A, (n=38)

Variable	Pre treatment (n=39)	Post treatment (n=38)	p value
	Mean ±SD	Mean ±SD	
Cholesterol (mg/dl)	226.04±55.30	187.89±47.97	<0.001^{s}
Triglyceride (mg/dl)	207.07±119.43	147.07±66.10	<0.001^{s}
LDL (mg/dl)	217.95±22.72	194.46±20.91	<0.001^{s}
HDL (mg/dl)	40.64±6.29	44.87±4.67	<0.001^{s}

Table 7 showed that in group A, Cholesterol (226.04±55.30 vs 187.89±47.97 mg/dl), Triglyceride (207.07±119.43 vs 147.07±66.10mg/dl), LDL (217.95±22.72 vs 194.46±20.91 mg/dl) were significantly (p<0.05) reduce and HDL (40.64±6.29 vs 44.87±4.67 mg/dl) were significantly increased when compared between pretreatment. vs post treatment patients.

Table 8: Pre-treatment and post-treatment of fasting plasma glucose, insulin and HOMA-IR in group A, (n=39)

Variable	Pre treatment (n=39)	Post treatment (n=38)	P value
	Mean ±SD	Mean ±SD	
Fasting blood sugar (mmol/l)	6.25±0.02	5.25±0.55	<0.001^{s}
Fasting insulin (µIU/ml)	15.5±5.9	9.8±3.9	0.001^{s}
HOMA-IR	3.6±1.5	2.1±0.9	0.001^{s}

Table 8 showed that in Levocarnitine group, fasting plasma glucose (6.25±0.02 vs 5.25±0.55) mmol/l, fasting insulin (15.5±5.9 vs 9.8±3.9 µIU/ml) and HOMA-IR (3.6±1.5 vs 2.1±0.9) were significantly reduce when compared with pretreatment.

Table 9: Pre-treatment and post-treatment of physical parameters in group B, (n=39)

Parameters	Pre treatment (n=39)	Post treatment (n=37)	p value
	(Mean ±SD)	(Mean ±SD)	
BMI (Kg/m^2)	31.67±3.16	31.22±3.23	0.536^{ns}
WC (cm)	103.10±7.69	102.33±7.99	0.666^{ns}

Table 9 showed that in post treatment group B, BMI (31.67±3.16 vs 31.22±3.23 kg/m^2) and waist circumference (103.10±7.69 vs102.33±7.99cm) reduced than pretreatment, but not significant.

Table 10: Pre-treatment and post-treatment of biochemical parameters in group B, (n=39)

Variable	Pretreatment (n=39)	Post treatment (n=37)	p value
	Mean ±SD	Mean ±SD	
Cholesterol (mg/dl)	227.14±60.23	226.35±87.23	0.963^{ns}
Triglyceride (mg/dl)	205.50±111.84	205.17±121.43	0.990^{ns}
LDL (mg/dl)	212.23±26.72	211.82±26.79	0.398^{ns}
HDL (mg/dl)	40.85±5.85	41.26±5.36	0.347^{ns}

Table 10 showed that in group B, Cholesterol (227.14±60.23 vs 226.35±87.23 mg/dl), Triglyceride (205.50±111.84 vs 205.17±121.43 mg/dl), LDL (212.23±26.72 vs 211.82±26.79 mg/dl) were reduced and HDL (40.85±5.85 vs 41.26±5.36 mg/dl) was increased in post treatment.

Table 11: Pre-treatment and post-treatment of fasting plasma glucose, insulin and HOMA-IR in group B, (n=39)

Variable	Pre treatment (n=39)	Post treatment (n=37)	P value
	Mean ±SD	Mean ±SD	
Fasting plasma glucose (mmol/l)	6.56±0.80	6.55±0.80	0.110^{ns}
Fasting insulin (µIU/ml)	13.9±4.6	13.4±4.4	0.040^{s}
HOMA-IR	3.2±1.1	3.1±1.1	0.089^{ns}

Table 11 showed that in group B, fasting insulin (13.9±4.6 vs 13.4±4.4 µIU/ml) was significantly reduced after treatment.

Table 12: Post treatment physical parameters in group A and group B, (N=78)

	Group A (n=38)	Group B (n=37)	p value
	Mean ±SD	Mean ±SD	
BMI (Kg/m^2)	-6.00±0.00	-0.45±0.07	<0.001^s
Waist circumference (cm)	-4.88±2.85	-0.77±0.30	<0.001^s

Table 12 showed that post treatment of BMI (-6.00±0.00 vs -0.45±0.07) and waist circumference (-4.88±2.85 vs -0.77±0.30) were significantly reduced in levocarnitine group than placebo group.

Table 13: Post treatment of biochemical parameters in two groups, (N=78)

Variable	Group A (Levocarnitine) (n=38)	Group B (placebo) (n=37)	p value
	Mean ±SD	Mean ±SD	
Cholesterol (mg/dl)	-38.15±7.33	-0.79±27.00	<0.001^s
Triglyceride (mg/dl)	-60.00±53.33	-0.33±9.59	<0.001^s
LDL (mg/dl)	-23.49±1.81	-0.41±0.07	0.002^s
HDL (mg/dl)	4.23±1.62	0.41±0.49	0.002^s
HOMA-IR	-1.49±0.95	-0.09±0.29	0.001^s

Table 13 showed that post treatment of cholesterol (-38.15±7.33 vs -0.79±27.00 mg/dl), triglycerides (-60.00±53.33 vs. -0.33±9.59 mg/d) and LDL (-23.49±1.81 vs. -0.41±0.07 mg/dl), and HOMA-IR were significantly decreased (-1.49±0.95 vs. 0.09±0.29) in Levocarnitine group. However, HDL level was significantly increased in Levocarnitine group (4.23±1.62 vs 0.41±0.49 mg/dl) than placebo group (0.41±0.49 mg/dl).

Table 14: Side effects of study population in both groups, (N=78)

Side effects	Group A (Levocarntine) (n=38)		Group B (Placebo) (n=37)		p value
	n	%	n	%	
Diarrhea	4	10.5	1	2.7	0.175^{ns}
Nausea	2	5.3	1	2.7	0.569^{ns}
Headache	2	5.3	0	0.0	0.158^{ns}
Weakness	1	2.6	0	0.0	0.322^{ns}

Table 14 showed that in Levocarnitine group, majority 4(10.5%) patients had diarrhea, Nausea 2(5.3%), Headache 2(5.3%) and Weakness 1(2.6%). In Placebo group patients had 1(2.7%) diarrhea, nausea 1(2.7%). Difference was not statistically significant when compared between two groups.

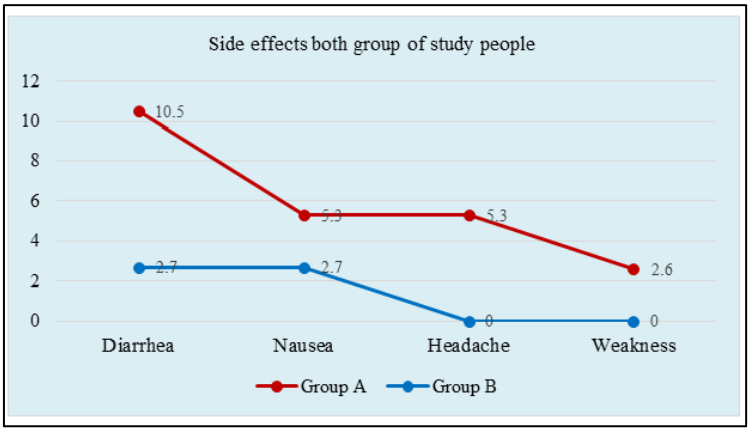

Figure V: Group wise side effects of study population, (N=78)

DISCUSSION

Polycystic ovary syndrome (PCOS) is an endocrine disorder affecting 6-10% of reproductive aged women [1, 2]. PCOS patients are at increased risk of infertility and metabolic disorders like diabetes and cardiovascular disease. Inadequate dietary intake of amino acid might play a key role in the pathogenesis of PCOS. Carnitine deficiency results from inadequate intake of amino acid. Levocarnitine exhibits antioxidant function as well as plays a vital role in mitochondrial bioenergetics. Previous study investigated the effects of Levocarnitine supplementation on biomarkers of oxidative stress, antioxidant capacity and lipid profile [6]. (Agarwal *et al*., 2018) [7] conducted a study and found the role of Levocarnitine in female infertility by regulating the oxidative and metabolic status. The aim of this study is to evaluate the effects of Levocarnitine supplementation on physical and biochemical parameters in polycystic ovary syndrome. In present study, majority patients belonged to age group 31-40 years in both groups. Mean age was found 23.2±2.3 years in Levocarnitine and 23.6±2.1 years in placebo. Most of the patients were educated up to HSC or above, housewives and came from middle class family in both groups. Both Levocarnitine and placebo groups were matched in age, educational status, occupational status and socioeconomic condition. Jamilian *et al*., (2017) [8] investigated a study in overweight and obese PCOS where the mean age was 29.6±4.3 and 27.4±5.3 years. In this study, patients were found to have primary or secondary infertility in both levocarnitine and placebo groups. Duration of infertility was 5.46±1.73 years in Group A and 5.57±1.97 in Group B. No significant difference was observed in types and duration of infertility between two groups. In present study, Oligomenorrhoea, acanthosis nigricans and hirsutism were found in both groups. Serum LH, FSH, TSH and AMH levels were observed in both groups. The difference between two groups were not statistically significant (p>0.05). All patients had bilateral PCO in both groups. In pretreatment stage, baseline physical parameters including BMI, waist circumference and biochemical parameters including serum cholesterol, triglyceride, LDL, HDL, fasting plasma glucose, fasting insulin, HOMA-IR were not statistically significant (p>0.05) when compared between two groups (Levocarnitine vs Placebo). BMI and waist circumference were significantly (p<0.05) reduced post treatment after administration of Levocarnitine. However, the reduction in BMI and waist circumference in placebo group was not statistically significant (p>0.05). Samimi *et al*., (2016) [9] found that oral carnitine supplementation reduced body weight in PCOS. They showed Levocarnitine 250 mg for three months in over weight PCOS patient caused significant reduction of BMI (-1.1±0.6 vs +0.1±0.7) and waist circumference (-2.0±1.3 vs -0.3±2.0). This finding were almost similar to my study. Pooyandjoo *et al*., (2016) [10] showed the effects of levocarnitine on weight loss. Their meta-analysis (nine studies, total n=911, duration from 1 months to 12 months) revealed that subjects who received levocarnitine had significant weight loss (p=0.002) and showed a decrease in body mass index (MD: -0.47 Kg/m^2. 95% CI -0.88 to -0.55) compared with the control group. My study findings were similar to their study. In present study, Cholesterol, Triglyceride and LDL were significantly (p<0.05) reduced and HDL was significantly (p<0.05) improved after Levocarnitine supplementation for 12 weeks. However, Cholesterol, Triglyceride, LDL were also reduced and HDL improved with placebo, but this difference was not statistically significant (p>0.05). Jamilian *et al*., (2020) [11] investigated the effect of Levocarnitine supplementation 1000 mg/day on 54 overweight PCOS women. After 12 week's period of treatment, they observed significant (P<0.001) decrease in triglyceride (-18.0±25.2 vs +5.5±14.4), total cholesterol and LDL (-13.3±19.2 vs +1.4±13.3) However, HDL cholesterol was not significantly increased in their study (P=0.56). They concluded that Levocarnitine supplementation for 12 weeks had beneficial effects on lipid profile except HDL level. Mohammadi *et al*., (2017) [6] conducted a study and found that administration of levocarnitine 2 g per day for 8 weeks reduced cholesterol, triglyceride, LDL (p<0.05) but did not improve HDL (P=0.06). This difference may be due to shorter duration of treatment. Samimi *et al*., (2016) [9] observed 60 overweight PCOS patients after Levocarnitine 250 mg supplementation. After 12 weeks they found that BMI, WC and insulin resistance were significantly reduced (p=<0.01) but lipid profile was not affected. My study findings were dissimilar to the findings. This disagreement may be due to different dose schedule. In this study, it was observed that levocarnitine supplementation significantly (P<0.001) reduced fasting plasma glucose, fasting insulin and HOMA-IR compared to placebo. These parameters were also reduced in placebo but was not statistically significant (p>0.05) except for fasting insulin. Sanagouni *et al*., (2021) [12] investigated the effect of L-carnitine 1000mg/day on insulin resistance in 62 overweight and obese PCOS. After 12 weeks they found significant improvement in fasting insulin {-0.7(-7.3 to 4.0) vs 0.7(-3.0 to 5.2); p=0.002} and HOMA-IR (homeostatic model assessment for insulin resistance) {-0.4(-1.7 to 1.1)} vs 0.0(-0.7 to 1.3); p=0.002}. A study conducted by Jamilian *et al*., (2020) [11] reported that 12 weeks levocarnitine supplementation significantly decreased fasting plasma glucose (-5.1±6.0 vs. -1.1±4.9) serum Insulin (-2.0±1.4) and HOMA-IR (-0.5±0.4). Agarwal *et al*., (2018) [7] suggested that Levocarnitine may improve female fertility through their integrated actions on reducing cellular stress, maintaining hormonal balance and enhancing energy production. It maintains oxidation in oocytes, cell membrane stability, prevents free radical induced DNA damage. These beneficial effects show a great promise in its application as a treatment option. During the course of the study no adverse event was observed. However, only diarrhea (4;

10.5%), nausea (2; 5.3%), headache (2; 5.3%) and generalized weakness (1; 2.6%) was reported by few patients in levocarnitine group. Diarrhea (1; 2.7%) and nausea (1; 2.7%) was reported by few patients in placebo group. Similar findings were observed in a study conducted by MFMER (2021) [13].

CONCLUSION

Levocarnitine supplementation in PCOS patients caused significant reduction of BMI and improved dyslipidaemia and insulin resistance. Therefore, by using these drugs, beneficial effects can be provided on physical and biochemical parameters in PCOS.

LIMITATIONS OF THE STUDY

- Small sample size.
- Short period of time.
- Study population was recruited from single selected center.
- The study was conducted during COVID pandemic situation and locked down period, so data collection and follow up was challenging.

RECOMMENDATIONS

- Further multicenter or community based studies can be undertaken by including larger number of patients.
- Further studies are necessary to evaluate the effect of levocarnitine when co-administered with other drugs compared to monotherapy
- To assess the effects of adding Levocarnitine with different ovarian stimulation protocol in PCOS.
- Supplementation with Levocarnitine may enhance the fertility potential and reproductive outcome in PCOS women.

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