Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/20086
DOI URL: http://dx.doi.org/10.21474/IJAR01/20086

RESEARCH ARTICLE

ROLE OF METFORMIN AND VITAMIN D3 IN OBESE PCOS PATIENTS

Veena Gupta

Manuscript Info

Manuscript History
Received: 17 October 2024
Final Accepted: 19 November 2024
Published: December 2024

Abstract

Polycystic ovarian syndrome (PCOS) is a common metabolic and endocrinological disorder affecting women of reproductive age, with a prevalence of 4-20%. It is characterized by symptoms such as oligoamenorrhea/amenorrhea, hyperandrogenism, hyperinsulinemia, and ultrasound (USG) features of polycystic ovaries. Risk factors include excessive weight gain, high BMI, dyslipidemia, stress, and chronic illness. Symptoms such as menstrual irregularity, infertility, male-pattern hair loss, facial hair, and acne are common due to anovulation and androgen excess. The exact cause of PCOS is unknown, but it is believed to be multifactorial, involving environmental and genetic factors. Studies suggest overexpression of LH receptors on theca cells as a potential mechanism. Metformin is recommended in addition to lifestyle interventions (LSI) for women with PCOS and BMI ?25 kg/m², irrespective of glucose disturbances or menstrual irregularity. It is effective for glucose intolerance and may be beneficial for long-term use, though the optimal duration is unclear. Vitamin D deficiency has been associated with insulin resistance and PCOS. Vitamin D enhances insulin synthesis, release, receptor expression, and reduces pro-inflammatory cytokines, improving insulin sensitivity. In conclusion, both metformin and vitamin D play significant roles in managing PCOS by addressing insulin resistance and hormonal imbalances.

Introduction:-

Polycystic ovarian syndrome (PCOS) is a metabolic and endocrinological disorder affecting the reproductive age groups and is characterised by presence of any of the symptoms like oligoamenorrhoea/amenorrhea, hyperandrogegism, hyperinsulinemia, USG features of polycystic ovary. Risk factors include excessive weight gain, high BMI, dyslipidemia, stress, chronic illness. This anovulation can cause menstrual irregularity and thus decrease fertility along with presence of sign of androgen excess like male pattern hair loss, appearance of facial hair, acne. Focusing on the characteristic's phenotypes the prevalence of PCOS, it is seen that it a common disorder in reproductive age women which represent 4-20%[1]of population. No specific reason has been found for the causation of PCOS, it is expected to be a multifactorial including combination of environmental factors, genetic. immunohistochemical studies have shown over expression of LH receptors on theca cells. When lifestyle intervention (LSI) is insufficient and for the management of menstrual irregularity and are unable to take oral contraceptives (OCPs) then Low-quality evidence supports the use of metformin for women with PCOS and glucose intolerance. The latest international guidelines update recommends considering metformin in addition to lifestyle intervention (LSI) also in women with PCOS with BMI ≥25 kg/m^2, independent of the presence of glucose

Corresponding Author:- Veena Gupta

disturbances and menstrual irregularity. However, there is no clearanswer for how long metformin should be prescribed in these subsets of patients, who would clearly benefit from long-term use of metformin in PCOS.Vitamin D is a fat soluble vitamin produced by the skin and a small amount is absorbed in the gut from dietary sources.Vitamin D deficiency has been linked to the insulin resistance and therefore PCOS and so 1-25hydroxy vitamin D is positively correlated with insulin sensitivity and negatively with beta cell function. Vitamin D3 enhances insulin action by enhancing insulin synthesis & release, increased insulin receptor expression and/ or suppression of pro inflammatory cytokines that are believed to mediate insulin resistance.

Aims And Objective:-

1) To study the effect of metformin and vitamin D3 in relation to weight, BMI , waist circumference.
2) To compare the effect of metformin and vitamin D 3 in relation to serum fasting insulin,serum total testosterone, serum sex hormone binding globulin.

Materials and Methods:-

Study Design

This study was prospective cohort studyconductedfor a period of 6 months from Jun 2023to Dec2023.

Study Setting

The research was conducted at the Department of Obstetrics and Gynaecology, Swaroop Rani Nehru Hospital, associated with Moti Lal Nehru Medical College, Prayagraj, India.

Study Population:-

The study included all reproductive female presenting with complains of oligomenorrhoea/amenorrhea, facial hair attending the outpatient department (OPD) at the tertiary care centre.

Methodology:-

100 Patient were enrolled on the basis of of criteria fulfilling for the diagnosis of PCOS and after informed written consent. They were randomly divided in two groups

Group A receiving metformin500mg BD for a period of 12 weeksandGroupB receivingvitamin D3 60,000U weekly for 12 weeks and then the parameters were compared after 3 months following treatment.

Inclusion Criteria

- HighBMI>25kg/m2 or waist circumference ≥ 85cm or more
- Infrequent menstrual cycles
- Clinicalhyperandrogegism (ferriman Gallway score>6) or total testosterone >58ng/dl
- Willing to participate.

Exclusion Criteria

- Women unwilling to participate.
- Patients lost to follow-up.
- Women with systemic and endocrine disorder, thyroid dysfunction, Cushing syndrome, hyperprolactinemia, coronary artery disease were excluded.

Data Collection

Participants were enrolled on the basis of criteria fulfilling for the diagnosis of PCOS and then obtaining informed written consent.

Clinical Examination

A detailed clinical history was recorded, including:

- General physical examination: Height, weight, BMI, pallor, and vitals, galactorrhea. Waist circumference
- Systemic examination: Cardiovascular, respiratory, and central nervous systems.
- Gynaecological examination: Per abdomen, per speculum, and per vaginal examinations.

Investigations
Routine and special investigations included:

- Blood group, haemoglobin, thyroid-stimulating hormone (TSH), HIV, HBsAg, anti-HCV, and VDRL.
- Serum calcium and vitamin D levels.
- Urine routine and microscopy.
- Fasting and post prandial sugar, fasting insulin
- Lipid profile- serum LDL, HDL, Triglycerides
- Hormonal profile- S. LH, S. FSH on day 2 of menses, Serum prolactin, serum testosterone

Ethical approval for the study was obtained from the Institutional Ethics Committee of Swaroop Rani Nehru Hospital, Prayagraj.

Data Analysis:-

Data were entered into Microsoft Excel and analysed using SPSS software version 24.0. Descriptive statistics, such as means, medians, and standard deviations, were used for continuous variables, while frequencies and percentages were used for categorical variables. and one-way ANOVA was used for continuous variables to determine statistical significance at a 5% level.

Results:-

This study was conducted in 100 patients in department of obstetrics and gynaecology from June 2023 to Dec 2023 where patients were divided into two groups receiving metformin and vitamin D3 and then compared.

Table 1 shows the baseline characteristics of study participants. This study included 100 patients with PCOS.The mean age of the participants in our study was 29.2 years while largest proportion of participants belongs to the Lower Middle class (34.6%), followed by the Upper Lower class (30%) whereas the Upper Middle class comprises 28%, and 14.2% fall into the Lower class.A higher proportion of participants reside in urban areas (64%), while 34% are from rural areas. The majority of participants are unmarried (71%), 21% were parity 1 and 0.8% were at their second parity.

Table 2Here are the paired t-test results for the pre- and post-treatment values for each parameter in both groups (Metformin and Vitamin D3) for **BMI**Group 1 (Metformin): $t = 5.88$, $p < 0.0001$, Group 2 (Vitamin D3): $t = 3.31$, $p = 0.0018$ while for **Weight**Group 1 (Metformin): $t = 3.57$, $p = 0.0008$ and Group 2 (Vitamin D3): $t = 2.16$, $p = 0.0357$. In **S. LH**Group 1 (Metformin): $t = 13.00$, $p < 0.0001$ and Group 2 (Vitamin D3): $t = 7.58$, $p < 0.0001$ whereas for **S. FSH**Group 1 (Metformin): $t = 7.39$, $p < 0.0001$ and Group 2 (Vitamin D3): $t = 3.25$, $p = 0.0021$ in **Serum Prolactin**Group 1 (Metformin): $t = 14.27$, $p < 0.0001$ and Group 2 (Vitamin D3): $t = 11.70$, $p < 0.0001$. **S. SHBG**Group 1 (Metformin): $t = -3.08$, $p = 0.0034$ and Group 2 (Vitamin D3): $t = -3.24$, $p = 0.0022$ while **S. Fasting Plasma Glucose**Group 1 (Metformin): $t = 11.45$, $p < 0.0001$andGroup 2 (Vitamin D3): $t = 10.11$, $p < 0.0001$and**Total Testosterone**Group 1 (Metformin): $t = 8.51$, $p < 0.0001$ and Group 2 (Vitamin D3): $t = 6.55$, $p < 0.0001$

Table 3 shows the comparative post treatment effect of metformin and vitamin D 3 on following parameters **Weight**:The post-treatment weight was slightly lower in the Metformin group (24 ± 2.2 kg) compared to the Vitamin D3 group (25.5 ± 2.45 kg) showing that Metformin appears more effective in reducing weight, likely due to its metabolic effects whereas in **BMI**:BMI values were slightly lower post-treatment in the Metformin group (61.7 ± 4.0) compared to the Vitamin D3 group (62.5 ± 3.5) suggesting that both treatments showed comparable effects on BMI, with Metformin showing a marginally greater improvement. Looking the **S. FSH (Follicle-Stimulating Hormone):**Post-treatment S. FSH was lower in the Metformin group (4.7 ± 0.51) than the Vitamin D3 group (5.4 ± 0.72) favouring that Metformin may have a stronger impact on regulating FSH levels, potentially aiding hormonal balance while **S. LH (Luteinizing Hormone)** post-treatment were slightly higher in the Metformin group (5.23 ± 0.45) compared to the Vitamin D3 group (5.11 ± 0.56) Both treatments effectively reduce LH levels, with Vitamin D3 showing a slightly greater reduction. Considering **Serum Prolactin**:Lower levels were observed post-treatment in the Vitamin D3 group (17.24 ± 2.74) compared to the Metformin group (18.64 ± 3.56) therefore Vitamin D3 shows a stronger effect in reducing prolactin levels, which could be beneficial for managing prolactin-related disorders. For**S. SHBG (Sex Hormone-Binding Globulin):** higher post-treatment levels in the Vitamin D3 group (20.82 ± 4.86) compared to the Metformin group (17.66 ± 4.41) showing that Vitamin D3 may enhance SHBG

levels more effectively, potentially improving hormonal regulation and insulin sensitivity. Looking in **S. Fasting Glucose** levels were slightly lower post-treatment in the Metformin group (110 ± 7.2 mg/dl) compared to the Vitamin D3 group (112 ± 6.1 mg/dl) suggesting that Metformin is slightly more effective in reducing fasting glucose, consistent with its known role in improving insulin sensitivity. Considering for **S. Total Testosterone**: Similar reductions were seen in both groups, with values of 1.9 ± 0.31 (Metformin) and 1.93 ± 0.7 (Vitamin D3) therefore Both treatments are equally effective in reducing testosterone levels, potentially beneficial for managing androgen excess.

Result:-

Table 1:- Baseline characteristics of the study participants.

Baseline Characteristics		**Mean±SD**	**N=50**	**%**
Age(years)		29.2	-	-
Socioeconomic Status	**UpperMiddle**	-	28	28%
	LowerMiddle	-	32	32%
	UpperLower	-	27	27%
	Lower	-	13	13%
Residence	**Rural**	-	36	36%
	Urban	-	64	64%%
Parity	**Unmarried**		71	71%
	1		21	21%
	2		8	.8%
BMI	**25-29.9**		65	65%
	30-35		28	28%
	>35		7	7%

Table 2:- Comparing The Hormonal And Biochemical Parameter Of Two Different Group.

	Metformin Group 1 (n=50)		**Vitamin D3 Group 2 (n=50)**	
	Pretreatment	Post treatment	Pre treatment	Post treatment
BMI (kg/m2)	26.6±2.6	24±2.2	26.8±2.47	25.5±2.45
Weight (kg)	64.2±4.5	61.7±4.0	63.6±4.1	62.5±3.5
S. LH (mg/dl)	6.5±.81	4.7±0.51	6.44±.74	5.4±0.72
S. FSH (mg/dl)	6.53±1.17	5.23±0.45	5.42±0.63	5.11±0.56
Serum prolactin (mg/dl)	28.45±3.43	18.64±3.56	24.15±3.21	17.24±2.74
S. SHBG	14.1±4.43	17.66±4.41	16.55±5.22	20.82±4.86
S. Fasting plasma glucose (mg/dl)	124±±5.6	110±7.2	124±6.2	112±6.1
Total testosterone	2.61±.51	1.9±.31	2.63±.48	1.93±.7

Table 3:- Comparison Of Biochemical And Hormonal Parameters Between The Two Studied Groups.

Parameters	Post treatment on metformin (n=50)	Post treatment on vitamin D3 (n=50)	P value	Remarks
Weight	24±2.2	25.5±2.45	0.001	Significant
BMI	61.7±4.0	62.5±3.5	0.289	Not significant
S. FSH	4.7±0.51	5.4±0.72	<0.001	Significant
S. LH	5.23±0.45	5.11±0.56	0.241	Not significant
Serum prolactin	18.64±3.56	17.24± 2.74	0.029	Significant
S. SHBG	17.66±4.41	20.82±4.86	<0.001	Significant
S. Fasting glucose	110±7.2	112±6.1	0.137	Not significant
S. Total testosterone	1.9±.31	1.93±.7	0.732	Not significant

Discussion:-

This study was conducted to find the impact and compare the efficacy of metformin and vitamin D3 in the treatment of polycystic ovarian syndrome in terms of post treatment reduction of BMI, weight, serum LH, FSH, serum prolactin, sex hormone binding globulin, serum total testosterone.

1. Considering the effect of metformin and vitamin D3 on **BMI**: Both Metformin (Group 1) and Vitamin D3 (Group 2) showed significant reductions in BMI after treatment, with a stronger effect in the Metformin group ($p < 0.0001$ vs. $p = 0.0018$)
2. Looking on to the effect of metformin and vitamin D3 on **Weight**: Significant weight reductions were observed in both groups, with a more pronounced effect in the Metformin group ($p = 0.0008$) compared to Vitamin D3 ($p = 0.0357$).
3. Analysing the effect of metformin and vitamin D3 on **S. LH (Luteinizing Hormone)**:Both treatments significantly reduced S. LH levels, with highly significant results in both groups ($p < 0.0001$), indicating a strong hormonal response to treatment.
4. Results of the effect of metformin and vitamin D3 on **S. FSH (Follicle-Stimulating Hormone):**Significant reductions in S. FSH were noted in both groups, with a stronger effect in the Metformin group ($p < 0.0001$) compared to Vitamin D3 ($p = 0.0021$).
5. Looking on to the effect of metformin and vitamin D3 on **Serum Prolactin**: Both groups showed substantial decreases in serum prolactin levels post-treatment, with highly significant results ($p < 0.0001$), particularly in the Metformin group similar to previous study done by R. Krysiak et al (2015)
6. Reviewing the effect of metformin and vitamin D3 on **S. SHBG (Sex Hormone-Binding Globulin):**Both groups experienced significant increases in SHBG levels, reflecting improved hormonal regulation (Metformin: $p = 0.0034$; Vitamin D3: $p = 0.0022$).
7. Results of the effect of metformin and vitamin D3 on**Fasting Plasma Glucose**: Both treatments significantly improved fasting plasma glucose levels, with highly significant reductions in both groups ($p < 0.0001$) which was in contrast to study done by A. Williams et al [4]
8. Analysing the effect of metformin and vitamin D3 on**Total Testosterone**: Significant reductions in total testosterone were observed post-treatment in both groups, with p-values indicating strong statistical significance ($p < 0.0001$).

Conclusion:-

Both Metformin and Vitamin D3 demonstrated significant improvements in metabolic and hormonal parameters post-treatment, with Metformin showing a slightly stronger effect across most measures. These results suggest that both interventions are effective in addressing the targeted conditions, with Metformin having a more pronounced impact on weight, BMI, fasting glucose, and FSH levels, making it effective for metabolic and hormonal regulation.Vitamin D3 had a greater effect on prolactin, SHBG, and LH levels, highlighting its role in hormonal modulation.

References:-

1. Deswal, R., Narwal, V., Dang, A., & Pundir, C. S. (2020). The prevalence of polycystic ovary syndrome: a brief systematic review. Journal of Human Reproductive Sciences, 13(4), 261.
2. Gokosmanoglu, F., Onmez, A., & Ergenç, H. (2020). The relationship between Vitamin D deficiency and polycystic ovary syndrome. African Health Sciences, 20(4), 1880–1886
3. Herman, R., Kravos, N. A., Jensterle, M., Janež, A., & Dolžan, V. (2022). Metformin and insulin resistance: A review of the underlying mechanisms behind changes in GLUT4-mediated glucose transport. International Journal of Molecular Sciences, 23(3), 1264.
4. Williams, A., Babu, J. R., Wadsworth, D. D., Burnett, D., & Geetha, T. (2020). The effects of vitamin D on metabolic profiles in women with polycystic ovary syndrome: a systematic review. Hormone and Metabolic Research, 52(07), 485–491.
5. Zainab nur elden azeez et al effect of metformin and vitamin D on metabolic and hormone profile in polycystic ovarian syndrome 2024.