EVALUATION OF CLINICAL EFFICACY AND SAFETY OF OVARYL TABLET AN HERBAL FORMULATION IN POLY CYSTIC OVARIAN SYNDROME (PCOS)

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ABSTRACT

Background: *To evaluate the clinical efficacy and safety effect of Ovaryl tablet a marketed herbal formulation of Mercury Laboratories Ltd., in Poly cystic Ovarian Syndrome.*

Methods: *58 women patients' age range between 20 to 40 years, suffering from Poly cystic Ovarian Syndrome symptoms like hirsutism, irregular periods, ovulation, volume of ovary, weight and serum insulin levels.*

Results: *A significant improvement was observed in clinical symptoms like hirsutism, irregular periods and ovulation after MOT medication.Laboratory investigation showed decrease in Serum Insulin levels. A minimum decrease of 2.87% and 36.73% maximum decrease of serum insulin levels were observed on 90th day of MOT treatment. 22.06% maximum and 1.55% minimum decrease of ovary volume in Right Ovary. 24.39% maximum and 1.37% minimum decrease of ovary volume in Left Ovary was observed. Upper Abdomen USG was normal in all the 58 patients, no cyst was reported.*

Conclusion*: Poly cystic Ovarian Syndrome symptoms like hirsutism, irregular periods, ovulation, and volume of ovary, weight and serum insulin levels were taken care off.*

Key words: *Ovaryl tablet, Poly cystic ovarian syndrome, Serum insulin level and Ovary volume.*

BACKGROUND

Motherhood is the crowning act in the women's feminine role of life. The very definition stree is "Sthyayathi Garbha Yasyamithi Stree" i.e. Stree means who possess womb (uterus) or who has capacity of conceiving a child. As per Ayurveda giving birth to a healthy offspring is dependent on four basic factors i.e. Ritu, Kshetra, Ambu and Beeja.[1] Abnormality of disturbance in anatomy and physiology of above factors may result in infertility (Vandhya). Infertility is a condition defined as a failure to achieve conception within one or years of regular unprotected coitus.[2] It may result by many causes of male and female factors. In that most frequent female causes are Tubal block, Anoyulatory cycles, Poly Cystic Ovarian Disease and some endometrial causes i.e. menstrual disorders like Menorrhagia, Metrorrhagia, Dysfunctional Uterine Bleeding, Dysmenorrhea etc.

Polycystic ovarian syndrome (PCOS) is sometimes called Stein-Leventhal Syndrome after the two doctors who first described it in 1935.[3] It is an extremely common disorderaffecting 4% to 12% of women of reproductive age.[4-5] A PCOS patient's ovaries have more than ten follicles visibleon ultrasound. The common symptoms like irregularmenstrual cycles, anovulation, infertility, hirsutism, hyperandrogenism, acne, the scalp hair thinning andfunctional ovarian hyperandrogenism are found in 70% ofthe patients with PCOS. PCOS is also associated withperipheral insulin resistance and hyper insulinemia and obesity amplifies the degree of both these abnormalities.[6] The presence of enlarged polycystic ovaries suggests that the ovaries are the primary sites of abnormality in PCOS.The etiology of PCOS remains unclear; however, several studies have suggested that insulin plays the basicpathologic role along with a genetic component to the syndrome.[7-9] As the condition progresses it may become associated with dysfunctional uterine bleeding, obesity, Type 2 diabetes, endometrial cancer, high cholesterol andcardiovascular disease.[10-11]

Traditional herbal medicines are naturally occurring substances with minimal or no industrial processing thathave been used to treat various illnesses.Traditionalmedicines have established preventive, curative and rehabilitative role.[12-16] Benefit of herbal therapy compared to conventional therapy is that it is safe with lesser sideeffects and presence of multiple active compounds in medicinal herbs altogether provides a potentiating effect.[17-18]

In this review, the treatment of different aspects of PCOS is discussed, with a particular emphasis on the natural products.

The Polycystic Ovary: In comparison to the normal ovary, the polycystic ovary is larger, has more follicles and has aparticularly dense centre – the stroma which is where testosterone is made. On average, the normal ovarycontains five follicles and is about the size of a walnut. Thepolycystic ovary contains 10 or more follicles, usuallythese are small follicles measuring between 2 and 10millimetres in diameter. The polycystic ovary is usuallythe size of a hen's egg but occasionally they may be thesize of an orange. The increased size of the polycysticovary is mainly due to an increased amount of stroma and not,

as may be expected, because of the extra follicles orcysts. Usually, the follicles are too small to contributemuch to the ovary size.[19]

Signs and symptoms of PCOS: The principal signs and symptoms of PCOS are: [19]

1) **Irregular or absence of periods:** Irregular and unpredictable uterine bleeding is the hallmark of PCOS. 85-90% women with PCOS have oligomenorrhoea while 30-40% present with amenorrhoea. These symptoms are clinical features of anovulation, but not all patients have anovulatory cycles as corpus luteum formation at the time of surgery has been found in approximately 16% of women with PCOS.[19]
2) **Hirsutism, Acne, temporal balding (Androgen Excess):** Approximately 80% of PCOS patients have excessive hair growth that usually has a male pattern. Prolonged exposure to high levels of circulating androgens may even cause temporal balding.[19] Acne is commonly seen but severe form of androgen excess such as clitoromegaly is absent.
3) **Weight gain or difficulty in losing weight:** The onset of obesity has been correlated with the appearance of menstrual dysfunction. Patients usually have an android pattern of obesity.18There are a variety of explanations why women with PCOS can be obese. Raised insulin levels might, however, be a drive to the appetite centers of the brain. Weight gain results in higher insulin levels which in turn drives the ovary to make more testosterone. Thus, as women gain weight the concentration of testosterone in the blood rises. The cause of obesity may uncertain but the fact of being overweight is clear.[20]
4) **Infertility:** PCOS causes infertility by preventing ovulation.[21] Usually the egg is released 14 days before a period. If the periods are very irregular then ovulation may be unreliable or indeed - it may not take place at all.
5) **Miscarriage**: Women with PCOS who also have a raised LH measurement are at an increased risk of miscarriage.[22]
6) **Changes in hormonal level:** Testosterone and other androgens: Ovary makes several androgens of which testosterone is the most prominent others include androstenedione and Dehydroepiandrosterone (DHEAS). The most typical feature of the polycystic ovary is that the stroma and theca cells make an excess of testosterone. The adrenal gland is another source of testosterone but the function of this gland is usually normal in women with PCOS.[23]

The gonadotropins, LH and FSH: The monthly timing of the menstrual cycle is controlled by a complex balance of hormones from the hypothalamus and pituitary gland which is situated behind the eyes. The gonadotropins, LH and FSH are made by the pituitary gland. The Luteinising Hormone (LH) drives the theca cells of the ovary to make testosterone. Testosterone is then passed to the granulosa cell of the ovarian follicle where it is turned into oestrogen under the influence of follicle stimulating hormone (FSH). In one third of women with PCOS, the level of LH is raised and there is a rough association between this finding and a tendency to infertility. Concentrations of FSH is seems to be decreased in women with PCOS.[24]

Insulin and the metabolism: The main role of insulin in the body is in regulating the level of glucose in the blood. In some individuals, high concentrations of insulin are required in order to maintain normal glucose levels insulin resistance. When insulin fails in this effort, diabetes occurs. Raised insulin concentrations have a side effect in the body of stimulating the ovary to produce more testosterone. About one third of lean women with PCOS have raised insulin levels and this proportion rises in those who are overweight. In obese women with PCOS about half have raised insulin levels and 10% have mild diabetes. Raised insulin levels are part of a metabolic syndrome which also includes high blood pressure and an adverse cholesterol profile - low HDL cholesterol and raised triglycerides.[25]

Causes of PCOS: Following are few important causes of PCOS: [26]

1. Genetic predisposition
2. Strong stimulation in adrenals in childhood
3. Raised insulin levels
4. Contraceptive pills
5. Hormonal imbalance
6. Stress

For the present study, this herbal formulation, Ovaryl tablet has been selected to evaluate its clinical efficacy and safety on human patients.

METHODS

Sample Size: 58 patients completed study (Total Enrolled: 60 i.e. 2 patient dropout during study)
Trial period: 03 months for each patient
Design of the study: Open Observational Trial.
Drug & dosage: Ovaryl tablet twice a day after food with a glass of Luke warm water (approx. 250 ml.) maintaining 12 hours gap in between, for 3 months (90 days).
Follow - Up: The follow-up was carried out after 15 days of treatment.

Duration of the study: 90 days drug therapy with a follow up for 30 days without drug.
Study period: 12 months.
Study Site: Mahavir Hospital, Latti Plot, Opp. District Library, Near C. J. Hospital, Surendranagar - 363001, Gujarat, India.

SUBJECT INCLUSION CRITERIA:
Enrollment: Patients found eligible were judged by the inclusion & exclusion criteria. Patients were formally informed about the study.
Informed consent: A written informed consent was obtained from all the patients, indicating purpose and nature of clinical trial-herbal formulation. The procedures to be carried out and the potential risks and benefits were explained to the study patients in detail in non-technical terms. They were assured that they can withdraw from the study at any time without explaining their action
Medication and treatment: The patients were treated with Ovaryl tablet, 1 tablet, twice daily and the treatment period was 3 months. The medicine was kept in secured storage in the office of the principle investigator and was allotted to the patients following a random number table.
Criteria for Exclusion: Patients who develop secondary complication of Colitis, intestinal obstruction etc. Any other serious illness e.g. Hepatic/ renal failure. Patient with diagnosed other than arthritis like Gallbladder stone, Hepatomegaly. Patient receiving any other method of treatment.

PARAMETERS FOR EVALUATION:
Clinical efficiency parameters: All patients enrolled into the study were subjected to through history taking and clinical examination and also questionnaire as part of the screening procedure and was re-evaluated at the end of the study (clinical research form). Apart from clinical examination and questionnaire, the selected investigation was done, before and after medication. Each subject visited at least 6 clinic visits during the study.
Safety information: Any serious adverse event is not expected but the clinical research form has the provision for recording any serious adverse event if it happens and the principle investigator of the trial would report the sponsor same on urgent basis.
Concomitant medication: Subject were advised not to use any concomitant medication unless absolutely necessary. If any concomitant medication was used, its record was maintained in a separate section of the clinical research form.
Confidentiality: All procedure in the study was carried out maintaining strict confidentiality. Patient identity, medical condition and trail data will not be disclosed to or discussed with any third party.

Criteria regarding PCOS symptoms were Weight, Hirsutism, Irregular Periods, Ovulation, No. of Cysts, Size of Ovary and Serum Insulin levels.

Routine Examination and Assessment

The full details of history and physical examination of the patients was recorded as per the Performa (Forms I & II).

1) Clinical assessment was done and recorded on '0' day (before MOT medication), 15th day, 30th day, 60th day and 90th day. Regularity or irregularity of menstrual cycle or menopause period along with Poly Cystic Ovarian Syndrome (PCOS)symptoms like Weight, Hirsutism, Irregular Periods, Ovulation, No. of Cysts, Size of Ovary and Serum Insulin levels.Grading score of symptoms was done as per its severity observed in an individual patient (like occasionally = 0, mild = 2, moderate = 4, sever = 6). All this parameters were observed during the period of MOT medication **(Figure No. 1-4)**.
2) No. of Cyst, Size of Ovary (volume of right and left ovary, **Table No 1-2 and Figure No. 5-6**) and Upper Abdomen USG study was performed on 0thand 90th day.
3) Serum Insulin levels was measured on '0th and 90th day **(Table No. 3 and Figure No. 7)**.

Table No. 1: Right Ovary Volume in cm^3 (0th & 90th day treatment of Ovaryl Tablet)

Patient Code	0th day	90th day	Patient Code	0th day	90th day	Patient Code	0th day	90th day	Patient Code	0th day	90th day	Patient Code	0th day	90th day	Patient Code	0th day	90th day
MOT-1	4.44	0.55	MOT-11	12.80	1.35	MOT-22	11.14	1.59	MOT-32	11.36	0.51	MOT-43	5.6	0.26	MOT-53	10.53	2.26
MOT-2	11.76	0.80	MOT-12	7.37	0.95	MOT-23	5.20	0.74	MOT-33	4.98	0.26	MOT-44	8.15	0.14	MOT-54	4.23	0.10
MOT-3	16.94	2.07	MOT-13	15.29	1.44	MOT-24	7.75	0.82	MOT-34	4.43	0.31	MOT-45	7.31	0.89	MOT-55	11.65	1.11
MOT-4	10.44	1.48	MOT-14	18.25	1.51	MOT-25	8.13	0.11	MOT-35	5.9	0.28	MOT-46	22.97	3.69	MOT-56	13.58	0.54
MOT-5	22.16	1.19	MOT-15	10.40	1.02	MOT-26	8.86	1.20	MOT-36	15.74	0.95	MOT-47	4.97	0.45	MOT-57	6.74	0.32
MOT-6	13.19	1.67	MOT-16	7.98	1.76	MOT-27	10.25	1.57	MOT-37	8.87	1.13	MOT-48	2.91	0.05	MOT-58	7.73	0.12
MOT-7	15.44	2.17	MOT-17	12.43	1.84	MOT-28	6.35	0.22	MOT-38	2.59	0.08	MOT-49	10.21	1.43	MOT-59	6.06	0.24
MOT-8	23.00	1.20	MOT-18	11.52	1.63	MOT-29	16.05	0.58	MOT-39	23.4	1.93	MOT-50	12.19	1.04	MOT-60	5.02	0.09
MOT-9	23.36	1.77	MOT-20	13.82	1.22	MOT-30	20.54	1.72	MOT-41	7.77	1.34	MOT-51	21.05	1.80			
MOT-10	31.36	2.73	MOT-21	13.49	1.32	MOT-31	18.16	0.77	MOT-42	12.12	0.07	MOT-52	3.43	0.28			

Table No. 2: Left Ovary Volume in cm^3 (0th & 90th day treatment of Ovaryl Tablet)

Patient Code	0th day	90th day	Patient Code	0th day	90th day	Patient Code	0th day	90th day	Patient Code	0th day	90th day	Patient Code	0th day	90th day	Patient Code	0th day	90th day
MOT-1	6.15	5.76	MOT-11	19.91	17.79	MOT-22	6.72	6.44	MOT-32	16.05	14.73	MOT-43	5.17	5.01	MOT-53	8.59	7.34
MOT-2	11.39	11.08	MOT-12	8.96	7.32	MOT-23	2.96	2.82	MOT-33	9.43	9.19	MOT-44	6.74	6.13	MOT-54	3.89	3.72
MOT-3	27.07	24.83	MOT-13	16.30	14.51	MOT-24	4.06	3.92	MOT-34	13.83	12.82	MOT-45	9.77	8.39	MOT-55	13.75	12.72
MOT-4	7.09	6.24	MOT-14	18.09	17.17	MOT-25	6.02	5.86	MOT-35	4.49	4.35	MOT-46	23.19	20.62	MOT-56	8.06	7.67
MOT-5	13.27	12.42	MOT-15	5.29	5.02	MOT-26	4.93	4.79	MOT-36	6.26	5.27	MOT-47	13.11	12.9	MOT-57	8.67	7.97
MOT-6	16.48	12.46	MOT-16	15.51	12.73	MOT-27	9.23	8.85	MOT-37	33.57	30.69	MOT-48	4.34	4.16	MOT-58	10.24	10.1
MOT-7	23.26	22.14	MOT-17	23.08	21.46	MOT-28	11.36	10.48	MOT-38	12.8	10.15	MOT-49	7.57	7.08	MOT-59	4.75	4.61
MOT-8	19.29	18.42	MOT-18	11.69	10.08	MOT-29	6.51	6.25	MOT-39	10.94	9.37	MOT-50	10.34	8.65	MOT-60	16.74	15.37
MOT-9	13.01	12.14	MOT-20	11.68	10.14	MOT-30	9.84	8.26	MOT-41	7.05	6.76	MOT-51	15.09	14.48			
MOT-10	26.08	24.72	MOT-21	19.91	17.79	MOT-31	16.60	15.70	MOT-42	8.27	8.11	MOT-52	5.97	5.58			

Table No. 3: Serum Insulin Levels in micro unit / ml (0th & 90th day of treatment with Ovaryl Tablet)

Patient Code	**0th day**	**90th day**	**Patient Code**	**0th day**	**90th day**	**Patient Code**	**0th day**	**90th day**	**Patient Code**	**0th day**	**90th day**	**Patient Code**	**0th day**	**90th day**	**Patient Code**	**0th day**	**90th day**
MOT-1	17.60	15.95	MOT-11	29.40	26.10	MOT-22	13.60	12.55	MOT-32	13.3	10.98	MOT-43	8.4	1.2	MOT-53	21.3	16.32
MOT-2	10.70	8.98	MOT-12	20.40	18.20	MOT-23	6.40	5.10	MOT-33	19.9	15.8	MOT-44	9.3	1.19	MOT-54	17.9	15.1
MOT-3	4.30	3.66	MOT-13	62.20	50.90	MOT-24	9.60	8.55	MOT-34	12.3	11.1	MOT-45	27.3	2.8	MOT-55	4.3	3.22
MOT-4	10.80	9.81	MOT-14	23.30	21.40	MOT-25	24.40	22.10	MOT-35	67.9	58.5	MOT-46	10.7	2.3	MOT-56	19.8	17.42
MOT-5	34.50	27.50	MOT-15	21.60	19.10	MOT-26	15.40	13.88	MOT-36	8.9	7.1	MOT-47	9.2	1.09	MOT-57	12.6	10.22
MOT-6	12.20	11.10	MOT-16	14.30	12.60	MOT-27	16.90	15.10	MOT-37	17.4	16.9	MOT-48	6.1	1	MOT-58	20.6	17.98
MOT-7	13.80	12.44	MOT-17	5.40	4.44	MOT-28	13.90	11.85	MOT-38	2.5	1.88	MOT-49	8	0.9	MOT-59	18.6	15.5
MOT-8	12.80	11.65	MOT-18	14.90	13.38	MOT-29	121.90	97.80	MOT-39	2.8	1.95	MOT-50	8.9	1.68	MOT-60	20.8	16.42
MOT-9	65.80	51.10	MOT-20	14.30	13.10	MOT-30	3.70	2.66	MOT-41	7.1	5.44	MOT-51	2.4	0.85			
MOT-10	85.66	67.90	MOT-21	32.20	26.10	MOT-31	13.3	10.98	MOT-42	113.9	86.85	MOT-52	3.8	1.16			

Figure No. 1: Weight symptom at 0th day, 15th day, 30th day, 60th, 90th and 120th day

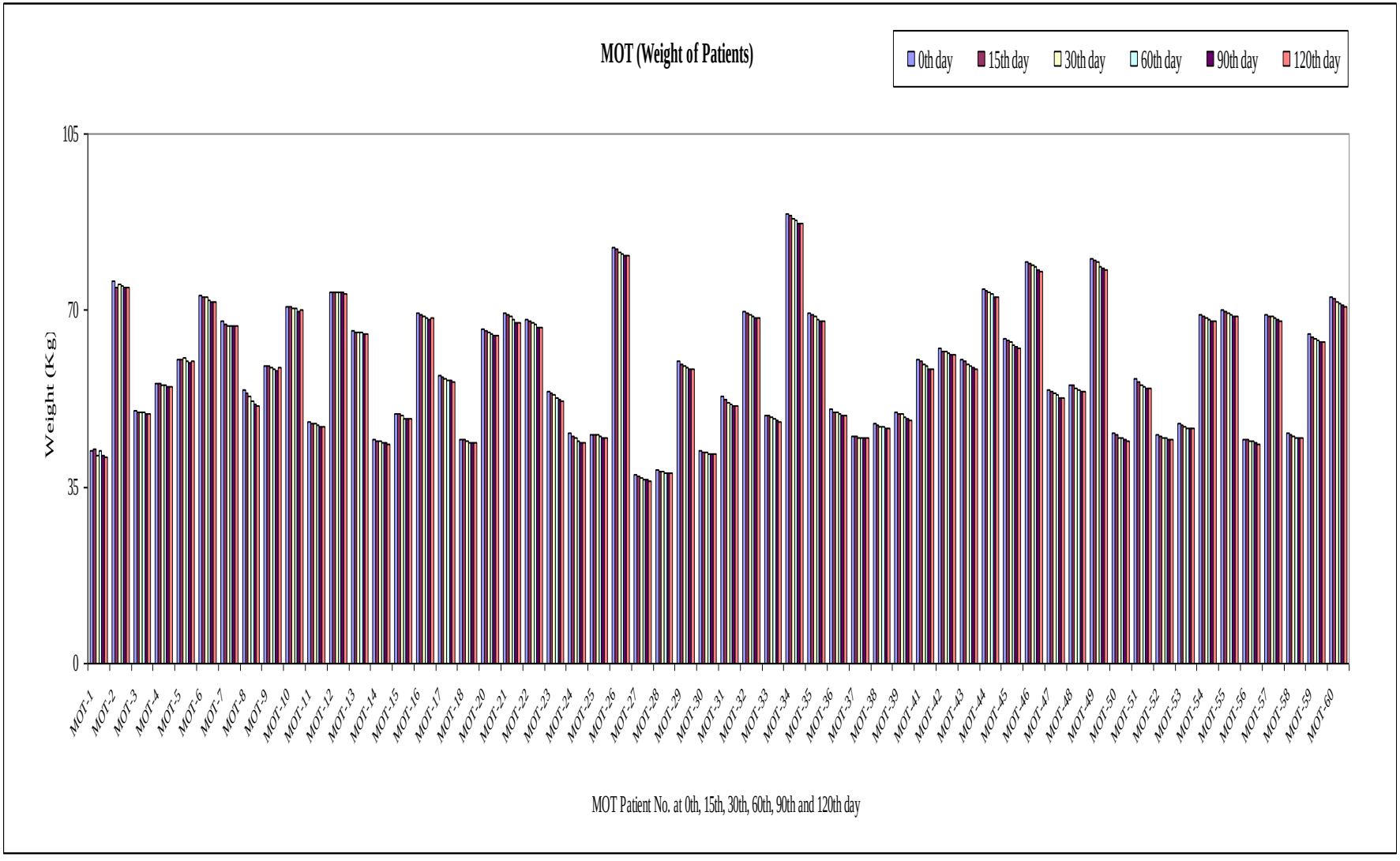


Figure No. 2: Hirsutism symptom at 0th day, 15th day, 30th day, 60th, 90th and 120th day

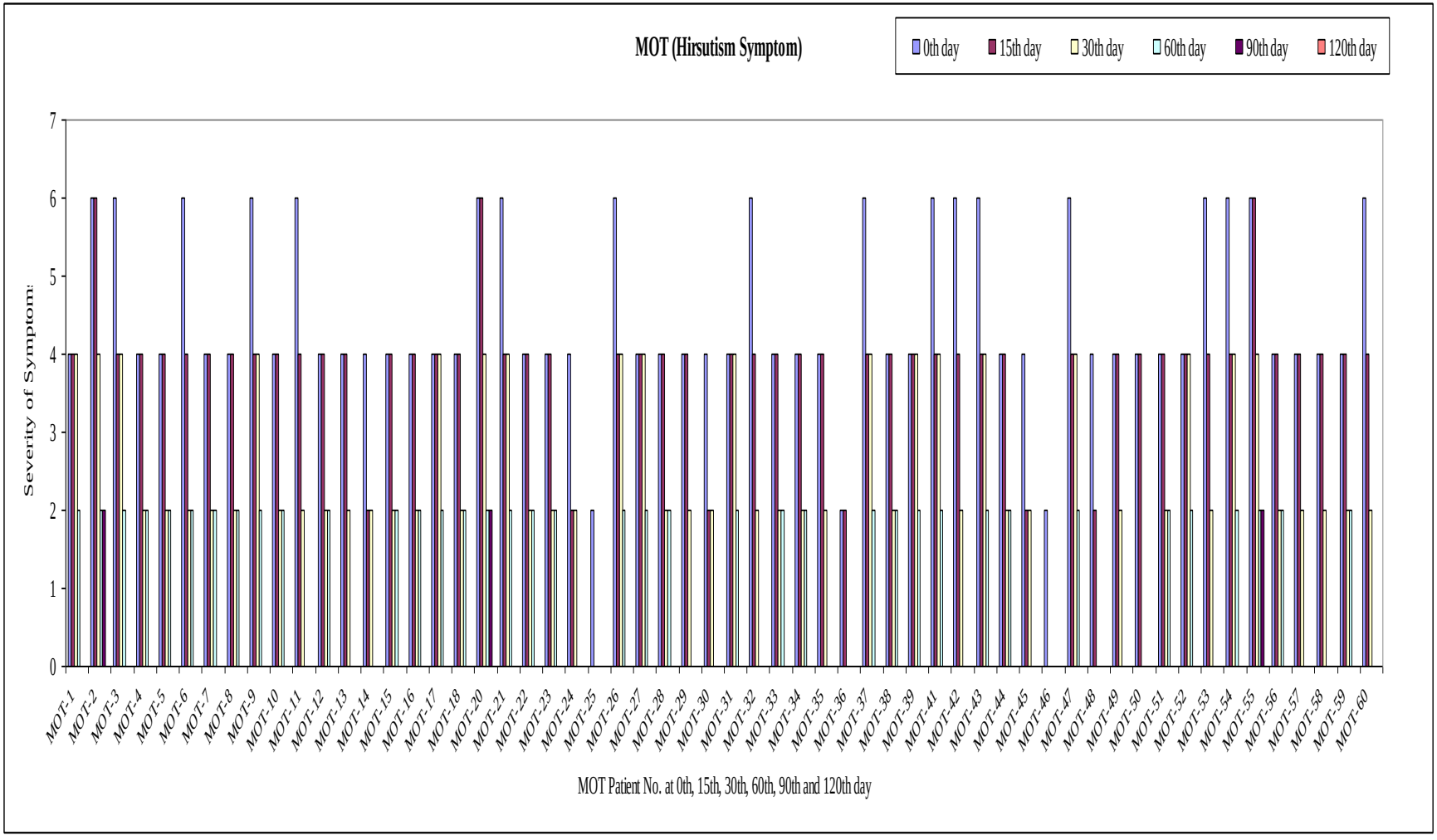


Figure No. 3: Irregular Periods symptom at 0th day, 15th day, 30th day, 60th, 90th and 120th day

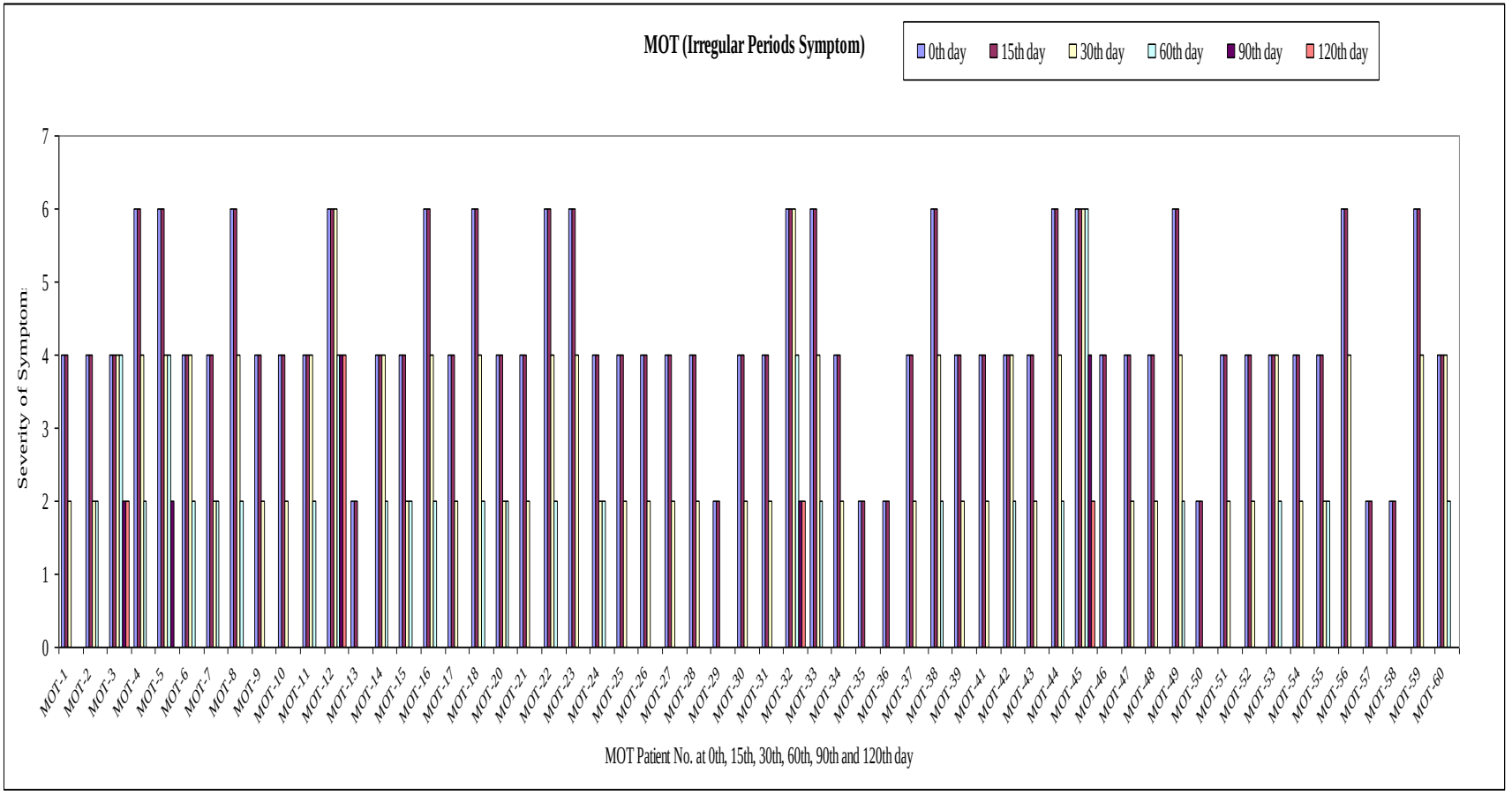


Figure No. 4: Ovulation symptom at 0th day, 15th day, 30th day, 60th, 90th and 120th day

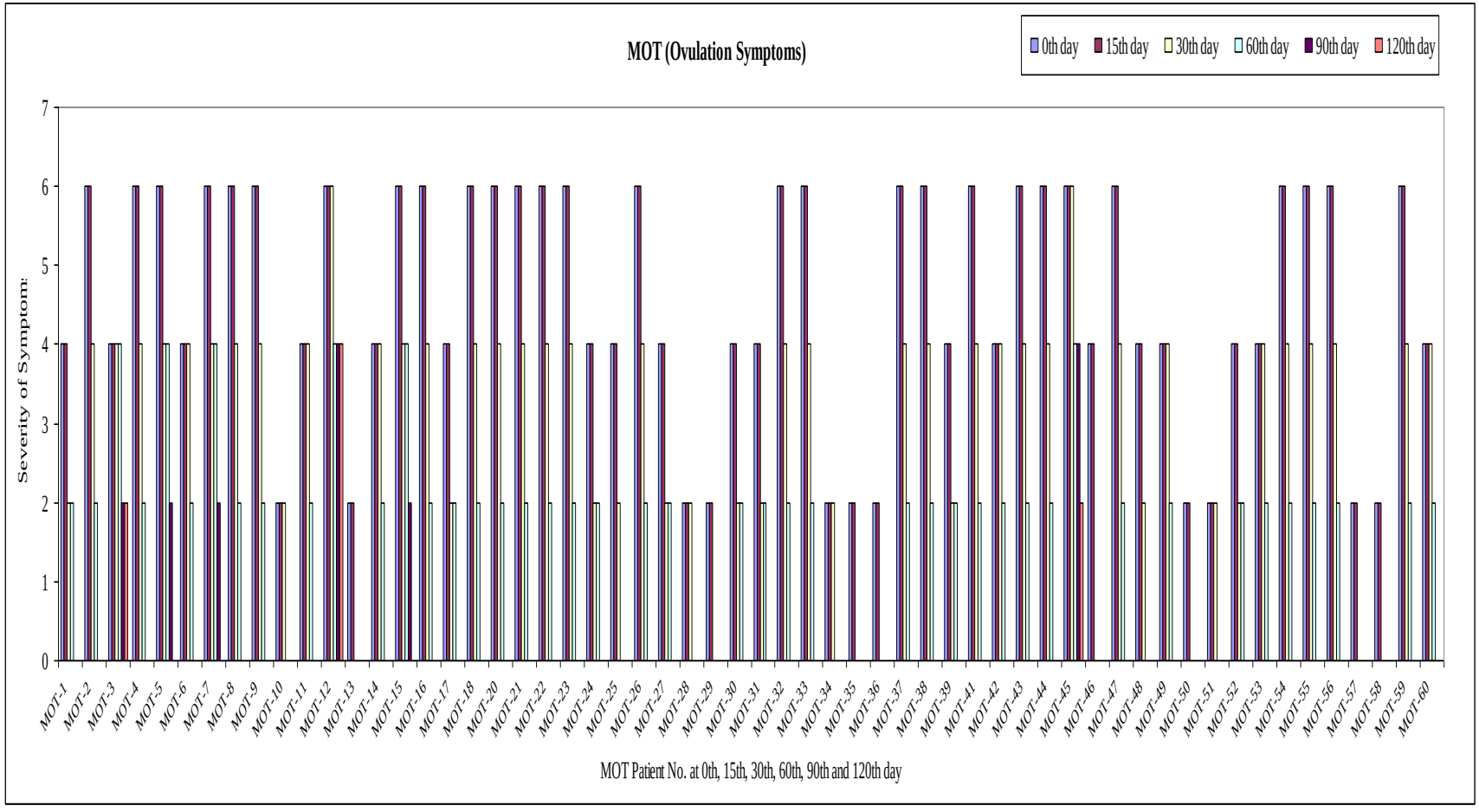


Figure No. 5: Right Ovary Volume (0th & 90th day treatment of Ovaryl Tablet)

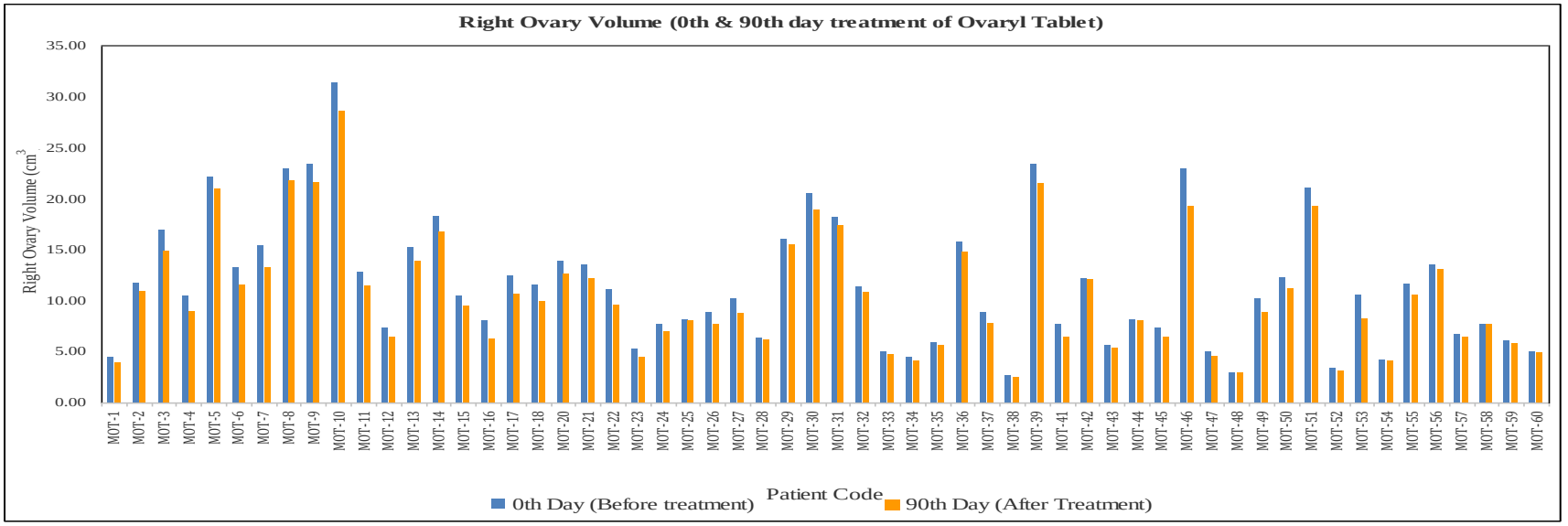


Figure No. 6: Left Ovary Volume (0th & 90th day treatment of Ovaryl Tablet)

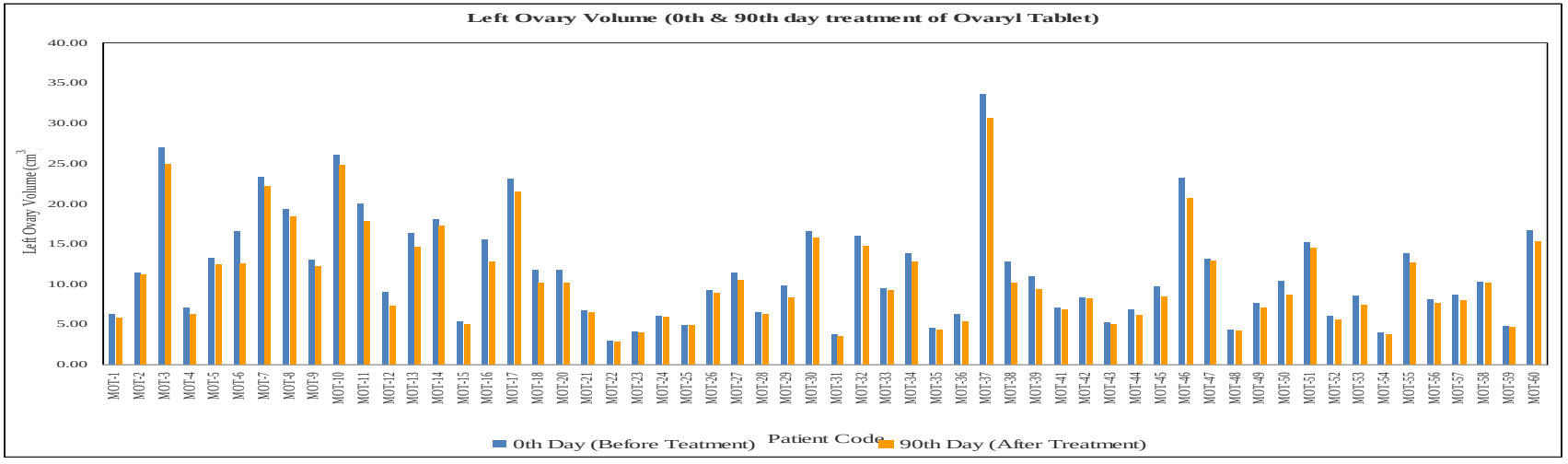
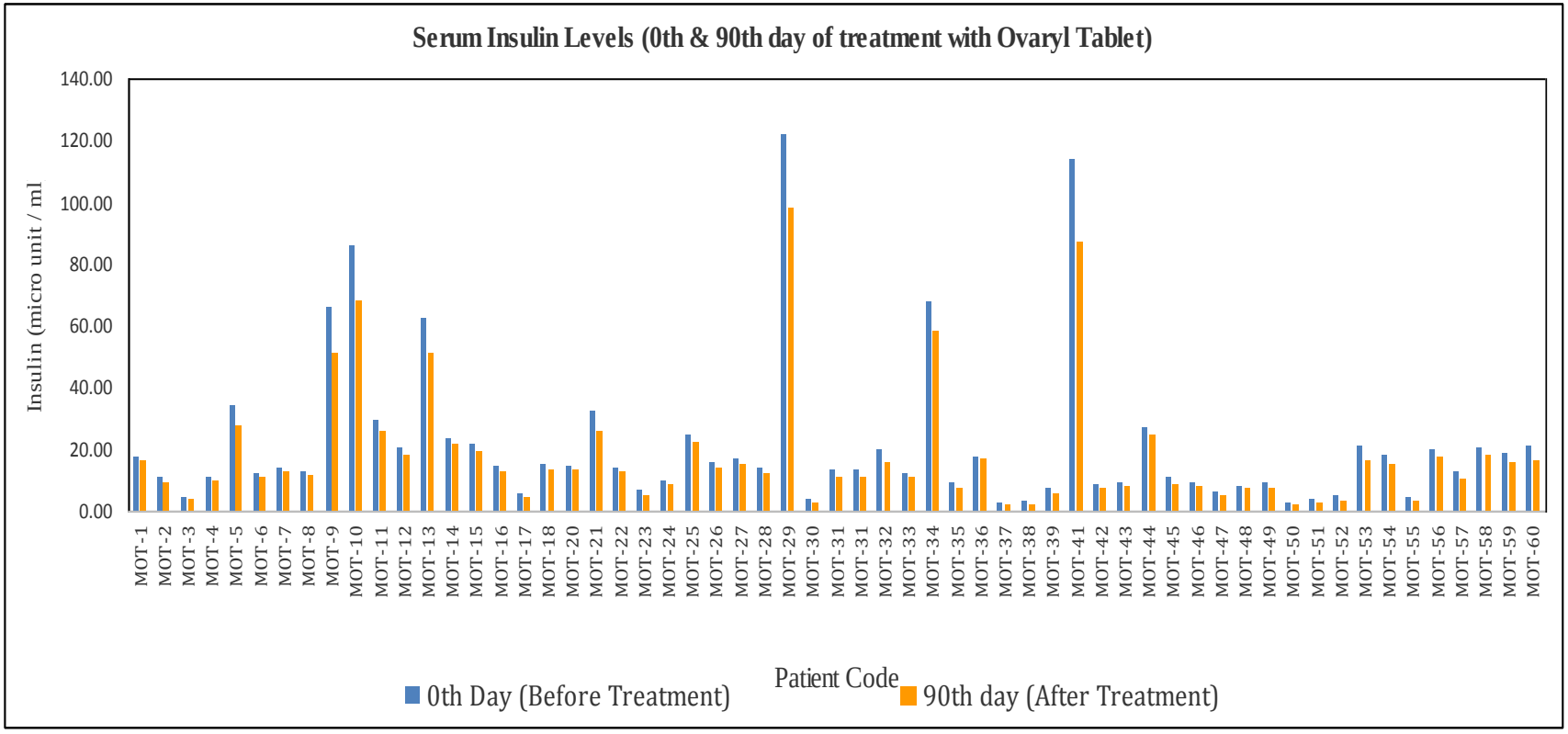


Figure No. 7: Serum Insulin Levels (0th & 90th day of treatment with Ovaryl Tablet)



RESULTS

Body Mass Index: The BMI is generally used as a means of correlation between groups related by general mass and can serve as a vague means of estimating adiposity **(Table 4)**.

Primary Outcome Measure: Improvements were observed in clinical, serum insulin and ovary volume of MOT medicated 58 women patients age range between 20 to 40 years old.

A significant improvement was observed in clinical symptoms like Weight, Hirsutism, and Irregularity of periods and Ovulation after MOT medication. % improvement was observed for different clinical symptoms, during the study.

1) Weight was measured in all the patients on '0' day but after MOT medication, maximum weight loss was 2.89 kg (5.34%) and minimum weight loss was 0.25 kg (0.34%) was observed at the end of 120th day.
2) Hirsutism were observed in all the patients on '0' day but after MOT medication 1.72% (15th day), 34.38% (30th day), 94.83% (60th day), 100% (90th day) and 100% (120th day) improvement was observed in all the 58 patients.
3) Irregularity of periods was a concern for PCOS. Irregular period days were improved from 30th day by 13.79%, 55.17% (60th day), 91.38% (90th day) and 93.10% (120th day).
4) Ovulation period was improved from 30th day by 13.79%, 24.14% (60th day), 89.66% (90th day) and 94.83% at the end of study **(Table No. 5 and Figure8 - 10)**.

Laboratory investigation showed decrease in Serum Insulin levels. A minimum decrease of 2.87% and 36.73% maximum decrease of serum insulin levels were observed on 90th day of MOT treatment.MOT medication showed a significant decrease in serum insulin level of patients.

22.06% maximum and 1.55% minimum decrease of ovary volume in Right Ovary. 24.39% maximum and 1.37% minimum decrease of ovary volume in Left Ovary was observed. Upper Abdomen USG was normal in all the 58 patients, no cyst was reported.

Statistical Analysis for Primary Outcome Measure:Clinical assessment was done (symptoms score Occasionally = 0 Score, Mild = 2 Score; Moderate = 4 Score and Sever = 6; as per the Clinical trial format) and recorded on the zero day (i.e. one day before administering the trial drug), 15th day, 30th day, 60th, 90th and 120th day final day of the follow-up.

As the score of PCOS symptoms were reduced towards the end of the trial 90th day with medication and other 30 days without medication (i.e. a total of 120 days), it revealed a significant activity of the Ovaryl tablet formulation, as shown in **Table No. 6 and Figure 11 - 14**. Results were reported by mean ± S.E.M., the test of significance was statistically analyzed by using one way ANOVA test, followed by Dunnett's multiple comparison test ($p < 0.05$ and $p < 0.01$). Statistical analysis was done by using software Graph pad Prism Demo version 3.

Table No. 4: BMI

Patient Code	BMI	Patient Code	BMI	Patient Code	BMI	Patient Code	BMI	Patient Code	BMI	Patient Code	BMI
MOT-1	19.20	MOT-11	20.08	MOT-22	27.60	MOT-32	26.73	MOT-43	26.50	MOT-53	20.08
MOT-2	30.99	MOT-12	26.57	MOT-23	29.05	MOT-33	23.19	MOT-44	39.02	MOT-54	28.51
MOT-3	23.66	MOT-13	27.76	MOT-24	21.90	MOT-34	34.48	MOT-45	25.60	MOT-55	25.48
MOT-4	22.00	MOT-14	18.79	MOT-25	18.60	MOT-35	28.51	MOT-46	29.66	MOT-56	17.05
MOT-5	26.50	MOT-15	19.52	MOT-26	18.00	MOT-36	23.66	MOT-47	21.60	MOT-57	27.60
MOT-6	27.89	MOT-16	18.98	MOT-27	35.03	MOT-37	18.60	MOT-48	24.30	MOT-58	18.60
MOT-7	25.15	MOT-17	25.90	MOT-28	16.91	MOT-38	20.08	MOT-49	37.86	MOT-59	27.76
MOT-8	20.27	MOT-18	23.56	MOT-29	17.37	MOT-39	19.60	MOT-50	18.60	MOT-60	27.03
MOT-9	24.38	MOT-20	26.93	MOT-30	25.54	MOT-41	22.53	MOT-51	24.74		
MOT-10	25.48	MOT-21	24.02	MOT-31	14.83	MOT-42	23.28	MOT-52	18.60		

Table No. 5: % Improvement for Hirsutism, Irregularity of periods and Ovulation.

Day/ Treatment	Hirsutism Present in Patient	Hirsutism Absent in Patients	% Improvement	Irregular Periods Present in Patient	Irregular Periods Absent in Patients	% Improvement	Ovulation Present in Patient	Ovulation Absent in Patients	% Improvement
0th day	58	0	0.00	58	0	0.00	58	0	0.00
15th day	57	1	1.72	58	0	0.00	58	0	0.00
30th day	38	20	34.48	50	8	13.79	50	8	13.79
60th day	3	55	94.83	26	32	55.17	44	14	24.14
90th day	0	58	100.00	5	53	91.38	6	52	89.66
120th day	0	58	100.00	4	54	93.10	3	55	94.83

Table No. 6: Treatment of PCOS Symptoms, Ovaryl tablet.

Day	Weight	Hirsutism	Irregular Periods	Ovulation
0th	58.9095± 1.6381	4.5172± 0.1439	4.3103± 0.1617	4.5862± 0.2029
15th	58.5936± 1.6308ns	3.7586± 0.1398**	4.3103±0.1617ns	4.5862± 0.2029 ns
30th	58.2936± 1.6315*	2.4483± 0.1559**	2.6207± 0.2041**	3.0345± 0.2043**
60th	58.0010± 1.6216*	1.3103± 0.1259**	1.1034± 0.1852**	1.7241± 0.1512**
90th	57.6919± 1.6147*	0.1034± 0.0587**	0.2414± 0.1108**	0.2759± 0.1148**
120th	57.6279 ± 1.6143*	0.0000± 0.0000**	0.1724 ± 0.0892	0.1379 ± 0.0832**

All values are in mean ± S.E.M., * p<0.05 = significant vs. Control (0th day untreated patients); ** p<0.01 = more significant vs. Control (0th day untreated patients); ns = Non Significant, n = 58

Figure No. 8: Hirsutism at 0th, 15th, 30th, 60th, 90th and 120th day

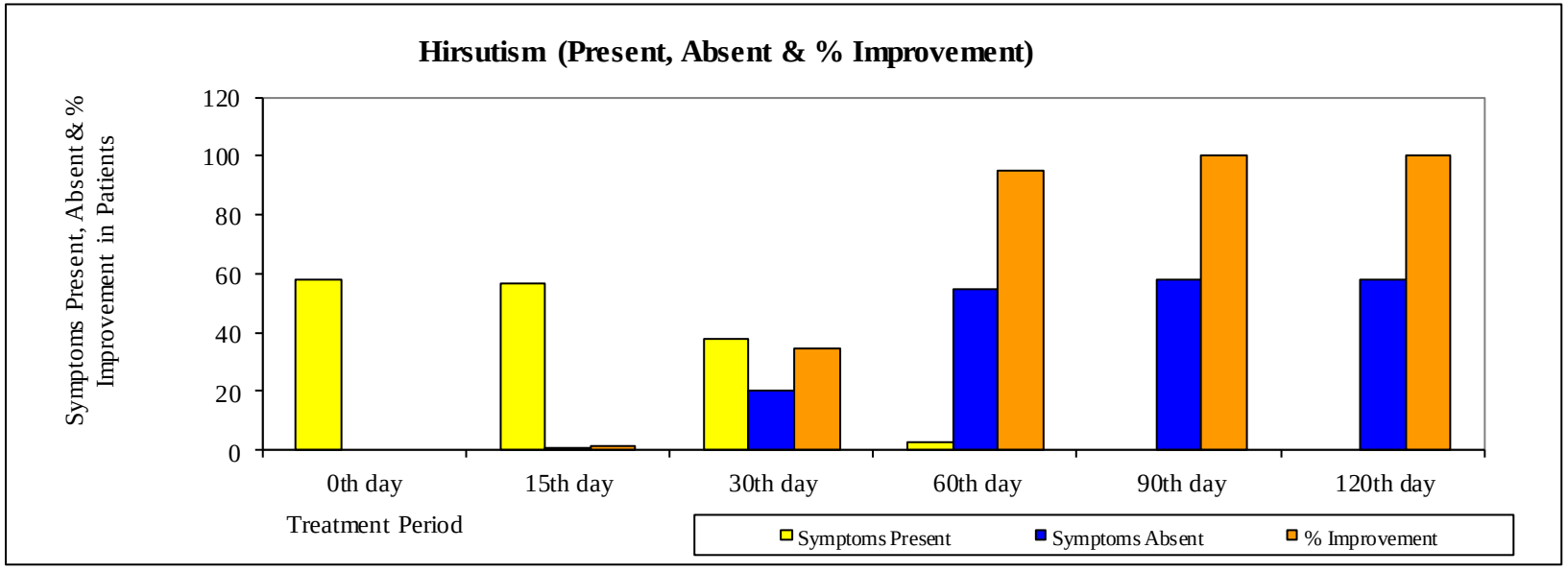


Figure No. 9: Irregular Periods at 0th, 15th, 30th, 60th, 90th and 120th day

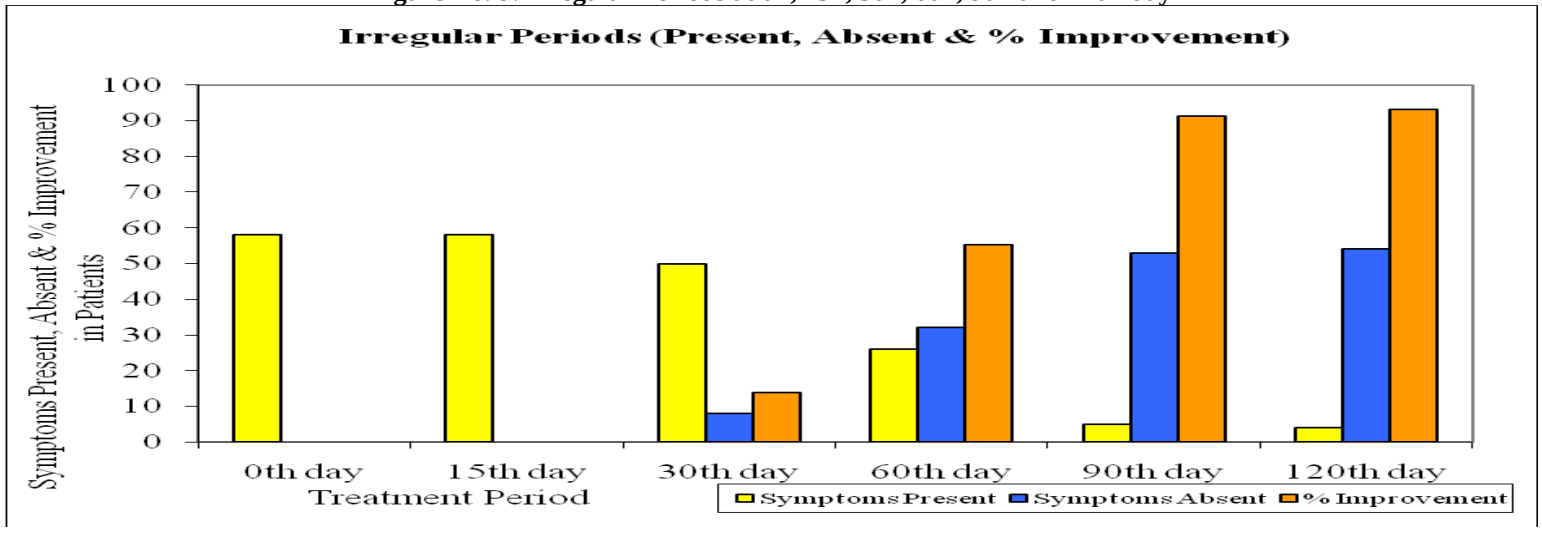


Figure No. 10: Ovulation at 0th, 15th, 30th, 60th, 90th and 120th day

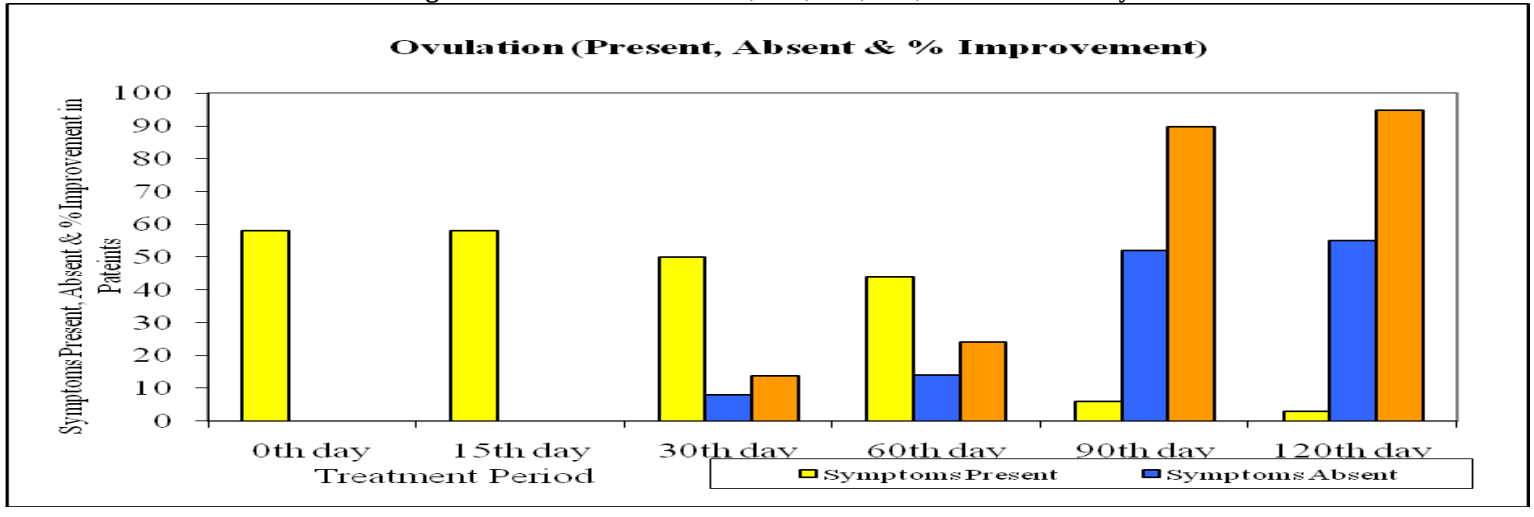
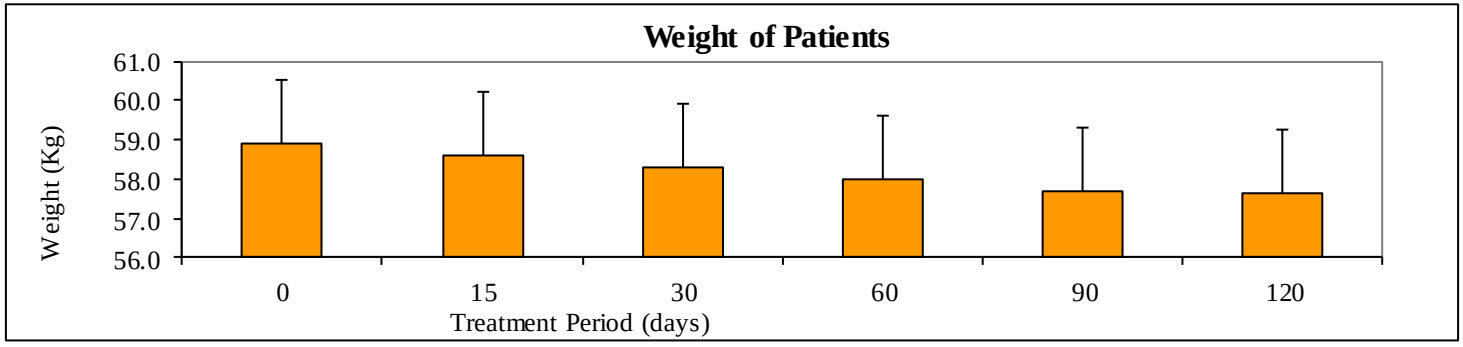
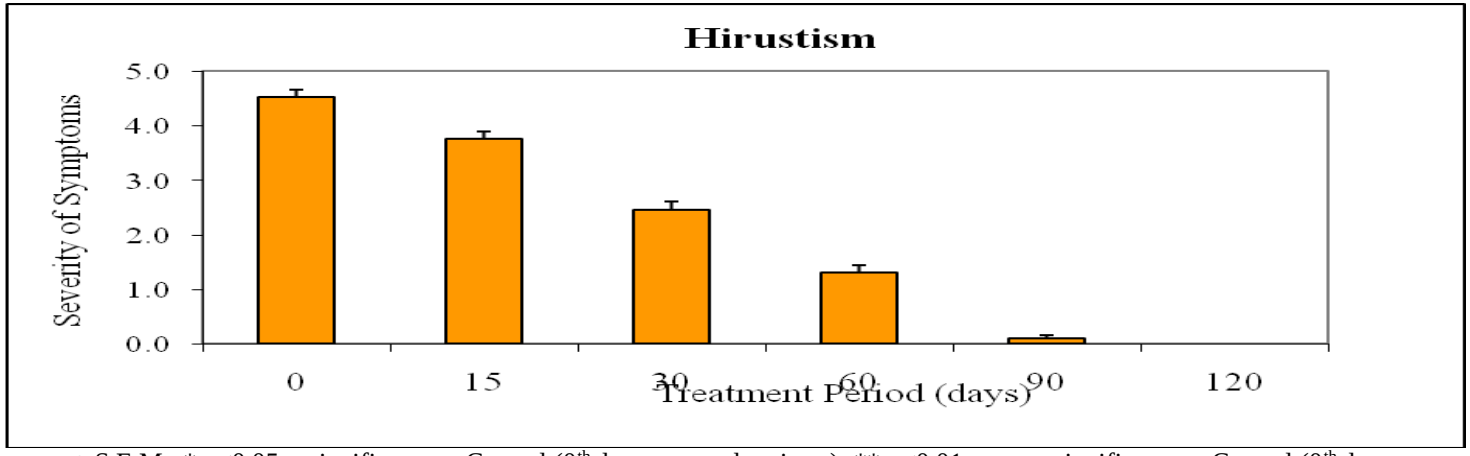


Figure No. 11: Graph of Weight of Patients, Weight (Kg) versus treatment period for Ovaryl tablet.



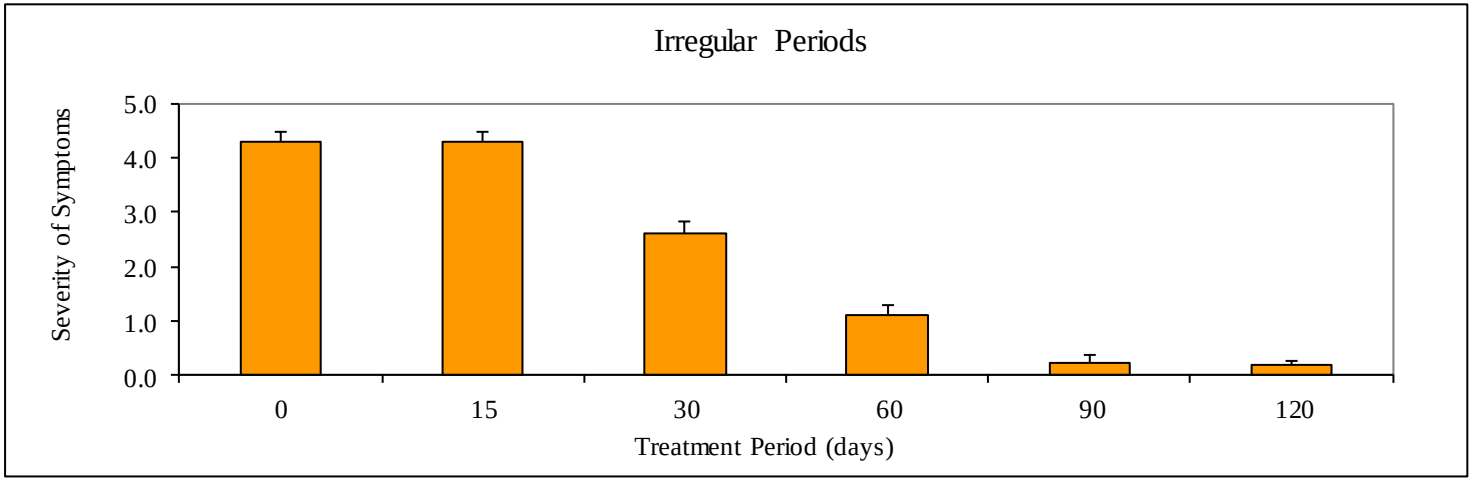
All values are in mean ± S.E.M., * p<0.05 = significant vs. Control (0th day untreated patients); ** p<0.01 = more significant vs. Control (0th day untreated patients); ns = Non Significant, n = 58

Figure No. 12: Graph of Hirsutism, Severity of Symptoms versus treatment period for Ovaryl tablet.



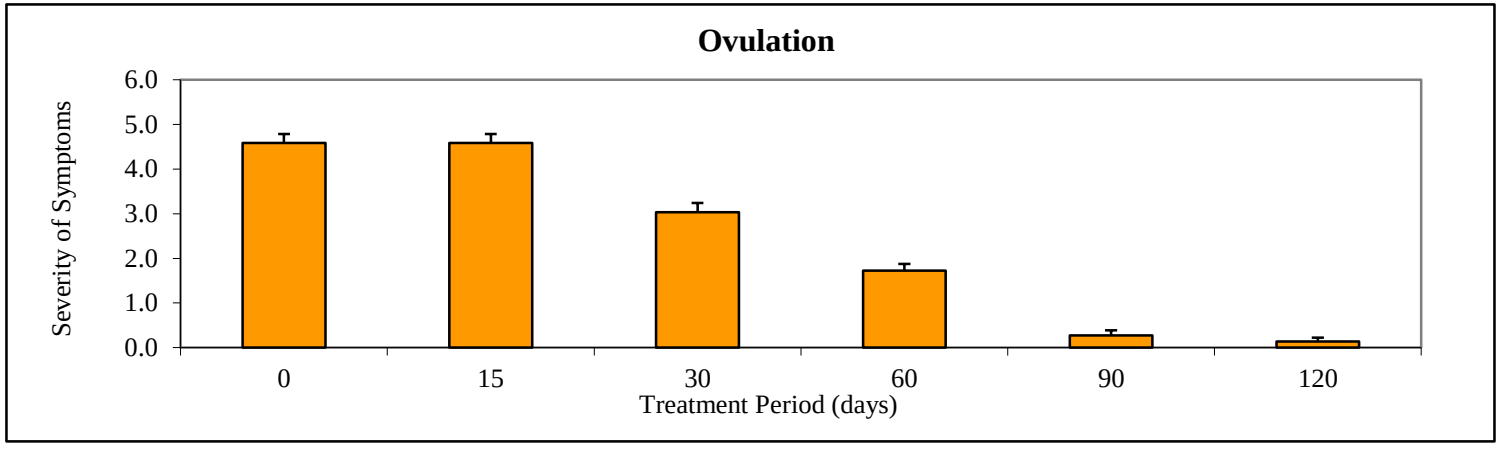
All values are in mean ± S.E.M., * p<0.05 = significant vs. Control (0th day untreated patients); ** p<0.01 = more significant vs. Control (0th day untreated patients); ns = Non Significant, n = 58

Figure No. 13: Graph of Irregular Periods, Severity of Symptoms versus treatment period for Ovaryl tablet



All values are in mean ± S.E.M., * p<0.05 = significant vs. Control (0th day untreated patients); ** p<0.01 = more significant vs. Control (0th day untreated patients); ns = Non Significant, n = 58

Figure No. 14: Graph of Ovulation, Severity of Symptoms versus treatment period for Ovaryl tablet.



All values are in mean ± S.E.M., * p<0.05 = significant vs. Control (0th day untreated patients); ** p<0.01 = more significant vs. Control (0th day untreated patients); ns = Non Significant, n = 58

DISCUSSION

As per the study design, total 60 patients were incorporated out of which 58 continued till the end of study. Patients were selected as per inclusion criteria and who doesn't fall in any one of the exclusion criteria. All necessary laboratory investigations were completed before starting the treatment with Ovaryl tablet. The patients selected had complaint of inadequate clinical symptoms like weight, hirsutism, irregularity of periods and ovulation along with serum insulin levels, ovary volume and no. of cyst.

0th Day Visit: All the patients were given the samples of test medicine, Ovaryl tablet. Patients were informed about the dose, effect of the drug and were advised to have followed up as per schedule, upto four monthsand if any harmful or unwanted or unexplained effect was noted and the drug should be stopped immediately and to inform as soon as possible. A complete general, systemic, laboratory (serum insulin levels) and upper abdominal USG examination of each patient was carried out in detail, to note any change in further visits.

15th Day Visit: All the patients were examined in detail after 15 days of starting the treatment. It was observed that subject was having no major changes in weight, hirsutism, irregularity of periods and ovulation. It was observed that no any major change in either of pulse, B.P., respiration etc. The systemic examination also was not altered at all. There was no any harmful effect noted either to patient.

30th Day Visit: After 15 days they were further called for the consultation. Each patient was examined in detail for their weight, hirsutism, irregularity of periods and ovulationsymptoms. No any significant harmful effect noted with the use of the product. The responses regarding the improvement in symptoms for patient were satisfactory at least. Pregnancy was reported positive in MOT-40.

60th Day Visit: At the end of 60th day they were further called for the consultation. Each subject was examined in detail for their clinical symptoms likeweight, hirsutism, irregularity of periods and ovulation symptoms were showing signs of improvement. Pregnancy was reported positive in MOT-19.

90th Day Visit: At the end of 90th day they were further called for the consultation. Each subject was examined in detail for their clinical, laboratory (serum insulin levels) and upper abdominal USG examination. Weight, hirsutism, irregularity of periods and ovulation symptoms were showing signs of improvement. Decrease in serum insulin levels and ovary volumes were observed, along with no cyst formation and normal upper abdominal USG were observed. Patients were told for last follow up after 30 days, the duration between 91stday to 120th day was observation period, for clinical symptoms without ovaryl tablet.

120th Day Visit: In that last visit they were examined as previously done, the difference in pre and post treatment parameters. The observations reported and the benefits noted from this product in PCOS women are discussed in detail.

Generally in clinical practice, the basic complaint almost by all the patients was weight, hirsutism, irregularity of periods and ovulation symptoms were significantly reduced.

With the use of the Ovaryl tablet which contains herbs, satisfactory and excellent results were observed within few days of use, in PCOS patients. During every routine visit, general and systemic examination was almost unchanged; there were no reporting of any harmful effect to the patient. Two patients reported pregnancy, positive.

With the pre and post investigations, all 58 patients showed significant decrease in weight, serum insulin levels and both ovary volume. Along with reduce PCOS symptoms weight, hirsutism, irregularity of periods and ovulation symptoms were significantly decreased with complete treatment of 3 months medication.

Stein-Leventhal syndrome or Polycystic Ovarian Syndrome (PCOS) is one of the most common female endocrine disorders which may leads to Infertility. Herbal drugs have promising role in treatment of PCOS and shows steady effect with minimal side effects. Herbal drugs enhance immunity of the body and also regularize menstrual cycle without fluctuating hormonal level.These herbal supplements, not only prevent ovarian cysts but also cure them. Herbal supplements may take time to cure PCOS but daily usage may treat the disease from its root. The review has successfully narrated all detail information regarding treatment of female infertility and prevention of recurrent abortions. The increased global warming, UV and cosmic rays, radiations of Silicon Medias, mobiles have generated the impairment of female infertility. Genetical disorder and hormonal imbalances are also can be rectified by drugs, alternatives medicines and physiotherapies.

Hence there is effective treatment for female infertility, proven to be as effective and safer alternatives to conventional drugs. The study indicates that Ovaryl tablet provides an effective and safer alternative for long term management since it improves symptoms score at the same time positive changes are observed radiographically.

CONCLUSION

1) PCOS symptoms weight, hirsutism, irregularity of periods and ovulation symptoms were taken care off.
2) Decrease in weight.
3) No cyst formation.

4) Decrease in Serum Insulin levels.
5) Decrease in right and left ovary volume.

LIST OF ABBREVIATIONS

MOT: Mercury Ovaryl Tablet
PCOS: Polycystic Ovarian Syndrome
USG: Ultrasonography
BMI: Body Mass Index

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