

**The Miracle of Iodine Complex in treatment of cases of polycystic ovarian disease induce by subclinical Hypothyroidism.**

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**ABSTRACT**

**Objective:** To determine the role of Iodine Complex in treatment of Cystic Ovaries due to subclinical Hypothyroidism.

**Study Design:** Pilot clinical study

**Duration of Study:** From 01-03-2012 to 30-10-2012 at Isra University Karachi

**Place of Study:** Isra University Karachi Campus.

**Methodology:** A total of 30 patients were included in the study. All of them were ensured that they were not taking any medication within the last 6 months. Investigations including complete blood picture, serum fasting insulin levels, thyroid stimulating hormone (TSH), serum free T4 (FT4), free T3 (FT3), serum FSH, LH, free testosterone, androstenedione and ultrasound of pelvis were carried out in all patients at the start of study and thereafter after four and eight weeks. Exclusion criteria were frank hypothyroidism, other metabolic and cardiac disease, hepatic and renal dysfunction. Capsule Iodomarine (Iodine Polymer) 50mg twice daily were prescribe for 8 weeks.

**Results:** The age of patients ranges between 18—35 years. Out of 30 patients 33.3% (n=10) were unmarried, 23.4% (n=7) were married with history of recurrent miscarriages and n=13 (43.3%) married woman with primary infertility. There was marked improvement in the symptoms with return of regular menstrual cycles in almost all patients. 6.6% (n=2) patients conceive within a period of 6 months time.

**Conclusion:** The Iodine complex marked by the name of Iodomarine capsules are found to be very effective in cases of PCO due to subclinical hypothyroidism.

**Keywords:** Iodine, Treatment, Polycystic ovarian disease, Hypothyroidism

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## **Introduction**

The polycystic ovarian syndrome affect 4% to 12% of women of reproductive age group and 6.5—6.7% of all perimenopausal women. The disorder originally described as cystic disease of the ovaries by Stein & Levanthal that is now considered to be associated with a barrage of endocrine and metabolic disturbances such as hypertension, impaired glucose tolerance (IGT), type 2 diabetes mellitus, coronary heart disease, increased risk of endometrial and perhaps breast cancer, menstrual disorders are most commonly seen in gynaecological practice.

The menstrual pattern is affected by number of endocrine derangement responsible for clinical manifestation of the disease. The thyroid acts directly on the ovaries which contain highest concentration of iodine after the thyroid gland(1).

Women are naturally prone to iodine deficiencies particularly during pregnancy (state of stress) and the need for iodine can double or triple (normal requirement for women is 150 gm and during pregnancy and lactation it increases from 220 gm and 270gm respectively). Treating thyroid dysfunction can reverse menstrual abnormalities and thus improves the infertility (2).

Most physicians & surgeons view Iodine from the narrow perspective of its use as an antiseptic and disinfectant for surgical wound. It is therefore that the international council for control of Iodine deficiency disorders recommend the use of Iodized salt. The life expectancy of Japanese is 81.25 years because they eat a lot of seaweed which includes brown, red and green algae rich in Iodine and it is internationally accepted that the infant mortality rate in Japan is lowest in the world even half of the infant mortality in US. Iodine in the body also acts as antioxidant. In organic Iodine neutralizes hydrogen peroxide thereby preventing it to become hydroxyl radical which is very specific for Kelp (algae) which absorbs increased amount of Iodine when placed under oxidative stress.(3,4)

The purpose of this study is to highlight the benefits of Iodine in the form of capsule Iodomarine containing Iodine, Iodine salt, Iodine polymer, extract of Kelp, Algae and ascorbic acid in the form of oral capsules 50mg. This product is found to be very effective in cases of PCO due to subclinical hypothyroidism with excellent results in regaining fertility and regulating menstrual pattern.

## **Methodology:**

The study was conducted from 1<sup>st</sup> March 2012 to 30<sup>th</sup> October 2012 at Isra University Karachi. 50 patients were enrolled but only 30 patients completed the study period. The patients included in the study were between 18—40 years and ensured that all of them were not taking any medication within the last six months. An informed consent was taken from all patients.

A protocol was designed for treatment of polycystic ovarian disease (anovulation, excessive androgen activity and ultrasound picture of ovaries- the Rotterdam criteria). The proforma includes Biodata of patients including date of enrolment for the study, clinical presentation including cyclical irregularity, hirsutism, infertility, obesity and recurrent miscarriages and the duration of symptoms. The positive findings in general physical examination including BMI, Pallor, hirsutism, acne, Galactorrhoea, cushingoid and acanthosis nigricans were noted.

Investigations including complete blood picture ultrasound of pelvis for size and volume of ovary number of follicles and their size, hyperechocity of central stroma of ovaries. (Rotterdam criteria) and it was repeated at 4 and 8 weeks of treatment to notice the changer following treatment. Serum fasting insulin level, blood sugar fasting and random, serum follicular stimulating and Leutinizing (FSH & LH) hormone levels , serum TSH, FT<sub>3</sub> and FT<sub>4</sub>, serum free testosterone and androstenedione at the start of study and then repeated on completion of study in order to note whether change in if any has occur in their levels after treatment.

Pelvic examination was carried out as routine procedure on enrollment and routinely at 4 and 8 weeks of treatment to note change in the clinical findings if any.

All cases were selected from consultant OPD and were explained about due benefits and risks of treatment including toxicity/overdose of iodine (burning of mouth, throat, and stomach and/or abdominal pain, nausea, vomiting, diarrhea, weak pulse and coma) and also the expense and monitoring. The patients were asked about family history of hypothyroidism, goiter and intake of drugs effecting the thyroid levels. All cases selected for the study had elevation of TSH upper limit of reference range (0.45—4.5miu/l) with normal T4 level. Obesity, infertility, hirsutism was found in all of the married patients; the unmarried group of patients were also suffering from same problem except infertility. The BMI was above the normal range (23—25) and ultrasound picture of PCO.

All patients receive 50 mg iodine complex in capsule form twice daily for a period of eight weeks. In addition to the medication an advice for life style changes including regular exercise and low glycogen foods was advice.

Exclusion criteria`s were patients above 40 years, frank hypothyroidism, patients on medication for other metabolic diseases, cardiac patients, patients with hepatic and renal dysfunction and patients with other chronic disease.

**Results:** The patients age were between 18—40 years. There werenn= 10 (33.3%) unmarried girls with age between 18—28 years having irregular menses, obesity, hirsutism, polycystic ovaries on ultrasound, serum TSH between 5—7 mu/L and serum FT<sub>4</sub> within normal limits .In this groups the periods become regular, weight and BMI decreases. The volume of ovaries also decrease and TSH become within normal range. They were further counselled regarding life style changes in future (Table I).

There were n= 7 (23.4%) married woman age between 20—30 years with same clinical findings and history of 3 consecutive miscarriages between 6-8 weeks .They were investigated for antiphospholipid syndrome, uterine anomalies, TORCH infection and other systemic infections etc. The only finding was serum TSH (6—8mu/L) on thyroid profile. They were prescribe capsule Iodomarine 50mg twice daily for 8 weeks. It was observed that the menses become regular in 5(16.6%) cases, 2(6.6%) cases conceived at the end of treatment and are booked with us and have crossed the critical period and are kept on tablet Idorine 300ugm as essential nutrients and are still being followed up. (Table I).

There were n= 13 (43.3%) married women age between (28—40 years) have oligo menorrhea, obesity, hirsutism, sign of polycystic ovaries on ultrasound, serum TSH between 6—8mu/L and serum FT<sub>4</sub> within normal limits and history of primary infertility. A complete work up was done before and after the treatment and were followed up regularly in OPD.

They were worked up for infertility as well. They were prescribed tablet Glucophage 50mg twice daily. Advice to reduce weight and regular exercise. All the investigations for fertility were found to be within normal limits the only abnormality was TSH (6—8 $\mu$ /L). These patients were kept on cap Idomarine 50mg twice daily and after eight weeks the cycles regain normality, weight and BMI show marked reduction and ovarian volume decreases as well. 1(3.3%) case conceived after this treatment. The remaining cases are still being treated with the hope of favourable results. (Table I).

**Table – I: Effect of capsule Idomarine in cases of PCO due to subclinical Hypothyroidism (n=30)**

<b>Type of patients</b>	<b>No of patients</b>	<b>percentages</b>	<b>Result of treatment</b>
Unmarried	10	33.3%	All patients (100%) recovered.
Married with recurrent miscarriage at 6—8 weeks	7	23.4%	Menses regularized in 5 (16.6%) patients, conceived and pregnancy continued beyond 8 weeks in 2 (6.6%) patients.
Married with infertility	13	43.3%	1 (3.3%) patient conceived.

## **Discussion:**

The menstrual pattern is influenced by thyroid hormones by its direct action on ovaries and in an indirect way via its impact on Sex hormone binding globulin (SHBG), Prolactin levels (PRL) and Gonadotropic releasing hormones (GnRH) secretion and coagulation factor (5,4).

The thyroid dysfunction not only affect the ovulation by interacting with ovarian function (5,6) but also affect the lipid metabolism and fertility of a woman. It only affect the menstrual pattern and interfere with foetal implantation which can be prevented by early recognition and treatment with thyroid hormone. (6) The polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders in women with reproductive age group (7). Treating thyroid dysfunction can reverse menstrual abnormalities and thus fertility in cases of PCO.(8,4)

The main endocrine derangement responsible for the clinical manifestations are hyper androgenemia and abnormal insulin response to glucose. Which are supported by biochemical and hormonal response by the insulin sensitizers. There is a trend in gynaecological practice that cystic ovaries are always taken as PCOS diagnose by a fix criteria of Rotterdam. The levels of FSH & LH plus ultrasound picture of PCO are taken as diagnostic features. Things like subnormal or little higher levels of other hormones are overlooked and not taking seriously like subclinical hypothyroidism which present with features of PCOS. (8,9)

The ovaries contain highest concentration of Iodine after thyroid gland. Research has shown that there is a cyclic change of ovarian Iodine content associated with ovarian activity, that is the Iodine content are highest at the peak of ovarian activity and decrease with the decline of ovarian activity. It is therefore that Iodine deficiency causes the ovaries to develop cysts, nodules and scar tissue. At its worse this ovarian pathology is very similar to that of Polycystic Ovarian syndrome (PCOS).

Women are naturally prone to Iodine deficiencies when they are under stress and the need for Iodine can double or triple. It is very interesting to note that prevalence of hypothyroidism is 0.2% in males as compare to 2% in females resulting in reduce fertility, menstrual abnormalities, miscarriage, premature delivery, placental abruption and poor perinatal outcome.(9) In cases of PCOS due to SCH also suffering from metabolic syndrome have more menstrual irregularity, significantly higher level of serum testosterone, higher TSH levels, total cholesterol and LDL. (10)

The scientific discoveries in human reproduction presented proof of the presence of thyroid stimulating hormone (TSH) as well as of T3- receptors in the ovary and thus indicating direct TSH - and T3- effect on steroidogenesis and oocyte maturation (11).

The under active thyroid if left untreated has severe consequences on the metabolism and function of various organs and systems of organism including the female reproductive system producing an ovulation disorders, reduce fertility in women of child bearing age, increased risk of miscarriages etc (12,9). SCH may affect the gonadotropic axis at different levels and lead to PCO.(12)

There was a case report presented by Kubotak et.al where the patient presented with multiple ovarian cysts and investigations determined that she was suffering from primary hypothyroidism and the cysts resolves completely after hormone replacement (13)

Hypothyroidism is an accepted cause of infertility and recurrent miscarriages. A study conducted in Bangladesh in Iodine deficient zone proves that Hypothyroidism is an accepted cause of infertility and habitual abortion because young infertile woman with menstrual dysfunction show improvement in cyclicity after iodine intake (14).

Regarding miscarriage and infertility the thyroid disease during pregnancy are related to maternal and fetal complications. Mild or subclinical hypothyroidism has been reported to increase the risk of first trimester miscarriages and low birth weight babies (15). There is a study reported from India conducted on 163 women with recurrent first trimester pregnancy loss compare with 170 healthy age-matched women without a history of abortion were included in the control group. In 4.29% women with recurrent pregnancy loss (RPL), hypothyroidism was found to be causative for abortion. In control group 1 0.61% woman was identified with hypothyroidism (16). The study concludes that treatment of hypothyroidism helps the couple to have a successful outcome in subsequent pregnancies. As far as infertility is concerned, hypothyroidism can effect fertility due to anovulatory cycles, luteal phase defects, hyperprolactinemia and sex hormone imbalance. There is a study concluded in India on 94 infertile women suffering from hypothyroidism out of which 23.9% had TSH > 4.2 u/u/ml. after treatment 76.6% conceived within 6 weeks to one year (17). There is another study which compare hypothyroid and control women with or without PCO and showed that PCO hypothyroidism is invariably followed by a lowering of sex hormone binding globulin and an increment in the free testosterone but further metabolism of testosterone may or may not be directed towards on overproduction of estrol,E<sub>3</sub>(18).

In a study conducted in Iran to assess the effect of metformin administration on thyroid function in overweight women with PCOS, 27 overweight women with PCOS and hypothyroidism were selected. 15 patients were treated with metformin for 6 months and 12 with placebo. There was a significant decrease in TSH in group I, but not in group II. Therefore metformin normalizes the TSH, without causing any reciprocal changes in other thyroid function parameters (19). There is another study conducted on the role of metformin in hypothyroid patients with PCO showing that metformin treatment results in significant reduction in serum TSH concentration in hypothyroid patients with PCO independent from concomitant substitution therapy with 1-thyroxine (20).

Our study is quite interesting in terms of its results as oral Iodine twice daily is found to be effective in reducing the ovarian volume, regaining menstrual irregularity and improving fertility. The Algea which is present in this Iodine polymer is a very rich source of Iodine, the addition of Ascorbic acid is also used for neutralizing Iodine and manufacturing of Iodine polymer. It proves that there is functional correlation between ovaries and thyroid gland thyroid disorders interact with ovarian function. Also treating thyroid dysfunction can reverse menstrual abnormalities and thus fertility in cases of polycystic ovarian syndrome (21).

**Conclusion:** Iodine complex used in the treatment of cystic ovaries, miscarriages and infertility is found to be very effective.

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