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Registered Address
Kwality House, 1st Floor,
August Kranti Marg, Kunds Corner,
Mumbai 400 026

Phone: 022 23802584, 022 23803965
Fax: 022 23804839
Email: thepcossociety@gmail.com
I do hope you all enjoy the academic exchange which will follow in this 3 days meeting, as much as the team at the PCOS Society has enjoyed putting it together!

I would personally like to convey my thanks to all the members of my team who have worked very hard to put this meeting together with a special thanks to Rochelle, a special thanks to ManjuBhargav for bringing in our Celebrity Guest of Honor Dr. Rustom Soonawala admired and loved by women all over our country, the experts from the Androgen Excess & PCOS Society, our national experts, all our esteemed sponsors who have come forward and contributed generously and our invited guests from the media and Society and last but not the least all the 650 delegates present here today.

Email: thepcossociety@gmail.com

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The first International Conference of the PCOS Society (India) entitled “PCOS – Understanding the Science and Practice” was held from the 17th- 19th June, 2016 at The Leela Hotel, Mumbai. It was jointly organized by the PCOS Society (India) and the Androgen Excess and PCOS Society (AE-PCOS Society) an International Society of Androgen Excess and PCOS, and endorsed by the Federation of International Societies of Gynecological Endocrinology (FISGE).

We had a galaxy of international speakers, which included Anuja Dokras, President of the AE-PCOS Society, Enrico Carmina, Executive Director and CEO of AE-PCOS Society along with Richard Legro, Kathy Hoeger and Maurizio Nordio.

The consequences of PCOS are seen across the entire lifespan of women requiring a multidisciplinary approach, hence faculty from various specialties such as endocrinologists, obstetricians, gynecologists, fertility specialists, dermatologists, sonologists, pulmonologists, physicians, obesity surgeons, nutritionists were all invited on the same platform to share their expertise. The Conference Sessions discussed all areas of PCOS from puberty to menopause, covering the entire lifespan of the women.

There were two Precongress Workshops, one on ‘Impact of PCOS on pregnancy’ and the other on “Management of cosmetic concerns in PCOS”. The Cosmetic Workshop was followed by a live demonstration of laser therapies. Both the Workshops were well attended and there was more than sufficient time for interaction between the delegates and the faculty at the end of the Session.

The Inaugural Function was preceded by two excellent Inaugural Lectures followed by a very elegant Inaugural Function where the Chief Guest was Mrs. Amruta Fadnavis the better half of the Maharashtra Chief Minister Shri. Devendra Fadnavis and a woman of substance in her own right. Our Guest of Honour was Padmashree Rustom Soonawalla, our respected senior gynaecologist, and both lent charm and grace to the function, which was attended by a full house followed by the Banquet.

The total number of delegates who had registered for our meeting were 650 and it was good to see that the majority of the delegates were present in the "Single Hall only". This goes to show the high academic standards maintained at this congress, which allowed a good 30 minutes interaction between the delegates and the faculty after every session. Overall this International Congress was well appreciated by all the delegates who gave a very positive feedback.

The evening Cocktails followed by Dinner was very enjoyable with music and a wonderful “Standup Comedy” show by Sahil Shah of the Canvas Club. Everyone had a totally relaxing time as they were in splits of laughter. We also had a guitarist and a violinist and all sang along with the musicians.

There was an excellent session by our scientists from the National Institute for Research in Reproductive Health (NIRRH) to showcase their research in this field and appraise the delegates on the excellent work happening in India. Their research involved community based studies giving us the prevalence of PCOS amongst young girls in Mumbai, along with a holistic approach of treating PCOS through women’s lives. They also showcased the research work done in their laboratory involving the pathophysiology of Folliculogenesis.

The Conference ended on Sunday afternoon after a Valedictory function followed by lunch.

During the Valedictory Function, Life Membership Awards of the PCOS Society were given to young delegates who presented free papers.

The President also thanked the sponsors of this Conference for their magnanimous support, without which this conference would not have been possible. We offer our gratitude to the following Sponsors –

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The lectures slides, which have the consent of the authors will be available free of cost to all as Continuing Medical Education on the PCOS Society Website.
Scientific session in progress – Round Tables

Some laughter and music...

Concerns of tomorrow...

Stand up comedian

NIRRH session

Valedictory

Understanding the Science and Practice

June 2016 - India

17th - 19th June 2016
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See page 9 for more pictures
PCOS is the commonest multi-organ endocrinopathy affecting women of reproductive age group. This reproductive and cardiometabolic syndrome greatly increasing a woman’s life time risk of infertility, menstrual abnormalities, type II Diabetes Mellitus and cardiovascular diseases. A cure is being highly sought after by researchers. But in the absence of a known pathophysiologic mechanism, this appears to be elusive. Currently, various investigational therapies, targeting the many symptoms of PCOS are being tried. Present article attempts to enumerate such therapies and explore their current status.

Insulin sensitizing agents
PCOS women, both obese and normal weight, have a very high prevalence of insulin resistance and hyperinsulinemia. Thus, the rationale to use insulin sensitizing agents in PCOS women is very strong. Biguanides and Thiazolidiones have been used extensively and large body of data exists on this subject. Some other novel agents which likely affect insulin resistance and metabolic profile of the PCOS woman have been discussed in this article.

Somatostatin analogs
Somatostatin is an endogenous hypothalamic peptide with 14 amino acids and a short half life. It inhibits pancreatic insulin release, pituitary growth hormone secretion and also LH release in response of gonadotropin releasing hormone (GnRH)1,2. This property therefore should be useful in PCOS management. Somatostatin analogue, octreotide, has been shown in few studies to improve pulsatile gonadotropin patterns, reduce LH, androgen and IGFI levels and improve ovulation4,5,6. Octreotide (LAR) long acting Somatostatin analog formulation, has also been tried and shown to directly influence insulin secretion14,15. Thus, this drug has potential role as insulin sensitizing agent, improve hyperinsulinemia, as well as have direct effect on the ovaries, as suggested by recent discovery of somatostatin receptors at ovarian levels17.

Inositols
“Inositol” is a group of naturally occurring carbohydrate compounds, which plays a small but significant role in “insulin” signaling. Many studies have reported defective inositol signaling as likely pathologic mechanism for insulin resistance of PCOS women. Three inositol family members have been tried in PCOS.

D-Chiro-inositol, Myo-inositol and D-Pinitol. These new molecules are thought to be having insulin sensitizing properties, likely to improve metabolic, cardiovascular and reproductive profile of PCOS women. There are many studies reporting the use of inositols in reducing insulin resistance and dyslipidemias in PCOS women18. In a recent paper, combination of myo-inositol and D-Chiro inositol, in a physiologic ratio of 40:1, was shown to improve metabolic profile of PCOS women19. Also, in another study this combination therapy was shown to improve oocyte, embryo quality and pregnancy rates in PCOS women undergoing IVF-ET20.

Artini et al studied 50 overweight PCOS women before and after a 12 weeks course of myo-inositol 2 gms with folic acid 200 mg daily. Patients were randomized to either the above combination or to only folic acid 200 mg daily21. They reported that after 12 weeks of myo-inositol administration, plasma LH, prolactin, testosterone, insulin levels and LH/FSH were significantly reduced. Insulin sensitivity, expressed as glucose to insulin ratio and HOMA index, significantly improved. Menstrual cyclicity was restored in all amenorrheic and oligomenorrheic subjects. No such improvement was seen in “Folic acid only” group. A systematic review published in 2011, looked into the effects of D-chiro-inositol on ovulation and insulin resistance in women with PCOS22. All studies published on PCOS and D-Chiro inositol (DCI) upto 2010 were included. Patients were women with PCOS receiving D-chiro inositol or where the relationship between insulin resistance and DCI had been investigated. Ovulation rates and insulin resistance were the main out come measures. They concluded that heterogeneity in study methodologies and small sample size used prohibit reliable conclusions to be drawn. More studies are needed to evaluate accurately the effects of DCI in PCOS. The inositols have potential to improve reproductive axis functioning by reducing hyper-insulinemia.

N Acetyl-Cysteine (NAC)
N-acetyl cysteine is a pharmaceutical drug and also a nutritional supplement. Acetly-cysteine is the N-acetyl derivative of amino acid L-Cysteine which forms antioxidant glutathione in the body. This compound is sold commonly as a dietary supplement, claiming antioxidant and liver protecting effects. Recent studies have shown beneficial effects from the use of NAC for patients with PCOS. Oner et al, reported clinical, endocrine and metabolic effects of metformin and NAC in PCOS women23. In this prospective trial, 100 women with PCOS were randomly divided to receive metformin (1500 mg/day) or NAC (1800 mg/day) for 24 weeks. Both treatments resulted in a significant decrease in body mass index, hirsutism score, fasting insulin, HOMA index, free testosterone and menstrual irregularity, compared with baseline values. Also both treatments had equal efficacy. NAC reduced both total and low density lipo-proteins, where as metformin only led to a decrease in total cholesterol.

Badawy et al24 studied NAC as a novel adjuvant to clomiphene citrate (CC) in clomiphene citrate resistant PCOS women. One hundred and fifty women diagnosed with CC resistant PCOS, aged 18-39 years, undergoing infertility treatment were included. The women were randomized to receive either NAC (1.2 gm/day) or placebo with CC 100 mg/day. Ovulation rates and pregnancy rates were reported. They concluded that NAC as an adjuvant was more effective than placebo for CC resistant PCOS women. Nasr, studied effect of NAC after ovarian drilling in CC-resistant PCOS women. Sixty CC-resistant women who had undergone unilateral laparoscopic ovarian drilling were randomized to receive placebo or NAC (1.2 gm/day) for 12 consecutive cycles. Ovulation rate, pregnancy rate and live birth rate were all significantly higher in the NAC group25. Thus, there is now a large body of evidence to support use of NAC in women with PCOS. It is likely to help to improve insulin sensitivity, to restore fertility and also to tackle homocysteine levels. It has been shown that many women with PCOS have high homocysteine levels26. Elevated homocysteine is associated with coronary artery disease, heart attack, chronic fatigue, fibromyalgia and cervical cancer. A 2009 study showed that people taking NAC for two months had a significant decrease in homocysteine levels27.

25-OH Vitamin D
Vitamin D deficiency has been shown to be prevalent in PCOS women28. About 65-85% of women with PCOS have serum concentration of 25-hydroxy vitamin-D (25-OH vit D) < 20 ng/ml. Some observational studies have shown that lower 25-OH vitD levels are associated with insulin resistance, ovulatory and menstrual irregularities, hirsutism, hyper-androgenism, obesity and elevated cardiovascular risk factors. Pal et al studied 12 overweight, Vitamin-D deficient, PCOS women. Blood pressure, plasma glucose, total testosterone, serum sex hormone binding globulin, 2 hr oral glucose tolerance test, were assessed at base line and after 3 months therapy with Vitamin-D and elemental calcium. Their results showed improved androgen and blood pressure profile. However, glucose and insulin resistance parameters remained unchanged.

Wehr et al studied 57 PCOS women, who received 20,000 IU of cholecalciferol weekly for 24 weeks. Anthropometric measures, oral glucose tolerance test and blood analyses of endocrine parameters were performed at baseline, after 12 weeks and after 24 weeks.
Introduction

Acne vulgaris is a common skin condition with 85% lifetime prevalence. While acne is commonly viewed as a disorder of adolescence, it may persist into adulthood and often may present for the first time in adulthood1. Adult acne is a common reason for patients to present for dermatological evaluation, and adults, in fact, make up a large portion of the patient population seen by dermatologists for acne.

Pathogenesis of acne

Pathogenesis of acne in adult women is complex, involving androgens in addition to other important factors well accepted for their role in the pathogenesis of acne: sebum production, follicular plugging, genetics, Propionibacterium acnes, diet, medications, innate immunity, and alterations in follicular keratinization and differentiation2.

Androgens in adult women with acne has been well supported in the literature3, and four clinical observations highlight this important role. First, androgen-insensitive individuals do not produce sebum and do not develop acne. Second, conditions of hyperandrogenism, such as polycystic ovary syndrome (PCOS), are associated with acne that is highly responsive to hormonal therapies4. Third, even in women with normal androgen levels, hormonal-based therapies such as oral contraceptives and anti-androgen medications are effective treatments for acne. Fourth, rising levels of dehydroepiandrosterone sulfate (DHEA-S) are associated with systemic retinoid therapy, and this is also correlated with clinical acne in a subset of menarchal females over the age of 14 years, even in those with normal androgen levels.

The PCOS Society (India)

Vice President

Dermatologist

Dr. Akshitha Shetty

Dermatologist

Dr. Rekha Sheth

MD, DVD

Dermatologist

The PCOS Society (India)

Treatment of acne

In the treatment of adult female patients with acne, it is important to treat the cause of acne; an endocrinological evaluation can be helpful. A systematic treatment algorithm for acne should be utilized5. Women over the age of 25 years have higher rates of treatment failure; 82% fail multiple courses of systemic antibiotics, and 32% relapse after isotretinoin6. Recurrence shortly after treatment with isotretinoin should trigger suspicion for an underlying hormonal disorder. A thorough review of systems for an underlying endocrine disorder should be performed prior to initiating isotretinoin5.

Isotretinoin

Isotretinoin remains a highly viable and important non-hormonal treatment option for acne in adult women7. In this patient population, there are special considerations of teratogenicity, and individuals over 35 years old may have increased risk of adverse skeletal side effects. Low-dose isotretinoin (10-20 mg/day) can be used to minimize side effects associated with systemic retinoid therapy, and this is an effective treatment of choice in this population8.

Hormones

Hormonal therapies, such as oral contraceptive pills (OCPs) and anti-androgen therapy, also provide an important and effective opportunity to increase treatment options for acne. As many adult women present with comedonal disease, hormonal therapies can be utilized across the entire clinical spectrum of acne, including mild and/or comedonal only disease9. Evidence-based recommendations supporting an algorithm for use of hormonal therapies in acne are currently lacking. An important goal of hormonal treatment is to reduce sebum production. The mainstay of hormonal acne therapy in the USA includes OCPs and spironolactone, other treatment options include flutamide and cyproterone10. Hormonal therapy provides an effective adjunct to the current acne treatments or may serve as primary therapy. Patients should be educated that this strategy will require time, up to several months, to see results, and may require long-term systemic treatment and ongoing monitoring for side effects. Hormonal therapy is safe and effective in post-menarchal females over the age of 14 years, even in those with normal androgen levels.

Spironolactone

Spironolactone is a highly effective treatment for acne in adult women and may surpass the efficacy of OCPs. A potassium-sparing diuretic, spironolactone at low doses (25 mg /day) blocks aldosterone and at higher doses (50-100 mg / day) blocks androgens at the receptor level. Drospirenone is a synthetic progestin that is an analog to spironolactone. In commonly-available OCP preparations, the 3 mg drospirenone is estimated to have anti-androgenic activity equivalent to 25 mg of spironolactone. Spironolactone is not FDA approved for the indication of acne, but spironolactone alone or combined with an OCP at a dose of 50-200 mg/day is effective in 33-85% reduction in acne lesion counts and also improves seborrhea. Studies with lower dose spironolactone (50-100 mg/day) demonstrate 33% improvement, suggesting a dosage effect. Studies with a higher dose of 100 mg plus drospirenone demonstrated an 85% improvement in acne, suggesting a highly effective combination treatment11,12,13.

Spironolactone is a safe and well-tolerated medication, yet patients should be counseled on potential side effects14. Side effects include breast tenderness (17%), menstrual irregularities (22%), headache (13%), fatigue (15%), blood pressure reduction (with mean decrease of 5 mmHg systolic, 2.6 mmHg diastolic blood pressure), and a minimal rise in serum potassium levels in 13% with no cardiovascular or renal sequelae. The investigators recommended checking potassium levels at baseline and at 4 weeks in certain patient populations, like patients over the age of 45 years, those with cardiac or renal disease, or those on concomitant drospirenone14. Importantly, spironolactone is a potential teratogen associated with hypospadias and feminization of male fetuses and is not recommended in pregnancy or in women contemplating pregnancy1,15.
Flutamide
Flutamide is a non steroidal androgen-receptor blocker used in prostate cancer and is effective in the treatment of hirsutism and acne in women\textsuperscript{1,11}. Typical doses are 250-500 mg/day. Due to its risk of hepatotoxicity, it is rarely used in the management of acne. Other side effects include gastrointestinal upset, hot flashes, and decreased libido\textsuperscript{2}.

Cyproterone acetate (CPA)
CPA is a 17-hydroxyprogesterone derivative with potent androgen blockade. CPA is available in two forms: in combination with OCPs or in a non-OCP form that can be used in combination with OCP or spironolactone. As a non-OCP medication, CPA is given on days 1-10 of the menstrual cycle (day 1 marking the first day of menstruation)\textsuperscript{2}.

Conclusion
Acne is common in adults and especially in women. Acne in adult women has significant psychosocial morbidity and may be challenging to treat. It may also be a sign of an underlying systemic disorder such as PCOS. Dermatologists likely play a critical role in the diagnosis of PCOS, as acne is a common cutaneous presenting sign. It is important to look for and ask about potential symptoms and signs of hyperandrogenism and to exclude an underlying hormonal disorder by complete history and physical examination. Isotretinoin remains a highly-viable treatment option. Hormonal therapies are also safe and effective, even when androgen levels are normal, and they provide an important opportunity to better treat this patient population. Hormonal therapies such as spironolactone and flutamide are effective even when other standard therapies for acne have failed, including antibiotics and isotretinoin. A strong therapeutic alliance with the patient is vital in this patient population, to attempt different combinations of therapies and to identify the best personalized treatment for acne.

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Systematic Reviews in PCOS – Abstracts

Abstract 1
Does Metformin help in assisted reproduction in PCOS patients?
Nine randomized controlled trials, with 816 PCOS women were included in this systematic review, where metformin was compared with placebo in women undergoing IVF/ICSI. The clinical pregnancy rates in metformin group compared to the placebo group were 32-49% and 31%, respectively. However, there was no conclusive evidence that metformin improved live birth rates in women with PCOS undergoing IVF/ICSI treatment.

Metformin treatment during or before IVF/ICSI in women with PCOS increases clinical pregnancy rates and decreases risk of ovarian hyperstimulation.

Abstract 2
Letrozole Vs. Clomiphene citrate for ovulation induction in PCOS – Which is better?
A systematic review & meta analysis was done on the results of randomized controlled trials (RCTs) which compared letrozole and clomiphene citrate (CC) for ovarian stimulation in women with Polycystic Ovary Syndrome (PCOS).
Seven RCTs with 1833 patients (906 in the letrozole group & 927 in the CC group) and 4999 ovulation induction cycles were included in the review. Live birth & pregnancy rates were statistically higher in the letrozole group, with no differences in the multiple gestations and miscarriage rates among the two groups.

Abstract 3
In vitro maturation (IVM) in PCOS & non-PCOS patients – Is it comparable?
In vitro maturation (IVM) was evaluated in sub fertile PCOS & non-PCOS women undergoing IVF.
Eleven studies with 268 PCOS & 440 non-PCOS patients undergoing IVM were included in the meta-analysis. A higher birth rate was observed among the PCOS patients who underwent IVM compared to non-PCOS controls. Clinical pregnancy and implantation rates were also higher, whereas cancellation rates lower among PCOS vs. non-PCOS patients.
However, there was no difference in the two groups as far as maturation and miscarriage rates were concerned.

PCOS Quiz

1. Which percentage of PCOS patients has elevated prolactin levels?
   a. <5%
   b. 5-10%
   c. 15%
   d. 25%

2. Which among the following statements is false?
   a. Androgen levels are elevated in obese as well as non PCOS patients
   b. Hyperandrogenemia is amplified by increasing obesity
   c. Hyperandrogenism is amplified by increasing insulin resistance
   d. Hyperandrogenemia occurs as a result of decreased Cytochrome P450 alpha enzyme activity

3. Which among the following statements is false?
   a. Gonadotropins stimulate adrenal androgen production directly
   b. Prolactin can stimulate DHEA-S production
   c. DHEA-S has low androgenic potential
   d. DHEA-S is co-secreted with cortisol from adrenals

4. Which of the following adipocytokines is not involved in pathogenesis of PCOS?
   a. TNF-ALHPA
   b. Retinol binding protein-4
   c. Monocyte chemoattractant protein-1
   d. None

5. Leptin intake is associated with which of the following options?
   a. Decreased hypothalamic Neuropeptide Y activity
   b. Increased GnRH activity
   c. Decrease in thermogenesis
   d. All of the above

6. Which of the following does not contribute to anovulation in PCOS patients?
   a. Increased insulin levels
   b. Deranged early follicular development
   c. Hyperresponsiveness of granulose cells to FSH in terms of estradiol production
   d. None of the above

7. The risk of developing moderate to severe OHSS in PCOS women undergoing gonadotropin stimulation is
   a. 5-8%
   b. 8-12%
   c. 10-18%
   d. 15-21%

8. The unfavourable reproductive outcomes in PCOS patients are related to all of these except
   a. High BMI
   b. Increased waist to hip ratio
   c. Insulin resistance
   d. None of the above

9. Using the NCEP criteria, what is the prevalence of Metabolic Syndrome in PCOS patients?
   a. <10%
   b. 20%
   c. 30%
   d. 40%

10. What percentage of PCOS patients have insulin resistance using the HOMA-IR index?
    a. 20%
    b. 30-45%
    c. 50-55%
    d. 65-80%
that Omega-3 fatty acid supplementation had a beneficial effect on liver fat content and other cardiovascular risk factors in women with PCOS, including those with hepatic steatosis38.

Mohammads et al, in a double blind randomised controlled trial conducted on 64 PCOS patients, concluded that Omega-3 fatty acids had some beneficial effects on serum adiponectin levels, insulin resistance and lipid profile in PCOS patients and may contribute to the improvement of metabolic complications in these women29.

References


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