Management of Adolescent PCOS

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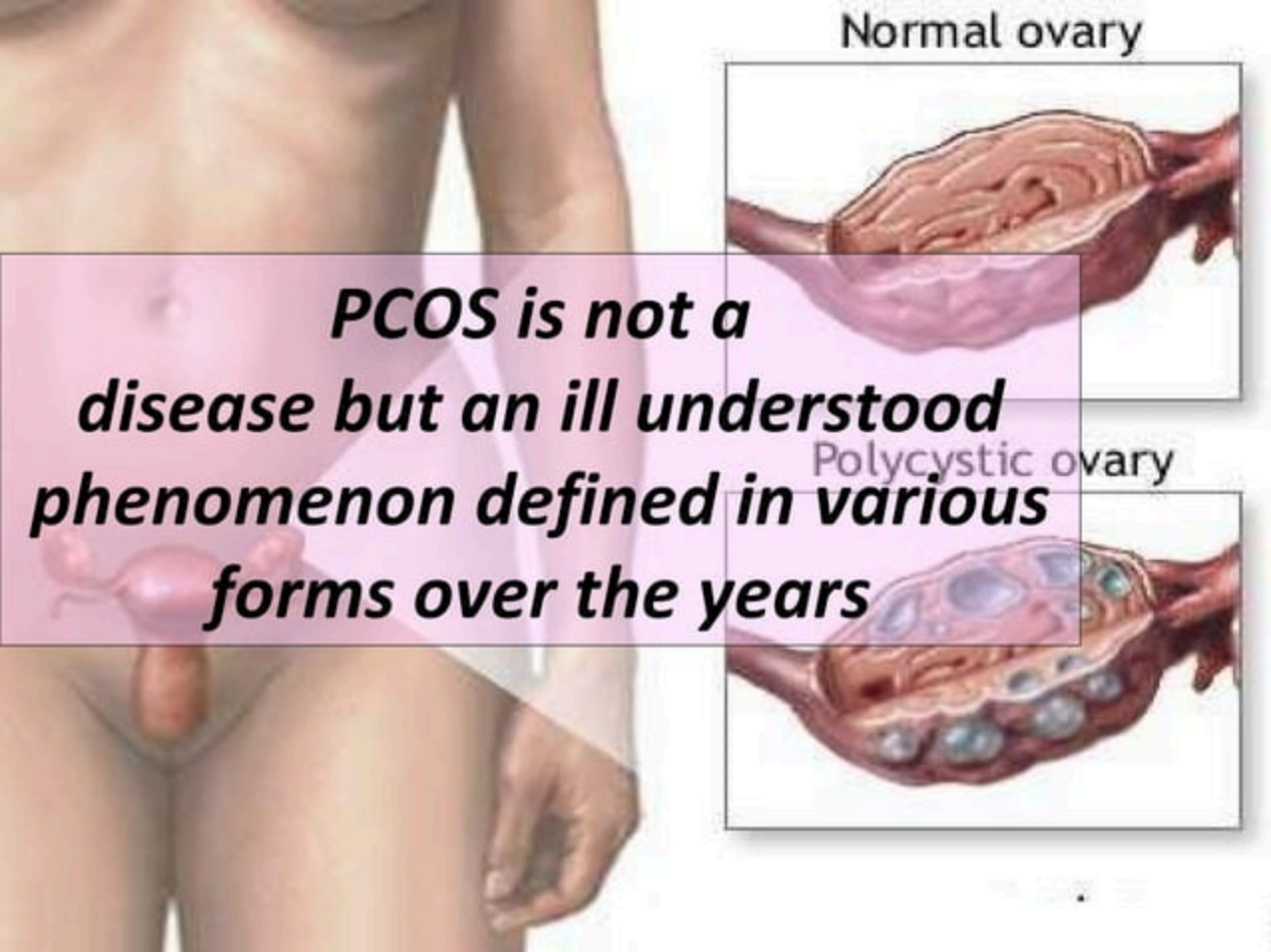
UNDERSTANDING OF PCOS IN VARIOUS AGE GROUPS

PCOS WORKSHOPS WERE THE THEME WORKSHOPS OF FOGSI FOR 2010 AND OF ICOG 2011
ALSO A NATIONAL SURVEY WAS DONE BY
DR JAIDEEP MALHOTRA AND DR BHARTI DHOREPATIL AND DR MANDAKINI



PCOS is not a disease but an ill understood phenomenon defined in various forms over the years

PCOS is defined as a heterogeneous disorder Presenting with a constellation of different manifestations throught the life of a women

"THIEF OF WOMENHOOD"

- **Recent increase in incidence of Adolescent PCOS.**
- **More commonly observed in urban areas.**

Fetal programming of PCOS

- It is now well established that fetal over an under nutrition programmes the fetus for many adulthood diseases and syndromes,which manifest in genetically predisposed fetuses.
- There has been an established co relation between low birth weight and insulin resistance/DM type-2/CVS risks and hypertension(metabolic syndrome)
- An androgen excess enviornment in pregnancy can also trigger the origins of PCOS in the female fetus(& metabolic defects in the male)
- A study on monkeys indicate that androgen excess exposure at any gestation during pregnancy, leads to PCOS in adult life

Pediatric origin of PCOS

- S/S of PCOS usually develop during or soon after puberty
- PCOS features are seen in girls with premature pubarche and adolescents with hyperandrogenism
- PCOS is the first component of METABOLIC SYNDROME to be recoginised in women at adolescent
- Early identification in pediatric /adolescent age group will have important implications in preventive and treatment options to prevent long term sequelae

Phsiology of puberty

- Is a transition from a state of sexually immature state to becoming capable of reproducing
- Gonadarche and adrenarche
- Normal puberty changes resemble PCOS(menstrual irregularities/hyperandrogenism/insulin resistance)
- Normal gonadarche sets in with maturing hypothalamic-pitutary axis and increase in FSH/LH
- Adenarche is onset of adrenal androgen production that preceded pubertal gonadotrophins and gonadarche
- There is a state of insulin resistance at puberty(25-30% reduction in insulin senstivity)
- IGF- 1 axis increases

Cont.....

- **Hence if there is an imbalance in normal pubertal develoment or they are genetically prone , these girls are likely to develop PCOS**
- **Premature pubarche,hyperandrogenimea and insulin resistance triggers of the development in genetically predisposed adolescent girls and those born low birth weight (Barker's hypothesis)**

CAUSES OF INCREASE IN ADOLESCENT PCOS

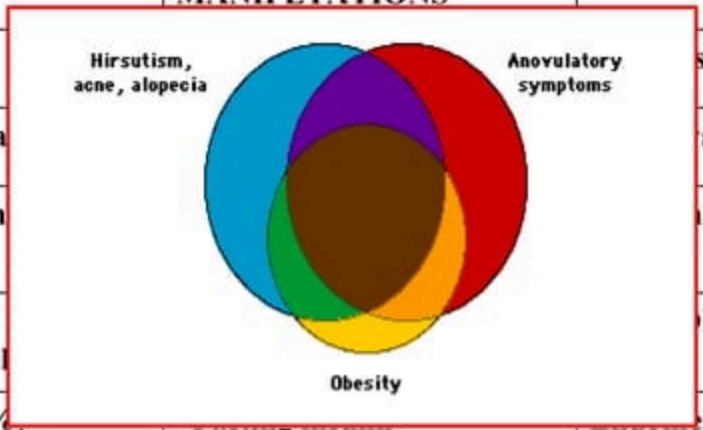
- Persistenceof physiological hyperinsulinemia
- Environmental factors.
- Changing lifestyle of modern society - overeating, eating more junk food like Ice creams, Cold drinks, Pizzas, Burgers.
- Competition for upliftment of social & financial status increases stress on growing children.
- Too much academic load with lack of outdoor exercise.
- Genetic factor.

PUBERTAL ENDOCRINE CHANGES RELATED TO ADOLESCENT PCOS

- In adolescent girls predisposed to PCOS, the abnormality of the regulatory mechanism continues.
- Increase in GnRH pulse frequency in the hypothalamus leads to LH hypersecretion resulting in excess thecal androgen production.
- Non ovulation and the absence of progesterone - a normal feature of early adolescence continues and leads to persistent LH hypersecretion.

CLINICAL MANIFESTATIONS

SYMPTOMS	ASSOCIATED ENDOCRINE MANIFETATIONS	POSSIBLE LATE SEQUALE
Obesity(38%)		s mellitus(29%)
Menstrual disturba		ascular disease
Hyperandrogenism		sulinemia
Infertility (73% of anovulatory infertil		L
Asymptomatic(20%		trial carcinoma
	Prolactin(27%)	hypertension
	Sex hormone binding globulin	



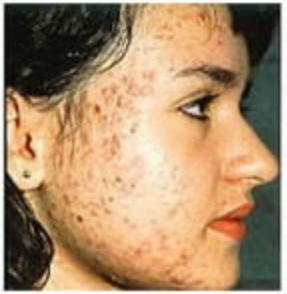
PCOS: Goals in Adolescent girls

- Identify patients with risks for or with diagnosis of PCOS
- Assess patients appropriately for PCOS and associated disease states
- Prescribe therapy to treat complaints and prevent sequelae

ADOLESCENTS

CONCERNS are;

- **Menstrual irregularities**
- **Obesity**
- **Hirsutism**



SPECIAL COUNSELING OF A PCOS PATIENT

Endocrine problems
Metabolic problems
Infertility
Risk of OHSS and multiple pregnancy
Pregnancy complications
Long term sequel

MOST IMP- Importance of life style modification

PROTOCOLS OF MANAGEMENT IN ADOLESCENTS

- Counselling for weight reduction and life style modification.
- Carbohydrate and fat restricted diet.
- Low glycemic index diet upto 85% will improve menstrual cycle regularity and ovulation in about six months.

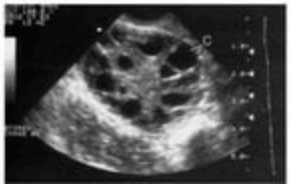
Diet restriction and exercise is the sheet anchor of treatment for overweight.

STANDARD DIAGNOSTIC ASSESSMENTS

- History taking, specifically for menstrual pattern, obesity, and absence of breast discharge.
- Obesity or increased BMI>25.
- Features of hyperandrogenism.
- Gynaecological ultrasonography – specifically looking for small ovarian follicles.
- According to Rotterdam criteria ≥12 follicles of 2-9 mm size arranged peripherally in ovary, size of ovary 1.5 - 3 times normal.

Imaging may be difficult in pediatric /adolescent groups

Experienced sonographer(abd scan)



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- Serum free testosterone.
- Fasting insulin/fasting glucose ratio.
- If abnormal, then follow up with 2 hour GTT and lipid profile.
- Serum LH to FSH ratio on day 3 of menstrual cycle.
- S.prolactin to rule out hyperprolactenemia.
- TSH to rule out hypothyroidism.
- 17-hydroxy progesterone to rule out 21-hydroxylase deficiency (CAH).

OBJECTIVES OF TREATMENT OF ADOLESCENT PCOS

- Treatment of oligomenorrhoea/ amenorrhoea.
- Management of hirsutism and acne.
- Reducing the far reaching consequences of insulin resistance and glucose intolerance.

PROTOCOLS OF MANAGEMENT

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OBESITY AND PCOS

- Associated in 35-60% of cases
- Usually android type
- Raised weight: hip ratio >0.85
- Increased waist circumference >90 cm
- Also associated with Insulin Resistance (IR)and Hyperinsulinemia
- But PCOS also seen in non obese girls.

IMPACT OF OBESITY IN REPRODUCTION

Condition	Associated risks
Mensturation	Ammenorhoea, oligomennorhoea, mennorhagia
Infertility	Anovualtion, poor response to infertility drugs
Miscarriage	Increased rate
Infertility treatment	Increased requirement of oral or injectable ovulation induction agent Decreased success rate of IVF
Glucose intolerance	Impaired glucose tolerance, type 2 DM
Pregnancy	Increased PIH, GDM,CS, Downs

- Even 7% weight reduction may lead to spontaneous resumption of menses.
- Moderate physical activity, 30-60 minutes per day

  should be goal of all patient with adolescent PCOS.
- M.O.A.- lowers circulating free androgen and

  insulin levels.
- Increases SHBG, thereby decreases level of free

  testosterone.

MENSTRUAL IRREGULARITIES

- Mostly managed by OCP
- **MPA 10 mg/day or micronized progesterone 300 mg at bedtime for 10 - 14 days effective in Rx of abnormal bleeding.**
- If oligomenorrhoea and amenorrhoea does not respond to oral contraceptives and antiandrogen combinations, insulin sensitizing agents have to be added.
- A lean PCOS may also have insulin resistance and therefore if they do not respond to oral contraceptive dose, insulin sensitizing drug has to be added.

ORAL CONTRACEPTIVE PILLS

- Estrogenic component of the oral contraceptive

  suppresses luteinising hormone and thus reduces

  ovarian androgen production.
- Estrogen also enhances hepatic production of

  SHBG ,thereby the level of free testosterone declines.
- Cyproterone acetate, Drospirenone and desogestrel can be used in combination with ethinyl estradiol.

Cyproterone acetate

Competitively inhibits th[illegible] of testosterone and also 5α[illegible] to the androgen recep[illegible]

Combination of[illegible] and cyproterone ace[illegible]ific in treating hyperand[illegible]as maintaining the menstrual cyclicity.

Ideal for Hirsuit PCOS.

Dose 1 tab. daily from D1 to D21 which has to be repeated cyclically for a period of six months.

DROSPIRENONE

- Combination of ethinyl estradiol (30 µg) with Drospirenone (3mg), an analogue of spironolactone
- Combination of ethinyl
with Desogestrel (20 µg) can also be used.

Ideal
for
Obese PCOS

- Combination of ethinyl estradiol (30 µg) with Drospirenone (3mg), an analogue of spironolactone with unique antimineralocorticoid and antiandrogenic action has also been used.

- Ideal for Obese PCOS

- Combination of ethinyl estradiol (30 µg) with Desogestrel (20 µg) can also be used.

OTHER DRUGS WHICH CAN BE USED IN ADDITION TO O.C.P.

- In cases of failure or where there is clinical or biochemical evidence of gross hyperandrogenicity or hyperinsulinemia, addition of **metformin** is recommended.
- **Spironolactone**- it has antiandrogenic effects in doses 100-200 mg daily.
- **Finasteride** - a competitive inhibitor of Type-2 5α reductase to treat hirsutism. Dose 1-5 mg/day.

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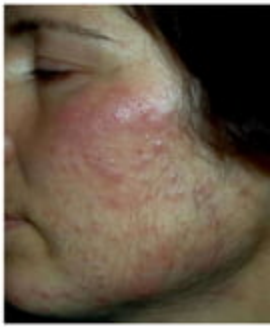
MOA of insulin sensitizing drug :-

- Improves hyperinsulinaemia.
- Regulates reproductive endocrine axis.

COSMETIC TREATMENT

- Antiandrogens used in PCOS will prevent further hair growth but the hair which have already grown have to be treated by COSMETIC TT

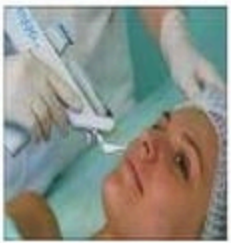
(epilation,waxing, by electrolysis or laser)



- Acne may require oral antibiotics like erythromycin and isotretinoin ointment.
- Acne also gets cleared in 6-9 months by use of oral contraceptive pills containing cyproterone acetate.

Excessive Hair

Mechanical method



Laser

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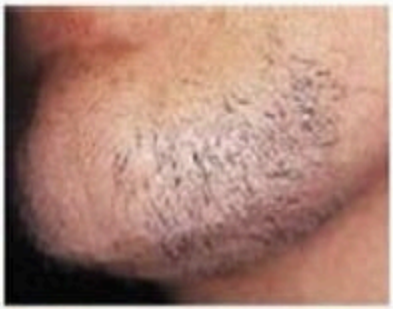
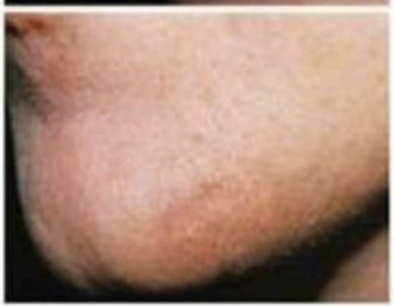
Waxing





Shaving

IMPROVEMENT OF HYPERINSULINEMIA BY INSULIN SENSITIZERS

- Directly sensitizing insulin receptors.
- Preventing neoglucogenesis.
- Reducing absorption of glucose from intestine.
- Increasing hepatic synthesis of SHBG level thereby

  reducing the level of bioactive free testosterone.

Metformin

Decreases basal hepatic glucose output in patients and lowers fasting plasma glucose concentration.

- It increases the uptake and oxidation of glucose by adipose tissue as well as lipogenesis.
- S/E- diarrhoea, nausea, vomiting ,specially initially.

To avoid them metformin should be taken with meals and the dose increased gradually.

- Increasing the level of SHBG and thereby decreasing the level of bioactive free testosterone.
- As the level of insulin is reduced, there is no LH mediated activity of theca cells for excess testosterone production.
- Reduces the level of leptin production.

In Adipose tissue:

Testosterone —Leptin→ Estrone

(Hyperestrogenism)

↓

Non ovulation

contd.

- Decrease in levels of leptin prevents excess estrogen formation and leads to normal restoration of HPO axis and hence ovulation.
- Metformin-

  Dosage 500-1500 mg daily in divided doses for six to nine months.

Sustained release formulations 1000 mg SR OD

OTHER DRUGS WHICH CAN BE USED

- Rosiglitazone ,
- Pioglitazone,
- D chiro inositol,
- N acetyl cysteine.

RESPONSE TO TREATMENT IS ASSESSED BY

- Resumption of menstrual cyclicity.
- Reduction in features of hyperandrogenicity.
- Improvement of biochemical parameters like reduction of free serum testosterone and normalization of fasting glucose insulin ratio.

CONCLUSION

Offering psychosocial support can be one of the most important aspects of managing this disease. This begins by building positive , supportive relationships with adolescents diagnosed PCOS. Such relationship will allow the adolescents to express her feelings and concerns regarding having a chronic disease whose signs and symptoms can greatly impact one's body image and self-esteem.

DEDICATED ADOLESCENT HEALTH CLINICS

PCOS HELP LINE


International Society of Ultrasound in Obstetrics and Gynecology (ISUOG)
8th International Symposium
India 2012
May 31 - June 3, 2012
Taj Palace Hotel, New Delhi
isuog
www.isuogsymposiuminindia.com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