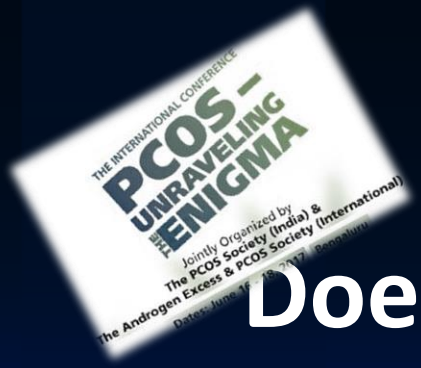


Does pre implantation genetic screening (PGS) followed by elective single embryo transfer (eSET) have a role in women with PCOS ?

SADHANA DESAI

ART in PCOS

- ART management is difficult because of associated endocrine and metabolic disorders
- Oocytes are sensitive to gonadotropin stimulation. Increased risk of ovarian hyperstimulation. Increased cancellation of cycles.
- Increase in miscarriage rate

ART in PCOS

Management

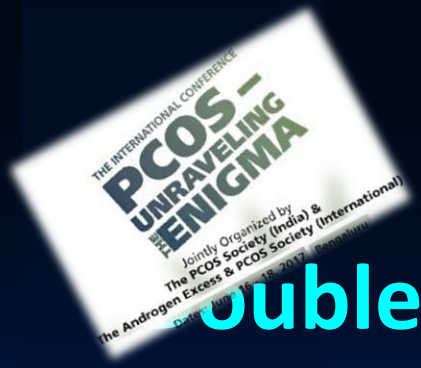
- Careful stimulation after correction of metabolic disorder
- Agonist trigger in Antagonist cycle
- Freeze all embryos and no transfer in stimulated cycle & transfer embryos in subsequent HRT cycle.
- Blastocyst stage transfer (if possible)
- Single blastocyst transfer is a gold standard

ART in PCOS

Advantages of Blastocyst stage transfer

- More physiological approach
- In human embryos enter uterine cavity 5 days after fertilization
- Culturing the embryos in lab. for 5 days evaluates genomic activation of embryos
- Higher preg. rate than day 2-3 transfer

Gverif et al 2004
Levitas et al 2004

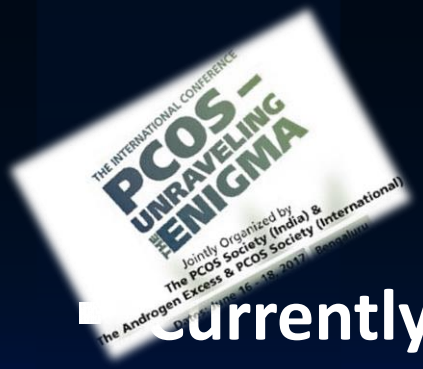


ART in PCOS
Double Vs. Single blastocyst transfer

Single blastocyst transfer prevents multiple pregnancy and its complications

The reluctance to accept eSET stems from diminished chance to delivery when only a single blastocyst is transferred compared to two blastocysts transferred

Cochrane database of systemic reviews 2009
Gelbaya T A Fertil. Steril 2010



Embryo Selection

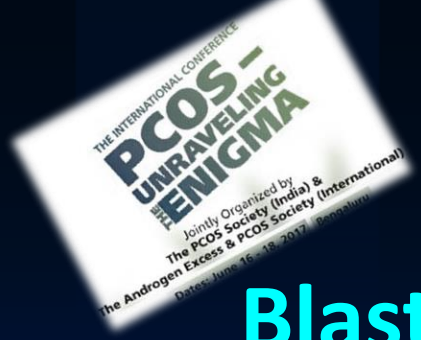
- Currently, the embryo chosen for transfer is selected on morphological grading and embryo kinetics that do not co-relate with chromosomal status

- Even morphological normal blastocyst has a risk of aneuploidy

- For single eSET to be more acceptable, a better embryo selection technique to be used to have equivalent preg. rate as two blastocysts transfer

Strategies to improve singleton delivery rate

One such strategy is to perform TE biopsy for New Generation Sequencing (NGS) and transfer a single euploid blastocyst to improve preg. rate and to reduce miscarriage rate



BEST TRIAL
Blastocyst Euploid selective transfer

Randomised non inferiority trial n=205

Single euploid blastocyst can result in an ongoing pregnancy rates that are same as transferring two untested blastocysts while dramatically reducing the risk of twins

Eric J Forman, Fertil. Steril, July, 2015

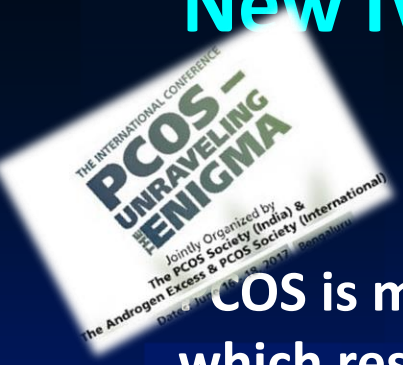
BEST TRIAL
Blastocyst Euploid selective transfer

Exclusion Criteria

1. > 42 Years
2. Poor responders, AMH < 1.2ng./ml.
3. Severe male factor requiring surgical sperm retrieval
4. B M I > 30 kg/m^2
5. Anovulatory PCOS

Eric J Forman, Fertil. Steril, July, 2015

New IVF paradigm for management of PCOS
PGS followed by eSET



COS is manifested by endocrine and metabolic dysfunction which results in a markedly altered ovarian milieu

This environment is characterised by mutations in cumulus cell complex of oocytes in some subset of PCOS.

It leads to poor quality oocytes & blastocysts with less implantation and high miscarriage rates.

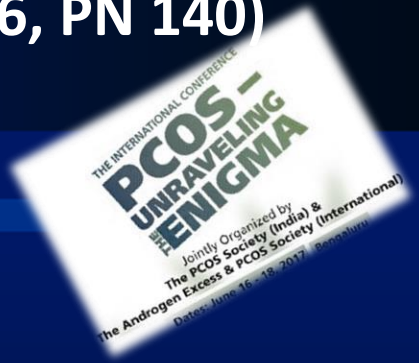
Suggest PGS followed by eSET

Dr. Angeline Beltsos, PCOS conference, Nov. 16-18, 2015, Seattle, USA

Impact of PCOS on early cleavage kinetics

Prospective study of assessment by time lapse analysis from fertilization to blastocyst stage

Hyperandrogenic PCOS (n=25, PN 110),
Normoandrogenic PCOS (n=26, PN 140)
Control (n=20, PN 97)



Conclusion :-

Embryos from hyperandrogenic PCOS were Slow to reach 8 cell stage.
However, this delay does not translate into decrease in implantation rate and is of no clinical significance

M L Wissing, Reproductive Health Care Ltd. 2014

Low aneuploidy rate in early pregnancy loss from patients with PCOS

Prospective cohort study of 1461 women who conceived following ART

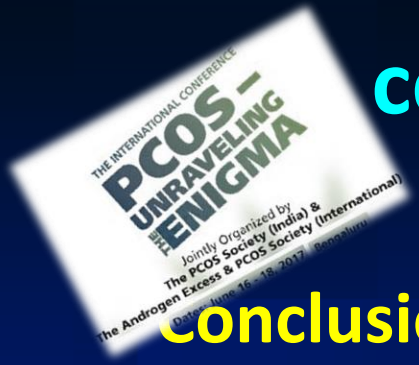
100 experienced clinical abortion, 32 were PCOS

In PCOS group 28% of abortus had aneuploidy which was lower than non PCOS group

Embryonic aneuploidy does not play a vital role in early spontaneous abortion in women with PCOS

Ref : Qiong Wang, Reproductive health care Ltd. 2016

Preimplantation screening worth the cost in high reserve patients?

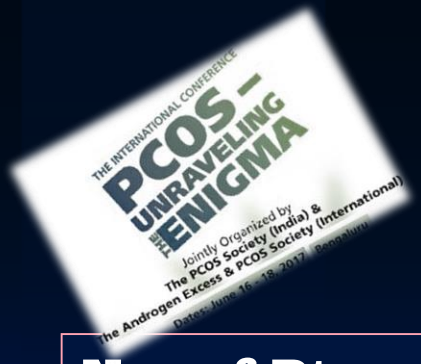


Conclusion:-

IVF with PGS is more expensive than traditional IVF but with similar cumulative preg. rate.

It has advantages only in older age group

AC Thyer et al, Seatle Reproductive Medicine, USA, Fertil.Steril.2015



ART in PCOS
Fertility Clinic Results

No. of Pts.	**406**
No. of OPU	**531**
OPU/pt	**1.3 cycle/pt**
No. of Embryo transfers	**712**
ET/pt	**1.7**
No. of pregnancies	**233**
Cumulative Preg.Rate /pt	**57.4%**
Multiple preg	**12.9%**
Miscarraige rate	**21%**

2012 to Dec 2016

The why, the how and when PGS_2 current practices & expert opinion of fertility specialists, molecular biologist and embryologist

30 Experts from Europe & USA participated

Consensus is lacking on which patient group, if any at all can benefit from PGS and a fortiori, whether all IVF patients should be offered PGS

Karen Sermon Norbert Gleicher
Mol. Hum. Reprod. 2016

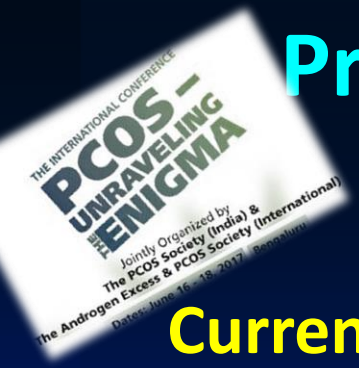

IVF rip-off exposed

26 out of 27 extra treatments sold by clinics are useless and one CUTS the chance of conceiving

Procedures that don't help you have a baby

PGS is one of the candidates for unnecessary add on treatments offered by fertility clinics along with immunology, time lapse imaging and endometrial scratching

U K Press and BBC programme, November, 2016



Preimplantation genetic screening who benefits ?

Current indications -

- **Older women, > 37 years old**
- **H/o. recurrent miscarriage due to enuploidy**
- **Recurrent IVF failure**

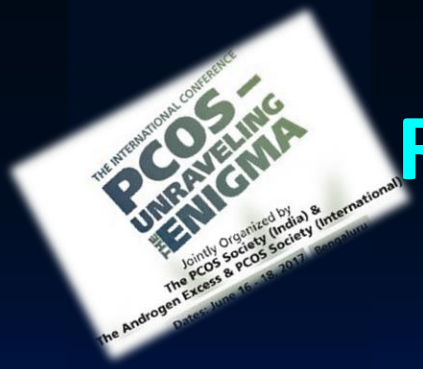
Universal application of PGS to all patients undergoing IVF is a matter of controversy.

Hey – Jookong, Zev Rosenwaks, Fertil. Steril. Sept.2016

PGS and the eSET of blastocyst in PCOS is debatable

Reasons for caution for PGS

- Limitations of available diagnostic techniques despite availability of New Generation Sequence (NGS) analysis
- Results obtained from chromosomal analysis are sometimes erroneous resulting in euploid embryo being incorrectly discarded
- Invasive biopsy procedure



Reasons for caution for PGS contd.

- Risk of erroneous interpretation of results on pre selection of embryo due to chromosomal mosaicism and segmental aneuploidy
- ↑↑ Cost
- One cycle of no transfer due to embryo not reaching blastocyst stage or, biopsy showing aneuploid embryos may lead to 3rd party reproduction in next cycle

PGS in PCOS

Case presentation:-

Mrs. N G, 27 years, PCOS with severe male factor referred for ART

Past H/o. 1st ICSI cycle- 27 oocytes, 20 fertilized, 3 FET cycle,

3rd ET cycle - missed abortion due to Trisomy 21

2nd ICSI Cycle, 38 oocytes, 18 fertilized,

PGS, 18 embryos, 16 abnormal,

ET of 2 normal embryo → → no pregnancy

4 ART centres advised egg donation.

At Fertility Clinic-

Counselling, long Agonist protocol instead of antagonist, chronic, low dose rFSH stimulation for (13 days), 13 oocytes 8 fertilised with IMSI, 2 blastocyst transfer → F T live birth

FERTILITY CLINIC, Mumbai, 2015

Conclusion

SET is the gold standard in IVF. Whenever possible, transfer one blastocyst with goal of healthy singleton pregnancy

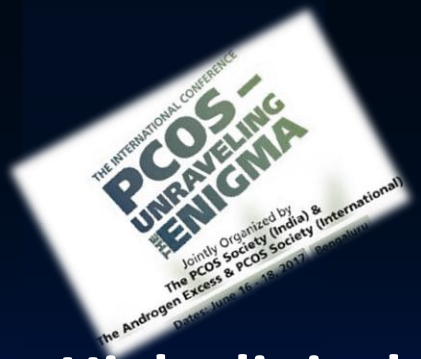
While it may benefit some patients, PGS adds to extra cost and invasiveness with limited benefit in younger women including PCOS.

Non-hypothetical prospective randomised large clinical trails are necessary for utility of PGS followed by eSET in PCOS


Thank you

Conclusion

Key to broad agreement within clinical and scientific community lies in our ability to react for evidence, improve technology where necessary and consider whether sufficient evidence exists to advise patient wisely and authentically



Advantages of FET

High clinical preg. rate following FET Vs. Fresh transfer in PCOS

In fresh cycle ↑↑ E2 levels and endometrial receptivity may be out of phase for implantation

Roque et al - 2012

Better placenta and better neonatal outcome

Pinborg et al - 2010

Birth weight significantly higher than fresh transfer

Hennigsen - 2011