OCP OF NEW GENERATION

- FOCUS ON DROSPIRENONE


1st time in India
Rasmin
(Drospirenone 3 mg +Ethinyl estradiol 30mcg)
21st Century Contraceptive Pill
Way Past Just "Contraception"

Rasmin - Composition

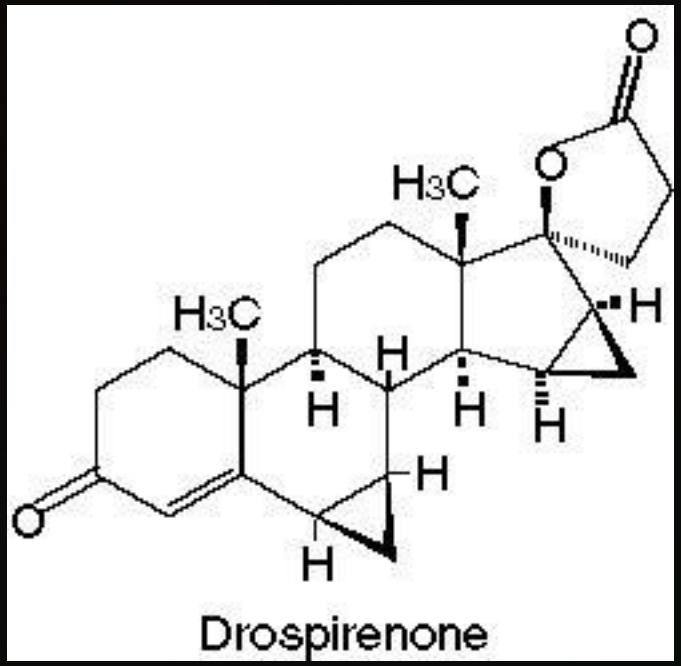
- An OC formulation based on drospirenone
- Each calender pack contains 21 hormone (yellow) tablets & 7 placebo(white) tablets
- Each hormone tablet contains:

  Drospirenone ----- 3 mg

  Ethinyl estradiol ----- 30 mcg

Drospirenone – The Novel Progestin

- Chemically a spirolactone derivative
- The newest progestin - combines progestational, antimineralocorticoid & anti-androgenic actions
- Closely resembles the natural progesterone in terms of its pharmacological actions



Drospirenone – Pharmacology*

Property	Clinical Benefit
Progestogenic	• Antigonadotropic action - Inhibits ovulation: contraceptive efficacy • Inhibits estrogen-induced proliferation of endometrium – Decreased menstrual bleeding • Transformation of cervical mucus to thick & viscid consistency – inhibits sperm penetration: additional contraceptive action

Complete inhibition of ovulation was achieved with DRSP+EE**

* - Ann N Y Acad Sci, 1995; 761: 311-35

** Eur J Contracept Reprod Health Care, 2000; 5:16 – 24

Drospirenone – Pharmacology*

Property	Clinical Benefit
Anti-mineralo-corticoid	• Promotes sodium and water excretion – decreased incidence of side effects such as bloating, weight gain, increase in BP, breast tenderness, mood changes etc • Inhibits estrogen-induced fluid retention

- DRSP+EE prevents the increase in total body water & extracellular water in the luteal phase**
- The changes in body water observed were similar to those seen at follicular phase**

*- Ann N Y Acad Sci, 1995; 761: 311-35;

** - Contraception, 2007; 75: 199 – 203

Drospirenone – Pharmacology*

Property	Clinical Benefit
Anti-androgenic	• Effective against acne and hirsutism – beneficial in adolescent girls as well as in women with acne or hirsutism • Also useful in women with PCOS • Increases HDL-C and decreases LDL-C

- Improves skin appearance
- Promotes better patient acceptance

* - Ann N Y Acad Sci, 1995; 761: 311-35

Drospirenone – Pharmacology*

Property	Clinical Benefit
No androgenic action	• Does not cause oily skin or acne • Does not promote weight gain • No adverse effects on lipid profile • No adverse effects on glucose tolerance

- Improves skin appearance
- Promotes better patient acceptance

* - Ann N Y Acad Sci, 1995; 761: 311-35

Drospirenone – Pharmacology*

Property	Clinical Benefit
No effect on glucocorticoid receptors	• No interference with glucose tolerance • May not adversely affect bone mineral density

In clinical studies, DRSP+EE was not associated with impairment of glucose tolerance[1] or adverse effects on BMD[2]

* - Ann N Y Acad Sci, 1995; 761: 311-35; 1. Contraception, 2003; 67: 423 – 9;
2. Obstet Gynecol, 2005; 105: 53-60

Drospirenone – Pharmacology*

Property	Clinical Benefit
No anti-estrogenic action	• Does not decrease estrogen-induced increase in Sex Hormone Binding Globulin (SHBG) levels • Therefore no increase in free androgen levels • Minimal chances of androgenic effects such as seborrhea, acne etc

* - Ann N Y Acad Sci, 1995; 761: 311-35

Drospirenone - Pharmacokinetics

- Well absorbed on oral dosing – t_{max} – 1-3 h
- Oral bioavailability – 76%
- Food delays the rate of absorption but does not affect the extent of absorption
- 97% bound to serum proteins but does not bind to SHBG or CBG
- Metabolized to minor extent by CYP3A4; metabolites inactive
- Excretion by fecal & urinary routes; half-life – 30 hours

Drugs, 2007; 67: 1749-65

Clinical Efficacy - Contraception

- Patients: 326 women requiring contraception
- Treatment: DRSP+EE for 13 cycles
- Assessments: Contraceptive efficacy, cycle control, Menstrual Health Asessments using a questionnaire on menstrually related symptoms and safety
- **Results:**
  - Effective contraception - corrected Pearl Index of 0.407
  - Cycle control was excellent; bleeding disturbances did not last beyond 1-2 cycles in the majority of the women

Contraception, 2000; 61: 105-11

Clinical Efficacy - Contraception

- **Results (cont'd):**
  - No effect on BP, weight or lipid levels were seen
  - No effect on laboratory tests – hematology, electrolytes & urinalysis
  - Good tolerability was observed – headache (4.9%) and breast pain (8.6%)
  - Discontinuation rate was low (6%)
  - Improvement in patient's well-being with regard to symptoms of water retention, negative affect and increased appetite was seen at cycle 6
  - The combination of EE + DRSP is an effective oral contraceptive that is safe and well tolerated

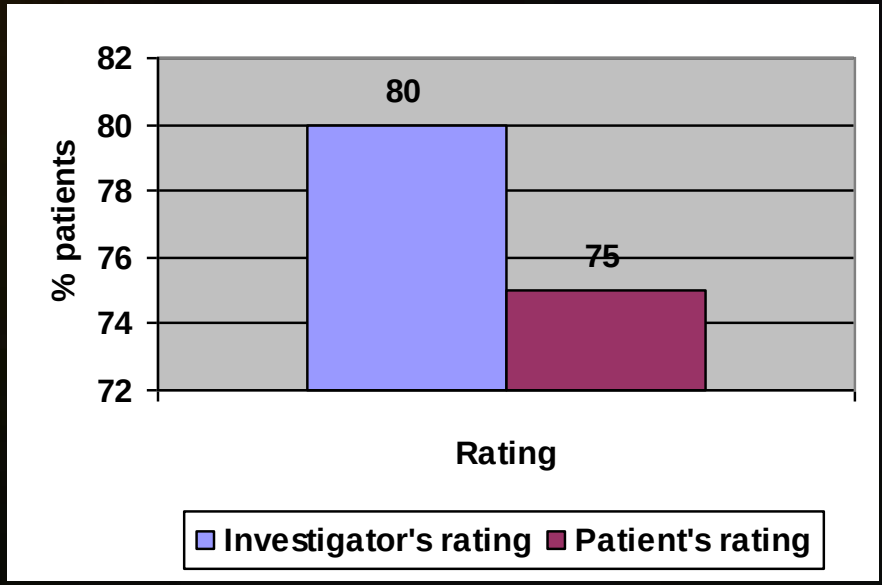
Cycle Control & QOL

- Patients: 336 women with PMS
- Treatment: DRSP+EE for 6 cycles
- Assessments: Cycle control, Psychological General Well being Index (PGWBI), body weight
- **Results:**
  - Cycle control was good
  - Body weight remained stable or decreased slightly

Eur J Contracept Reprod Health Care, 2003; 8: 37-51

Cycle Control & QOL

- **Results (cont'd):**
  - Improvement in patient's psychological well-being as per PGWBI was seen at cycle 3 and maintained at cycle 6
  - Reductions in incidence & severity of somatic symptoms related to menstruation was observed



% Patients with improvement in somatic symptoms

These results suggest a beneficial effect of the antimineralocorticoid action of drospirenone.

Comparative Studies

Rasmin vs levonorgestrel + EE*:

- Comparable cycle control
- Side effects e.g. headache & breast tenderness more frequent in levonorgestrel + EE group

Parameter	DRSP+EE	Levonorgestrel + EE
Body Weight	Decrease	Increase
BP	Decrease	Increase
LDL-C	Decrease	Unchanged
HDL-C	Increase	Decrease

* - J Clin Endocrinol Metab, 1995; 80: 1816-21

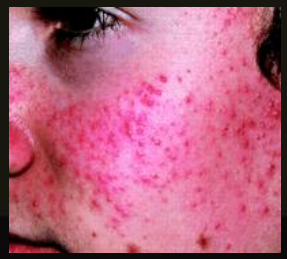
Comparative Studies

Compared to desogestrel + EE*:

- Comparable contraceptive efficacy & cycle control
- Tolerability was similar
- With DRSP+EE, a distinct decrease in body weight was seen
- Effect on dysmenorrhea – similar
- Effect on PMS – better with DRSP+EE
- DRSP+EE is beneficial in women having tendency to gain wt

* - Eur J Contracept Reprod Health Care, 2000; 5: 25-34; 124-34

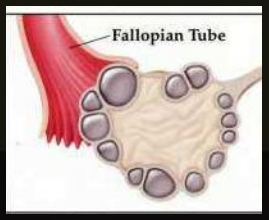
Efficacy in Acne & Hirsutism



- Increase in SHBG levels[1]
- Decrease in LH & androgen levels[1]
- Reduction in sebum production[1]
- Reduction in total & inflammatory acne lesion count[2]
- Decrease in hair growth in upper lip & chin[1]
- Comparable efficacy to cyproterone+EE OCs[1,3]
- DRSP+EE (6 -12 cycles) useful in the treatment of facial acne & hirsutism

1. Cutis, 2002; 69(4 suppl): 2-15 Cutis, 2004; 74: 123-30
2. Gynecol Endocrinol, 2007; 23: 38-44

Efficacy in PCOS

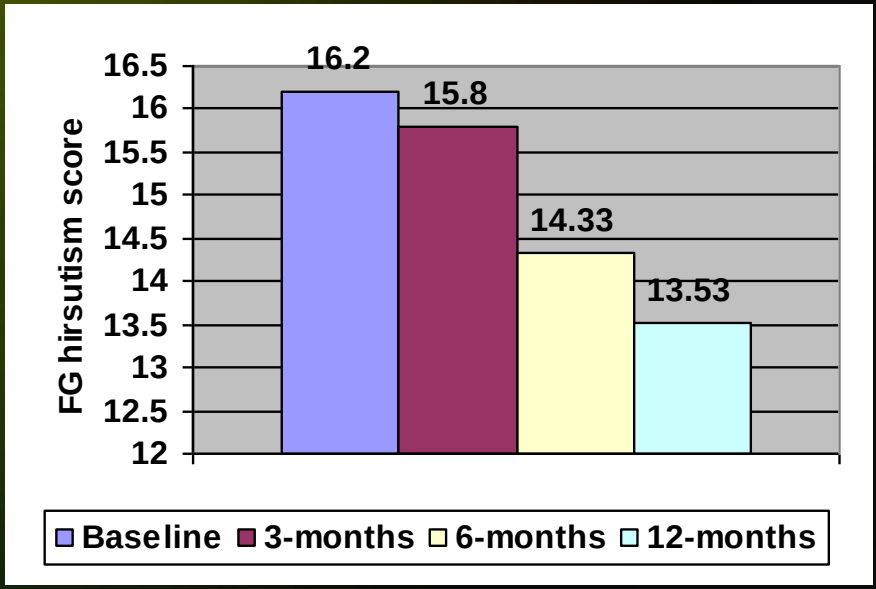


- Patients: 15 women with hirsutism & PCOS
- Treatment: DRSP+EE for 12 cycles
- Assessments: Serum hormones, lipid profile, hirsutism score (FG scale), USG, glucose tolerance
- **Results:**
  - Cycle control was satisfactory in all women
  - Body weight, fat distribution & BP remained stable
  - No significant effect on glucose tolerance & total-C to HDL-C & LDL-C to HDL-C ratios
  - Plasma LH, testosterone levels & free androgen index decreased

J Clin Endocrinol Metab, 2004; 89: 2817-23

Efficacy in PCOS (cont'd)

- **Results:**
  - –Hirsutism score decreased from 6th cycle



- **DRSP+EE effective in improving clinical & hormonal features of PCOS**

Safety Aspects of DRSP+EE

- Used by over 4 million women worldwide[1]
- The most widely used contraceptive[1]
- Safe and devoid of any serious safety concerns[1,2]
- Improved tolerability with regard to weight gain, mood changes and acne[2]
- Improves QOL & well-being
- Decreases BP[1]

1. Drugs, 2007; 67: 647-55; 2. Treat Endocrinol, 2003; 2: 49-70

Safety Aspects of DRSP+EE

- Risk of VTE similar to levonorgestrel-OCs[1]
- No serious adverse events e.g. hyperkalemia, cardiac arrhythmias or birth defects[1]
- EE+DRSP results in a decrease in bone turnover[2]
- Does not affect the BMD adversely[2]
- A bone-sparing effect in young post-adolescent women[2]
- The continuous use of DRSP+EE for 126 days was safe, efficacious, well accepted by the users & resulted in a considerable reduction of bleeding[3]

1. Drug Saf, 2004; 27: 1001-18; 2. Obstet Gynecol, 2005; 105: 53-60;
3. Contraception, 2006; 73: 34-40;

Effect on QOL

- EE+DRSP has positive effects on body weight, skin, hair, cycle, attractivity & mental well-being & on premenstrual symptoms
- It improves QOL, thus facilitating better patient compliance

Eur J Contracept Reprod Health Care, 2002; 7(suppl 3): 35-41;
Schweiz Rundsch Med Prax, 2003; 92: 1177-84

Effect on Metabolic Parameters

- Increase in HDL-Cholesterol
- Decrease in LDL-Cholesterol
- Slight increase in the apolipoproteins Apo A-I, Apo A-II and Apo B
- Increase in triglycerides
- No effect on Lipoprotein (a)
- Decrease in free fatty acid levels
- No clinically significant impairment of glucose metabolism or glucose tolerance

J Women's Health, 2006; 15: 585 – 90; Contraception, 2003; 67: 423 – 9;
Contraception, 2004; 69: 271 – 78

Drospirenone – Clinical Benefits Over Other COCs*

- Reduced incidences of side effects e.g. weight gain, bloating, breast tenderness
- Improves seborrhea, acne & hirsutism
- Improvement in premenstrual symptoms
- Improves patient well-being

Improves patient acceptance

*- Human Reprod Update, 2006; 12: 169-178 ; Ann N Y Acad Sci, 1995; 761: 311-35; Drugs, 2007; 67:1749-65; Drugs, 2007; 67: 647-55

Drospirenone – Clinical Benefits Over Other COCs*

- No increase in BP
- Improvement in lipid profile (↑ HDL-C & ↓ LDL-C)
- Possible decrease in risk of CVD
- Decreases bone turnover, no adverse effects on BMD
- No additional safety concerns

Allays fears about safety

*- Human Reprod Update, 2006, 12: 169-178 ; Ann N Y Acad Sci, 1995; 761: 311-35; Drugs, 2007; 67:1749-65; Drugs, 2007; 67: 647-55