Handout
SGIM 26th Annual Meeting

Workshop Handout
WE03

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Update in Contraceptive Technology

Saturday, May 3, 2003
9:00 - 10:30 AM

Pan Pacific Hotel
Gazebo 1
Contraceptive Updates
Things to Remember

Background:
We can still do better!
- 2-3% of reproductive-age women have elective abortions each year[1]
- Over 40% of American women have had an abortion[2]

Barrier Methods/Spermicides:
Still less effective than hormonal methods but decrease sexually transmitted infections

Condoms
- polyurethane are less effective than latex, but offer an alternative for those with latex allergies, or a desire to use oil-based lubricants
  - Total clinical failures (breakage and slippage) were 8.4% for the polyurethane condom and 3.2% for the latex condom (difference 5.3%, 90% CI 2.8, 7.7) [3]

Diaphragms
- Lea’s Shield™ was FDA approved March 2002 as a prescription device
  - Silicone, so for those with latex allergy
  - typical failure rate is about 20% in first year
  - One size fits all
  - OTC since 1993 in Germany, Austria, Switzerland, Canada

Cervical Caps
- Less effective in parous women (60-74% vs 80-91% in nullips)
- Prentif™ cap is as effective as a diaphragm[4]
- Femcap™ is less effective

Sponges
- Less effective than diaphragms[5] but available
- Efficacy is about 84-87% with typical use
- Today™ sponge, available in Canada and on the web, returning to the US market
- Protectaid™ sponge-polyurethane foam with F-5 gel (nonoxynol-9, benzalkonium chloride, sodium cholate)[6] [7, 8]
  - Efficacy of 77% [9]
  - Sperm were found in cervix of 4 of 9 women studied[10]

Carraguard
- a microbicide under study by the Population Council
- has been shown to block infection by HIV, HSV-2, HPV and N. gonorrhoeae both in vitro and in vivo.
- A Phase III effectiveness trial is scheduled to begin in late 2003 and will last approximately four years. If it is shown to be effective, a New Drug Application will be filed with the U.S FDA
Emergency Contraception

- Sooner is Better
- Efficacy up to 5 days with a single dose of 1.5 mg levonorgestrel[11]
  - both “PlanB™” pills taken at once resulted in a pregnancy rate of 1.5%
  - More effective than the Yuzpe regimen (“Preven™”, combination OCPs)
  - Fewer side effects than the Yuzpe regimen (only 6% vomit, 20% nausea)
  - Not teratogenic or abortifacient
- Advance provision increases use, decreases unwanted pregnancy rates [12]
- Advance provision does not adversely affect routine contraception
  - Pharmacist direct dispensing in Washington since 7/98 & CA since Jan ’02
- Over the counter status in the USA is hopefully coming soon [13]
  - Currently available over the counter in 7 countries around the world
  - Meets FDA standards for over the counter status.
  - The Women's Capitol Corporation, maker of Plan B™, submitted an application to the FDA to make Plan B™ available over the counter on March 20th, 2003

Oral Agents

- No need to do a pap, pelvic, or breast exam before prescribing[14, 15]
- Starting the same day patient was seen by MD (rather than waiting for the first Sunday of menses) may increase rates of continuation,[16, 17]
  - No increase in side effects such as breakthrough bleeding or nausea
  - Need to use a backup method for a whole 28 day cycle (rather than only for 7 days if you use a first-Sunday-of-menses start)
- Consider recommending continuous use to increase efficacy
  - Especially for those with endometriosis, dysmenorrhea, anemia, and menstrually-related seizures or migraines
  - Seasonale™- 84 active pills then 1 week off (4 pill-free intervals per year)[20]
    - Expected to reach market in 2003
    - Intermenstrual bleeding main concern
- Drospirenone, a new progestational agent
  - Analogue of spironolactone, an aldosterone antagonist
  - Contraindicated in renal disease
  - Concern of increased risk of DVTs[18]
  - Theoretically good for cyclic “bloating,” breast pain
  - Yasmin™ is a combination with ethinyl estradiol
- Start most women on 30µg or 35µg monophasic pills
- Reserve ultra-low dose (20µg) pills for >40- year-olds[19]
- Special conditions:
  - Diabetes: May alter glucose control (especially progestin only methods)[22], but OK to use if no vascular complications
  - Hypertension: OK to use if well controlled on meds and <35 yo[23]
  - Seizures: Dilantin and carbamazepine decrease efficacy—can use higher dose pill or DMPA (which decreases seizures)
  - Depression: St. John’s Wort may decrease efficacy
Migraine: OK to try as long as no focal neuro sx.  
- May improve menstrual migraines

Anticoagulated: USE to prevent ovulation and resultant hemoperitoneum

Sickle cell anemia: No study has shown increase in sickling, but DMPA decreases sickle crises[21]

Breastfeeding: Progestin only pills are preferred as they do not decrease milk supply, although combination pills are safe for breastfed babies and more effective
- Do need a method to prevent pregnancy unless all three of the following conditions are met:
  - Baby is less than 6 months of age
  - No formula supplementation
  - No return of menses

**The Patch (Ortho Evra™)**
- on market since early 2002
- Norelgestromin 150 mcg + ethinyl estradiol 20 mcg daily
- Contraindications similar to those for OCPs
- Efficacy similar to Triphasil OCP (failure rate=1-2%) in industry-sponsored, non blinded trial[24]
- Less effective for women over 200 lbs (92% vs 99%)
- Regimen: one patch weekly x 3 weeks, followed by one patch-free week
- Apply patch anywhere except breasts (must peel off liner before applying)
- No need for backup unless patch falls off for more than a day
  - 1-2% of patches detached completely during study
- Skin Patch site reaction was mild for 20% of women, limited method use for 2%
  - decrease by rotating site, using a topical steroid PRN

**The Ring (NuvaRing™)**
- FDA approved 10/01, Available since 8/02
- 54-mm diameter, transparent, flexible, soft ring
- delivers etonogestrel 120 mcg + ethinyl estradiol 15 mcg daily
- Cost, contraindications, side effects similar to combination OCPs
- One ring inserted vaginally per week
- Use rings for three weeks followed by one ring-free week
- Failure rate: 0.65-1.18%[25, 26]
- Package insert allows for removal for 3 hours at a time without compromising efficacy

**Injectables**
- **Lunelle™**: Once-monthly injection
  - FDA approved October, 2000. **Recalled** by manufacturer October, 2002 due to lack of assurance of prefilled syringes (vials were not recalled) subpotency.of preparation
Medroxyprogesterone acetate 25 mg + estradiol cypionate 5 mg, IM q 28-33 days
- Side effects/acceptability similar to OCPs [27]
- Failure rate: 0.1% [28]
- Irregular bleeding lead ~2.5% of users to discontinue method

**IUDs**
- Extremely effective (Mirena™ is most effective)
- Worldwide, is the most frequently used reversible contraceptive
  - 15-20% of European women use IUDs
- Misperceptions & historical concerns and limit use in the United States
  - <1% of U.S. women now choose IUDs
  - 28% of U.S. women have undergone surgical sterilization
- Rapidly reversible. No delay in return to fertility [29]
  - No effect on fertility among nulliparas [30-32]
- Minimal to no increased risk of PID except in 20 days after insertion [33, 34]
  - Asymptomatic patients with GC/CT can be treated without IUD removal
- Protect against ectopic as well as intrauterine pregnancy.
- Uterine anomalies should not limit use [35]
- Parity not essential
  - Nulliparous/younger women have higher rates of expulsion and of inability to insert device
- *Not* abortifacient
  - Mechanism of action is the creation of a spermicidal uterine environment, & endometrial changes preventing implantation
  - Can be used as a highly effective form of emergency contraception for 5 days
- Can be placed immediately after abortion

**Levonorgestrel IUD (Mirena®)**
- 32-mm² T-shaped device with reservoir containing 52 mg of levonorgestrel
- Failure rate: 0-0.3% (better than tubal ligation)
- Duration of efficacy: FDA approved for 5 years, used in Finland for up to 10 years
- Return to fertility: 80% at one year
- Minimal systemic hormonal effects
  - Acne, breast tenderness, headaches, mood changes, nausea can occur
- Reduce Menorrhagia/dysmenorrheal/menstrual dysfunction
  - Decreases average menstrual blood loss by 80-90%
    - 16.8% of women reported amenorrhea at 1 year
  - An alternative to hysterectomy for symptomatic women
    - Of 102 women referred for hysterectomy, only 19 underwent procedure [36],[37]
- Can provide endometrial protection for women requiring tamoxifen [38]
- Irregular spotting/bleeding is most common reason for discontinuing method
Copper IUD (ParaGard T 380A)
- Failure rate: 0.7% first year, Cumulative 10-year failure rate: 1.9%
- Duration of efficacy: 10 years
- Adverse effects = Increased menstrual bleeding and cramping
- Cu may protect vs. endometrial[39] and cervical cancer [40]
- Can image with MRI without a problem

Progesterone IUD (Progestasert)
- No longer used as only lasted 1 year, and risk of ascending infection is highest at insertion

Implants

Norplant® is on hold

Implanon® Anticipated FDA approval: 2003
- Single rod releases etonogestrel/desogestrel 60-70 mcg/day initially (dose decreases over time)
- Insertion and removal are faster/less painful than Norplant™[41]
- Less androgenic progestin than Norplant™ so theoretically, fewer androgenic SE
- Lasts 3 years
- Failure rate: 0-0.2%[42]
- Irregular bleeding was most common reason for requesting early removal: 17.2% for irregular bleeding, 1.7% for amenorrhea

Jadelle (Finnish product) FDA approved July 2001, not currently available in the US
- 2 rods containing levonorgestrel, effective for 5 years[43]

Early Medical Abortion

Mifepristone (RU486)
- You can do this![44]
  - sign up at http://www.earlyoptionpill.com/hcp_providing.php3
  - Arrange for vacuum aspiration back up (only needed 3-4% of the time) and transfusion (very rarely needed)
  - Date pregnancy at less than 9 weeks
  - Rule out ectopic
  - Check need for rhogam
- Evidence Based regimen up to 9 weeks[45]
  - Mifepristone dose: 200 mg p.o., in office, Day 1
  - Intravaginal misoprostol (800 mcg) self-administered at home on Day 3
  - Better than the FDA approved regimen as it has fewer side effects, is cheaper, leads to more rapid completion of abortion, and is equally safe
Follow up in one to two weeks to check drop in hCG

Common side effects:
- pelvic pain…Rx ibuprofen & vicodin (10-30% require vicodin)
- GI symptoms (N/V-31%, diarrhea-18%, cramping) due to misoprostol
- Bleeding for mean of 8-17 days

Also
- Very effective and well tolerated as Emergency Contraception
  - 10 mg of mifepristone resulted in a pregnancy rate of 1.1% per RCT in China[46]
  - cost & hassle currently limits use in US
- Effective for shrinking fibroids[47]

In Development

Intraluminal vas occlusion plug
- being developed in China [48]

Immunocontraception
- Concerns include reversibility, and genetically based variations in the population that would lead to resistance among some[49]

WEB RESOURCES
American College of Obstetricians-Gynecologists: http://www.acog.org
Alan Guttmacher Institute: http://www.agi-usa.org/index.html
Association of Reproductive Health Professionals: http://www.arhp.org
Cochrane Library: http://hiru.mcmaster.ca/cochrane/cochrane/cdsr.htm
CONRAD: http://www.conrad.org
WHO Medical Eligibility Criteria: http://www.who.int/reproductive-healthpublications/RHR_002_medical_eligibility_criteria_secondEdition
Emergency Contraception information: http://www.not-2-late.org
Managing Contraception: www.managingcontraception.com
Nuvaring Website: www.nuvaring.com
Mifpristone: http://www.earlyoptionpill.com/hcp_providing.php3
Carraguard: http://www.popcouncil.org/biomed/carraguard.html
Contraception while Breastfeeding: http://www.lalecheleague.org/ba/Nov01.html


