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Current Status of Contraception

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During the past decade great advance has been made in contraceptive technology. The development and subsequent modification of oral steroid contraceptive together with the improved design of other contraceptives have tremendously altered the contraceptive practise of complete throughout the world.

At the present time one of most complex issue is the population explosion. In Korea the population growth rate is remarkably decreased from 3% in 1960s to 1.7% in 1984.

Increasing proportion of women practising family planning and improved contraceptive methods have contributed on remarkable reduction of fertility rate. But still about half of married women not involved in family planning practise. One of the reasons why that so many women haven't participated in family planning should be undesirable side effects or inconvenience of currently available contraceptives.

So we need more research to develop newer, safer and more effective contraceptive to solve the problems.

According to recent report on the family planning program achievement in Korea, sterilization (male and female) is most popular, leading contraceptive method (330 cases/1000 fertile persons) and the I.U.D. (167.5/1000), condom (132.9/1000) and oral pill (61.1/1000) were followed by in the order of favorite choice of contraceptive (KIPH, Family planning evaluation report, 1984; KIPH Family plan Service Statistics, 1981-1984).

In present paper the present status and knowledge of contraceptives will be summarized.

CURRENT STATUS OF CONTRACEPTIVES

I. Oral contraceptives

Since 1960s a surge of contraceptive research and technologic development has provided highly effective hormonal contraceptives and intrauterine device (IUD). Since 1968 Oral pill became popular and available in Korea. Between 1970 and 1980, oral pill and IUD were the most popular method of contraception in those years. Today female sterilization by laparoscopy tend to be selected as major contraceptive methods. According to national fertility study of 1970 we can see similar patterns in USA like our country (Bernstein 1974).

There are two major types of oral steroid contraceptives: combination and sequential. The former is made up of a combination of estrogen and progestogen given continuously for three weeks, while the latter is made up with a regimen of estrogen alone given for about 2 weeks followed by one week of combination mimicking natural horomal profile in woman. But sequential pill already were withdrawn from market because of adverse effect (Roy 1985).

A third type of oral contraceptives is administration of a small dose of progesterone without estrogen every day. This regimen was considered safer due to total elimination of estrogen.

Also it is associated with a relatively high incidence of irrequlars veginal bleeding and pregnancy rate of 2-8%/yrs (Bernstein 1974). It is believed that effect on cervical mucosa and endometrium are unfavorable for fertility. So far the advantage of oral pill far outweigh the disadvantage and the most effective and reliable method of birth control available. They do not interfere with the sexual intercourse and few immediate effects.

As noncontraceptive health benefit Oral contraceptives alleviate premenstrual syndrome and dysmenorrhea by inhibition of ovulation (Roy 1985). OCs is known to be associated with fewer breast

cancer, fewer endometrial cancer, and fewer ovarian cancer (The Center for Disease Control Cancer and Hormone study 1983). One recent research study have suggested that cervical dysplasia was more likely to progress carcinoma in situ in women who use OCs than in women who don't, particularly in those with longer duration of the (Stern et al. 1977). But other report indicated that OCs users have only increased risk of cervical dysplasia but there was no evidence for increased risks of invasive carcinoma of cervix due to OCs use (Stern 1977). Those difference can be fully explained by the effects of different sexual behavior among user and non-users (Roy 1985; Rotkin 1973; Peritz et al. 1977).

Benign hepatocellular tumors are most closely associated with high-estrogen OCs but benign adenoma do not become malignant (Child Health and Human Development (A) 1981; Roy 1985).

Data from the Walnut Creek study have indicated that OCs users are more likely than non-users to develop melanoma, with increasing with duration of use (Beral et al. 1977).

In relation with future childbearing OCs do not cause permanent sterility. Although return of fertility delayed, but after 30 to 42 months fertility rate are same as other contraceptives (Vessey et al. 1978) Impairment seems to be independant of the length of use of oral contraceptives (Porter et al. 1982). Spontaneous abortion rate and congenital anomaly rate in babies conceived after stopping OCs were not increased among users in several studies (Roy 1985).

The chief causes of morbidity and mortality among OCs users are vascular and each of these may be influenced by oral contraceptives. Some case-control studies and follow-up studies have consistently found positive association between OCs and venous thromboembolism but there has been some disagreement among these about the relation between oral contraceptives and stroke and myocardial infarction. Walnut Creek study found a positive association with subarachnoid hemorrhage but not with thrombotic stroke or myocardial infarction (Porter 1982; Petitti 1979).

Royal College of General Practitioner's oral contraceptive study (1981) suggested that the positive association of myocardial infarction risk with OCs use but this relative risk increased with age, cigarette smoking but not related with duration of OC use (Jain 1976,; Royal College General Practioner's Oral Contraceptive Study 1981). It has been demonstrated that some contraceptive preparation lower High Density Lipoprotein-Cholesterol as does smoking (Bradly et al. 1978; Criqui 1979). Lower level of HDL-C have been associated with increased risk of coronary heart disease. Some progestin lower the contents of HDL-c and so a cautious approach toward progestin only contraceptives has resulted (Gordon 1977).

Oral contraceptives have wide-ranging metabolic effect on many organs and tissues. In OCs users serum vitamin A level is raised, and the serum vitamin B_2, vitamin B_6, vitamin E, folic acid, vitamin B_{12} reduced. Clinical effects due to vitamin deficiency have been described for vitamin B_6 namely depression, and impaired glucose tolerance (Wynn 1975; Adams et al. 1976; Spellacy 1969). Also altered typtophan metabolism resulting from vitamin B_6 deficiency caused depression, mood change and sleep disturbance. Generally Ethinyl estradiol, one of main component of Oral pill, induced increased triglyceride and HDH-c with decreasing LDL-c. It decrease glucose tolerance with increasing insulin concentration. Chloasma, breast tenderness and endometrial hyperplasia but less acne were induced by Ethinyl estradiol. Oral pill produced impressive abnormality in renin-substrates concentration and in its reactivity to exogenous renin as well as endogenous renin activity and aldosterone secretion (Laragh et al. 1967; Roy et al. 1980). It might be associated with arterial hypertension.

Detailed information about the possible mechanism by which OCs exert the various health effects discussed above would be extremely valuable to physician and their patients in their choice of contraceptive method.

II. Intrauterine Device (IUD)

In our country 167.5 married women per 1000

fertile women selected IUD as reversible contraceptive method. IUD has been very popularly used before and after introduction of oral pill. The mechanism of its contraceptive action is still poorly understood but it seems to interfere with gamete transport, changes in uterine environment and interfere with implantation. IUD require minimal motivation. Its acceptability has been limited result of such complication as perforation of the uterine wall, pelvic inflammatory disease and pregnancy with IUD in place. Bleeding, Pain, ectopic preginancy and expulsion have contributed to lower acceptability and high drop out rate (Child Health and Human Development (B) 1983). The continuation rate in first one year is about 49 percent in Korea. Mechanism of infection is not clear but ascending infection along the tail of the IUD has been suggested (Tatum et al. 1975).

FDA has recently recommended that IUD should not be inserted during postpartum period because of excess risk of perforation (Lanctot 1979).

Some study suggested progeterone containing IUD reduced the possibility of PID.

III. Barrier Method

The directness, simplicity, relative safety and reversability of barrier methods seem to account for their growing acceptability. Although failure rate is high, interest in barrier method has been renewed because of numerous side effect of OCs and IUD. But their main drawback is direct association with coital act, inconvenience and esthenic unattractiveness.

IV. Natural family Planning (NFP) — Periodic Abstinence (Child Health and Human Development (B), 1983)

A couple must abstain from intercourse during the women's fertile period. The three commonly used NFP method are Basal Body Temperature (BBT) method, the cervical mucus or Ovulation method (OM) and symptothermal method (SM). In BBT method the postovulatory infertile phase begins on the third night of rising temperature. In OM the quality and quantity of cervical mucus are observed. The appearance of the mucus signs the beginning of the fertile period. The end of the fertile period occurs four days after the peak day. In the SM cervical mucus is used to determine the beginning of the fertile phase and BBT to define the end of the fertile phase. Failure rate as high as 25% has been reported (Wade et al. 1979; Klaus 1979).

Because of unnecessary prolonged period of abstinence, research is being undertaken to pinpoint ovulation based on hormonal determination using readily accessible body fluid (Annual report, National Institute of Child Health and Human Devemopment 1980).

V. Female Sterilization

During the past decade sterilization has gained popularity throughout the world. It is currently considered the world's leading method of contraception.

In Korea in 1974 only one percent of women in reproductive years took female sterilization but in 1984 it has increased to thirty four percent. Sterilization failure rate of overall technique combined would be one per 1000 procedures per year. Overall complication is 30 to 50 per 1000 cases. Major complication rate of 4.6 per 1000 cases caused by bleeding (Andrew 1979). Other complications are infection, bowel burn or injury and ectopic pregnancy. Recently major concern involved reversability, Modern microsurgical technique have yield subsequent pregnancy rate of 40 to 75% (Gomel 1978; Winston 1980).

VI. Regulation of Male Fertility

Vasectomy has gained increasing acceptance as a method of permanent contraception throughout the world. Aiso in Korea 109.2 married men per 1000 fertile persons took vasectomy for permanent sterilization. Since past 5 years the number of men accepting the vasectomy has increase five times. Vasectomy is readily accepted because it is simple, inexpensive, effective and apparently without serious medical complication. The failure rate ranged from 0 to 6 percent.

Vasectomy involves the potential for inducing

an autoimmune reaction. It is well established that from one-half to two-third of vasectomized men and animal develop circulating antibodies to sperm (Mumford 1979).

VII. New method of Contraception

1. Long acting steroid formulation

A. Injection Suspension

Long acting steroid can be administered through the injection, subdermal implant and contraceptive vaginal rings (CVRs). As injectable suspension Depomedroxyprogesterone acetate (DMPA). Norethindrone Enanthate (NET-EN) and Gestagen-estrogen formulation have been evaluated for contraceptive availability. The most widely use of this injectable steroid is DMPA. Most studies indicated that the effectiveness of the injectable steroid formula is 99 percent. DMPA is effective for 3-6 months after single injection (Ortit 1977). Major problem is breakthrough bleeding. Usually fertility returns within at least by 18 months (Gardner 1970).

B. Subdermal implants

Norplant I^R and norpland II^R are currently applied for subdermal implants. This method involves a silastic-based drug delivery system implanted subdermally that continuously and steadily release the contraceptive drug by diffusion. This system are attractive because they can function over extended period of time (6 month or longer). The primary difficulty has been breakthrough bleeding and the devise must be surgically removed when the drug is depleted (Moore et al. 1978; Population Council, International Committee for contraception (A) & (B) 1978).

C. Contraceptive Vaginal Rings (CVRs)

Readily absorption of steroid through vagina permit us to utilize natural steroids that are readily inactivated by oral ingestion. To take advantage of this fact research have designed silastic vaginal rings that fit the cervix and release contraceptive drug. The vaginal method are attractive to users because they can be self administered and ther is minimal interference in normal reproductive function. CVRs has shown not to produce certain estrogen-related metabolic change (Roy et al. 1980).

2. LHRH Analogs

Most current clinical research on LHRH is focused on the synthetic analog with agonistic activity (agonist). Considerable research, however, has been undertaken on the synthesis of analogs with antagonistic activity (antagonist). Clinical trials currently in progress are intended to assess the safety and utility (Child Health and Human Development (B) 1983).

3. Medicated or bioactive Intrauterine Device (IUD)

At least two main products have developed. One is the progesterone-releasing device, Progestaset and two Cu^{++}-ion releasing device, the cupper "T" and "7". Copper interfere with migration of spermatozoa as well as with implantation, probably by disrupting sulfhydryl group in the endometrium and in spermatozoa (Romney et al. 1981). Replacement is required periodically as the drug is exhausted. Pregnancy rate is 2 percent at 4 years (Sivin et al. 1981).

4. Regulation of male fertility

Numerous attempts have been made to develop a drug like oral contraceptives for women, that produce male infertility. Most of trials have focused on the use of androgen or on progestational drugs in combination with androgen. The time needed to suppression of sperm production and the effect varies considerably. Cyproterone acetate and α-cholorohydrate, some antimetabolite & Gossypol are known to interfere with sperm maturation (Mischell 1984).

5. Antifertility Vaccine

Much attention has recently been given to immune approaches to the management of fertility. It is important to have an antigen to which antibodies will be highly specific. The mostly wide investigated vaccine is based on a derivatives of human Chorionic Gonadotropin (HCG). But it has low antigenecity and inconsistent titers of antibody following vaccination. Vaccine also developed to ar-

rest spermatogenesis by neutralization of FSH with limited experience. Development of a vaccine based on unique antigen in the egg (Zona pellucida) and the sperm is the subject of current basic research (Sacco et al. 1978: Ownby et al. 1972).

CONCLUSION

Since 1960s a reavaluation of contraceptive research and technology development has provided highly effective contraceptive methods. They have tremendously contributed on reduction of fertility rate during the past decade.

But so far no any contraceptives method is perfect in terms of safety, convenience and effectiveness. Until newer, well-motivated, safer and effective contraceptives is available, we have to apply existing contraceptives through continuous monitoring of adverse effect to assist the users and then to give intellegent choice among numerous contraceptives. Also there is continuing need in research on contraceptives development to meet our goal.

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