CURRENT DEVELOPMENTS IN CONTRACEPTION

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SUMMARY

Contraception (birth control) prevents pregnancy by interfering with the normal process of ovulation, fertilization and implantation. There are different kinds of birth control that act at different points in the process.
The rapid increase in the world population makes it mandatory to develop new contraceptive methods. According to WHO data, every year 200 billion new pregnancies occur and more than 50 billion of them are classified as unintended.
To avoid complications of these unintended pregnancies and abortions, the contraception and kinds of contraceptive methods should be well known and understood. Recently, new hormonal contraceptive choices and regimen were adminestered and studies about male contraception and immunocontraception were performed. In this review, we discussed about the new development and progress on contraception.

Key words: *contraception, current, immunocontraception, male*
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KONTRASEPSİYONDA GÜNCEL GELİŞMELER

ÖZET

Kontrasepsiyon (doğum kontrolü) ovulasyon, fertilizasyon ve implantasyonun normal oluşum basamaklarını bozarak gebeliği önleyen hadisedir. Sürecin değişik noktalarını hedef alan birbirinden farklı doğum kontrol yolları vardır.
Dünya nüfusunun hızla artması yeni kontrasepsiyon metodlarının gelişimini zorunlu kılmaktadır. Dünya Sağlık Örgütü'nün verilerine göre her yıl 200 milyon yeni gebelik oluşmaktadır. Bunların 50 milyondan fazlası istenmeyen gebelik grubuna girmektedir.
Bu istenmeyen gebelik ve düşük komplikasyonlarından kaçınmak için, kontraseptif seçenekler iyice bilinmeli ve kavranmalıdır. Özellikle son dönemde yeni hormonal kontrasepsiyon seçenekleri ve rejimleri geliştirilmiş, erkek kontrasepsiyonu ve immunokontrasepsiyonda çalışmalar ve deneyler yapılmıştır. Bu derlemede kontrasepsiyonda mevcut güncel gelişmeler ele alınmıştır.

Anahtar kelimeler: *erkek, güncel, immunokontrasepsiyon, kontrasepsiyon*
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Definition, Aim and Prevalence of Family Planning

Family planning may be briefly and simply defined as the fact that married couples have a number of children that they desire at a time that they want and the prevention of the unplanned pregnancies. Thanks to family planning programs, in the entire world, annually, 187 millions of unwanted pregnancies, 60 millions of unplanned delivery and 105 millions of abortus are prevented and 2.7 millions of infant death and 215.000 cases of pregnancy-related deaths are avoided[1].

Inter-community contraception use rates depend on several factors such as the desired number of children, education, awareness and service procurement. Based on the investigation performed by United Nations Economic and Social Relations, Population Unit, world-wide prevalence of contraception use is 63%[1].

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Based on Turkish Population and Health Investigation performed in collaboration with Minister of Health, General Directorate of Maternal and Infant Health and General Directorate of Family Planning by Hacettepe University, the Institute of Population Studies in 2003, information about both modern and traditional methods of family planning is very prevalent in Turkey. Almost all of the women with whom an interview was performed during the study were informed about at least one method. While the contraceptive pills and RIA were the most commonly known methods with a rate of 98%, female condom (14%) and emergency contraception pills (16%) were the least known modern methods. At the time of the study, in Turkey, of all married women, 71% has been using a contraceptive method, 43% using a modern and 29% using a traditional method. Among the married women, the most commonly used method was withdrawal method with a rate of 26%. While one of each five married women used RIA, the use of condom followed this method with a rate of 11%. It is seen that the use of contraceptive method varied by the residential area, the region, educational level and the number of alive children. Use of any contraceptive method is more prevalent among the married women who live in the cities compared to the women who live in the rural areas (74% and 65%, respectively). Use of a contraceptive method had the lowest prevalence in Eastern region (58%) and highest prevalence in Western and Central regions (74%). The prevalence of the use of a contraceptive method shows a marked increased starting from the group of women who were graduated from the first-step primary education (5-year education) and maintains its high level at highest-level education groups. Its usage rate increases to 78% among the women with 1-4 children and decreases to 62% among the women with at least five children[2]. This study was repeated by the same institutions in 2008. Accordingly, the usage rate for any contraception method is 73%. (Users of a modern method, 46%; users of pills, 5.3%; users of RIA, 16.9%; users of condom, 26.9%)[3].

Contraceptive Methods

Today, 48% of the unwanted pregnancies occur during the use of any contraceptive method[4]. This suggests the importance of the selection and of the use of the contraceptive modality which is the most appropriate to the use of the couple. Table I shows all contraceptive methods.

Table I: *Contraceptive methods.*

Hormonal Contraceptives	- Combined oral contraceptives
	- Mini pills
	- Post-coital pills
	- Depot injections
	- Hormone-containing IUDs
	- Vaginal rings
Intrauterine Devices	
Barrier Methods	- Condom
	- Diaphragm
	- Spermicides
Surgical Sterilization	- Tube Ligation
	- Vasectomy
Natural Family Planning	
Prevention of the Pregnancy by Lactation	

Hormonal Contraceptives

Combined Hormonal Contraceptives

This group includes combined oral contraceptives, transdermal combined patches, monthly injectable preparations and combined vaginal rings. These drugs inhibit the ovulations via estrogen and progesteron that they contain. Estrogen suppresses FSH, regulates the bleeding pattern by stimulating the endometrium and increases the number and the efficacy of the progesteron receptors in the target organs. Progesteron suppresses LH, condenses the cervical mucus, decreases tubal motility and ciliary activity and decreases the endometrial receptivity[5]. Combined oral contraceptives, patches and combined vaginal rings may be used in a cyclic or continuous manner. Fertility is restored approximately five months after the discontinuation of the injectable methods and immediately after the discontinuation of the other methods[5].

Combined Oral Contraceptives (COC)

COCs, which are traditionally initiated to be taken within the first 5 days of the menses, which are received one tablet per day for 21 days and then which are discontinued for 7 days, have been included in various regimen for the last period. Table II shows the latest preparations[6].

In the regimen, which was called as 24/4, the number of hormone-free days was reduced from 7 to 4. When compared to classical regimen, it was detected to increase the suppression of the ovulation in the

efficiency and safety profile and to decrease the number of days with withdrawal bleeding in the control of cycle[7,8]. In a meta-analysis that compared classical 21/7 regimen and new formulations, although it was stated that the differences between the tablet contents and the durations of the regimens rendered the comparison more difficult, contraceptive efficacy and safety profiles, compliance rates, satisfaction rates and the discontinuation rates due to bleeding problems were found to be similar[9].

Combined Injectable Hormonal Contraceptives

This group, which is especially consisted of the drugs that may be selected in the patient population with a low socio-cultural level that does not use other alternative methods, may be used a monthly intramuscular injections. While these preparations have some disadvantages such as an amenorrhea rate of 14.6%, weight increase and a fertility restoration time of approximately 5 months, they also have some advantages such as the rarity of the breakthrough bleedings compared to depot medroxyprogesteron acetate[5]. In our country, their examples include 5 mg estradiol valerate and 50 mg norethisterone (Mesigyna).

Combined Vaginal Ring

Combined vaginal ring is placed inside of the vagina during the menses. It remains in the vagina for 3 weeks and then it is removed. One week later, it is replaced inside of the vagina with the menses. It releases 15 mcg ethynlestradiol and 120 mcg ethonogestrel per day. In the control of the cycle, it is an efficient and well-tolerated method[10]. In an analysis that compared combined vaginal ring and COCs that contained 30 mcg ethynlestradiol, the group of vaginal ring showed lower systemic estrogen exposure and better cycle control and better long-term continuation to use[11]. While the parameters such as contraceptive efficacy, patient compliance, breast tenderness, headache and nausea-vomiting, the percentages of the discontinuation of the method because of local and ring-related problems were determined to be 12% and 9.9% respectively[11].

Failure rate of the contraceptive method is expressed as a parameter called Pearl index, which means the pregnancy rate per 100 woman-years (100x12=1200 cycles). When combined hormonal contraceptives were collectively examined, we saw that COC, transdermal patch and vaginal rings had similar efficacies[12]. Mean rate was 0.3/100 woman-year with excellent use and 8/100 woman-year with typical use[12]. Transdermal patches had a worse side effect and complication profile compared to COCs and vaginal rings (breakthrough bleedings, headache, nausea-vomiting, fluid retention, weight increase). furthermore, these drugs similarly increase the risk for deep vein thrombosis and pulmonary embolism by 2-fold and the risk for myocardial infarction, stroke, hypertension, glucometabolic irregularities in diabetics and cervical, hepatocellular and breast cancer in the actual users by varying percentages[12,13]. When an examination was done in terms of breast cancer, especially for oral contraceptives, the determinant factor appeared to be the time at which the drug was discontinued rather than the duration of the use[14]. The relative risk was 1.24 in the current users, 1.16 in those who were using 1-4 years ago and 1.07 in those who were using 5-9 years ago. When the duration exceeded 10 years, no additional risk increase was observed[14]. Table III presented the precise and relative contraindications of the combined hormonal contraceptives[5].

Table II: New OK formulations.

Commerical name	Dose	Characteristics
Loestrin 24 Fe	Norethindrone acetate 1 mg Ethynilestradiol 20 mcg	24 active pills Monthly withdrawal bleeding (+) Milder bleeding
Yazz	Drospirenone 3 mg Ethynilestradiol 20 mcg	24 active pills Monthly withdrawal bleeding (+) Milder bleeding
Seasonale	Levonorgestrel 150 mcg Ethynilestradiol 30 mcg	84 active pills 4 withdrawal bleeding per year
Seasonique	Levonorgestrel 150 mcg Ethynilestradiol 30 mcg Ethynilestradiol 10 mcg/ for the last 7 days	91 active pills No intermediate period without hormone 4 withdrawal bleeding per year
Lybrel	Levonorgestrel/Ethynilestradiol 90mcg/20mcg	365 active pills High likelihood of amenorrhea

Table III: *Contraindications of combined hormonal contraceptives.*

Definitive Contraindications	Relative Contraindications
- Pregnancy	- > 35 years-old, smokers
- Undiagnosed genital bleeding	- Hypertension (TA>140/90mmHg)
- Breast cancer	- Diabetes mellitus
- History of cardiovascular disease	- Hyperprolactinemia
- Active hepatic disease	- Bill bladder disease
- Thrombophilia	- migraine without aura
- İlacın indüklediği hipertansiyon	- Autosclerosis
- Drug-induced hypertension	- Sickle cell disease
- Systemic lupus erythematosus	
- Haemolytic uremic syndrome	
- Thrombotic thrombocytopenic purpura	

Contraceptives that Contain Only Progesteron

This group of drugs leads to dose-related inhibition of the ovulation. Their other effects include rendering the endometrium inappropriate for the nidation, thickening of the cervical mucus and decreasing the tubal motility and ciliary activity[15]. To avoid estrogen-related metabolic and clinical side effects in the conditions in which mainly estrogen-containing combined preparations are precisely or relatively contraindicated, they are preferred during the lactation, menarche or menopause[16]. The convenience that they provide for the long-term use is their main characteristics. These drugs don't increase the risk for venous thromboembolism, myocardial infarction and stroke[17].

Injectable Preparations that Contains Only Progestine

Intramuscular administration of 150 mg depot medroxyprogesteron acetate (Depo Provera) inhibits the ovulation for 3 months and thereby, provides high efficacy of contraception. While the continuous use provides 60% amenorrhea at the end of 1 year and 70% amenorrhea at the end of 2 years, its unfavorable effects include a fertility restoration time as long as 10 months and its reducing effect on the bone mineral density[18]. It may be given at Day 7 after the elective abortus, at postpartum 3rd week if the mother is not breast-feeding and at postpartum 6th week if the mother is breast-feeding[18]. Recently, a new formulation, which contained 104 mg depot medroxyprogesteron acetate, which is subcutaneously administered, which has an efficacy that lasts for 3 months and which provided the absence of pregnancy for 16.000 cycles. The convenience provided by this preparation is the ability of the patient to self-administer the drug via subcutaneous route[19].

Pills That Contains Only Progestin

They should be regularly taken every day at the same hour. While the ability to be used during the lactation is their advantage, their disadvantage is the irregularities that they create in the menstrual cycle. The contraindications of these drugs include breast carcinoma, known or suspected pregnancy status and unexplained vaginal bleeding[20]. Table IV presents the preparations included in this group.

Table IV: *Drugs that contain only progestin.*

Commerical name	Dose
Cerazette	Desogestrel 75 mcg
Microval	Levonorgestrel 30 mcg
Ovral	Norgestrel 500 mcg
Micronor	Norethisterone 350 mcg

Implants that Contains Only Progestin

The use of this group aims to ensure a long-term contraception without user errors and without the side effects of the estrogen. Table V shows the preparations. Serum concentrations of the active substances depend on the weight of the user and on the time passed after the administration. For Norplant-6 and Jadelle, Pearl indexes were 0-0.3 for the first year and 5-year cumulative pregnancy rates were 1[21,22]. Unlike others, contraceptive efficacy of Implanon is 3 years. For Implanon, 3-year Pearl index is 0[23].

Table V: *Implants that contain only progestin.*

Commericial name	Characteristics
Norplant-6	6 Levonorgestrel-releasing sticks
Jadelle	2 Levonorgestrel-releasing sticks
Implanon	Single ethenogestrel-relesing sticks
Uniplant	Single nomegestrol acetate-releasing sticks

Some drugs to be used in the patients who use hormonal contraception may decrease the efficacy of the drugs by inducing hepatic enzymes (Table VI).

Table VI: *Drugs that interact with hormonal contraceptives.*

Barbituratles	Rifampicin
Carbamazepine/Oxcarbamazepine	Griseofulvin
Phenytoin	Ritonavire/Nevirapine
Primidone	Lamotrigine
Topiramate	Cyclosporine
Modaphynile	Potassium-sparing diuretics

Intrauterine Devices (IUD)

There are 3 types of IUD: copper-containing IUDs, inert and hormone-containing IUDs. They act by preventing the migration of the sperms to upper genital tract and by creating unfavorable environment for the implantation as a result of their inflammatory effect in the endometrium. Their indications include the conditions in which hormonal contraception is contraindicated, lactation, emergency post-coital contraception and the wish of using a coitus-independent method[24].Their positive aspects include the absence of need for patient compliance, their long-term efficacy near to those of the sterilization methods, the ability to use during the lactation and the restoration of the fertility[24]. Their negative aspects include the requirement of health staff for the administration, the likelihood of menstrual irregularity and high risk for sexual transmission of diseases[24]. The incidence of ectopic pregnancy is lower compared to non-users of contraceptive methods, but, if a pregnancy develops during the use of IUD, the likelihood to observe an ectopic pregnancy is higher and the incidence of pelvic inflammatory disease development is not different from the normal population[24,25]. For IUDs, the contraindications include pregnancy, uterine anomaly, acute PID, post-partum endometritis, post-abortal sepsis, idiopathical vaginal bleeding, suspicion of cervical or uterine malignancy and hypersensitivity [26]. The insertion time of the IUD is within the first 7 days of the cycle in the interval practice and immediately after the 1st trimester abortus in the post-abortal practice.

Risk for expulsion is lower when it is placed within the first 10 minutes following the placental separation in the post-partum period, compared to the first 48 hours. The risk is higher between 48 hours and 4 weeks. There is no restriction about the application after the 4th week[27].When IUD is being placed, prophylactic antibiotics are not routinely recommended and excessive reducing effects of the non-steroidal anti-inflammatory drugs were not demonstrated. While 2% local lidocain was found to be efficient in the excessive reduction, misoprostol was found to be efficient for the reduction of the cervical resistance[25,28].

Levonorgestrel-containing IUD

It is placed within the first 7 days of the menstrual cycle. It releases 20 mcg levonorgestrel per day. It thickens the cervical mucus and releases levonorgestrel. It suppresses the proliferation in the endometrium, causes fragility of the superficial vessels and thereby, prevents the implantation. In addition, an unfavorable environment for the sperm is prepared, motility and capacitation are inhibited and fertilization is prevented. In many women, while the ovulation continues, the levels of hormones secreted from the ovary are decreased. During the first 3 months, irregular spotting bleedings occur. Its cost is high, but its efficacy lasts for approximately 5 years. Pearl index is 0.1/100 woman-year[29].

In a large, randomized, controlled study conducted on 2244 women, pregnancy rate following 7-year use was 1.1% with levonorgestrel-containing IUD and 1.4% with copper-containing IUD[30]. Other benefits of these devices include protective effect against PID, improved hemogram parameters in the women with menorrhage and anemia, avoiding the negative effects of systemic progesteron on lipid profile, decreased dysmenorrheal and premenstrual dysphoria, palliation of the pain in the endometriosis and regressed endometrial hyperplasia [5]. Adverse events that developed during their use included amenorrhea (20-35%), functional ovarian cysts (12-30%), bleeding (8%), depression (2.9%), acne and skin impairment (2.3%), headache (1.9%) and breast tenderness (0.8%)[31]. Their contraindications include active PID, serious cervicitis, undiagnosed genital bleedings, pregnancy, uterine anomaly and suspected malignancy[32].

Post-coital Contraception (Emergency Contraception)

These applications target the post-coital and pre-implant time point, on any day of the cycle, as soon as possible. COCs, the pills that contain only progesteron, copper-containing IUD and mifepriston are used for post-coital contraception. 1500 mcg levonorgestrel (one single dose or two doses of 750 mcg taken with 12-hour interval) used within the first 72 hours after the coitus is more efficient and are better tolerated compared to COCs[33]. RU-486 (Mifepriston), which is taken as a 10 mg single dose within the first 120 hours after the coitus has the same efficacy as levonorgestrel[34]. Two doses of 50 mcg ethynlestradiol and 250 mcg levonorgestrel tablets taken two times with 12-hour interval or, again, 30 mcg ethynlestradiol and 300 mcg norgestrel taken 4 times with 12-hour intervals, which are known to form Yuzpe method, are other alternatives used for emergency contraception. IUD is administered within the first 5 days and its efficacy is 99%[33].

Contraception in Specific Groups

Lactational Amenorrhea and Contraception

While the lactation decreases the releases of GnRH and gonadotropin, the elevation of endorphins results to decreased release of dopamine and, ultimately, increased release of prolactin[34]. All these hormonal changes result to anovulation and amenorrhea[34,35]. The requirements to ensure a successful lactational contraception include feeding the infant only with breast milk, the presence of amenorrhea in the mother and duration of lactation shorter than 6 months. If properly administered, the efficacy is 98%[26].

Contraception in the Postpartum Period

The patients, which are not breast-feeding, should begin to take such drugs 3 weeks after the delivery, because combined hormonal methods increase the risk for early thrombosis. While the pills that contain only progestin may be initiated immediately after the delivery, injectable preparations that contain only progestin may be initiated at 6th week after the delivery. IUD may be implanted immediately or at 4th week in a mother that breast-feeds or not[37].

In breast-feeding patients, all hormonal methods except the pills that contain only progestin are contraindicated. There are some insights that suggest that combined preparations may be initiated at 6th week after the delivery[38]. In both groups, vasectomy and condom may also be recommended for the male partners of the patients.

Contraception in the Perimenopausal and Postmenopausal Periods

For the patients in the perimenopausal period, COCs that contain 20 mcg ethynlestradiol, the pills that contain only progestin or, in those with menorrhage, levonorgestrel-containing IUDs may be recommended [37,38].

Even if they are taking hormone replacement therapy (HRT), the patients that had the menopause below the age of 49 years-old should continue to use contraceptive methods for an additional 2 years and those aged above 50 years-old for an additional 1 year[39]. FSH may be determined between 5th and 7th days of the week during which no pill was taken in the patients who used COCs within perimenopausal period and at any day in those who used only progestin and, when the results are above 30 IU/L, the therapy should be switched to HRT[39].

Male Hormonal Contraception

Today, hormonal contraception is out of the conventional contraceptive methods such as condom and vasectomy and is a method which is investigated for routine use. Hormonal contraceptive method should be efficient, reversible and well-tolerable. In male hormonal contraception, different forms of testosterone are given and thereby, the suppression of pituitary LH and FSH releases is aimed. As a result, stimulating signals required for the spermatogenesis are prevented, sperm counting is decreased in many men and the infertility is ensured[40].

When we reviewed the literature, two studies supported by World Health Organization, which included a total of 700 men, were remarkable. Weekly administration of testosterone enanthate led to the development of azoospermia or severe oligospermia in 98% of the subjects and its contraceptive efficacy was found to be high. Weekly administration of this hormone with a low side effect profile was stated to be a disadvantage [41,42]. Similarly, in phase 3 study for contraceptive efficacy, which investigated male hormonal contraception on 1045 patients, contraceptive efficacy phase of 500 mg testosterone andecanoate administered monthly for 30 months occurred along with oligozospermia (<1.000.000/ml). While 4.8% of the subjects did not show suppression, 1.3% of the subjects developed post-suppression sperm rebound effect. Method-related failure rate was 6.1%. Contraceptive efficacy was 1.1/100 person-years, whereas it was determined to be an efficient, safe and well-tolerated and reversible method for the future[43].Thereafter, to ensure a higher efficacy, combined therapy with testosterone and progestin was considered.

In a double-blind, randomized, controlled study, 354 healthy males were given 750-1000 mg testosterone andecanoate and ethonogestrel implants each 10-12 weeks for 42-44 weeks. The patients of the control group were implanted or injected placebo. While 94% of the males achieved the suppression of spermatogenesis, weight increase, mood changes, acne, sweating and libido changes were found to be higher compared to placebo group. As a result of the study, it was concluded that the combination of testosterone andecaonate and ethonogestrel was a well-tolerated method that provides efficient suppression, but it should be ameliorated[44]. As a result of all these studies, the factors that affected the suppression of spermatogenesis included the addition of progestin to testosterone, race, low baseline

sperm count, low baseline testosterone level and younger age. The factors that affected the normalization (averagely 20 millions/ml at 3rd month) included advanced age, Asian ethnicity, short time of therapy, high baseline sperm count, fast suppression and low baseline LH levels and it was stated that, to render narrower the side effect profile, the studies about selective androgen and progesteron receptor modulators were warranted[45].

Immunocontraception - Vaccines

Although an attempt to develop a contraceptive vaccine has been performed for long years, no successful result was obtained. A suitable contraceptive vaccine should be safe (minimal side effect), reversible, manageable by the doctor and the patients and efficient with an efficacy rate near to 100%. In the development of fertility vaccine, targeted antigen should be an essential component of the human fertility, the vaccine should be highly antigenic and, to ensure the infertility, the immunological response should be long-lasting[46]. Only anti-HCG vaccine could clinically reach phase 2 study stage[47]. Although this vaccine showed contraceptive properties, it was efficient in only 2/3 of the study population[48].

GnRH hormone is a decapeptide which has a vital importance for reproductive functions. The vaccination for GnRH is being developed as a potential method for the control of fertility and gender-related behaviors in male and female laboratory animals[49]. As a result of the studies conducted on deers, pigs, mice and horses, it was seen that contraceptive effects were weak and short-termed and, additionally, non-contraceptional endocrinological side effects were found[50]. It was reported that better results could be obtained with modified adjuvants and re-immunization[49].

Vaccines that contained target antigens present in the ovary (Zona Pellicuda proteins A,B,C) were studied in the kangaroos and in the deers. The formation of the zona matrix is one of the prequisites for a normal ovarian follicular development, fertilization, the formation of blastocyst and the transportation of the embryo. It is required to ensure the self-tolerance in the presence of a physiological endogenous antigen [50]. Immunization with homologous or heterologous zona proteins results to the loss of immune tolerance and ovary-specific autoimmunity[51].

The investigators, in the searching of alternative immunocontraceptive antigens, found that, in the sheeps, bone morphogenetic protein 15 (BMP15) and growth differentiation factor 9 (GDF9) had immunogenous properties[52]. It was revealed that the antibodies that developed after the administration of specific agents targeting N-terminal led to the formation of an anestrous status, together with the inhibition of a normal ovarial follicular development and anovulation, but endocrinologic side effects consist an obstacle for clinical use[53].

Appropriate preparation of the uterine endometrium plays the key role for a successful embryonic implantation[54]. Optimal uterine receptivity period is associated with epithelial interleukin 11 (IL-11), interleukin-11 receptor (IL-11 RA) and leukemia inhibitor factor (LIF) and the deficiency of these elements resulted to an impairment in the invasion of the blastocysts to the uterus wall in the mice[55,56]. Intraperitoneal administration of the agents that are prepared using special immunological analyses and that contain IL-11 antagonist and LIF antagonist led to serious decidual damage and a full implantation disorder[55,56].

High immunogenic property of the sperm in the male and in the women has been known for long years[57]. In 5% of the infertile couples and in 70% of the vasectomized men, sperm antibodies were detected in the serum and in the accessorial glands[58]. Accordingly, the development of human immunocontraception vaccines based on sperm- or male-specific antigens seems to be a logical approach[59]. For this purpose, many sperm protein antigens were examined and some animal studies showed marked spermicidal activity and the occurrence of the inhibition of sperm-ovum interaction that resulted to infertility[60]. Capacitation, which is an essential function in the preparation to the fertilization, is controlled by four sperm-specific ion channels. These ion channels are called as CatSper 1-2-3 ve 4. In human studies, selective damage of these channels resulted to the loss of sperm motility, the inhibition of sperm-ovum interaction and the inhibition of the pregnancy[61]. Many sperm antigens have potential contraceptive property, but none of them fully meets the criteria to be used as a human vaccine[51].

Conclusion

Number of the studies conducted in the field of contraception is incrementally increasing. In our country's circumstances, the doctor should do a good medical and

socio-cultural evaluation of the couple and be careful to select the most appropriate method for them.

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