Contraceptive Vaccine : New Hope for the Overcrowded World?

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Abstract

The overall rate of fertilization in humans has contributed to sustained increases in the world population and the added urgency of the need to develop new, effective contraceptive strategies. One potential approach to preventing fertility is to disrupt sperm-egg interaction or embryonic-maternal communication during early pregnancy with immunological reagents. This has lead to the principal concept of "contraceptive vaccine" which may become available in the near future.

Key word : Contraceptive Vaccine, New Hope for Fertility Control

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The world population continues to grow at a steadily increasing rate, currently by more than 220,000 per day. By the end of the year 2000, the human population will reach 6.3 billion, double the number of 1960. It is estimated that 80 per cent of these people live in third-world countries(1). These demographic statistics emphasize the need for new means of contraception. The methods of birth control presently available can be grouped as follows: (1) hormonal such as oral pills, injectable contraceptives, and contraceptive implants; (2) chemical such as spermicides; (3) mechanical such as condoms, caps, intrauterine devices; (4) surgical such as tubal ligation, vasectomy; and (5) natural such as safety period and withdrawal. Although these methods have found widespread acceptance in various parts of the world, this range of options is still inadequate to meet the widely different cultural, social, and religious demands existing in different cultures, particularly in third-world countries.

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Contraceptive vaccine: A new approach in fertility control

A new method of human contraception presently being investigated is the development of immunologic vaccines that will generate antibodies to gamete-associated antigens or reproductive hormones. Major advantages of this mode of contraception include ease of administration, lack of failure, long-lasting protection, low cost, and potential reversibility. Several different criteria for the ideal antigen to be used in the development of a contraceptive vaccine have been proposed. First, the antigen should have a response confined to the reproductive processes. It should be present in the circulation temporarily and/or at low concentration. The formation of the immune complexes should not lead to autoimmune disease and the contraceptive effect should be reversible. Finally, the contraceptive effects should not cause danger to future offspring(1).

Three of the immunogens currently being evaluated are subunits of human chorionic gonadotropin (hCG), zona pellucida antigens, and sperm antigens. Progress in the developmental process of each group of these contraceptive vaccines as well as their potential benefits and drawbacks will be discussed as follows.

The hCG vaccine

The preimplantation embryo produces and secretes hCG as early as 5 days postfertilization, stimulating the corpus luteum to maintain the production of progesterone needed for maintaining the uterine endometrium for embryo attachment and implantation. HCG travels by the maternal circulation from the embryonic trophoblast to the corpus luteum and therefore could be inactivated systematically by circulating antibodies.

Based on the experimental data in three species of primates, two candidates of hCG vaccines have be assessed. The first type, being tested by the Population Council in New York and the National Institute of Immunology (NII) in New Delhi, is the whole Beta subunit of the hormone (B-hCG)(2).

The other type of vaccine is being developed with the support of the World Health Organization (WHO) and relies on a synthetic peptide homologous to the carboxy-terminal region of the B subunit of the hormone (B-hCG-CTP)(3).

The vaccine being tested by the Population Council consists of B-hCG conjugated to tetanus toxoid (carrier molecule). Phase I clinical trials in human volunteers have demonstrated the immunogenicity of this preparation and no adverse side effects have been reported(4,5). The anti-hCG vaccine being tested by the NII is a heterospecies dimer with B-hCG associated with the alpha-subunit of ovine luteinizing hormone conjugated to tetanus toxoid and diphtheria toxoid carriers. In phase II clinical trials with this vaccine it has been reported that antibody titers above the estimated efficacy threshold were achieved by 80 per cent of the women and only one pregnancy has been reported in 1000 otherwise unprotected menstrual cycles in study participants(1,6).

While vaccines against hCG hold promise for an effective and safe method of contraception, their application may be restricted due to their action as an early abortificant rather than antifertility treatment. Ideally immunologic disruption of fertility should occur before fertilization.

Antizona pellucida vaccine

The concept of a zona pellucida vaccine was based on studies concerning the influence of antiovarian antisera on mammalian IVF systems. Anti serum against ovarian tissue inhibited sperm binding to the zona pellucida and blocked fertilization(1). The responsible antigens are present in the zona pellucida. Antibody against zona pellucida proteins has blocked IVF in laboratory rodents by inhibiting sperm binding to the zona surface(1).

The zona pellucida of all mammals appears to be composed of three major glycoproteins which has been designated ZP1, ZP2, and ZP3(7). Since the 1970's, the zona pellucida has been viewed as a potential target for immunocontraception. More recently, it has been demonstrated that the zona genes are expressed in oocytes, and the resultant proteins are secreted to form an extracellular matrix unique to the ovary. The presence of antibodies directed against specific epitopes on the zona proteins have effectively blocked fertilization in several experimentally useful species(8). A possible drawback to immunization against zona antigens is that antizona antibodies bind ovulated oocytes as well as those still in the follicles, resulting in prolonged infertility(1).

Ethical factors and limitations to the availability of human antigens prevent the collection of sufficient amounts of human zona for experimantation. Thus, the use of heterlogous zona is an essential element for development of a human contraceptive vaccine. Because the zona proteins are conserved among mammals, contraceptive strategies developed in laboratory or veterinary settings may eventually be transferable to humans. However, the immune response varies among species, and additional investigations are required to consistently elicit an effective immune response in all members of a target population. In addition, there remains considerable concern about the safety of active vaccination with "self"- peptides[9].

Antisperm antigen vaccines

It has been observed in patients with subfertility that antisperm antibodies can contribute to human infertility[1]. Based on this, sperm-specific antigens have been sought as potential immunogens in contraceptive vaccines. Intact sperm can generate antibodies that induce infertility but this antigen is not appropriate for a contraceptive vaccine because some antigens are shared with brain and kidney cells, erythrocytes and lymphocytes[10].

Antibodies to acrosin or hyaluronidase do not reduce fertility in females. In contrast, immunization with LDH-C4 reduces fertility in female rabbits, mice, and baboons[1]. The human sperm protein SP-10 is a differentiation antigen localized within the acrosomal vesicles of spermatids and appear to be testis specific. This protein has been designated as a "primary vaccine candidate" by a WHO task force on contraceptive vaccines due to its tissue specificity and evidence that antibody to SP-10 inhibited fertilization in the hamster egg penetration test[1,11]. Other sperm-related proteins such as RSA-1, FA-1, and GA-1 also have been evaluated as potential immunogens for contraceptive vaccine.

SUMMARY

Most vaccines are developed to protect a host from infectious agents such as virus, bacteria and parasites. The primary goal of this ordinary vaccine is to provide long-lasting, preferably lifelong immunity. The development of a contraceptive vaccine, however, requires the realization of a different set of goals. The target of these vaccines are endogenous and essential to reproduction. Thus, while the immunological response must effectively prevent fertility, it must avoid demonstrable hazards to the host or any offspring born subsequent to vaccine users. Ideally, the contraceptive vaccine will affect fertilization rather than early development and would be reversible at the discretion of the host. In summary, the hCG as well as specific sperm and zona pellucida antigens may serve as potential immunogens for a contraceptive vaccine. Although a number of questions need to be resolved, it is very likely that immunologic contraception will play an important role in the future management of the world population growth.

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วัคซีนคุมกำเนิด : ความหวังใหม่สำหรับการควบคุมประชากรโลก?

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ปัจจุบันประชากรของโลกเพิ่มจำนวนขึ้นอย่างรวดเร็วทำให้ทรัพยากรที่มีอยู่อย่างจำกัดต้องถูกจัดสรรด้วยความยากลำบาก การคุมกำเนิดจึงมีบทบาทสำคัญในการควบคุมประชากรของโลก แม้ว่าวิธีการคุมกำเนิดต่าง ๆ ที่มีใช้อยู่แล้วในขณะนี้จะมีประสิทธิภาพดีและได้รับการยอมรับค่อนข้างสูง แต่ทว่าในบางส่วนของโลกวิธีการคุมกำเนิดต่าง ๆ ก็ยังเข้าไปไม่ถึงเนื่องจากลักษณะเฉพาะด้านวัฒนธรรม ความเชื่อ ตลอดจนลัทธิศาสนาต่าง ๆ โดยเฉพาะในกลุ่มประเทศโลกที่สามประกอบกับวิธีคุมกำเนิดต่าง ๆ ที่มีใช้ในปัจจุบันยังมีอาการข้างเคียงบางอย่างที่ก่อให้เกิดความไม่สะดวกในการใช้ และผู้ใช้อาจขาดความมั่นใจในความปลอดภัยหลังการใช้เป็นเวลานาน จึงได้มีการคิดค้นวิธีคุมกำเนิดแนวใหม่ขึ้น คือวัคซีนคุมกำเนิด ซึ่งมีข้อดีคือเตรียมได้ง่าย ราคาไม่แพง มีประสิทธิภาพสูง ออกฤทธิ์อยู่ได้นาน และสามารถกลับมาตั้งครรภ์ได้เมื่อต้องการ แม้ว่าวัคซีนคุมกำเนิดจะเป็นวิธีการใหม่ซึ่งยังต้องได้รับการปรับปรุงและทดสอบอีกหลายขั้นตอนกว่าจะได้รับอนุญาตให้นำมาใช้ได้จริง แต่ก็มีความเป็นไปได้ค่อนข้างสูงว่าวัคซีนคุมกำเนิดจะถูกนำมาใช้ได้อย่างแพร่หลายในอนาคตอันใกล้นี้

คำสำคัญ : วัคซีนคุมกำเนิด, ความหวังใหม่ในการควบคุมประชากร

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