Male Contraceptive Methods in Development

Wilson de Jesús Terán-Fonseca[1], Amely Olalde-Apaseo[1], Christian Joshué Monge-Ortega[1], María Fernanda Miranda-Corona[2].

[1] Faculty of Medicine, Autonomous University of San Luis Potosi, San Luis Potosí, S.L.P., Mexico.
[2] Anáhuac University Querétaro, Santiago de Querétaro, Querétaro, Mexico.

Corresponding author: Wilson de Jesús Terán-Fonseca, teranfonsecawilson@gmail.com
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ABSTRACT

The article highlights that, despite approximately 50% of pregnancies worldwide being unplanned, modern contraceptive options for men are almost exclusively limited to condoms and vasectomy. The document analyzes the development of hormonal methods, such as dimethandrolone undecanoate (DMAU) and 11β-MNTDC, which aim to suppress sperm production by inhibiting gonadotropic hormones. It also describes promising non-hormonal alternatives, including reversible polymeric barriers such as VasalGel and RISUG, and the disruption of retinoic acid synthesis through enzyme inhibition.

The development of new male contraceptives represents a critical advance for public health and equity in reproductive responsibility. Although many of these methods still require further research on their safety and reversibility, their future implementation could significantly transform family planning practices globally.

The aim of this work is to review recent advances in the development of male contraceptive methods, exploring both hormonal and non-hormonal options, in order to encourage greater male participation in family planning and reduce the rate of unwanted pregnancies.

Keywords: male contraceptives, family planning, reproductive health.

INTRODUCTION

The oldest method of contraception is the male condom, which remains one of the most widely used methods today. There are reports that early versions were used in ancient Egypt; however, the first documented reports on condoms date back to 1564, published by Gabriello Falloppio, in which they were described as a method to prevent syphilis infection.

Currently, approximately 50% of all pregnancies are unplanned, and these figures are even higher among adolescents in the United States. Of the half of modern contraceptives available, only two are for men: condoms or vasectomy.

Hormonal methods can successfully block sperm production, thus interfering with spermatogenesis. Contraceptive options for men are based on various hormonal regimens that achieved 94% effectiveness in clinical studies, but have been abandoned due to undesirable side effects such as acne, behavioral changes, etc.

The development of contraceptive methods has had a major impact on fertility rates, women's health, the role of women in society, and the sexual practices of adults and adolescents.

The failure rate in these methods ranges from <1% to >20%, depending on the method.

The aspects that still generate debate regarding the mechanisms of action these methods should have are the site and time at which they should act.

In this respect, there are three opinions:

1.- That their result is azoospermia.

- Advantages: Their effect can be measured quantitatively, and their result in infertility is easily obtained through testing.
- Disadvantages: They are slow to establish and reverse, as they target meiotic divisions.

2.- That they act against mature sperm.

- Advantages: They are quick to establish and reverse; there is no testicular change.
- Disadvantages: These methods are effective against all viable sperm present in ejaculation.

3.- That they produce morphologically abnormal sperm.

- Advantages: They are quick to establish.
- Disadvantages: Some viable sperm may remain for fertilization.

HORMONAL METHODS

Hormonal contraceptives for men involve administering exogenous hormones to prevent spermatogenesis. These hormones affect the hypothalamic-pituitary axis, inducing negative feedback from testosterone on this axis, ultimately suppressing the secretion of FSH and LH.

Currently, various types of male contraception are being researched, with oral formulations being one group of options.

Dimethandrolone undecanoate (known as DMAU) is a compound that shows great promise. It is administered to patients in ester form and is then metabolized in the body to DMA (dimethandrolone). After 28 days of oral administration, a decrease was observed in plasma levels of luteinizing hormone (LH), responsible for the proper functioning of the interstitial cells of the testes where testosterone is produced; follicle-stimulating hormone (FSH), responsible for stimulating sperm production and increasing the production of androgen-binding protein (ABP); and testosterone levels, which affected male fertility.

After seven days of taking DMAU, a significant decrease was observed in the levels of gonadotropic hormones and testosterone (median <24 ng/dL) produced in the body. DMAU binds to progesterone and androgen receptors located in the pituitary gland and hypothalamus, thereby inhibiting the secretion of pituitary hormones that affect testicular hormonal activity. Specifically, the hypothalamus stops secreting GnRH, and the pituitary gland stops secreting LH and FSH, through negative feedback.

11β-Methyl-19-nortestosterone-17β-dodecylcarbonate (11β-MNTDC) is another substance tested as a male oral contraceptive. It is a prodrug in ester form that is converted in vivo to the active substance: 11β-methyl-19-nortestosterone. Like DMA, it inhibits androgen secretion by binding to androgen and progesterone receptors. Taking this substance with food has been found to significantly increase its serum concentration. Doses of 200, 400, and 800 mg effectively reduced sex hormone levels.

Segesterone acetate is a novel progestin (Nestorone) that has been formulated as a transdermal gel for daily use in combination with a topical testosterone gel in male contraceptives. A study has shown that over 80% of men who received 8 mg per day of segesterone acetate with testosterone, and who applied Nestorona gel daily with testosterone gel, experienced a reduction in sperm concentration to less than one million per milliliter.

NON-HORMONAL METHODS

VasalGel, a high molecular weight (360 kDa) styrene-malic acid (SMA) polymer, is administered intramuscularly. This polymer acts as a barrier that sperm cannot cross and can be removed by dimethyl sulfoxide (DMSO). This preparation has already been tested in rabbits and rhesus monkeys. Studies show that this method is also very effective, but further research is needed to determine its absolute safety.

One of the most promising drugs could be **Reversible Inhibition of Sperm Under Guidance (RISUG)**. This styrene-maleic anhydride copolymer, injected into the vas deferens, lowers the pH level and creates a positive charge, thus preventing the proper transport of male reproductive cells through the female reproductive tract.

Sperm counts have been found to be reduced by disrupting retinoic acid synthesis. This can be achieved by **inhibiting the enzyme aldehyde dehydrogenase-1A2 (ALDH1A2) in human germ cells**, which is a catalyst for the conversion of retinaldehyde to retinoic acid.

CONCLUSIONS AND PERSPECTIVES

With the advent of hormonal birth control pills in 1960, women's control over their own bodies and their decision to have children was revolutionized. However, unintended pregnancies remain common.

Advances in hormonal contraceptives for men are a major area of research today, as they present a challenge for the health sector and the scientific community. The goal is not only to improve contraception but also to eliminate societal negative impacts and, most importantly, to increase men's involvement in family planning.

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Conflict of interest

The authors declare no conflicts of interest.

Ethical considerations

This work did not involve the participation of human subjects or animals, nor the collection of primary data; therefore, it did not require approval from a research ethics committee. All data used came from previously published and publicly accessible secondary sources.

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