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REVIEW ARTICLE

Male Contraception: Review

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ABSTRACT

Unintended pregnancies represent a significant public health challenge on a global scale. While there exists a diverse array of contraceptive methods available for women, the options for men remain largely restricted to condoms and vasectomy. The efficacy of condoms is often compromised by high failure rates, and vasectomy, being a surgical procedure, lacks reversibility. Consequently, there is a pressing need and a widespread interest in the development of male contraceptive methods across the world.

KEYWORDS

• Male contraception • Testosterone • Reversible • Vaso-occlusive methods • Vaccines

INTRODUCTION

Recent studies show that men have knowledge of family planning and are inclined for small family for economic and social reasons. In spite of this, there is reluctance to use male contraceptive methods.[1] It is argued that male methods of contraception are limited and unlike female contraceptive methods, there is limited choice for the male.[2]

Vasectomy and condom are the only two modern methods available to male. Traditional methods like coitus interruptus and safe period require very good spouse communication and understanding.[3]

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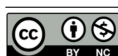

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Mechanism of Male contraception

Hormonal male contraception operates by targeting the hypothalamic-pituitary-gonadal (HPG) axis to inhibit spermatogenesis. The HPG axis begins with the hypothalamus, which releases gonadotropin releasing hormone (GnRH).[3] This hormone prompts the pituitary gland to secrete luteinizing hormone (LH) and follicle-stimulating hormone (FSH). FSH is essential for the proper functioning of Sertoli cells in the testes, which are crucial for the maturation of spermatogonia. Meanwhile, LH stimulates Leydig cells in the testes to produce testosterone. For normal spermatogenesis to occur, a significantly elevated level of intratesticular testosterone approximately 100 times greater than that found in the bloodstream is necessary. Additionally, circulating testosterone exerts a negative feedback effect, inhibiting the release of GnRH, LH, and FSH, thereby completing the regulatory feedback loop.[4]

HORMONAL MALE CONTRACEPTION

Oral Male contraceptive's

1) DMAU (Dimethandrolone undecanoate)

DMAU is a testosterone-derived pro-drug, DMAU was shown to effectively, reversibly suppress gonadotropins and spermatogenesis while maintaining physiologic androgenic effects without serious side effects importantly, there were no signs of liver toxicity, a well-characterized side effect of many exogenous androgens.[5]

2) MENT (7Î-Methyl-19-Nortestosterone)

MENT is an experimental hormonal male contraceptive being developed as an alternative to testosterone-based methods. It is a synthetic androgen that is more potent than natural testosterone and has both contraceptive and therapeutic potential.[6]

Mechanism of action

Suppresses sperm production by inhibiting follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which are essential for sperm development. Maintains male characteristics (muscle mass, libido.) without needing additional testosterone replacement. Delivered via implants placed under the skin, slowly releasing MENT over time.

Advantages of MENT

- More potent than testosterone, meaning lower doses are needed.
- Does not require additional testosterone replacement, unlike some other hormonal male contraceptives.
- Potential for reversibility after discontinuation.
- Alternative to traditional testosterone therapy

3) 11-Beta MNTDC (11β-methyl-19-nortestosterone dodecylcarbonate)

MNTDC is a testosterone derivative; it does not undergo aromatization and therefore lacks estrogenic effects.

11β-MNTDC was shown to effectively suppress serum gonadotropins and exert even less liver toxicity than other androgens side effects were mild or moderate. The most common sides effects were headache, acne, and decreased libido.[6]

4) NES-T (Nestorone -T)

Segesterone acetate, most often identified by its trade name Nestorone (NES), is a potent progestin with virtually no affinity for androgen receptors (AR) or estrogen receptors (ER) and minimal glucocorticoid activity. NES shows low bioavailability when taken orally but is readily absorbed by transdermal application.

NES is now compounded with Testosterone in a transdermal gel. Testosterone is added to improve suppression of spermatogenesis and minimize potential symptoms of androgen deficiency.[6]

Non hormonal Male contraception

Non-hormonal male contraceptive approaches include physically blocking sperm passage through the male reproductive tract (vaso-occlusion), altering sperm motility, and interrupting intratesticular sperm maturation, among others.

Vasoocculsive Methods

1) Intra-Vas Device (IVD)

The Intra-Vas Device (IVD) known as Shug, is implanted into vas. Two plugs are kept in each vas so that sperms passing through one

plug will be stopped by the second plug. In animal studies the IVD resulted in no sperms in the ejaculate and after removal of the device sperms were seen in the ejaculate.[7]

2) Vasagel

RISUG (Reversible Inhibition of Sperm Under Guidance) is a long-term, reversible male contraceptive currently in advanced clinical trials in India. It involves a clear polymer gel made of styrene maleic anhydride (SMA) mixed with dimethyl sulfoxide (DMSO) into the vas deferens which blocks sperm from passing through.This technique was developed at the Indian Institute of Technology and All India Institute of Medical Sciences.[8]

How It Works

The gel creates a charge-based barrier that damages sperm as they pass, rendering them incapable of fertilization. Unlike a vasectomy, the vas deferens is not cut, just blocked. If a man decides to regain fertility, the gel can be flushed out with another injection of a solvent.[8]

Advantages

- Long-lasting (up to 10-15 years with one injection)
- Reversible with another injection
- Highly effective in preventing pregnancy
- No major hormonal side effects

MALE CONTRACEPTIVE IMPLANTS

A desogestral pill of 75-300 mcg daily, with subcutaneous testosterone pellets, suppress gonadotropin secretion profoundly and within eight weeks in 300 mcg group, azoospermia can be achieved in some cases. The HDL cholesterol level in the blood does not change. The combination of 4 LNG implants (75 mg each) followed 4 weeks later by 1000mg of testosterone by intramuscular injection every 8 weeks for 24 weeks is a promising candidate for hormonal male contraception with marked suppression of spermatogenesis.[8]

Spermatogenesis returns to normal range after the implants are removed and no serious adverse events and no significant changes in serum chemistry have been reported.[8]

Vaccines for Control of Fertility of Males

The LHRH vaccine is usable in males and stops spermatogenesis. However as it also stops the production of testosterone, it will not be acceptable and would demand supplementation with androgens.

Moudgil et al developed a vaccine reacting against FSH. The approach was effective in monkeys. Oligospermia was induced without decline of testosterone. The vaccine underwent preliminary Phase I clinical trials in India but lies abandoned.[8]

Transdermal Patches

The transdermal route of testosterone (5 mg/day) has been tried but resulted in lesser efficacy. This demonstrates that the dose or route of administration of androgens is critical for sperm suppression in combined androgen-progestogen regimen for hormonal male contraception.[9]

Adverse effects reported with this mode of contraception are mila asymptomatic gynecomastia, mild acne, emotional irritability and anger and transient decrease in libido.

Recent advancements in male contraception

1. Plan A: Injectable Hydrogel

NEXT Life Sciences, a Los Angeles-based startup, is developing Plan A, an injectable hydrogel designed to provide long-term, reversible contraception for men. The procedure involves a non-invasive injection into the vas deferens to block sperm movement, effective for up to 10 years. Reversal is achieved through a second injection that dissolves the gel.

2. Hormone-Free Male Contraceptive Pill

Researchers at Monash University in Australia have made significant progress toward a hormone-free male contraceptive pill. By mapping the 3D structure of the P2X1 receptor protein, they aim to develop a drug that inhibits sperm transport without affecting long-term sperm viability or overall health. This approach could offer a non-hormonal contraceptive option for men, addressing concerns associated with hormonal methods.[9]

3. NES/T: Male Contraceptive Gel

The NES/T gel is a hormonal contraceptive applied daily to the skin. It combines progestogen to suppress sperm production and testosterone to maintain hormonal balance. In global trials involving around 200 couples,

participants reported effective contraception with minimal side effects. This method represents a shift toward shared contraceptive responsibility between partners.[10]

CONCLUSION

New male contraceptives are needed and desired worldwide. Effective, safe, completely reversible, and available to a wide range of potential users are the characteristics of the perfect male contraceptive. Male contraception has the ability to give couples another family planning alternative in addition to lowering the high rate of unwanted pregnancies that occur globally. Numerous androgen-alone and androgen + progestin methods have been assessed in hormonal male contraceptive efficacy studies. Among these, the most promising strategies involve androgen and progestin regimens administered via injections and transdermal gels, although new oral formulations are currently being researched. Preliminary findings suggest that these methods are safe for short-term use, reversible, and generally more effective than condoms in most men, particularly within the confines of clinical trials.

Ongoing research aims to identify regimens that minimize adverse effects, reduce the time required for effectiveness and reversibility, and address the challenges posed by "non-responders," while also assessing long-term safety. In contrast, efficacy studies on non-hormonal methods have primarily focused on vas-occlusive techniques, highlighting the need for further research to establish their safety and reversibility. Several alternative non-hormonal targets are currently in preclinical development, but it may take several years before they become commercially available. Research indicates a high level of acceptability and the potential for a positive impact from the introduction of novel male contraceptives into the family planning sector. The advancement of reversible and safe male contraceptive options represents a significant move towards reproductive justice, empowering men to take control of their fertility and share family planning responsibilities with their partners.[10]

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