Safety, Efficacy, and Reversibility of Novel Male Contraceptives for Improved Pregnancy Prevention

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Abstract

Unintended pregnancy is a global issue that can result from contraceptive failure or from a lack of contraceptive use. A literature search was conducted to explore novel methods of male contraceptives being developed for improved pregnancy prevention. Seven articles were selected, reporting on either oral contraceptive pills, transdermal gel, injectable hormonal, or intravas polymer injection. The most common adverse events reported across all studies include changes in libido, mood, weight gain, acne, and headache. After reaching hormone and sperm concentration levels sufficient for pregnancy prevention, authors reported complete reversibility of contraceptive effects. Four studies described changes in various safety laboratory tests, including cholesterol and hemoglobin. Though more research is needed, novel male contraceptives may be effective in preventing unintended pregnancy.

Introduction

Nearly half (45%) of all pregnancies in the U.S. are estimated to be unintended.[1] Unintended pregnancies are associated with increased risk of negative outcomes for mothers and babies.[2,3] Currently, contraception is heavily reliant on female methods, as modern male methods only include condoms and vasectomy. Novel male methods being developed include both nonhormonal and hormonal methods. The availability of these new methods would broaden contraceptive choice and allow men to take a more active role in family planning. This review analyzes evidence to evaluate the safety, efficacy, and reversibility of novel male contraceptives compared to current methods in adult patients seeking to prevent pregnancy.

Methods

A literature search was completed using PubMed, Academic Search Ultimate, and Google Scholar. Seven articles were selected based on relevance to the research question and fulfillment of eligibility criteria.

- Inclusion Criteria
  - Adult participants
  - Clinical trial or randomized controlled trial of novel contraceptive method
  - Published between 2016 and 2022
  - Full text
  - In English (studies not limited to U.S.)

Results

Of the seven articles included, six studied novel male hormonal methods and one studied a nonhormonal method of intravas deferens polymer injection. All studies measured efficacy, either by serum gonadotropin suppression, sperm concentration, or pregnancy rate. All evaluated the safety of each given method, and some reported on the reversibility of its effects.

Table 1. Study and Method Characteristics

Study	Type	Contraceptive Method	Contraceptive Administration
1[4]	Double Blind RCT	Combination T and progestin gel	Daily
2[5]	Double Blind RCT	Modified testosterone oral contraceptive pill	Daily
3[6]	Non-blinded RCT	Combination T and progestin gel	Daily
4[7]	Double Blind RCT	Dimethandrolone oral contraceptive pill	Daily
5[8]	Phase III clinical trial	Intravas polymer Injection	Once
6[9]	Phase II clinical trial	Gluteal progesterone and testosterone injection	Every 3 months
7[10]	Double Blind RCT	Dimethandrolone oral contraceptive pill	Daily

Note: RCT= randomized controlled trial; T= testosterone

Table 2. Study Outcomes

Study	Efficacy	Safety	Reversibility
1	G.T. suppression ($p<0.001$)	rash, sunburn at gel site	Fully reversible
2	G.T. suppression ($p<0.029$)	↑ LDL-C, ↓ HDL-C, weight gain, acne, HA	N.S.
3	G.T. suppression, ↓ sperm conc. ($p<0.001$)	↓ hemoglobin, hematocrit, insulin sensitivity, △mood	Fully reversible
4	G.T. not significantly suppressed ($p>0.05$)	↑ LDL-C, ↓ HDL-C	N.S.
5	100% azoospermia by 6m; 0% pregnancy rate	Temporary scrotal and inguinal pain	N.S.
6	95.9% azoospermia by 6m; 1.57% preg. rate	Acne, injection site pain, increased libido, △mood	Fully reversible
7	G.T. suppression ($p<0.001$)	↑ weight, ↓ HDL-C, HA, decreased libido	Fully reversible

Note: G.T.= gonadotropins; LDL-C= low-density lipoprotein cholesterol; HDL-C= high-density lipoprotein cholesterol; HA= headache; N.S.= not studied

Discussion

- When reported, efficacy of novel male contraceptives was found to be higher than condoms (~18% failure rate).
  - While the data indicates that these methods will provide effective contraception, long term studies are necessary to measure the incidence of pregnancy and azoospermia after a complete cycle of spermatogenesis- approximately 72 days.
- Common adverse effects of these methods include acne, weight gain, and mood changes. No significant adverse effects were reported.
  - These side effects are comparable to those seen with current use of female hormonal contraceptives but may be viewed as unfavorable by some men.
- Common changes in safety laboratory tests included changes in lipid panels and complete blood counts.
  - Providers will need to be aware of these effects to determine which method is appropriate for a given patient.
- When reported, participants experienced full recovery of either serum hormones or sperm concentrations to baseline after discontinuing use. These methods may leave long term fertility intact, which would appeal to patients compared to poorly reversible vasectomy.
- Condoms remain the only method that protect against sexually transmitted infections.

Conclusion

The evidence from this paper demonstrates that both hormonal and nonhormonal methods of novel male contraception are well tolerated by most men, have acceptable safety profiles, and can be effective for pregnancy prevention. While they demonstrated overall safety in short term trials, long term studies are needed to demonstrate lasting safety and reversibility of each respective method for males seeking to utilize them. Longer studies that evaluate pregnancy rates will provide more evidence for or against use of novel contraceptives for pregnancy prevention compared to methods currently available.

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