Published in final edited form as:
Contraception. 2014 October ; 90(4): 407–412. doi:10.1016/j.contraception.2014.05.013.

Acceptability of a transdermal gel-based male hormonal contraceptive in a randomized controlled trial☆, ☆☆, ★

Mara Y. Roth[a,*], **Grace Shih**[b], **Niloufar Ilani**[c], **Christina Wang**[c], **Stephanie T. Page**[a], **William J. Bremner**[a], **Ronald S. Swerdloff**[c], **Regine Sitruk-Ware**[d], **Diana L. Blithe**[e], and **John K. Amory**[a]

[a]University of Washington, Department of Medicine and Center for Research in Reproduction and Contraception

[b]University of Washington, Department of Family Medicine

[c]Harbor-UCLA Medical Center and Los Angeles Biomedical Research Institute, Department of Medicine, Torrance, CA

[d]Center for Biomedical Research, Population Council, New York City, NY

[e]Contraceptive Discovery and Development Branch, NICHD, Bethesda, MD

Abstract

Objective—Fifty percent of pregnancies in the United States are unintended despite numerous contraceptive methods available to women. The only male contraceptive methods, vasectomy and condoms, are used by 10% and 16% of couples, respectively. Prior studies have shown efficacy of male hormonal contraceptives in development, but few have evaluated patient acceptability and potential use if commercially available. The objective of this study is to determine if a transdermal gel-based male hormonal contraceptive regimen, containing testosterone and Nestorone® gels, would be acceptable to study participants as a primary contraceptive method.

Study Design—As part of a three-arm, 6-month, double-blind, randomized controlled trial of testosterone and nestorone gels at two academic medical centers, subjects completed a questionnaire to assess the acceptability of the regimen. Of the 99 men randomized, 79 provided data for analysis.

☆Funding Sources: The study was supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development contracts HHSN 2752004033691 and HHSN 2751008060044U and the Population Council. The University of Washington site was supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development through cooperative agreement U54 HD-42454 as part of the Cooperative Contraceptive Research Centers Program and through K12 HD053984 and K23 HD073164-02. The Los Angeles Center was supported by the Endocrinology, Metabolism and Nutrition training Grant (T32 DK007571) and the UCLA Clinical and Translational Science Institute (UL1TR000124) at Harbor-UCLA Medical Center and Los Angeles Biomedical Research Institute.

☆☆Trial registration number: National Clinical Trial no. 00891228 and 00229593.

★Disclosure Statement:
MYR, GS, NI, RSW and DLB having nothing to disclose.

*Corresponding author at: University of Washington, 1959NE Pacific Street, Box 357138, Seattle,WA, 98195. Tel.: +1-206-543-3470; fax: +1-206-616-0499. mylang@u.washington.edu (M.Y. Roth).

Results—Overall, 56% (44/79) of men were satisfied or extremely satisfied with this gel-based method of contraception, and 51% (40/79) reported that they would recommend this method to others. One third of subjects (26/79) reported that they would use this as their primary method of contraception if it were commercially available today. However, men with concerns about sexually transmitted disease were significantly less satisfied than men without such concerns (p=0.03).

Conclusions—A majority of the men who volunteered to participate in this trial of an experimental male hormonal contraceptive were satisfied with this transdermal male hormonal contraceptive. If commercially available, a combination of topical nesterone and testosterone gels could provide a reversible, effective method of contraception that is appealing to men.

Implications—A substantial portion of men report they would use this transdermal male contraceptive regimen if commercially available. This method would provide a novel, reversible method of contraception for men, whose current choices are limited to condoms and vasectomy.

Keywords

Contraception; Acceptability; Testosterone; Nestorone; Spermatogenesis

1. Introduction

Unintended pregnancies account for 50% of pregnancies in the United States despite numerous contraceptive methods available to women. The only contraceptive methods currently available to men are vasectomy and condoms, used by 10% and 16% of couples, respectively [1]. Development of male hormonal contraceptives has been ongoing for many years and requires the administration of exogenous testosterone (T) combined with a progestin to effectively suppress the secretion of gonadotropins and subsequently suppress spermatogenesis [2]. Suppression of sperm concentrations to below 1 million/mL results in fertility rates commensurate with female oral contraceptive pills [3].

General interest regarding hypothetical male hormonal contraceptives is high across various cultures and ethnic groups [4–6], and women in stable monogamous relationships report that they would trust their partner to use a male hormonal contraceptive [7]. While no commercially available male hormonal contraceptive exists, several efficacy trials have studied various methods of hormone administration, including injections, implants, gels and combinations thereof [3,8–12]. However, little information regarding the acceptability of these approaches to men has been reported, and no information on a gel-based male hormonal contraceptive regimen is available.

To assess the acceptability of a transdermal male hormonal contraceptive regimen in men participating in a 6-month, two-site, double-blind, randomized controlled trial of T and nestorone (NES) gels, we asked subjects to complete an acceptability questionnaire to assess overall contraceptive attitudes and acceptability of the method. We hypothesized that the majority of subjects would find a gelbased male hormonal contraceptive regimen acceptable for long-term use if it were commercially available.

2. Materials and methods

2.1. Study design

The study design has been previously reported [13,14]. In brief, healthy male volunteers were enrolled at two academic medical centers as part of the Contraceptive Clinical Trial Network. After randomization to one of three treatment groups: (a) T gel 10 g+placebo gel (T+NES 0); (b) T gel 10 g+8 mg NES gel (T+NES 8); (c) T gel 10 g+12 mg NES gel (T +NES 12); gels were applied daily for 20–24 weeks. Subjects completed acceptability questionnaires at 12 and 24 weeks of treatment. Subjects who dropped out of the study early but returned for an end-of-study visit completed an "end of treatment" acceptability questionnaire at their exit visit. All subjects provided written consent prior to the initiation of screening and study procedures.

NES, a 19-norprogesterone-derived progestin with no androgenic, estrogenic or glucocorticoid activity [15,16], is effective at suppressing gonadotropins when combined with T gel in men [17]. T gel (Testogel®) was manufactured by Besins Healthcare S.A. (Brussels, Belgium) and supplied by GOOGLIFE Healthcare (Den Haag, the Netherlands). NES and placebo gels were produced by Antares Pharma (Basel, Switzerland) based on a formulation developed by the Population Council (New York City, NY, USA). This trial was registered at www.clinicaltrials.gov, National Clinical Trial no. 00891228 and 00229593.

2.2. Acceptability questionnaire

As no validated instruments exist to assess the acceptability of male hormonal contraceptives, we adapted a previously published acceptability questionnaire [18]. The questionnaire was based upon earlier questionnaires published in male contraceptive acceptability studies [10,19–22] and included questions about specific characteristics of the gels applied, overall acceptability, likelihood of using the regimen if commercially available and current contraceptive use.

Using a 5-point Likert scale, subjects were asked to select *strongly disagree, disagree, undecided, agree or strongly agree* to the following statements: "Overall, I was satisfied with this investigational method of contraception," "If available today, I would use this method of contraception as my primary method of contraception" and "I would recommend this method of contraception to others." Using the same scale, subjects were asked to respond to the following statements about each gel: "The gel was easy to use," "The gel smelled good," "The gel dried quickly on my skin," "The gel left my skin feeling sticky or greasy," "Applying the gel interfered with my daily routine," "The gel was messy to use," "The gel irritated my skin" and "The gel interfered with my sexual activities."

Subjects were asked a series of questions about current contraceptive practices including relationship status and the current method used by the subject or their partner most often. Subjects were asked to select *very dissatisfied, mostly dissatisfied, neutral or mixed, mostly satisfied* and *very* satisfied to the question, "How satisfied are you with the contraceptive method you or your partner have used most often?" Subjects were asked to select *a lot better, a little better, about the same, a little worse* or *a lot worse* to the following

statements: “How did this method of contraception compare with your expectations?” and “How would you compare this method of contraception to the method of contraception you or your partner has usedmost often?” Lastly, subjects were asked to select *very important, important, moderately important, of little importance* or *unimportant* to the question, “How important is protection from sexually transmitted diseases in your contraceptive choice?”

2.3. Statistical analysis

There were no significant differences in the responses between the three treatment groups; so all treatment groups were combined for this analysis. In addition, there were no differences in Week 12 versus Week 20–24 responses; therefore, only the Week 20–24 data are presented. Analysis was done as an intent-to-treat analysis including all 79 subjects who completed the questionnaires. A sensitivity analysis was also completed using the 55 subjects who were considered efficacy evaluable and were compliant with the full 20–24 weeks of treatment. For ease of presentation and analysis, answers are grouped as *strongly disagree/disagree, strongly agree/agree, a lot better/better* and *a lot worse/worse*. Outcomes were compared using an extended chi-square test, or Fisher's Exact Test as appropriate. For all comparisons, an alpha <0.05 was considered significant. Statistical analyses were performed using STATA Version 12.1 (College Park, TX, USA).

3. Results

3.1. Baseline characteristics

Of the 99 subjects randomized, 79 subjects completed the end-of-treatment acceptability questionnaire, including 17 of 37 subjects who dropped out of the study prior to Week 20–24. Twenty subjects terminated the study early and did not return for an end-of-treatment visit.

The mean age of the enrolled subjects was 27, ranging from age 18 to 50. Sixty-seven percent were Caucasian, 15% African American, 14% Asian and 4% of Native American or Native Hawaiian descent. Baseline contraceptive use and relationship characteristics are shown in Table 1. Contraceptive use did not differ by age (p=0.8) or ethnicity (p=0.6). Fifty-eight percent (46/79) of subjects reported satisfaction with their current method of contraception and 11% (9/79) of subjects reported dissatisfaction with their current method of contraception. Of those “most dissatisfied” or “somewhat dissatisfied,” all were either using condoms or a combination of condoms and a female pill or patch for their current method of contraception.

In comparing the full cohort of 79 subjects to the 55 men deemed efficacy evaluable, there was no statistically significant differences in baseline contraceptive use or relationship characteristics. While 60% (33/55) of efficacy evaluable subjects reported satisfaction with their current method of contraception and 13% (7/55) reported dissatisfaction, which was not statistically different from the full cohort.

3.2. Overall acceptability

A majority of subjects were satisfied with this investigational method of contraception (58%, 44/79) and would recommend this method of contraception to others if it were commercially available (53%, 40/79). About a third of subjects (34%, 26/79) reported that they would use this gel-based male hormonal contraceptive as their primary method of contraception if it were available today. There was no association between likelihood of using this contraceptive regimen and age (p=0.31) or relationship status (p=0.47). There was an interaction between ethnicity and likelihood of using this form of contraception (p=0.05), with African American men reporting the least interest in using this contraceptive regimen, and Asian and Caucasian men most likely to use this regimen.

In comparison to current contraceptive use, 34% (27/79) of subjects answered that this experimental method of contraception was better than their current method of contraception, whereas 35% (28/79) answered that this method was worse. There was no significant interaction between current use of condoms for contraception and overall satisfaction (p=0.46) or likelihood of using this method as a primary method of contraception (p=0.23). However, there was a strong negative association between concern about sexually transmitted disease and both overall satisfaction (p=0.03) and likelihood of using this method as a primary form of contraception (p=0.02). Subjects who reported that protection from sexually transmitted diseases was important in their contraceptive choice were significantly less likely to agree with the statement, “Overall, I was satisfied with this method of contraception” and “I would use this method of contraception as my primary method.”

Among the 55 subjects who were efficacy evaluable, there was no difference when compared to the full cohort of 79 subjects in the overall satisfaction, likelihood of using or recommending this male hormonal contraceptive regimen. Similarly, neither overall satisfaction with this method of contraception nor likelihood of using this contraceptive regimen if it were commercially available was affected by current condom use (p=0.21 and p=0.08, respectively). As seen with the full group of subjects, there was a strong negative association between overall satisfaction with this gel-based contraceptive method and concern for protection from sexually transmitted diseases (p=0.004).

3.3. Assessment of gel formulation

T gel and NES gels were applied separately in this study as either two sachets applied to the arms and chest daily (T) or dispensed in a pump and applied to the abdomen daily (NES). The assessment of gel characteristics was similar for the two gels (Table 2), except in response to the statement, “The gel dried quickly on my skin.” Significantly more subjects agreed or strongly agreed with this statement for the T gel than the NES gel (p=0.001).

The responses to the gel acceptability questions were not different among the 55 subjects who were efficacy evaluable as compared to the full cohort of 79 subjects.

4. Discussion

In this report, we demonstrate that daily application of T and NES gels is an acceptable form of contraception for the majority of subjects in a 6-month male hormonal contraceptive trial. Given that this regimen was previously shown to be effective for nearly 90% of men at suppressing sperm concentrations down to a level effective for preventing pregnancy (<1 million/mL) [13], its acceptability is of great interest to further develop this contraceptive method into a commercially available one.

Overall acceptability of this regimen was high and comparable to both an injection-only male hormonal contraceptive regimen [19] and a combination of T gel and injections of depomedroxyprogesterone acetate every 3 months [18]. Although it is difficult to compare results from clinical trials with population data, it is worth noting that the probability of women discontinuing oral contraceptive pills is estimated to be 31% and 47% within 6 and 12 months of use, respectively, in a general population study [23]. Discontinuation rates were higher with all other contraceptive methods.

While overall acceptability was high, a smaller number of subjects, 34%, reported that they would use this method as their primary method of contraception. The concern about risk of sexually transmitted diseases was a significant confounder when addressing whether men would use this method of contraception. The acceptability questionnaire did not address secondary forms of contraception or why a subject would choose not to use this method as a primary method of contraception. In addition, this study did not ask about sexual preference, which could confound the results regarding whether a man would use this for contraception. Future studies will include questions tailored to improve our understanding of overall contraceptive choices among men, and why fewer men would use this regimen than would recommend it to peers.

In this study, the test medication was administered as two separate gels — one administered by sachets and one by pump. Both gels dry in less than 5 min, and inconvenience of the daily gel routine did not appear to be a large factor in acceptability. In terms of the two different gels used in this study, they were similarly acceptable to men with no differences in ease of use or perceptions of interference with other activities. While no studies have directly compared acceptability of hormone replacement by gel versus patch, prior studies of T and estradiol topical preparations show consistently fewer adverse events related to skin irritation or rashes among the gels [24–26]. In addition, gel formulations account for the majority of T replacement in the United States [27]. Future studies will test a single gel regimen that contains both T and NES, which could improve appeal to men.

This study has several limitations, including the lack of a validated questionnaire to assess general acceptability of a contraceptive regimen in men. In addition, this randomized controlled trial enrolled healthy volunteers which may not be representative of the general population of men. However, this analysis included acceptability data from all men enrolled in the study, including those who exited the study early, thus including subjects who may have dropped out due to their dislike of the medication regimen. A sensitivity analysis was performed looking specifically at men who completed the full 20–24-week treatment phase

of the study and specifically at men who dropped out early from the study and found no significant differences in any of the acceptability questions. In addition, none of the subjects who dropped out early from the study cited dislike of the study drug as their reason for leaving the study. Lastly, this study did not assess the acceptability of the gel-based regimen to the study subjects' partners. Only one prior contraceptive study enrolling married men solicited input regarding acceptability of the regimen from the subjects' wives [21].

In conclusion, this study demonstrates that daily application of a topical gel-based male hormonal contraceptive regimen is acceptable to over half of men enrolled in a male hormonal contraceptive trial. Over a third of men report they would use this as their primary form of contraception if it were commercially available. These data support further development of a daily gel-based male hormonal contraceptive regimen with the ultimate goal of a safe, effective, reversible and easy-to-use contraceptive option for men.

Acknowledgments

The authors acknowledge the gift of T gel through Paul Piette, MD, Besins Health Care International; the help and assistance provided by Sharon Midler and her team for monitoring the study at Health Decisions; Elizabeth Ruiz, Xiao-Dan Han, Kathy Winter, Robert Bale Jr., Iris Nielsen, Connie Pete and Dorothy McGuinness for their help in coordinating the study; Christin Snyder, MD, for helping recruit and evaluate patients at the UW site; Andrew Leung, HTC, Sima Baravarian, PhD, and technologists of the Hormone and Metabolic Research Laboratory at Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center for all the hormone analyses.

CW receives research support from Clarus Therapeutics, Lilly, Besins Health Care and Lipocine.

STP serves on the Advisory Board for Besins Health Care.

WJB serves as a consultant for Repros Pharmaceuticals.

RSS receives research support from Clarus Therapeutics and Novartis.

JKA receives research support from Clarus Therapeutics.

References

1. Mosher, WD.; Jones, J. Use of Contraception in the United States: 1982–2008. Hyattsville, MD: U. S. Department of Health and Human Services Hyattsville; 2010.
2. Page ST, Kalhorn TF, Bremner WJ, Anawalt BD, Matsumoto AM, Amory JK. Intratesticular androgens and spermatogenesis during severe gonadotropin suppression induced by male hormonal contraceptive treatment. J Androl. 2007; 28(5):734–741. [PubMed: 17494097]
3. Gu Y, Liang X, Wu W, Liu M, Song S, Cheng L, et al. Multicenter contraceptive efficacy trial of injectable testosterone undecanoate in Chinese men. J Clin Endocrinol Metab. 2009; 94(6):1910–1915. [PubMed: 19293262]
4. Heinemann K, Saad F, Wiesemes M, Heinemann LA. Expectations toward a novel male fertility control method and potential user types: results of a multinational survey. J Androl. 2005; 26(2): 155–162. [PubMed: 15713817]
5. Martin CW, Anderson RA, Cheng L, Ho PC, van der Spuy Z, Smith KB, et al. Potential impact of hormonal male contraception: cross-cultural implications for development of novel preparations. Hum Reprod. 2000; 15(3):637–645. [PubMed: 10686211]
6. Heinemann K, Saad F, Wiesemes M, White S, Heinemann L. Attitudes toward male fertility control: results of a multinational survey on four continents. Hum Reprod. 2005; 20(2):549–556. [PubMed: 15608042]
7. Glasier AF, Anakwe R, Everington D, Martin CW, van der Spuy Z, Cheng L, et al. Would women trust their partners to use a male pill? Hum Reprod. 2000; 15(3):646–649. [PubMed: 10686212]

8. Liu PY, Swerdloff RS, Anawalt BD, Anderson RA, Bremner WJ, Elliesen J, et al. Determinants of the rate and extent of spermatogenic suppression during hormonal male contraception: an integrated analysis. J Clin Endocrinol Metab. 2008; 93(5):1774–1783. [PubMed: 18303073]

9. World Health Organization Task Force on Methods for the Regulation of Male Fertility. Contraceptive efficacy of testosterone-induced azoospermia in normal men. Lancet. 1990; 336(8721):955–959. [PubMed: 1977002]

10. World Health Organization. Contraceptive efficacy of testosterone-induced azoospermia and oligozoospermia in normal men. Fertil Steril. 1996; 65(4):821–829. [PubMed: 8654646]

11. Turner L, Conway AJ, Jimenez M, Liu PY, Forbes E, McLachlan RI, et al. Contraceptive efficacy of a depot progestin and androgen combination in men. J Clin Endocrinol Metab. 2003; 88(10): 4659–4667. [PubMed: 14557437]

12. Wang C, Swerdloff RS. Hormonal approaches to male contraception. Curr Opin Urol. 2010; 20(6): 520–524. [PubMed: 20808223]

13. Ilani N, Roth MY, Amory JK, Swerdloff RS, Dart C, Page ST, et al. A new combination of testosterone and nestorone transdermal gels for male hormonal contraception. J Clin Endocrinol Metab. 2012; 97(10):3476–3486. [PubMed: 22791756]

14. Roth MY, Ilani N, Wang C, Page ST, Bremner WJ, Swerdloff RS, et al. Characteristics associated with suppression of spermatogenesis in a male hormonal contraceptive trial using testosterone and Nestorone(r) gels. Andrology. 2013; 1(6):899–905. [PubMed: 24123845]

15. Kumar N, Koide SS, Tsong Y, Sundaram K. Nestorone: a progestin with a unique pharmacological profile. Steroids. 2000; 65(10–11):629–636. [PubMed: 11108869]

16. Sitruk-Ware R, Small M, Kumar N, Tsong YY, Sundaram K, Jackanicz T. Nestorone: clinical applications for contraception and HRT. Steroids. 2003; 68(10–13):907–913. [PubMed: 14667982]

17. Mahabadi V, Amory JK, Swerdloff RS, Bremner WJ, Page ST, Sitruk-Ware R, et al. Combined transdermal testosterone gel and the progestin nestorone suppresses serum gonadotropins in men. J Clin Endocrinol Metab. 2009; 94(7):2313–2320. [PubMed: 19366848]

18. Amory JK, Page ST, Anawalt BD, Matsumoto AM, Bremner WJ. Acceptability of a combination testosterone gel and depomedroxyprogesterone acetate male contraceptive regimen. Contraception. 2007; 75(3):218–223. [PubMed: 17303493]

19. Meriggiola MC, Cerpolini S, Bremner WJ, Mbizvo MT, Vogelsong KM, Martorana G, et al. Acceptability of an injectable male contraceptive regimen of norethisterone enanthate and testosterone undecanoate for men. Hum Reprod. 2006; 21(8):2033–2040. [PubMed: 16731547]

20. Ringheim K. Evidence for the acceptability of an injectable hormonal method for men. Fam Plann Perspect. 1995; 27(3):123–128. [PubMed: 7672104]

21. Zhang L, Shah IH, Liu Y, Vogelsong KM. The acceptability of an injectable, once-a-month male contraceptive in China. Contraception. 2006; 73(5):548–553. [PubMed: 16627044]

22. Sjogren B, Gottlieb C. Testosterone for male contraception during one year: attitudes, well-being and quality of sex life. Contraception. 2001; 64(1):59–65. [PubMed: 11535215]

23. Vaughan B, Trussell J, Kost K, Singh S, Jones R. Discontinuation and resumption of contraceptive use: results from the 2002 National Survey of Family Growth. Contraception. 2008; 78(4):271–283. [PubMed: 18847574]

24. Steidle C, Schwartz S, Jacoby K, Sebree T, Smith T, Bachand R, et al. AA2500 testosterone gel normalizes androgen levels in aging males with improvements in body composition and sexual function. J Clin Endocrinol Metab. 2003; 88(6):2673–2681. [PubMed: 12788872]

25. Mazer N, Bell D, Wu J, Fischer J, Cosgrove M, Eilers B. Comparison of the steady-state pharmacokinetics, metabolism, and variability of a transdermal testosterone patch versus a transdermal testosterone gel in hypogonadal men. J Sex Med. 2005; 2(2):213–226. [PubMed: 16422889]

26. Hirvonen E, Cacciatore B, Wahlström T, Rita H, Wilén-Rosenqvist G. Effects of transdermal oestrogen therapy in postmenopausal women: a comparative study of an oestradiol gel and an oestradiol delivering patch. Br J Obstet Gynaecol. 1997; 104(Suppl 16):26–31. [PubMed: 9389780]

27. Layton JB, Li D, Meier CR, Sharpless JL, Stürmer T, Jick SS, et al. Testosterone lab testing and initiation in the United Kingdom and the United States, 2000 to 2011. J Clin Endocrinol Metab. 2014; 99(3):835–842. [PubMed: 24423353]

Table 1

Baseline current relationship and contraceptive use of all study subjects (and their female partner)

Current relationship	*N*=79 (%)	Mean age (range)
Steady dating	29 (37)	28 (19–48)
Casual partners	11(14)	25 (19–50)
Married	11(14)	36 (23–44)
Cohabitating	9 (11)	31 (19–46)
No current partner	19 (24)	33 (18–50)
Current contraception	*N*=79 (%)	Mean age (range)
Condoms only	33 (42)	33 (19–50)
Condoms and female pill/patch	13 (16)	30 (19–48)
Female pill/patch only	13 (16)	29 (21–48)
Rhythm method/withdrawal	6 (8)	28 (19–42)
Intrauterine device/vaginal ring	5 (6)	31 (23–44)
Depomedroxyprogesterone acetate injection	1 (1)	27
Do not know/none	8 (10)	33 (18–46)

Table 2

Assessment of T gel and NES gel during treatment (*N*=79)

Questionnaire statement	T gel, *n* (%)			NES gel, *n* (%)		
	Strongly disagree/disagree	Undecided	Agree/Strongly agree	Strongly disagree/disagree	Undecided	Agree/Strongly agree
The gel was easy to use	11 (14)	10 (13)	55 (70)	9 (11)	8 (10)	59 (75)
The gel smelled good	38 (48)	25 (32)	13 (16)	28 (35)	32 (41)	16 (20)
The gel dried quickly on my skin*	14 (18)	8 (10)	54 (68)	35 (44)	9 (11)	32 (41)
The gel left my skin feeling sticky or greasy	36 (46)	13 (16)	25 (32)	29 (37)	14 (18)	33 (42)
Applying the gel interfered with my daily routine	43 (54)	14 (18)	19 (24)	45 (57)	13 (16)	18 (23)
The gel was messy to use	29 (37)	14 (18)	32 (41)	39 (49)	9 (11)	28 (35)
The gel irritated my skin	71 (90)	2 (3)	3 (4)	71 (90)	4 (5)	1 (1)
The gel interfered with my sexual activities	51 (65)	10 (13)	15 (19)	52 (66)	12 (15)	12 (15)

Note: Percentages do not add up to 100% as three subjects did not answer these questions.

*p=0.001, p value was not significant for all other comparisons.