Adolescents and Young Women's Use of a Microbicide Surrogate Product When Receiving Oral Sex

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Abstract

Study Objective—Genital herpes, which can be spread through oral sex, is an important target for microbicides. We examined episode-specific predictors of young women's receptive oral sex and of microbicide surrogate use.

Design—Longitudinal study

Setting—Participants were recruited to participate in a microbicide acceptability study from adolescent clinics and local colleges and through snowballing.

Participants—Young women (ages 14 to 21 years) who reported sexual contact on at least one weekly phone interview (n = 181) were included from the larger sample of 208 young women.

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Main Outcome Measures—On weekly diary phone interviews, participants reported whether or not their last sexual contact included receptive oral sex and whether or not their last sexual contact included use of a microbicide surrogate.

Results and Conclusions—Participants reported a total of 1042 episodes of sexual contact; 311 included receptive oral sex and 354 included microbicide surrogate use. Being older, having sex for the first time with a partner, and having given oral sex were associated with having received oral sex during a sexual episode. Being older, being African American, and having discussed the microbicide surrogate with their partner were associated with having used the microbicide surrogate use during a sexual episode. These results indicate that oral sex should be considered in the design of clinical trials. Future studies need to evaluate ways to promote consistent microbicide use in the context of receiving oral sex as well as those factors (e.g., taste, pleasure) which may serve as a barrier.

Keywords

sexually transmitted infections; genital herpes; oral sex; microbicides; adolescents

Introduction

Recently, clinical trials of topical microbicides have had promising results for the prevention of both HIV and herpes simplex virus (HSV) type 2 infections.[1-3] However, these products must be used during each sexual encounter, as reduction rates of HIV acquisition were found to be greater when the product was used more consistently.[2] Little is known about women's use of microbicides during oral sex, although it has been hypothesized that a woman may be less likely to use a microbicide when she receives oral sex due to users/partners' concerns regarding taste and smell of the microbicide.

Genital herpes is an important target for microbicides, because of its' significant physical and psychosocial morbidities for the individual[4], serious consequences for neonates,[5] and its' association with increased HIV transmission and acquisition.[6, 7] HSV types 1 and 2 infect the mouth and the genitals and the virus is shed in the absence of symptoms, so can be transmitted at any time from the mouth to the genitals.[8] In recent years and across several countries, the rates of genital herpes attributable to HSV-1 have increased dramatically,[9-14] which may be due to an increase in oral sex practices.[15] Thus, the relationship between microbicide use and oral sex is particularly relevant for genital herpes prevention and for the design of a microbicide trial with acquisition of genital herpes as an endpoint.

Since microbicides are still in development, surrogate products have been used to increase understanding of the behavioral and attitudinal issues associated with microbicide acceptability.[16] There may be some product-specific issues which will impact use of microbicides during receptive oral sex (e.g., taste) that will have to be understood in the context of each candidate microbicide. However, studies of surrogates can help us understand oral sex practices and help to design clinical trials of candidate microbicides.

Previously, in a study of adolescent girls and young women's use of a surrogate product, we found that African-American girls were significantly less likely to report a history of oral

sex than whites and Hispanics and also reported a later age of initiating oral sex than the other two race/ethnicities.[17] While most young women were willing to try the microbicide surrogate, initial use and frequency of use depended on their characteristics (i.e., age and sexual experience) and perceptions of the product (e.g., comparison to condoms, experience of sexual pleasure).[15, 18] We did not, however, examine episode predictors of use. Thus, the purpose of this analysis was to examine episode specific predictors of: 1) young women's receptive oral sex and 2) their use of a microbicide surrogate.

Material and Methods

As previously described,[18] 208 females (14 to 21 years) who had ever had penile-vaginal sex were recruited from clinics and colleges and through snowball sampling to participate in a 6 month longitudinal study examining the use of a microbicide surrogate, either a gel-filled applicator -Replens® Vaginal Moisturizer (Warner Wellcome, Morris Plains, NJ) or a suppository- Lubrin® Insert (Bradley Pharmaceuticals, Fairfield, NJ). Participants were asked to use the product of their choice with sexual intercourse. Participants received $30 for each completed face- to-face interview and an additional $3 for each completed "weekly" telephone interview. The study was approved by the Institutional Review Board at the University of Texas Medical Branch in Galveston.

The present sample was limited to those who reported sexual contact on at least one weekly interview. Analyses were based on data collected at intake (i.e., age and race- ethnicity), and data collected weekly regarding their last sexual contact. Race/ethnicity was collapsed into: Non-Hispanic white/other, African-American, and Hispanic. Questions regarding their last sexual contact relevant to this analysis were: gender of their partner, whether this was the first time they had sex with that partner (partner type), whether the sexual experience included vaginal sex, receptive oral sex, and giving oral sex, whether they talked to the partner about using the surrogate, and whether they used the surrogate.

Data were analyzed using SAS 9.2.[19] To assess the first objective of examining episode specific predictors of young women's receptive oral sex, age, race/ethnicity, partner type (first time having sex with that partner), and oral sex (giving) were entered into a repeated measure logistic regression model utilizing generalized estimating equations (GEE) to predict receptive oral sex at each sexual episode. To evaluate the second objective of examining episode specific predictors of young women's use of a microbicide surrogate, age, race/ethnicity, first time having sex with that partner, oral sex (giving), oral sex (receptive), and discussion with partner about use were entered into a repeated measure logistic regression model utilizing GEE to predict surrogate use during a sexual episode. Significance was set at the $p < 0.05$ level.

Results

Of the 208 participants, 181 reported on a last episode of sexual contact at least once. Participants had a mean age of 18.3 years (sd = 1.92); 38.7% were African-American, 33.2% were Hispanic, and 28.2% were Non-Hispanic White/other. Participants completed an average of 5.8 (sd = 4.43) weekly interviews wherein they reported on their last sexual

contact, an average of 1.73 (sd = 2.56) weekly interviews wherein they reported receiving oral sex, and an average of 1.97 (sd = 2.93) weekly interviews wherein they reported surrogate use.

A total of 1042 episodes of sexual contact were reported. Most of the episodes were heterosexual (n = 1014); 105 of the episodes were with a person with whom they had not previously had sex. The 1042 episodes included 727 of vaginal sex only, 304 of both oral and vaginal sex, 5 in which only oral sex was received, 4 in which only oral sex was given, and 2 in which oral sex was given and received without vaginal intercourse. Ninety-seven participants (54%) reported receiving oral sex across 311 of the 1042 sexual episodes. Product use was discussed in 289 episodes. Use of the product occurred in 354 episodes with 110 (61%) participants reporting using the product.

The odds ratios and confidences intervals for the prediction of receptive oral sex are presented in Table 1. Age, partner type (first time having sex with that person), oral sex (i.e., given) significantly predicted having received oral sex. Contrary to previous research,[17] race/ethnicity did not significantly predict receptive oral sex. As age increased by one year, the odds of having received oral sex increased by 1.16 (CI 1.02-1.32). Those who gave oral sex were 8.62 (CI 5.58, 13.33) times more likely than those who did not give oral sex to have received oral sex. Participants who had sex with a partner with whom they had not previously had sex were 1.85 times (CI 1.12, 3.04) more likely to have received oral sex than those who had previously had sex with that partner.

The odds ratios and confidence intervals for the prediction of surrogate use are presented in Table 2. Age, race/ethnicity, and having discussed the surrogate with their partner were significantly associated with surrogate use in a sexual episode. As age increased by one year, the odds of having used the microbicide surrogate increased by 1.20 (CI 1.06, 1.37). African-Americans were 2.09 (CI 1.08, 4.01) times more likely than Non- Hispanic white women and 2.02 (CI 1.09, 3.74) times more likely than Hispanic women to have used the surrogate during a sexual episode. Non-Hispanic white and Hispanic women did not significantly differ from each other. Giving oral sex, partner type (first time having sex with that person), and having received oral sex were not related to surrogate use during a sexual episode. Oral sex occurred in 111/311 (36%) episodes in which the surrogate was used and in 243/731 (33%) in which there was no surrogate use.

Discussion

During this 6-month study, more than half of the young women received oral sex with approximately 30% of sexual episodes including receptive oral sex. Those with a new partner were more likely to have received oral sex. Thus, the design of microbicide trials for prevention of genital herpes will need to consider the risk of acquiring genital HSV through oral sex, particularly since these results suggest that those women mostly likely to be in the clinical trials (young adults and those with new partners) are more likely to receive oral sex.

Receiving oral sex was not associated with a decreased likelihood of using the microbicide surrogate which suggests that microbicides could be used during oral sex. However, the lack

of relationship should be interpreted with caution given the following limitations: a) information about the timing of decision-making or timing of oral sex and use was not available, and b) relatively little surrogate use was reported. Episodes in which microbicide surrogate use was discussed with a sexual partner were associated with a greater likelihood of surrogate use. Thus, if there were partner concerns about the use with oral sex, perhaps these concerns could be integrated into discussions prior to use.

There were limitations to this study. First, the analyses were based on a sample of sexual experienced young women who were willing to participate in a microbicide surrogate acceptability study and therefore may not generalize to other populations (e.g., older women). Secondly, as mentioned, the larger study on which these analyses are based was not specifically designed to examine oral sex in the context of surrogate use. Thus it may have been possible for young women to have had oral sex and to use the product during a sexual episode but to have timed them in a way that the two were not concurrent. Finally, the products used in this study were surrogates that were over the counter lubricants, and therefore results could possibly differ in the context of a sexual encounter using an actual microbicide.

The results of this study demonstrated that receptive oral sex will occur in the context of microbicide studies, at non-trivial rates. Some of these episodes may be protected by a microbicide and some may not, and the timing of oral sex relative to microbicide use may vary. Understanding how couples make decisions about oral sex and how that would relate to microbicide use is critical in providing anticipatory guidance to foster the use of microbicides across all episodes of sexual contact. Finally, researchers should consider the frequency of oral sex in designing microbicide trials in which the outcome (i.e., genital herpes) could be acquired either through vaginal or oral sex.

Acknowledgments

References

1. Andrei G, Lisco A, Vanpouille C, et al. Topical tenofovir, a microbicide effective against HIV, inhibits herpes simplex virus-2 replication. Cell Host Microbe. 2011; 10:379–89. [PubMed: 22018238]

2. Abdool Karim Q, Abdool Karim S, Frohlich J, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. Science. 2010; 329:1168–74. [PubMed: 20643915]

3. Mesquita P, Rastogi R, Segarra T, et al. Intravaginal ring delivery of tenofovir disoproxil fumarate for prevention of HIV and herpes simplex virus infection. J Antimicrob Chemother. 2012; 67:1730–8. [PubMed: 22467632]

4. Bickford J, Barton SE, Madalia S. Chronic genital herpes and disclosure…. The influence of stigma. Int J STD AIDS. 2007; 18:589–92. [PubMed: 17784999]

5. Nahmias AJ, Josey WE, Naib ZM, et al. Perinatal risk associated with maternal genital herpes simplex virus infection. Am J Obstet Gynecol. 1971; 110:825–37. [PubMed: 4327295]

6. Gupta R, Warren T, Wald A. Genital herpes. Lancet. 2007; 370:2127–37. [PubMed: 18156035]

7. Drake A, John-Stewart G, Wald A, et al. Herpes simplex virus type 2 and risk of intrapartum human immunodeficiency virus transmission. Obstet Gynecol. 2007; 109:403–9. [PubMed: 17267842]

8. Mertz GJ. Asymptomatic shedding of herpes simplex virus 1 and 2: implications for prevention of transmission. J Infect Dis. 2008; 198:1098–100. [PubMed: 18783317]

9. Kortekangas-Savolainen O, Vuorinen T. Trends in herpes simplex virus Type 1 and Type 2 Infections among patients diagnosed with genital herpes in a Finnish sexually transmitted disease clinic, 1994-2002. Sex Transm Dis. 2007; 34:37–40. [PubMed: 17195754]

10. Ribes J, Steele A, Seabolt J, et al. Six-years study of the incidence of herpes in genital and nongenital cultures in a Central Kentucky Medical Center patient population. J Clin Microbiol. 2001; 39:3321–5. [PubMed: 11526170]

11. Nilsen A, Myrmel H. Changing trends in genital herpes simplex virus infection in Bergen, Norway. Acta Obstet Gynecol Scand. 2000; 79:693–6. [PubMed: 10949236]

12. Christie S, McCaughey C, McBride M, et al. Herpes simplex type 1 and genital herpes in Northern Ireland. Int J STD AIDS. 8:68–9. [PubMed: 9043990]

13. Roberts C, Pfister J, Spear S. Increasing proportion of herpes simplex virus type 1 as a cause of genital herpes infection in college students. Sex Transm Dis. 2003; 30:797–800. [PubMed: 14520181]

14. Xu F, Sternberg MR, Kottiri BJ, et al. Trends in herpes simplex virus type 1 and type 2 seroprevalence in the United States. JAMA. 2006; 296:964–73. [PubMed: 16926356]

15. Lafferty WE, Downey L, Celum C, et al. Herpes simplex virus type I as a cause of genital herpes: Impact on surveillance and prevention. J Infect Dis. 2000; 181:1454–7. [PubMed: 10762576]

16. Tanner AE, Fortenberry JD, Zimet GD, et al. Young women's use of a microbicide surrogate: The complex influence of relationship characteristics and perceived male partners' evaluations. Arch Sex Behav. 2010; 39:735–47. [PubMed: 19224355]

17. Auslander B, Biro F, Succop P, et al. Racial/ethnic differences in patterns of sexual behavior and STI risk among sexually experienced adolescent girls. J Pediatr Adolesc Gynecol. 2009; 22:33–9. [PubMed: 19232300]

18. Short M, Succop P, Ugueto A, et al. Predictors of using a microbicide-like product among adolescent girls. J Adolesc Health. 2007; 41:357–62. [PubMed: 17875461]

19. SAS Institute. SAS for Windows, 9.2. Cary, NC: SAS Institute, Inc; 2002-2008.

Table 1

Univariate and Multivariate Repeated Measures Logistic Regression Analyses: Associations with Receptive Oral Sex

	Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (**per year**)	1.19 (1.04, 1.37)	.01	1.16 (1.02, 1.32)	.02
Race/ethnicity				
Non-Hispanic white vs Hispanic	1.96 (1.11, 3.46)	.02	1.16 (.64, 2.10)	.62
African-American vs Hispanic	1.24 (.66, 2.34)	.50	1.15 (.63, 2.08)	.65
African-American vs Non-Hispanic white	.63 (.35, 1.45)	.13	.99 (.54, 1.79)	.96
First time having sex with that person (yes vs no)	1.42 (.93, 2.20)	.11	1.85 (1.12., 3.04)	.02
Oral sex (given; yes versus no)	8.25 (5.32, 12.82)	<.0001	8.62 (5.58, 13.33)	<.0001

Table 2

Univariate and Multivariate Repeated Measures Logistic Regression Analyses: Associations with Microbicide Surrogate Use

	Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (**per year**)	1.18 (1.03, 1.35)	.02	1.20 (1.06, 1.37)	.02
Race/ethnicity				
Non-Hispanic white vs Hispanic	1.21 (.64, 2.27)	.56	.97 (.52, 1.81)	.92
African-American vs Hispanic	2.08 (1.16, 3.77)	.01	2.02 (1.09, 3.74)	.03
African-American vs Non-Hispanic white	1.73 (.92, 3.24)	.09	2.09 (1.08, 4.01)	.03
First time having sex with that person (yes versus no)	.75 (.52, 1.06)	.10	.75 (.50. 1.14)	.18
Oral sex (given; yes versus no)	1.03 (.70, 1.50)	.89	1.02 (.64, 1.62)	.93
Oral sex (receptive; yes versus no)	.96 (1.35, 1.47)	.80	.89 (.58, 1.37)	.60
Discussion with partner about surrogate (yes vs no)	4.93 (3.40, 7.13)	<.0001	5.38 (3.71. 7.81)	<.0001