Culture, Health & Sexuality: An International Journal for Research, Intervention and Care

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/tchs20

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Published online: 14 Apr 2010.

To cite this article: Elizabeth Greene, Georges Batona, Jyoti Hallad, Sethulakshmi Johnson, Stella Neema & Elizabeth E. Tolley (2010) Acceptability and adherence of a candidate microbicide gel among high-risk women in Africa and India, Culture, Health & Sexuality: An International Journal for Research, Intervention and Care, 12:7, 739-754, DOI: 10.1080/13691051003728599

To link to this article: http://dx.doi.org/10.1080/13691051003728599

Culture, Health & Sexuality
Vol. 12, No. 7, October 2010, 739–754

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(*Received 14 July 2009; final version received 24 February 2010*)

Vaginal microbicides currently under development are substances that may prevent the transmission of HIV. Qualitative, in-depth post-trial interview data from a Phase III clinical trial of 6% Cellulose Sulfate microbicide gel in two sites in Africa (Uganda and Benin) and two in India (Chennai and Bagalkot) were examined in order to better understand factors that influence microbicide acceptability and adherence in a clinical trial setting. Women found the gel relatively easy to use with partners with whom there were no expectations of fidelity, in situations where they had access to private space and at times when they were expecting to engage in sexual intercourse. Adherence to gel seemed significantly more difficult with primary partners due to decreased perceptions of risk, inconvenience or fear of partner disapproval. Findings suggest that women in a variety of settings may find a microbicide gel to be highly acceptable for its lubricant qualities and protective benefits but that adherence and consistent use may depend greatly on contextual and partner-related factors. These findings have important implications for future trial designs, predicting determinants of microbicide use and acceptability and marketing and educational efforts should a safe and efficacious microbicide be found.

Keywords: microbicide; acceptability; Africa; India; HIV prevention; adherence

Introduction

An estimated 33 million people were living with HIV in 2007; women account for half of all infections worldwide and for 75% of infections among young people aged 15–24 years in sub-Saharan Africa (UNAIDS 2008). Socio-political, economic, biological and sexual power imbalances leave women particularly vulnerable to HIV, especially as woman-initiated HIV prevention technologies are lacking (Beyrer 2007; Exner et al. 2003; Gupta 2002; Quinn and Overbaugh 2005). While condoms are highly effective at preventing HIV, the need for an acceptable, safe and effective method of protection that is not controlled by men is critical. Topical microbicides, which are applied vaginally or rectally to reduce transmission of HIV or other STIs, are in various stages of development and can potentially provide this much needed alternative.

There are currently six microbicide candidates in ongoing clinical trials and many more in early stages of development (Alliance for Microbicide Development 2009).

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ISSN 1369-1058 print/ISSN 1464-5351 online

DOI: 10.1080/13691051003728599
http://www.informaworld.com

Understanding factors that contribute to acceptability and consistent use is imperative to developing a successful microbicide. Previous microbicide acceptability research has focused on product attributes (Joglekar et al. 2007; Jones et al. 2008; Kilmarx et al. 2008; Mantell et al. 2005; Morrow et al. 2007; Ramjee et al. 2007). While product-associated characteristics are essential components of microbicide acceptability (Morrow and Ruiz 2008), inter-personal and contextual factors that shape adherence and actual use have emerged as critical issues to understand, both in a clinical trial setting and in considering how microbicides may realistically be used (Mantell et al. 2005; Montgomery et al. 2008; Rosen et al. 2008; Salter et al. 2008; Severy et al. 2005; Tanner et al. 2009; Woodsong and Alleman 2008).

Microbicide researchers commonly refer to the term 'acceptability' to mean satisfaction with the product and willingness to use it, as well as actual correct and consistent use (Mantell et al. 2005, 320; Severy and Newcomer 2005, 122; Severy et al. 2005, 47). However, recent literature suggests that acceptance of microbicides does not necessarily predict consistent or long-term use (Morrow and Ruiz 2008; Severy et al. 2005). Thus it is important to examine the concept of 'adherence' as well, defined as correct, consistent and sustained use. For the purposes of this paper, acceptability is defined as product satisfaction and intention to use.

A safe and effective microbicide has not been identified and, thus, Phase III effectiveness trials are currently the best approximation for a 'real world' context. They can provide valuable insights into the interpersonal, social and cultural factors affecting microbicide acceptability and adherence; however, few findings from these trials have yet been published, particularly pertaining to use-associated factors (Mantell et al. 2005; Morrow and Ruiz 2008). This paper aims to address current gaps in the literature by examining qualitative, in-depth data from a Phase III clinical trial of 6% Cellulose Sulfate microbicide gel from two sites in Africa and two in India in order to better understand various factors that influence the relationship between microbicide acceptability and adherence in a clinical trial setting with high-risk women.

Methods

Clinical trial

From 2004–2007, a randomised, double-blind, placebo-controlled Phase III clinical trial was carried out to assess the effectiveness of Cellulose Sulfate 6% vaginal microbicide gel in preventing transmission of HIV and other STIs. Women from three sites in Africa (South Africa, Uganda, Benin) and two sites in India (Chennai, Bagalkot), who were at least 18 years of age and at high risk for STIs and HIV, were recruited for the trial. Clinic staff and local non-governmental organisations working with these high-risk populations assisted in recruitment. Site initiation was staggered, beginning with South Africa and ending with Bagalkot (approximately one month before trial closure), resulting in a low number of participants in Bagalkot as compared to the other sites (Table 1). All participants provided written informed consent, had three or more sex partners in the three months before screening, had an average of three or more sex acts per week and were HIV-negative at the time of screening (Family Health International 2008; Van Damme et al. 2008). The trial ended prematurely in January 2007 after an interim analysis by an independent data monitoring committee found the Cellulose Sulfate 6% gel may have increased the risk of HIV infection as compared to the placebo (Van Damme et al. 2008).

Table 1. Behavioural and Social Sciences (BSS) data sources, with reference to clinical trial enrolment.

	India		Africa	
Data Sources	Bagalkot	Chennai	Benin	Uganda
Clinical trial participants[a]	23	255	238	306
BSS participants[b]	10	13	10	20

Notes: [a]Number randomised; [b]number who completed post-trial interview.

Behavioural and social sciences activities

Qualitative data collection activities in support of the clinical trial were carried out in three phases: (1) preparedness – conducted pre-trial with community groups and potential participants to assess hypothetical acceptability of gel and inform trial recruitment and retention; (2) on-going – conducted during the trial with community members and clinic staff only, to monitor community reactions to the trial; and (3) exit – conducted post-trial with former trial participants to explore their understanding and use of the study gel and assess how they understood the decision to end the trial (Family Health International 2008). The post-trial exit phase was added in a protocol amendment in February 2007 after the trial was terminated. Findings presented in this paper derive solely from analysis of these exit phase post-trial interviews with a subset of former trial participants (Table 1) from four sites (Uganda, Benin, Chennai, India and Bagalkot, India).[1] Family Health International's Protection of Human Subjects Committee and local Institutional Review Boards (IRB) for each site reviewed and approved the study. Local staff members were trained on research ethics, study procedures, including informed consent processes and qualitative data collection methods, and were purposely separate from clinical trial staff in order to reduce potential for social desirability bias in interviews.

Sample

Study participants for the post-trial interviews were selected non-randomly using convenience sampling and are not considered representative of the larger clinical trial study population. Because no permission was originally sought to contact participants for post-trial interviews, only those who returned to the clinic to learn the results after they were informed that the trial had ended prematurely and who agreed to be contacted to provide more information about their experiences were invited to participate in a post-trial interview. Staff in each site determined the number of interviews they would conduct (between 10 and 20) depending on the resources, staff, time available and number of women agreeing to participate. Interviews were initiated as soon as each site obtained local IRB approval for these activities, between February and August 2007.

Recruitment of high-risk women for the clinical trial resulted in most participants of the post-trial interviews being formal or informal sex workers. The social context of sex work is complex and differed greatly between the four sites; it is important to note some general differences. In Chennai, participants were self-identified sex workers, mostly street-based, though some also worked from lodges. Most Bagalkot participants were traditional *Devadasi* sex workers who lived in colonies, were brothel- or home-based and were accepted by their community. Some worked under *Gharwallis*, or madams, and others were independent; as a whole, they were highly organized. In Benin, most participants were brothel-based, self-declared sex workers, although some engaged in less

formal transactional sex and did not consider themselves sex workers. Ugandan participants included sex worker peer educators, as well as street- or bar/hotel-based sex workers.

Data analysis

Analysis focused on (1) participants' acceptance of the study gel and (2) their adherence to the study gel during the trial. Data analysed for this paper were exclusively in the form of in-depth interviews conducted post-trial closure with trial participants; each participant was interviewed once. Interviews were tape recorded with participant consent, transcribed and translated into either English or French (in the case of Benin).

Five members of the research team conducted a preliminary analysis of the post-trial interviews, following a process of reading, coding, data display and reduction (Ulin et al. 2005, 144). Broad themes were identified, a code list was developed by consensus and interpretations and results were summarised jointly to inform a final report (Family Health International 2008). Content was analysed using NVivo8. Adherence and acceptability codes were extracted and further analysed by two members of the research team. Emergent sub-themes were identified, recoded when applicable and entered into Excel matrices under broader thematic categories to track, quantify and compare themes (e.g. reasons for acceptability) and sub-themes (e.g. lubrication, protective benefits) within and between study sites. Memos based on these matrices were developed to summarise major findings.

Theoretical framework

A variation of the socio-ecological model (Mcleroy et al. 1988) provided an organizing framework. The model, presented in Figure 1, describes the multi-dimensional relationship between microbicide acceptability and adherence. Five concentric circles

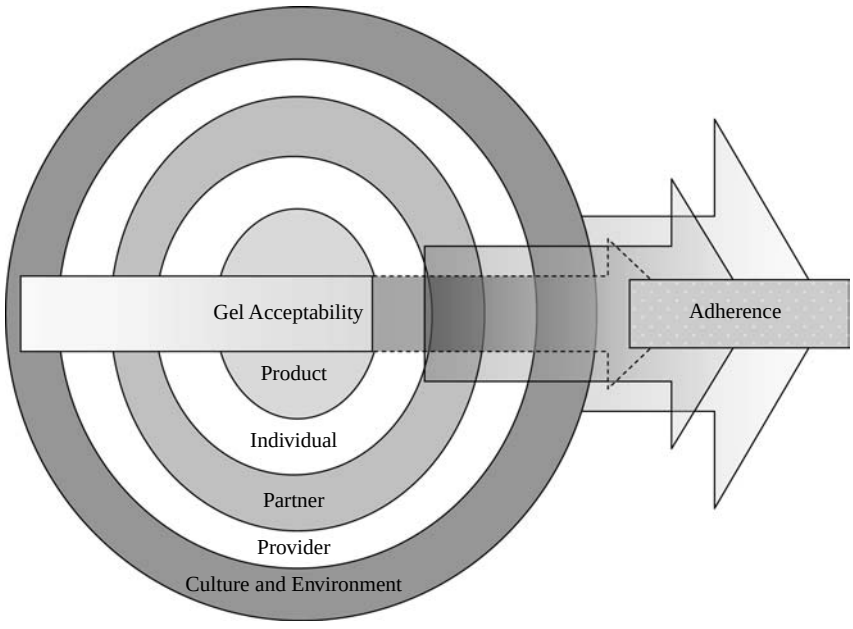

Figure 1. Socio-ecological framework.

represent different levels of influence: product, individual, partner, provider and culture and environment. As the figure demonstrates, acceptability influenced adherence and factors on all levels influenced both acceptability and adherence. While the findings are categorised into their most relevant level of influence, interconnections exist between the various levels. The following sections identify key issues that emerged in the analysis.

Results

Acceptability of the study gel

Product, individual, partner and cultural and environmental factors affected participants' acceptance of the study gel, which was overall very high. Table 2 presents some of these factors and the variations that exist between sites.

Product-related factors

Lubrication

Acceptability of the study gel was most strongly linked to the gel's physical characteristics. In particular, over two thirds of all participants stated they liked the gel because of its lubricant qualities, which facilitated sex. Variations in this attitude were linked to individual and partner preferences as well as cultural factors. While some participants did not specifically identify the lubricant trait as what they liked, many reported liking the gel because it made sex less painful or prevented the condom from breaking:

> It makes our work easier. We felt no pain. … When we use a condom alone we feel pain and we would even be unable to walk. Since using the gel, we had no pain. (Lakshmi, 38 years old, Chennai)

Table 2. Factors affecting study gel acceptability.

	Total ($n = 53$) *n* (%)	Bagalkot ($n = 10$)	Chennai ($n = 13$)	Benin ($n = 10$)	Uganda ($n = 20$)
Factors facilitating acceptability					
Product-related factors					
Lubrication/facilitation of sex	37 (70)	3	8	6	20
Other gel characteristics	11 (21)	1	2	0	8
Individual-related factors					
Protective benefits	23 (43)	6	10	4	3
Lack of adverse effects	15 (28)	7	1	5	2
Partner-related factors					
Partner accepts	12 (23)	0	3	1	8
Woman-controlled method	17 (32)	3	9	2	3
Factors inhibiting acceptability					
Product-related factors					
Application issues	18 (34)	0	6	2	10
Quantity of gel	8 (15)	0	0	1	7
Other gel characteristics	8 (15)	0	1	1	6
Partner-related factors					
Partner dislikes	9 (17)	1	3	0	5
Environmental factors					
Covert application	13 (25)	2	6	2	3

At least five participants from Uganda and two from Chennai also noted that this characteristic allowed them to increase their number of clients per day and thus make more money, a positive outcome in their opinion.

Application issues

Problems applying the gel accounted for most of the negative sentiments surrounding gel use. Overall, roughly one third of participants, mainly from Chennai, Benin and Uganda, cited some difficulty inserting the applicator at the beginning of the study. Most women who initially had difficulty inserting the gel were later counselled by clinic staff on proper insertion techniques. As one Chennai participant said:

> Gel use was easy for me. For two days to one month it was sticky because I didn't know how to use it. In the second month the doctor told me to insert it deeply and it would be fine. After that it was fine. (Radhika, 28 years old)

Other product characteristics

Seventeen participants indicated that other gel characteristics, such as odour, colour, temperature or consistency influenced their acceptance of the gel, either positively or negatively. This was most often discussed by Ugandan participants, six of whom liked the odourless nature of the gel. This may have been more important in Uganda as some women mentioned that traditional lubricants caused foul-smelling discharge. Most participants felt that the quantity of gel in the applicator was sufficient; however, several Ugandan participants felt the quantity was too much.

Individual factors

Perceived protective benefits of gel

Nearly half of all participants liked the gel because they felt it protected them from HIV and other infections. This sentiment varied by site and was more common in Bagalkot and Chennai, where women had the highest faith in the gel's effectiveness and the majority believed they were using Cellulose Sulfate as opposed to the placebo, despite trainings and other mechanisms undertaken to ensure all participants understood the study design. Several Bagalkot participants equated the presence of any gel in their applicators to 'medicine' or the Cellulose Sulfate gel. Chennai participants had a better understanding of the placebo concept, yet many reported they 'had a feeling' or just believed that their gel contained the active ingredient.

In some cases, participants' faith in the gel's effectiveness related to their own perceptions of risk. Many women in Chennai spoke of the importance of protecting their health yet frequently mentioned encounters with 'rowdies' or violent, often intoxicated clients who refused to wear condoms, suggesting their perceived risk of HIV may have been high. This increased perception of risk, desire to protect their health and lack of control over condom use may have amplified participants' faith in the protective capabilities of the gel, which seemed to be integral to acceptability. As one Chennai participant said:

> Some rowdies or policemen will have sex violently and so at that time we cannot use the condoms, but if we can use the gel at that time, it will help protect us. I have courage that for the clients like this we are able to use the gel. (Vidya, 38 years old)

This finding did not seem to hold true in Uganda and Benin, where, according to one Ugandan participant, women 'didn't care whether it healed the disease or not, but it lubricated them. Some women don't have the love and sexual urge for men and after one client another one follows' (Edith, 27 years old). Participants in these sites demonstrated a strong understanding of the placebo concept, felt it was impossible to know which gel they had been assigned and were less trusting of the gel's protective capabilities. As one woman from Benin stated, 'if I had believed in [the gel], I would have used it without a condom' (Justine, 22 years old).

Lack of adverse effects

Several participants reported at first being fearful of expected adverse effects from gel use; many, particularly in Bagalkot, felt positively about the gel when these effects failed to materialise:

> I never had any problems when I was using the gel. Some people do not adjust with these things. … Sometimes they lead to itching and many other problems. I never got any of those problems. (Priyanka, 28 years old, Bagalkot, when asked why she liked the gel)

In all sites, women reported their fears subsided after counselling and positive experiences with gel use.

Partner-related factors

Partner preferences

For some women, their partners' acceptance of the gel shaped their own acceptance, particularly in Uganda and Chennai. Partner preference for gel often related to lubrication:

> We liked the gel because it would lubricate us. It was also good because when you applied it before sex, the man would say 'you have lots of fluid'; some would even praise you because of the way they felt while with you. Because of the lubrication, the partner would say you are soft and nice. Even the condom would not tear. (Salma, 29 years old, Uganda)

In Uganda in particular, there seemed to be ethnic differences in preference for lubrication that affected male acceptance of the gel:

> A man can come when he is a Muganda [ethnic group] and he loves a Munyarwanda woman. And he may find a lot of vaginal fluid in that woman. … Now for the Baganda women if you are using that gel, a man may wonder and say 'Eeeh. I have never seen a Muganda woman with a lot of vaginal fluid like that.' … Women liked it because it helped them to perform like the Banyankole were performing. (Christine, 23 years old)

One third of participants in Chennai reported that partners complained of the gel's 'stickiness'. However, Uganda was the only site in which participants suggested that men may have a preference either for or against lubricated sex based on cultural inclinations.

Woman-controlled method of protection

Some participants in all sites, but particularly Chennai, liked the gel because they felt that it could be used without a partner's consent and sometimes without his knowledge, allowing them control over their own protection, unlike condoms:

> We go to different types of men. … We give them condoms and some men will be good and some others will be bad. We were using the gel for our sake, to keep our body healthy. It was good to us. (Divya, 23 years old, Bagalkot)

Cultural and environmental factors

Prior lubricant use

There seemed to be a relationship between culture of lubricant use in each site and how strongly participants liked the gel because of lubrication. Most Ugandan participants knew of herbs or traditional millet porridges commonly ingested or inserted vaginally to produce lubrication but said they dry quickly and produce foul-smelling discharge. Similarly, almost all Benin participants knew of other lubricants and many had used them in the past. Most participants from Uganda and Benin felt the Cellulose Sulfate gel was of superior quality to other lubricant options and said they would use a lubricant gel similar to it if one was available and affordable, regardless of whether it protected against HIV.

In contrast, few participants in Chennai and none in Bagalkot had previously used or heard of other lubricants. While most Chennai participants were open to the idea of using lubricants in the future, others suggested that they could stigmatise a woman as a prostitute. No participants in Bagalkot were receptive to this idea and many were distrusting of products that were not distributed by medical personnel.

Need for covert application of gel

Nearly half the women in Chennai, and several from Benin, Bagalkot and Uganda, felt that the requirement for pre-coital insertion of the gel was inconvenient when 'going outside' (conducting sex work from the street or lodges as opposed to homes) or when travelling. Women preferred to covertly apply gel but could not in these situations due to a lack of privacy.

Adherence to the study gel

Most participants initially reported adhering to gel and condoms at every sexual encounter, but further questioning revealed evidence of non-adherence (non-use or incorrect use of gel at every sexual encounter) by over three quarters of the post-trial interview participants. Bagalkot participants reported the highest adherence to gel and Chennai the lowest. Main reasons for non-adherence are presented in Table 3 and discussed below. Just over half of the participants reported consistently using a condom when using the gel.

Table 3. Factors contributing to non-adherence of study gel.

Factors contributing to non-adherence	Total ($n = 53$) n (%)	Bagalkot ($n = 10$)	Chennai ($n = 13$)	Benin ($n = 10$)	Uganda ($n = 20$)
Product-related factors					
Quantity and texture	6 (11)	1	2	1	2
Partner-related factors					
Non-use with primary partners	21 (40)	0	7	5	9
Non-use with certain clients	5 (9)	0	4	0	1
Provider-related factors					
Gel supply	7 (13)	0	3	2	2
Environmental factors					
Inconvenient location	10 (19)	2	6	0	2

While several women mentioned occasionally using condoms without gel, only a few reported ever using the gel without condoms.

Product and individual factors

Product characteristics

One or two participants from each site admitted to partial application of the gel because they felt the quantity was too much. While several women contended that the applicator design made partial application impossible, some circumvented this barrier by using one application for multiple sex acts:

> Inserting the gel was easy; the applicator was easy to use. The only problem was that if you insert the gel for every sex act, it would be messy and drip. So I would insert it once and have sex with about four customers, then afterwards I would insert it again. (Lulu, 32 years old, Uganda)

Partner related factors

Non-use with certain partners

Partner dynamics had the strongest influence on adherence. Participants reported high adherence with clients or casual sex partners, but gel and condom use were much less frequent with primary partners (Table 4). Two thirds of all participants identified themselves as having a primary partner. Nearly half of all participants reported partner type as a reason for non-use of gel.

Women in Benin, Chennai and Uganda often viewed gel use, similar to condom use, as inappropriate for long-term or romantic relationships. Some women felt that gel use was difficult if sex was unplanned and using gels or condoms would ruin the trust, intimacy or romance they had established with their partner:

> It's simple. Because a boyfriend isn't just anyone, he's like your husband. There's trust, and love. (Miriama, 20 years old, Benin – when asked why she does not use gel with her boyfriend)

> It was a problem for me because most of them (long-term partners) are characterised by romance. So it was difficult to let them kiss my vagina after I had applied the gel. … My husband is a man I stay with at home. I cannot tell when we are going to have sex, so I cannot come out to apply this gel. So this is a problem. (Helen, 27 years old, Uganda)

Some women were fearful that their partners would notice the gel and accuse them of being unfaithful, diseased or have a negative reaction and thus avoided using the gel altogether with them:

> I cannot use the gel in front of my uncle [term of endearment for older man] because he will doubt me. He doesn't know that I am participating in this research and he will abuse me. (Gunjita, 40 years old, Chennai)

Some women first attempted gel use with their primary partner, but subsequently stopped because of partner disapproval, as was the case with at least four participants in Uganda. However, as discussed in the acceptability section, some women continued to use gel because both they and their partners found it highly acceptable.

Several women in Chennai reported difficulty in using gel with certain clients who were violent, rowdies or rogues:

> There would be rogues and they would be in urgency. As soon as we meet they would finish off their work [sex] without any patience. There would be no time to concentrate on the gel. (Shruti, 37 years old, Chennai)

Table 4. Use of gel and condoms with primary partners.

Self-reported gel and condom use with primary partners	Total ($n = 35$)*	Bagalkot ($n = 6$)*	Chennai ($n = 9$)*	Benin ($n = 7$)*	Uganda ($n = 13$)*
Ever gel use	23	6	4	2	11
Always gel use	14	6	2	2	4
Always condom use	10	5	2	1	2
Always gel and condom use	7	5	0	1	1

Note: *Number of participants who reported having a primary partner.

Conversely, some women in Chennai expected to not be able to use condoms with certain clients and, as one woman reported, would 'be prepared by using the gel at these circumstances' (Shruti, 37 years old). For some women who faced the risk of unprotected sex on a regular basis, gel use provided them some level of reassurance that they were protecting themselves.

Communication and covert use

The majority of women from all sites preferred not to disclose their gel use or study participation to their partners because they liked the gel and preferred to continue using it, but were either afraid that their partner would not approve, would question their fidelity or health status or because they simply felt there was no need for their partner to know. One Beninois woman, when asked if she was afraid to tell her boyfriend about the gel, replied 'Of course. It wouldn't please him. It's best he knows nothing' (Miriama, 20 years old). Women in Uganda reported that some clients distrusted sex workers, feared the gel, and would withhold payment if they found out they were using it:

> One of our workmates told us that as she was applying it, she was seen by the client and the client refused her saying, 'you want to cheat me, is this chloroform?' That is why it is important to apply it when nobody is seeing you; the clients fear it. (Judith, 23 years old)

About one third of all women reported having partners who recognised the increase in lubrication or stickiness from the gel or noticed the applicator and inquired about it. Women found many ways to address these questions while still keeping their gel use a secret when they feared a negative reaction:

> I told them that it is nothing, it is the oil from the inside layer of the condom … they accepted it. (Bharati, 33 years old, Bagalkot)

> If they question, I will tell them it's because I hugged you [had sex with you] that I am having this kind of a discharge. (Jayani, 28 years old, Chennai)

> I would be able to tackle [questions] by saying that since I had some itching problems, I have applied some ointment. (Padmini, 37 years old, Chennai)

> They find me with this gel but still I lie to them that I sell it to other women. (Helen, 27 years old, Uganda)

> I told him that I do not know [why there is so much vaginal fluid], but it has just come, then he told me that you are so nice this time. (Mirembe, 20 years old, Uganda)

Disclosure of gel use

A minority of women chose to communicate openly with their partners about the gel and their desire to protect themselves. Nearly half the women in Chennai reported that they told

certain partners about the gel, often because they felt the men would notice that a product had been applied. Open communication about gel use allowed some women to feel more comfortable using the gel and, ultimately, use it more consistently. Most women reported that their partner accepted the gel once they were informed of its purpose, yet women were often selective about whom they disclosed gel use to. One woman in Bagalkot only told her boyfriend, a lay health worker, because she knew he would understand. Some women reported some initial resistance, but eventual acceptance, of the gel from their partners:

> I told the customers '... if [gel] is used, it is good for both of us and even if I have a disease it will not spread to you and if you have any disease it will not spread to me ...' And later step by step they [accepted using] it ... for the past two months it is not there and they are asking us why it has stopped now and what has happened to you ... they are asking for gels. (Lakshmi, 38 years old, Chennai)

Provider-related factors

Accessibility and gel supply

Seven women reported not using gel when their supply finished before their next appointment at the clinic. While they knew they could go to the clinic at any time to replenish their gels, they often chose to use condoms until they returned for their regularly scheduled appointment:

> For the gel, if it would get finished I would use condoms only, but in most cases they would get finished when we are left with about 3 to 4 days before our next visit [to the clinic]. (Nantale, 28 years old, Uganda)

Physical environment factors

Inconvenient location

At least 10 out of the 53 participants reported difficulty finding private or convenient locations in which to insert the gel at the appropriate time and thus could not use it in all situations. This was most often reported by women in Chennai, who seemed to frequently find sex partners while working outside or from the street. As one woman explains:

> When we have to go to the areas where there is not much space, we are unable to use gel and unable to use condoms too. ... If I go taking four [gels] and get eight clients ... I may have to go to different places and I might have only four gels which I could use only with four people and I cannot use it with everyone. I cannot keep many in my bag since there could be sudden raids and they will question what it is. (Prita, 35 years old, Chennai)

Women found it easier to use the gels when engaging in sex from home or an established location where they could keep a supply of gel on-site and had access to a private area to insert it and wash after having sex. Most women in these situations reported no problems requesting their partner or client wait for them. Some women in Chennai and Uganda arranged meetings with clients by phone and inserted the gel before leaving their home. However, at least nine women, mostly in Chennai and Uganda, reported difficulty in reapplying the gel if the timing between partners was short, if partners wanted multiple rounds or if they were staying the night, as this made it more difficult for the women to find time or a private space to insert the gel before the next sex act without their partner knowing.

Discussion

Our findings support prior research that suggests it is becoming increasingly important to consider contextual factors surrounding consistent and sustained use of microbicides (Lees

et al. 2009; Mantell et al. 2005; Severy et al. 2005; Tolley et al. 2006). Multiple levels of influence within the socio-ecological framework (Figure 1) impacted both acceptability of and adherence to the microbicide gel. While there were variations both between and within countries, experiences in each site were generally similar: women found the gel to be highly acceptable for its lubricant qualities and protective benefits, but adherence and consistent use were more dependent on contextual and partner-related factors. These findings indicate that acceptance does not necessarily coincide with adherence and underscore the critical role that relationship dynamics and social context factors play in the consistent and sustained use of microbicides and, ultimately, in the effectiveness of microbicides in preventing HIV.

Overall, given acceptance of the gel and preference to use it, women found adherence to be relatively easy with partners with whom there were no expectations of fidelity, in situations where private space was accessible and at times when sexual intercourse was expected. Gel adherence seemed significantly more difficult with primary partners due to decreased perceptions of risk, inconvenience or fear of partner disapproval. Other studies have, likewise, found a strong link between women's acceptance of and willingness to use a microbicide gel and their perceptions of their partner's acceptance of the gel (Montgomery et al. 2008; Salter et al. 2008; Tolley et al. 2006; Woodsong and Alleman 2008).

Ability to use the gel with a variety of partners may also depend on cultural sexual norms and factors within a relationship. In this study, most Bagalkot participants were traditional *devadasi* sex workers who engage in sex from homes or brothels and have lovers considered equal to husbands but who know the women have other partners. They operate within a highly organised, almost unionised, structure, which may help enforce regular condom use. This may have made it easier for them to adhere to gel use with a variety of partners. Primary partners of participants in Chennai, Benin and Uganda were not always aware of the women's occupation. Condom use within these partnerships was not socially normative; like condoms, women feared microbicides would be associated with infidelity, thus presenting a major barrier to use. In these sites, gel adherence was easier with casual partners; if these partners noticed the gel, they had less power to control women's use of it except where violence or coercion were used. Particularly in Chennai, women felt empowered by their ability to use microbicides with casual partners who consistently resisted condom use. While this situation is not ideal, as any new microbicide is likely to be less effective than condoms when used consistently, effective microbicides may nonetheless provide some level of protection to women who would not otherwise be able to use condoms.

Though difficult to fully understand without the perspective of men, our findings suggest that the gel's physical properties may prevent the possibility of true covert use, particularly with regular partners. Consistent with findings of other studies (Lees et al. 2009; Montgomery et al. 2008; Woodsong and Alleman 2008), despite being a 'woman-controlled' method, some negotiation for use may still be required. Indirect covert use, or finding ways of explaining the gel that are not threatening to fidelity, trust or power dynamics within relationships, may be a viable option to reduce the potential for gel use to create conflict within a relationship. More research is needed to better understand how microbicides should be introduced and negotiated within different sexual contexts.

One possible advantage of microbicides is their potential for use both as a lubricant and a protective substance, which could reduce stigmatisation as an HIV prevention method. However, this may only be possible in contexts where lubricant use is seen as somewhat normative, as was the case in Benin and Uganda. Evidence from these sites

suggests that lubricant properties contributed to sexual pleasure, which, as suggested by other studies (Lees et al. 2009; Woodsong and Alleman 2008), may increase the likelihood of gel acceptance by men, thus giving microbicides a paramount advantage over condoms. Even in contexts where lubricant use was not the norm, this property often increased levels of sexual pleasure and decreased discomfort. Marketing efforts of any future approved microbicide may benefit from examining the social acceptability of lubricants as compared to HIV prevention methods to select the least stigmatising strategy.

Women participating in this study were at high risk and engaging in frequent sex acts with multiple casual and long-term partners, thus they were not representative of the general female population in the study sites and may have had higher perceptions of risk and lower expectations of fidelity than many other women. The findings may only be transferable to similar high-risk populations, but the multi-site design of the study indicates that high-risk women across different contexts may experience similar issues surrounding lubrication effects, perceived protection, partnership dynamics and contextual factors related to gel adherence and acceptability. It is therefore also important to examine adherence and acceptability in low-risk women and those who incur risk due to a partner's behaviour rather than their own, as the barriers and facilitators to acceptability and adherence may be different for those populations.

Women participated in these post-trial interviews after being informed of the reason for trial closure. This may have influenced their perceptions of the gel and how they retrospectively viewed the trial. Additionally, the manner in which participants were recruited for the post-trial interviews may have biased the information that was collected, though in which direction is unclear. Women who were most positively affected by the trial may have been first to return to the clinic and agree to participate in the interviews, but participants could have also been those who were most concerned or upset by the trial results.

Conclusion

The confidential nature of clinical trials makes it difficult to fully explore the effects of social and political influences on gel use and acceptability. If the relationships posited in the socio-ecological model hold true, these factors are likely to impact how a microbicide gel is perceived and used. Likewise, as the relationship between the community, implementing organisation, participants and clinical trial were different in each site, we assume that some differences in acceptability and adherence may be due to these dynamics. The effects that these factors may have on adherence, acceptability and reliability of interview data warrant more investigation and direct study.

Findings on perceptions of efficacy, particularly from the India sites, underscore the need for careful message testing for each site in future microbicide trials. While participants were counselled correctly, certain concepts, such as placebos, seemed to have been difficult for some to understand and messages may have been complicated by translation. Future trials can benefit from careful attention to messages and how they may be interpreted by the study population.

Proof of effectiveness of microbicide gels requires adherence, which the results of this study suggest may not always be possible in a real-world or even clinical trial context. Subsequent research aimed at further operationalising factors that may influence adherence, such as partner type and physical environment, may improve the ability of future trials to address and monitor these issues. Due to the study design, clinical trial data were not linked directly to the qualitative interviews. This was particularly problematic for

this study as it is difficult to determine if evidence for increased risk of HIV from gel use was a result of the gel or of participants' behaviour, underscoring a need to find better methods of monitoring gel adherence. Self-report is the most common measure of gel use as there are no validated biomarkers of adherence, but the post-trial interview data collection mode presents the potential for recall bias and misreporting and the sensitive nature of the questions may have led to socially desirable responses. Triangulation of clinical trial data with qualitative and behavioural data during future trials may improve the ability of researchers to monitor adherence. Recent studies also suggest the use of stained applicators or coital diaries is feasible, inexpensive and more accurate than self-report in measuring and monitoring sexual behaviour and adherence to microbicide gels (Allen et al. 2007; Hogarty et al. 2007; Wallace et al. 2007). Additionally, future trials should pay careful consideration to concerns about privacy in the environments where women must use the gel.

Microbicide gels have the potential to be accepted by women across geographic and cultural lines; however, consistent and sustained use of microbicides cannot be expected based solely on acceptance of the gel, but likely will depend on interpersonal and contextual factors. Context should be taken into consideration when designing future trials, when examining the usefulness of a microbicide gel and when exploring how to market a microbicide should a safe and efficacious one be found.

Acknowledgements

The authors are grateful to the participants of the CONRAD Cellulose Sulfate 6% gel clinical trial, as well as the dedicated research and clinical trial teams at CONRAD, Family Health International and the study sites in India, Benin, Uganda and South Africa. The authors would also like to thank Laura Johnson, Kate Gilles, Aurelie Brunie and Christina Wong for their data analysis efforts, as well as Lut Van Damme, Marianne Callahan, Jill Schwartz, Chris Mauck, Mary Secret and Donna McCarraher for their thoughtful reviews of earlier drafts of the manuscript. This study was funded by the US Agency for International Development (USAID).

Note

1. The local Institutional Review Board in South Africa did not approve the final protocol amendment, which included the post-trial interviews, due to concerns of site contamination prior to an audit and fears that the social and behavioural research team would not be entirely independent from the clinical trial team. Thus no data were collected from this site that could be included in this paper.

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Résumé

Les microbicides vaginaux actuellement en développement sont des substances qui pourraient prévenir la transmission du VIH. Les données issues d'entretiens en profondeur et qualitatifs qui ont succédé à un essai clinique de Phase III sur un gel de microbicide à base de 6 % de sulfate de cellulose s'étant déroulé sur deux sites en Afrique (Ouganda et Bénin) et deux en Inde (Chennai et Balgakot) ont été analysées afin d'approfondir la compréhension des facteurs qui influencent l'acceptabilité et l'adhésion du/au microbicide dans le cadre d'un essai clinique. Les femmes ont trouvé le gel relativement facile à utiliser avec les partenaires dont elles n'attendaient aucune fidélité, dans des situations où elles avaient accès à un espace privé, et à des moments où il était attendu d'elles qu'elles s'engagent dans des rapports sexuels. L'adhésion au gel semble avoir été considérablement plus difficile avec les partenaires principaux, en raison des perceptions moins fortes du risque, de l'inconfort dû au produit ou de la crainte de la désapprobation du partenaire. Les résultats suggèrent que dans une diversité de contextes les femmes peuvent considérer qu'un microbicide est très acceptable pour ses propriétés lubrifiantes et ses avantages protecteurs, mais que l'adhésion à ce produit et son usage régulier peuvent dépendre fortement de facteurs contextuels et en rapport avec les partenaires. Ces résultats ont des implications importantes pour l'élaboration des futurs essais, la prise en compte des déterminants de l'usage et de l'acceptabilité des microbicides, et les stratégies de commercialisation et d'éducation, si un microbicide sûr et efficace devait être découvert.

Resumen

Los microbicidas vaginales actualmente en desarrollo son sustancias que pueden prevenir la transmisión del virus del sida. Con el objetivo de conocer mejor los factores que influyen a aceptar y cumplir con el uso de un microbicida en un entorno de ensayo clínico, se analizaron los datos cualitativos de entrevistas exhaustivas tras los ensayos de un estudio clínico en fase III sobre un gel microbicida con un 6% de sulfato de celulosa en dos lugares de África (Uganda y Benín) y dos en India (Chennai y Bagalkot). Se observó que para las mujeres era relativamente fácil usar el gel con compañeros que no esperaban que fueran fieles, en situaciones donde tenían acceso a un espacio privado y a veces cuando preveían que iban a tener relaciones sexuales. Cumplir con el uso del gel parecía mucho más difícil con las parejas principales debido a una menor percepción de riesgo, incomodidad o temor a que los compañeros lo desaprobaran. Los resultados indican que las mujeres en entornos distintos podrían considerar que un gel microbicida es altamente aceptable por sus cualidades de lubricación y beneficios de protección pero que usarlo de forma constante y correcta depende en gran medida de los factores contextuales y los tipos de compañeros. Estos resultados tienen repercusiones importantes para otros estudios futuros, en los que se predigan los determinantes del uso de microbicidas y su aceptación. Asimismo, cuando se haya desarrollado un microbicida seguro y eficaz, se deberían aunar esfuerzos para comercializarlo y enseñar a usarlo.