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Australian men's experiences during a microbicide male tolerance study

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Abstract

Microbicides currently in development have the potential to provide new options for the prevention of sexually transmitted infections if proven safe and efficacious. We examined the experiences of healthy male volunteers in a male tolerance study in Victoria, Australia in relation to trial participation and product use. Men ($N = 36$) enrolled in a seven-day, phase 1 clinical safety trial of SPL7013 were interviewed pre and post-use of the gel using a semi-structured interview guide. Interviews were digitally recorded and transcribed verbatim, and transcripts were analysed using a framework approach. All but one man completed the trial. The median age was 34 years (range 22–67 years). Most men had little pre-study knowledge of microbicides and almost all participated for altruistic or personal reasons. Men expressed few concerns about product safety during the trial and indicated trust in the information received through the consent process and from study staff. Three men were non-adherent to the request to be abstinent and an additional two did not refrain from masturbation. Most were positive about the gel, although they described it as “sticky” and found that it stuck to clothes, bed sheets and pubic hair. The type of applicator used was unfamiliar to the men, and some found it “clinical” in appearance. Men are willing to participate in male tolerance studies, often for altruistic reasons. However, counseling about ways to maintain abstinence and further research to inform anticipatory guidance regarding the “sticky” quality of gels, may be important.

Keywords

topical microbicides; sexuality; sexually transmitted infections; male tolerance studies; clinical trial participation

Introduction

Topical microbicides are creams, gels or foams to be applied to the vaginal or rectal mucosa that are being developed to protect against sexually transmitted infections (STIs), including the human immunodeficiency virus (HIV) (Nuttall et al., 2007). These products will be used by otherwise healthy individuals so they must be safe for both women and men. Phase 1 male tolerance studies, in which men apply candidate microbicide products to their penis (without use during intercourse), are necessary to establish safety (Mauck, Rosenberg, & Van Damme, 2001; Tabet et al., 2003).

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Studying men's attitudes to microbicides is important because, although microbicides are anticipated as a female-initiated prevention option, many women indicate they would inform their partners if they used one (Coggins, Blanchard, & Friedland, 2000; Green, Pool, & Harrison, 2001) and it may be difficult to use these products without male partners knowing (Bentley et al., 2004; Bentley et al., 2000; Morrow et al., 2003). Understanding men's perceptions of the characteristics of candidate microbicides can assist the development of appropriate anticipatory guidance. Identifying and understanding men's experiences and perspectives of participating in safety studies may enhance male participation in future clinical trials and guide the development of research questions for studies of microbicide use during sex.

Based on pre and post-use qualitative interviews with men enrolled in a placebo controlled, clinical safety study of the candidate vaginal microbicide, SPL7013 Gel, we explored:

1. Reasons for participating in the study
2. Description of, and concerns about, the product's characteristics
3. Experiences of trial participation.

Methods

The study was approved by the Alfred Hospital Human Research Ethics Committee and conducted at the Melbourne Sexual Health Centre (MSHC). A detailed description of the study method has been published elsewhere (Chen et al., in press).

The need for study volunteers was publicised through posters at the MSHC, local hospitals, universities, and research institutes, through advertisements on radio and in newspapers, through a letter mail out, and through word of mouth. After initial telephone screening, potentially eligible men were invited to attend MSHC for screening. Inclusion criteria were "aged over 18 years", "HIV negative", "in good health" and "had sexual intercourse with a female partner at least once in the past year". The trial required men to attend the MSHC for five visits *each between one and one and a half hours*. Participants were reimbursed US \$50 per visit for travel expenses, inconvenience and missed work. They were asked to apply the gel to their penis and allow to air dry for seven nights and to wash it off in the morning. Participants were asked to abstain from vaginal, anal and oral sex for the seven-day study period. In order to assess potential effects of the product on the skin of the penis, men were also asked to refrain from masturbation. The gel was provided to the men in the applicator planned for future vaginal use.

As part of the qualitative acceptability aspect of the study, men were interviewed by a trained male interviewer using a semi-structured interview guide at enrollment, after they had been given the gel and instructions for use, and again at the final visit after clinical aspects of the study were completed. Interviews lasted between 5 and 30 minutes and were digitally recorded and transcribed verbatim. In four cases, the interviewer reconstructed the conversation from memory and notes because recording failed; an additional three transcripts were incomplete.

Data were analysed following a "framework" procedure similar to that described by Ritchie and Spencer (1994). Transcripts were read several times to become familiar with the data. Initial themes were identified through consensus. Each transcript was coded and the coding scheme was refined as new themes emerged within and across interviews.

Results

Recruitment and sample characteristics

Recruitment was completed in 19 weeks. There were 359 enquiries, 65 men were formally screened, and 36 were eligible. The protocol required that half the participants be circumcised; the uncircumcised quota of 18 was recruited more quickly than the circumcised. Interestingly, some of the men screened by telephone could not say whether or not they were circumcised.

Eight of the 36 men were in their 20s, 15 were in their 30s, seven in their 40s, five in their 50s and one was 67 years of age. Thirty of the men were Caucasian, two were Asian, one was a native Alaskan, one was a Native Hawaiian/Pacific Islander, and for two men race/ethnicity is unknown (Chen et al., in press). None of the men reported having had sex with a man in the past year. Sixteen of the men reported having had only one sexual partner in the previous year. Among the 20 men who reported more than one sexual partner the median number of partners in the previous year was 3 (range 2–10). The number of sexual partners in the previous three months varied between 0 and 5. The men were not asked systematically about their relationship status. Of those who mentioned their status, six were married, eight were in a serious relationship, and four were in a casual relationship or were “single”. Two men spontaneously reported being in serodiscordant relationships (one for HIV and one for herpes simplex virus).

All 36 men completed a pre-use interview, and 35 completed a post-use interview. It is not known why one man did not attend his final study appointment. Five men did not adhere to the protocol requirement to abstain from sexual activity. Two reported that they had masturbated, one reported masturbating and having vaginal intercourse, one reported oral and vaginal sex, and another had vaginal intercourse. Twenty-four men received 3% w/w SPL7013 Gel, and 12 participants received placebo gel.

Trial participation

Knowledge—Men were asked whether they had heard of microbicides before the study. Only eight of the 36 reported that they had. These participants clearly drew on existing frames of reference to interpret and understand “microbicides” and few had specific knowledge about the concept of microbicides to prevent STIs. For example, one man said “... *my father’s a farmer as well so I’ve come across microbicides as part of herbicides, so they target, like, um, they’ll target the insects but they’ll also target, perhaps, the particular thing on plants or something that attracts the insects, so it counters that, or something like that ...*”. Another man referred to the use of antiseptics to kill off microbes.

Reasons for participation—Most men indicated that they chose to participate in the study because of its importance to society. For example, one noted that the gel “*could potentially prevent the transmission of a deadly disease or a disease that has a lot of social stigma*”, while another said: “*I don’t want to donate money and I cannot go over there to help people – I feel that maybe being part of this study is a little thing*”. Some men were motivated by their personal experiences, such as the man whose partner had genital herpes and the one with an HIV-positive partner. Another man reported “*I am from a country where AIDS is aggressive. In fact all of my friends have HIV/AIDS so if this gel is on the market they will benefit from this*”. Only one man reported being motivated by the reimbursement.

Reactions of others—Some men spontaneously described discussing the study with partners or friends with varied reactions. One man commented, “When I discussed it with male friends of mine they were really surprised that I would do that. They consider that it is a huge risk doing a test and putting something on your penis”. Another reported being teased by male friends, but that women had been supportive. Men in relationships reported that their female

partners were generally supportive although one said: “She was mortified and shocked and never going to touch me again for the rest of my life and I said, ‘Oh, that’s a nice surprise’”. This participant subsequently reported having intercourse on day six of the trial.

Perceptions of safety—In general, men reported few concerns about safety during the pre-use interview. Some based their confidence on data from animal studies and studies with women, which were described to them as part of the consent process. Other men expressed trust in the clinic staff conducting the trial, or had faith in their own health. One man described himself lightheartedly as follows: “*I’m fairly experimental. I’ll try ice cubes or hot wax. I’m thirty nine years old and my penis has served its useful life as far as I am concerned so anything extra is an adventure*”. At the post-use interview, some men appeared to have expected something to happen as part of the trial, such as the man who said: “*I was expecting a little more of a reaction, I was expecting to at least tick some boxes you know – about itching and burning but it was all straightforward*”.

Experiences of trial participation—Several men mentioned in the post-use interview that they had enjoyed taking part and that the idea of a microbicide was “*very interesting*” or “*exciting*”. Most men reported that participation was not onerous and some enjoyed the experience. However, some men reported that the time it took the product to dry before they could dress or go to bed was frustrating and longer than expected. One man found completing the diary card difficult. The most common comment about trial demands concerned the requirement to abstain from sex, including masturbation, “*being a week without sex we seemed to barely manage*”. Most did abstain, with one man noting that, “*once I committed to the trial I was going to do it and get it done and just a couple of times that I had to refrain from masturbating where I thought ‘oh, well no, I’m on a trial I better wait.’*”. One man who discussed his lack of adherence justified it based on the earlier safety studies in women: “*She [partner] heard the results were safe. We had intercourse knowing it was day six, basically day seven of the study*”.

Experience of the gel

The characteristics of the gel were acceptable to most men. They described it as clear and having a “nothingness” quality, suggesting that they might find it imperceptible in use. While almost all men mentioned the stickiness of the gel, they expressed different views about it. Some men reported that this was a good quality because it might help the gel to “*stay on*”. A few thought the stickiness might interfere with sexual pleasure by increasing friction, although for the most part men assumed that the gel would act as a lubricant during sex. Some men reported that it stuck to their clothes, bed sheets and pubic hair, and was difficult to wash off their hands or genitals. They described that the product tended to flake as it dried. One used the comparison with skin peeling after a sunburn to describe the flakiness. Some men related these characteristics of the gel to perceptions of how it might work. For example, one man described how the gel dried like “*cement*”, which led him to wonder whether the gel worked by forming a barrier against microbes. Most men thought the gel had no smell, which they felt was an advantage, but those who detected a smell did not dislike it.

Men found the gel easy to apply and did not express strong views about the applicator. Not unexpectedly some men reported that they were unfamiliar with vaginal applicators but reported that this delivery mechanism would probably be familiar to their female partners. However, some suggested that from their perspective a sachet (a single dose sealed packet) would be discreet and easy to carry. Others thought the gel could be packaged in a tube in the same way as toothpaste. Two men expressed concerns about the environmental implications of the plastic applicator. Some mentioned that the applicator had a “*clinical*” appearance. One man who thought it was “*clinical and cold and horrible*”, also noted that: “*my partner, on the*

other side, was like 'I want it to look clinical and look like it comes from a doctor and will protect me against something, especially something so vague as a clear gel that will do the job of a condom – that is quite worrying to me'".

Discussion

Although there is a great need for microbicides to reduce the spread of HIV infection in high prevalence countries, microbicides could also have an important role in protecting against herpes simplex and other STIs in developed countries. There have been few studies of the views of Western men about use of microbicides for protection against STIs and HIV during vaginal intercourse (Carballo-Diéguez et al., 2007; Mauck et al., 2001), and little is known about this group's attitudes to participating in clinical trials.

Our study has several limitations. In addition to the artificial context of product use, many men did not perceive themselves to be at risk or in need of a microbicide. Our sample was determined by the trial need to investigate the safety of the product on normal skin, so there were many exclusion criteria, and the study required several clinic visits. *In addition, the sample size was too small to examine differences in attitudes across men of varying demographic characteristics.* There has been debate about the appropriateness of integrating behavioural and social research with clinical trials where participants are carefully selected and unlikely to be representative of those likely to use the product (Tolley et al., 2006). Nevertheless, we believe that participants in early phase clinical trials can provide useful and relevant insights because of their actual daily use of the product (Carballo-Diéguez et al., 2007). It would also be possible to plan to recruit an additional sample from the study population for focus group discussions to complement the perspectives of those who have tried the product (Morrow & Ruiz, 2007).

Despite the need to change their sexual behaviour for a week and to describe intimate aspects of their personal life, we found a high level of interest and motivation to participate among our sample of Australian men who have sex with women. Similar men have also been found to be willing to take part in and adhere to studies of candidate microbicides (Low-Beer et al., 2002; Tabet et al., 2003) and lubricant use with condoms (Smith, Jolley, Hocking, Benton, & Gerofi, 1998). Consistent with the literature on willingness to participate in HIV vaccine and microbicide trials (Sengupta et al., 2000; Tharawan et al., 2001) altruism and personal interest were common reasons for participating in this study.

Studies of willingness to participate in HIV clinical trials have identified perceived physical and social risks as potential barriers to trial participation (Priddy, Cheng, Salazar, & Frew, 2006). Participants in the current study appeared confident that they were not placing themselves at undue physical risk and expressed confidence in the study staff and setting. Future research could evaluate characteristics of settings, staff, and methods of conveying information that enhance confidence. Participants' spontaneous descriptions of their conversations with others were a reminder that trial participation occurs in the context of broader social networks and that participants may be influenced by partners, families and friends.

Veldhuijzen et al. (2006) have pointed out that the acceptability and feasibility of microbicide studies is influenced by existing norms and values regarding sexual and contraceptive behaviour. In general, men were adherent to study demands. A potential barrier to participating in the trial may have been the requirement to abstain from sex and masturbation for seven *days*, with five of the 36 men reported not adhering to this requirement. Men who admitted to having sex early in the study were again counseled to refrain and subsequently said that they abstained. Future research should seek to identify factors associated with failure to adhere to these

expectations in order to increase the effectiveness of counseling *and evaluate the usefulness of involving the female partners of male participants in order to enhance adherence. It would also be useful to study women's experience of meeting abstinence requirements as participants in female safety studies.*

In addition to informing the planning and conduct of future clinical trials, the results of this study can be used to inform future acceptability research and anticipatory guidance for products shown to be safe and effective. Most men had not heard of microbicides, and a few associated the gel with other products which are not sexually enticing, such as insecticides. However, most men viewed the product as similar to lubricants, which were familiar even to men that did not use them, indicating a potentially effective marketing strategy. Men's perceptions also suggest that packaging may need to strike a balance between indicating a product that potentially enhances sexual pleasure while appearing sufficiently "clinical" to inspire confidence. Finally, men found the trial product sticky and difficult to wash off. These perceptions need to be assessed in the context of use during sexual activities in order to develop appropriate anticipatory guidance.

Our findings provide several suggestions for the planning and design of future studies. While men are willing to participate in microbicide safety and acceptability trials, motivated by altruistic reasons, planning of trials should allow ample time for recruitment. Recruitment may be enhanced by paying attention to the social contexts of participation, perhaps using snowball sampling or recruiting such that eligible men can obtain the support of their partners and/or friends. Finally, consideration must be given to improving counseling methods to support abstinence requirements and to developing anticipatory guidance procedures for trial participation, and for products once they are developed. Enhancing the participation of men in microbicide clinical trials will foster the development of a product that will offer individuals an additional option for the prevention of HIV and other STIs.

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