Acceptability of Praneem polyherbal vaginal tablet among HIV uninfected women & their male partners in Pune India - Phase I study

N.S. Joglekar, S.N. Joshi*, S.N. Navlakha, U.R. Katti* & S.M. Mehendale*

Departments of Social Sciences & *Epidemiology, National AIDS Research Institute (ICMR), Pune, India

Received October 26, 2004

Background & objectives: The number of HIV infected women is steadily increasing worldwide and women controlled methods to prevent HIV are urgently needed. Vaginal microbicides are products for vaginal administration that can be used to prevent HIV infection and other sexually transmitted diseases (STDs). We conducted a Phase I safety and acceptability study of Praneem polyherbal tablet, a candidate microbicide, among HIV uninfected women in Pune, India.

Methods: Twenty eligible women were requested to use the product intravaginally once daily for 14 consecutive days between menses. Safety was assessed by clinical examination, laboratory monitoring and colposcopy. Acceptability was assessed after 14 days of product use through structured questionnaires, focus group discussions among participating women, and in-depth interviews with a subset of 5 randomly selected male partners.

Results: Praneem polyherbal tablet was found acceptable by the study participants with 90 per cent of the participants showing 80 per cent and more acceptability score. Discharge of the product residue was reported as a concern by 6 (30%) of participants. Nineteen (95%) female participants liked the smell and the same number reported that the product was easy to use and did not affect the usual sexual pleasure. However, men reported lack of sexual satisfaction.

Interpretation & conclusion: Product characteristics received good acceptability score in women. However, studies of long-term safety and acceptability among at-risk population would provide more detailed information about its long term acceptability.

Key words Acceptability - HIV - microbicide - Praneem polyherbal tablet - scores

Over 86 per cent of the reported HIV infections in India have been contracted through heterosexual intercourse1. Negotiating male condom use to prevent HIV infection may not be always possible for women owing to social, cultural and gender inequalities2. Thus women urgently need female controlled methods to protect themselves against HIV infection.
Vaginal microbicides can be used to prevent HIV infection and other sexually transmitted diseases (STDs). Over 60 products are currently being evaluated as possible microbicides and are in various stages of clinical development. Praneem polyherbal tablet is one such product, indigenously developed in India. It contains purified extracts of *Azadirachta indica* (Neem) along with purified Saponins from *Sapindus mukerosi* and *Mentha citrata* oil with sodium alginate as an excepient.

A considerable work has been done to explore biological activities and medicinal applications of Neem during the last five decades. We undertook a Phase I study to evaluate the acceptability of Praneem polyherbal vaginal tablet, a candidate microbicide, among women at low risk for HIV infection. The safety of the product is reported elsewhere.

**Material & Methods**

*Clinical procedures:* The study was conducted by National AIDS Research Institute (NARI), Pune, India, in collaboration with Department of Obstetrics and Gynaecology, Sassoon General Hospital, Pune. The study protocol was approved by the Scientific Advisory Committee and the Ethics Committee of NARI, the ethics committee of Sassoon General Hospital and the Drug Controller General of India. Participants were recruited from the community involvement plan of NARI, in which AIDS awareness and the need for female controlled methods for HIV prevention were stressed. Willing and potentially eligible volunteers were referred to the study clinic.

Thirty six women volunteers were screened to decide eligibility and 20 participants (mean age 30 ± 4.8 yr, range 20-40 yr) were enrolled between July 2003 to January 2004. Demography, reproductive health history and safer sex behaviour data have been described in the safety report. Twenty women were enrolled into the study three to five days post menstruation, after establishing their eligibility based on clinical, colposcopic and laboratory evaluations. They were instructed to use the product once daily for 14 consecutive days starting on the day of enrollment. They were clinically and colposcopically evaluated for safety on day 7 and day 14 of the product use respectively.

**Acceptability assessment**

Acceptability scores – A structured pre-coded questionnaire was administered on day 14, which included questions to assess acceptability regarding colour of the product, odour of the product, product usage related acceptability, symptoms experienced and experiences during sexual contacts. These five characteristics of the product were rated as 0 or 1, with ‘0’ indicating non acceptability and ‘1’ indicating positive acceptability. Sum of these scores was considered as the total score for acceptability.

Qualitative assessment of acceptability – Participants were asked about the properties that they liked and disliked the most with open-ended questions at their day 14 visit. Their responses were tabulated to determine acceptability.

Acceptability assessment also included exit focus group discussions (FGDs) with the participants. A total of four FGDs were conducted among the participants completing 14 days of product use within one month of completion of the study. A focus group guide was developed to explore the acceptability related issues that were not captured in the quantitative data instrument. Each focus group discussion required up to one hour and 4-6 participants participated in each of the four FGDs. A study counselor trained in qualitative data collection methods facilitated the discussion and one note-taker attended the group discussion. The discussions included topics related to the decision-making process for participation in the study, product acceptability, and difficulties related to the product use, willingness to consider using the product in future, and experiences and reactions of the male partners.

In depth interviews of five randomly selected male partners of the participating women were conducted to explore their views on the product acceptability and attitude towards a possible female controlled method for HIV prevention.
These interviews were conducted with the help of an in-depth interview guide, which included questions related to male involvement in microbicide trials, acceptability of the products and concerns related to the product use. Each interview lasted for about 45 to 60 min. The FGDs and interviews were audio taped with the permission of the participants, transcribed into the local language and then translated into English.

The FGD and interview transcripts were analyzed after coding into specific themes, e.g., ‘willingness to use the product in future’, ‘difficulties faced during product usage’, ‘liked characteristics’, ‘disliked characteristics’ etc.

Results

Of the 20 enrolled participants, 12 (60%) were housewives and 8 (40%) were unskilled labourers. Five participants were illiterate and 15 (75%) had some education. All of them were married and monogamous except one participant who had two lifetime sexual partners. The mean age at marriage was 16.5 ± 2.9 yr and the mean duration of marriage was 14.5 ± 6.7 yr.

Benefit of investigations done, as a part of screening for the study, curiosity and wish to have pelvic exam with novel technology (colposcopy), interest in experiencing vaginal product and strive to save women of future generations were the main motives behind participation as reported by the participants during FGDs. One participant reported trust in the medicinal qualities of Neem. All of the female participants had consulted their spouses before deciding about study participation in order to avoid unnecessary problems and suspicion by their male partners subsequently.

The main reason for male partners consenting for the study was altruistic motivation to save the community from the dangerous disease. Although they had fear about side effects initially, assurance of management of side effects by the study team during the informed consent process helped them in making an informed choice of study participation.

Product adherence: All the 20 enrolled participants completed all of their scheduled follow up visits. Nineteen of them completed the full schedule of product applications. The product use was extended for three days for one participant who had missed three applications.

Acceptability of the product characteristics: The maximum acceptability score that could be attained was 5. Acceptability score was 5 for 9 subjects, 4 for 9 others and 3 for the remaining 2, the mean being 4.35. Only one participant out of twenty, perceived herself at risk of STDs and she had acceptability score of 5.

Majority of the women liked the product. All the participants liked its ‘cream’ colour and 19 (95%) liked its smell too. Out of the 19 (95%) participants who found the product easy to use, 12 (63.2%) had not used any vaginal product in the past, and all of them had 80 per cent and more acceptability scores. Product storage was not perceived as a problem by most of the women. Smell was rated as the most liked characteristic by 15 (75%) participants, the same was reiterated during FGDs. Being a tablet, women liked the easy mode of insertion.

Product experience: Of the twenty participants, 9 (45%, 95% CI 22.8-68.7) reported total 17 episodes of some genital irritation, possibly related to the product use. However, 7 of these 9 had a maximum acceptability score and two of these 7 had experienced multiple symptoms. The data indicated willingness to accept the product in spite of irritative symptoms.

The median number of sexual contacts reported by the participating women during the study period was two. Leaking of the product before sex was reported by two participants, one woman reported leaking of the product during sex and 9 (45%) participants reported leaking after sex. Only one participant who was married for 15 yr reported that she did not get sexual pleasure while using the product and also reported leakage of the product after sex. Sexual pleasure was perceived to be as good as the one without product use by rest of the participants and the same was reported during FGDs. One
participant commented that vaginal products would not affect sexual pleasure, as the products will be used by women.

During male in-depth interviews, smell of the product and lack of sexual pleasure were the main reported concerns, however, product use did not affect men’s routine sexual activity.

Concerns related to the product: Discharge of the product remains was reported to be the most disliked characteristic by 6 (30%) women; of these 2 were most concerned about soiling of the clothes. In the focus group discussions, most participants expressed a concern over intermittent discharge, which continued up to 8 h after the product insertion. Some participants informed that ‘curd like discharge’ appeared intermittently which soiled their clothes and that made them feel miserable. Discharge was usually noticed at the time of micturation. Other problems reported included the large size of the tablet, and transient itching related to the product use. Almost half of the participants (9/20, 45%) did not mention anything that they did not like about the tablet.

During FGDs, storing the study product was mentioned as a problem due to lack of privacy and inquisitiveness of children. Men did not like the use of condom during the study period and three of them reported tightness, uneasiness and inconvenience.

Acceptance of vaginal products by Indian women and men: Women participants felt that Indian women would accept such a product, as its use would be under their own control and products free from side effects would have greater acceptability. During male in-depth interviews all men expressed willingness to use the product in future.

Overall, both men and women felt that male involvement is crucial in vaginal microbicides trials in order to avoid conflicts. It was felt that a joint decision to participate in the study would be a better option. However, two men who were better educated than the others (7th grade and above) opined that male involvement should be left to the women’s discretion.

Discussion

A 30 per cent efficacious vaginal microbicide, if used 60 per cent of the times would provide more protection than a method that is 90 per cent efficacious but used only 20 per cent of the times. Thus consistent use is the most crucial factor in deciding effectiveness of a particular product. Ability and willingness of a potential user to use a product or technology in every day life, depends on individual perceptions of susceptibility to certain conditions, benefits of that particular method, concerns about the potential side effects, behavioural choice, cost and access. Acceptability of the product has been reported to be a function of interaction between product characteristics and perceptions of the users.

Praneem polyherbal tablet was acceptable to the participating women in terms of its aesthetic characteristics like appearance and smell. All the participants completed their scheduled follow up visits and adhered to the treatment regimen. Nearly 90 per cent of the participants showed 80 per cent and more acceptability scores. This can be considered as indicative of consistent usage of the product.

Product usage was perceived as easy by a majority of the participants. Product acceptability was good even among those women who had never used a vaginal product and hence a hypothetical apprehension about possible non-acceptability of vaginal products among Indian women should not become a barrier for microbicides advocacy.

Safety of the product could definitely affect its acceptability. This product was found to be safe in the study population in once daily application for 14 consecutive days. This finding would be of great value in the post trial promotion of this product in the community.

Sexual experience was expected to influence the product acceptability in men. This has been reported earlier in South African studies. Effect of the physical presence of the product on sexual experience in men could have been altered by the confounding effect of condom use by men during the study.
As opposed to men, women did not experience any negative effect following the product use on sexual satisfaction. Moreover, sexual pleasure was perceived to be a man’s issue by the participants. This finding again substantiates that sexual preferences of men are considered as more important in the Indian cultural setting and their perceptions would greatly affect acceptability of vaginal microbicides in future. Both men and women expressed a need for vaginal products for HIV prevention, but had concerns about their covert and uninformed use.

Perceived risk could positively affect the acceptance for vaginal microbicides in women as reported in the earlier literature\textsuperscript{13,14} and we made the same observation.

Post-usage discharge of the product residue seemed to be a major concern to the women. Similar finding has been reported in earlier studies\textsuperscript{14-16}. This needs to be addressed by making necessary modifications in the manufacturing process and product formulation.

Acceptability measurements involving actual testing of the real product and monitoring effects following its long term use and reactions are considered as more objective\textsuperscript{17}, our data provided assessment of the acceptability of praneem tablet based on actual experiences following the product use. The primary objective of this study was a short-term assessment for safety.

The generalizability of our findings may be limited as this trial was done with the population selected according to study specific criteria, and large-scale efficacy studies among high risk women would provide wider acceptability data.

As per UNAIDS, less than 20 per cent of married Indian women have ever heard of AIDS\textsuperscript{16}. Awareness and education programmes should aim at informing women of the risks they face. There is also a need for awareness on microbicides as a female controlled option for prevention of HIV and STDs and as a possible alternative to male condoms.

Indigenously developed products like 'Praneem' might help to serve the urgent need for a female controlled option like a vaginal microbicide, for Indian women. To conclude, Praneem polyherbal tablet was found to be acceptable by the study participants in Pune. However, studies among at risk populations will provide data on its acceptability among the potential users in that category. Product characteristics, perceptions about the risk for HIV infection, product usage and related sexual experience were the factors that influenced acceptability of vaginal products in women, whereas sexual satisfaction related to the product use was the main determinant of acceptability in men.

**Acknowledgment**

Authors acknowledge Dr R.S. Paranjape, Director, NARI, Pune, for his continuous help and encouragement. We thank Dr G.P. Talwar and Panacea Biotech Ltd., New Delhi, India, for providing the study product, and National AIDS Control Organization (NACO), New Delhi for providing financial support. We also thank Dr Kapila Bharucha, Sassoon General Hospital, Pune, for making the study implementation possible, data entry staff and other staff of National AIDS Research Institute and Sassoon General Hospital, Obstetrics and Gynaecology department for technical help. We gratefully acknowledge the participation and co-operation by the participants without whom the study would not have been possible.

**References**

1. Surveillance for AIDS cases in India as reported to NACO as on 31\textsuperscript{st} March 2004 (webpage: http:\textsuperscript{/}/www.naco.nic.in/ AIDS Cases/overv.htm), accessed on May 22, 2004.


Reprint requests: Mrs Neelam S. Joglekar, Behavioural Scientist, National AIDS Research Institute (ICMR) G-73, MIDC, Post Box 1895, Bhosari, Pune 411026, India e-mail: joglekarneelam@yahoo.com