MICROBICIDES IN INDIA- PRESENT AND FUTURE

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Abstract

India continues to wage a battle against the human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) epidemic. Despite an array of preventive and control efforts directed against the disease, it continues to find its way from the high risk groups to the general population. Women are more vulnerable to HIV/AIDS because of biological as well as socio-cultural factors. Microbicides appear to provide an attractive option as a means of protection to be used by women. At present, microbicide trials are in study phases I and II in India. The development of an ideal microbicide candidate which would be effective and confirms to user satisfaction poses a major challenge to researchers.

Key words: HIV/AIDS, India, microbicides, trials, women

Introduction

“Women in India and worldwide are still left out of equation. The issue of trust and violence against women increases their vulnerability to human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS). Look at the current tools for women’s protection - usage of condoms is in men’s hands and women lack the power to take this with their primary partners. I wish we could have a product like microbicides yesterday in the hands of women” (A leading HIV/AIDS activist, India) [1]

With a total of 2.5 million people living with HIV/AIDS (PLHA), India is in the grip of the HIV/AIDS epidemic.[2] Women are increasingly vulnerable to HIV/AIDS and account for around one million cases.[3] A significant number of women have been infected by husbands who have frequented sex workers.[4] Women have fewer and rather unfeasible options such as abstinence and condom usage, available, to protect themselves. Microbicides appear to serve as a convenient option for women wanting to protect themselves from sexually transmitted infections (STIs) and HIV/AIDS. A model projection predicts that widespread use of microbicides in low income countries would lead to US$ 2.7 billion savings for health systems.[5] Research trials for an effective microbicide are extensively being conducted in India and other parts of the world. In this article, we will review the current status of microbicide trials and its scope of use in the socio-cultural context in India.

Action of microbicides[6]

Microbicides are compounds that can be applied inside the vagina or rectum and can be formulated as gels, creams, films, or suppositories. Microbicides may help prevent HIV infection by: (i) Preventing HIV and other pathogens from reaching the target cells by creating a physical barrier. (ii) Maintaining an acidic vaginal pH which enhances the natural defense mechanism (iii) Killing or disabling pathogens by disruption of the protective outer cover (iv) Preventing virus replication after it enters the cell.

Microbicide Clinical Trials[7]

Broadly speaking, microbicide trials may be categorized as:

a) Pre-clinical: This includes laboratory and in-vivo animal studies

b) Clinical Safety trials (Phase I to II trials): These trials involve testing a microbicide in a small number of people to determine its safety, side effects, and provide preliminary data of effectiveness. In addition, there exist Phase 1/2 trials, which are, either a combination of Phase I and II designs, or designed for Phase I to merge with Phase II.

c) Acceptability studies: Microbicide clinical

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trials often also undergo acceptability studies, to determine acceptability of the microbicide in partners of the women using the candidate microbicide.

**Ongoing Microbicide Trials**

At present, there are more than 50 microbicide candidates in the stages of pre-clinical testing and more than 40 microbicide products in various stages of clinical development [Table 1].

**Microbicide trials in India**

While phase I and II of studies with certain microbicide products have undergone completion, currently there are no phase III trials in India because of less than expected HIV incidence to conduct such research. Phase I trials of Buffer gel and PRO 2005 have been completed in Pune. Tenofovir gel and Praneem Polyherbal vaginal tablets have completed Phase II trials. With regard to Cellulose Sulfate, while Phase I and II studies reported satisfying results, the Phase III study which was expected to end in 2009 had to be stopped in January 2007 because more participants using the gel were becoming infected than those in the placebo group. Similar experience was reported in studies pertaining to Carraguard gel conducted in other country sites.

Questions with regard to acceptability of microbicides have been raised by program managers and policy makers in India. Certain barriers to use such as cost factor, lack of privacy for use, storage and disposal have been anticipated. However, certain studies point towards a willingness to use a microbicide. High acceptability for Praneem and PRO 2000/5 has been reported. Nonoxynol-9, a vaginal pessary was also found to be acceptable among Indian women during a Phase I trial. At present preclinical research of products like NIM 76, Basant, NISIN, Maganin A, Haemolymp of Indian crab is underway.

**Future of microbicides in India**

Although clinical trials have demonstrated safety and acceptability of candidate microbicides, its effectiveness yet remains to be proven. Before that, it is vital to raise awareness about the potential availability of a device such as a microbicide against HIV/AIDS in the community. Also programs should continue to address the social and cultural barriers to good sexual and reproductive health practices. Greater advocacy with involvement of Non-Governmental Organizations and community stakeholders along with political commitment is required to prioritize microbicide research. It also calls for commitment from policy-makers, the public and the private sector to invest the necessary resources. Phase III trials should be conducted with due attention to ethical concerns given the lesson learnt from Carraguard and Cellulose Sulfate trials. It is also imperative to encourage young professionals and scientists to pursue microbicide research. Public health professionals could also play a major role by sensitizing the community about microbicides and creating motivation to participate in clinical trials. It is hoped that a safe, effective, easy to use and affordable microbicide would soon be available.

**References**


**Table 1: Ongoing microbicide trials**

<table>
<thead>
<tr>
<th>Candidate Name</th>
<th>Phase</th>
<th>Sites by Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRO 2000/5</td>
<td>III</td>
<td>South Africa, Tanzania, Uganda and Zambia</td>
</tr>
<tr>
<td>PRO 2000/5 gel and buffer gel</td>
<td>II/IIB</td>
<td>Malawi, South Africa, United States, Zambia and Zimbabwe</td>
</tr>
<tr>
<td>Tenofovir gel</td>
<td>II B</td>
<td>South Africa</td>
</tr>
<tr>
<td>Tenofovir gel</td>
<td>II</td>
<td>South Africa, Uganda, United States</td>
</tr>
<tr>
<td>VivaGel® (SPL7013 gel)</td>
<td>½</td>
<td>Australia</td>
</tr>
<tr>
<td>HEC/CS/N-9†</td>
<td>I</td>
<td>USA</td>
</tr>
<tr>
<td>PRO 2000</td>
<td>I</td>
<td>USA</td>
</tr>
<tr>
<td>Dapivirine</td>
<td>I</td>
<td>Belgium</td>
</tr>
<tr>
<td>Ethanol in emollient gel</td>
<td>I</td>
<td>Kenya</td>
</tr>
<tr>
<td>Tenofovir gel</td>
<td>I</td>
<td>United States, Dominican Republic</td>
</tr>
<tr>
<td>UC-781</td>
<td>I</td>
<td>United States, Thailand</td>
</tr>
<tr>
<td>SPL7013 gel</td>
<td>I</td>
<td>United States, Puerto Rico</td>
</tr>
</tbody>
</table>

Source[9]


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