Overview of Microbicides and Research – in Malawi

Tchangani Tembo

UNC Project 13 MAY 15

OVERVIEW

- Microbicides
- Background
- Why are they needed?
- How do they work?
- Microbicides in Malawi

OVERVIEW

- What are Clinical Trials?
- Status of MTN 020 – ASPIRE
- Primary Objectives
- Eligibility Criteria
- Methods
- Challenges

MICROBICIDES

- These are gels, films, rings or suppositories that are mainly used to neutralize viruses and bacteria.

- There are both vaginal and rectal Microbicides.

BACKGROUND

- UNAIDS report of 2009 indicate that 1.8 million people became newly infected with HIV and 2 million lost their lives to AIDS.
- 2009 Global Report indicated an estimated total number of individuals living with HIV to be 33.3 million, of these 22.5 million reside in sub-Saharan Africa.

BACKGROUND

- UNAIDS/WHO “AIDS Epidemic Report 2009” show that women and girls continue to be affected disproportionately by HIV in sub-Saharan Africa, where women account for approximately 60% of people living with HIV.1
- The development of safe and effective HIV prevention technologies that can be made easily accessible to developing countries remains a public health priority.

WHY ARE THEY NEEDED?

- Unprotected heterosexual intercourse is currently the leading mode of HIV transmission among women.
- Correct and consistent use of latex condoms is one proven method of preventing HIV transmission
- Condoms are widely regarded as inadequate prevention options for women, many women are unable to negotiate condom use with their partners.

WHY ARE THEY NEEDED?

- Condoms, mutual monogamy and STI treatment are not feasible options especially for women
- Many women do not have the social or economic power to insist on condom use they require the consent of the male partner.
- Microbicides would not require a partner's cooperation, they would put the power to protect into women's hands

HOW DO THEY WORK

- Killing or Inactivating pathogens
- Strengthening the body's normal defenses. (maintaining vaginal pH)
- Blocking infection by creating a barrier between the pathogen and target cells
- Preventing infection from spreading to other cells

MICROBICIDES IN MALAWI

- In Malawi there are mainly two clinical trial sites that carry out microbicide studies.
- University of North Carolina(UNC) Project- situated at KCH campus

- Johns Hopkins University (JHU) – situated at QECH campus
- These sites mainly conduct research in vaginal microbicides and Pre exposure prophylaxis studies for the prevent ion of sexual transmission of HIV amongst other studies.

TIDZIWE CENTER

JOHNS HOPKINS UNIVERSITY

WHAT IS A CLINICAL TRIAL?

- A clinical trial is a planned experiment designed to evaluate the benefits of one or more treatments.
- “Clinical” includes both therapeutic, prophylactic or preventative trials.

WHAT IS A CLINICAL TRIAL?

- There are many different types of treatment or intervention that can be evaluated with a clinical trial i.e.
- Drug Therapy
- Medical Procedures
- Educational Intervention
- Screening Trial
- Vaccine Trial

KEY DESIGN ISSUES

- The primary aim of a clinical trial is to provide reliable evidence of treatment efficacy or effectiveness and safety.
- There are a number of design issues in clinical trials that are key to enable reliable conclusions to be made

KEY DESIGN ISSUES

Controlled

- Any treatment needs to be compared to one or more other treatments. This is often a new treatment compared to standard treatment. In drug therapy trials there will often be a **placebo** control.

Unbiased

- There needs to be a fair comparison between the treatments with no bias whether deliberate or accidental.

KEY DESIGN ISSUES

- **Randomization** ensures that patients are randomly allocated to a particular treatment group without bias.
- **Blinding** of patients/participant, investigators and evaluators ensures that bias is reduced.

Large

- Patients vary considerably in their response to treatment. In order to obtain a precise estimate of any treatment effect sufficiently large numbers are required

PHASES OF CLINICAL TRIALS

- There are four phases of clinical trials in drug trials
- Pre- Clinical studies – Lab and animal models

Phase I (20-80 subjects)

- Relates to the safety of the drug under investigation in healthy volunteers.
- To establish the appropriate doses of a drug to be used and understand how the drug is dealt with in the body(pharmacology and Pharmacokinetic).

PHASES OF CLINICAL TRIALS

Phase II (100-200 Subjects)

- To establish short term safety and to determine efficacy.
- These trials are also used establish which therapies have the potential to be investigated in full-scale, phase III randomised trials.

PHASES OF CLINICAL TRIALS

Phase III (200 – 4000 or even more)

- Gather data to confirm **safety and effectiveness** and assess the risk-to-benefit ratio (Benefits of a drug against a placebo or standard therapy).

Phase IV (200 – Thousands)

- Relates to the stage after a drug has been approved and involves the long-term monitoring of the safety of the drug.

STATUS OF ASPIRE (MTN 020)

- A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Phase III Safety and Effectiveness Trial.
- Vaginal matrix ring containing 25mg Dapivirine.
- Conducted by Microbicides Trials Network (MTN)

SITES

Malawi- Blantyre and Lilongwe

South Africa – 9 Sites

STATUS OF ASPIRE (MTN 020)

- Zimbabwe - 3 sites
- Uganda – 1 site

MALAWI

- Lilongwe enrolled142
- Blantyre enrolled 130
- 2629 across sites
- Follow up of participants to be finalized by 25 June 2015
- Results expected end 2015 or early 2016

PRIMARY OBJECTIVES

- To determine the *effectiveness* of 25mg dapivirine vaginal matrix ring when inserted once every 4 weeks, in preventing HIV-1 infection among healthy sexually active HIV-uninfected women
- To assess the *safety* of 25 mg dapivirine vaginal matrix ring when inserted once every 4 weeks over the investigational product use period

ELIGIBILITY CRITERIA

- Aged between 18 – 45
- Able and willing to provide informed consent
- Able and willing to provide locator information
- HIV uninfected
- Sexually active
- Using an effective contraceptive method
- Not pregnant and not breastfeeding

METHODS

- Sensitization
- Consenting
- Screening
- Enrollment
- Follow up
- Endpoints
- Termination
- End of Study

CHALLENGES

- Adherence to investigational product.
- Husbands/partners not allowing spouses to participate in trials.
- Principles of research not well understood by communities.
- Sometimes studies are delayed in getting necessary approvals from regulatory bodies as such sites fail to meet certain international deadlines .

CHALLENGES

- Rumors and misconceptions
- Retention
- Relocations
- Social Harms

AKNOWLEDGEMENTS

- MTN 020 Protocol and SSP Manual
- UNC Staff
- All MTN 020 Participants
- JOURNAIDS
- UNC Management
- MTN
- IPM
- KCH Management and staff

REMARKS

- Thank U
- Questions?