ARISE

African Research And Innovative Initiative For Sickle Cell Education

Train-the-Trainer Workshop
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Day 1

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Recent studies in Africa – REACH & NoHARM

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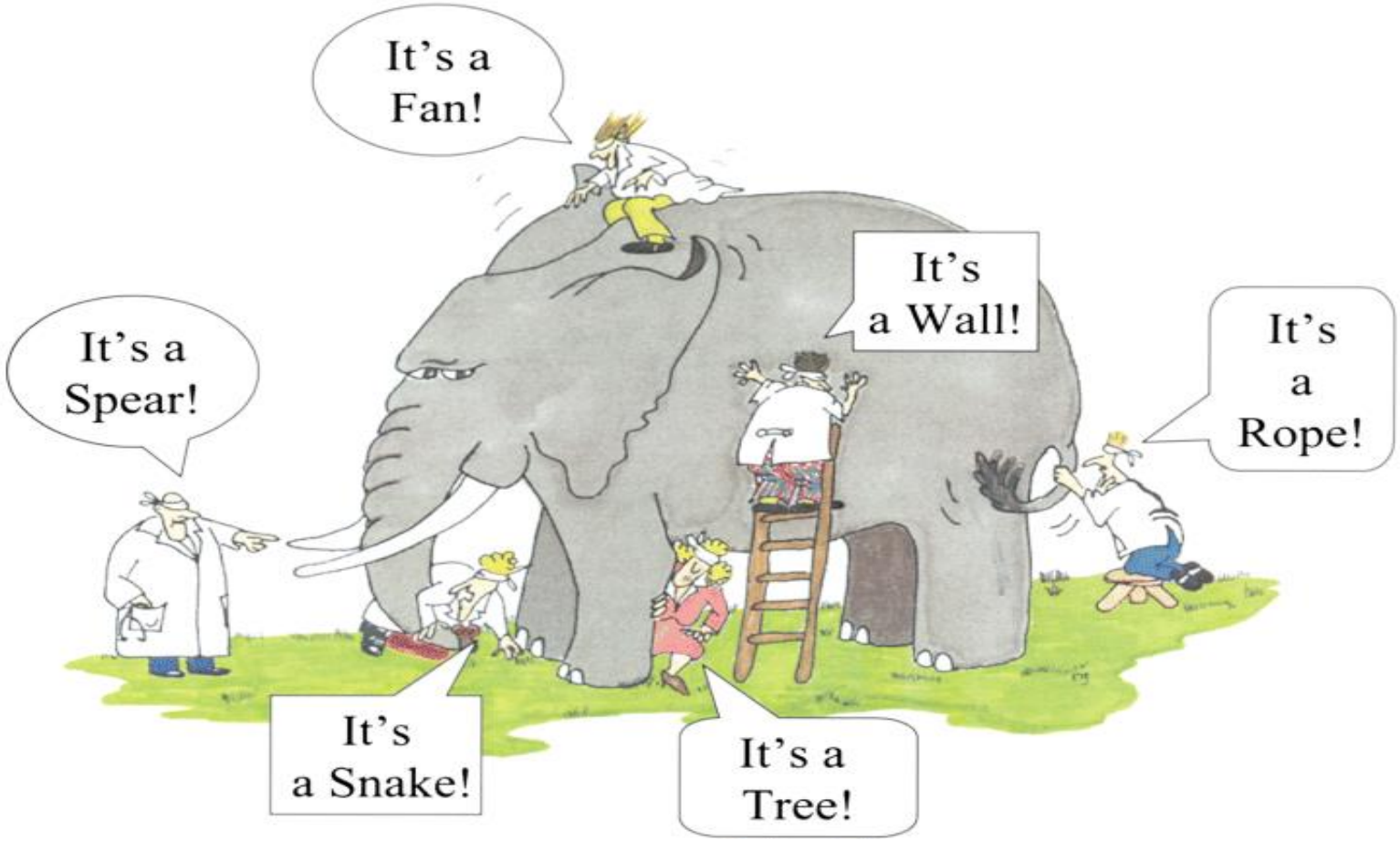
SCD: RECENT STUDIES IN AFRICA

- Courtesies

Icebreaker: Research Subjects



ICEBREAKER

Introduction

- In 1986 it was demonstrated that prophylactic penicillin remarkedly reduced the incidence of pneumococcal sepsis
- That provided a great motivation for the widespread implementation of neonatal screening for sickle cell disease
- Subsequent experience demonstrated that neonatal screening, when linked to timely diagnostic testing, parental education, and comprehensive care, markedly reduces morbidity and mortality from sickle cell disease in infancy and early childhood
- BUT we and many SSA Countries do not yet have national policy for Newborn screening for SCD – that is the reason we're here!

- Globally about 5.7 million neonates were estimated to have variant haemoglobin in different combinations with an average of 350,000 babies with severe forms of the disease are born each year.[11]
- The developed world accounts for just 10% of the world's haemoglobinopathy patient population.[12]
- Seventy-five to eighty-five percent of children born with this disease are born in Africa with the highest prevalence seen in Sub-Saharan Africa which accounts for eighty-four percent.
- The West African region accounts for sixty percent of affected newborns worldwide and seventy-one percent of the sub-saharan Africa figures.[10,11]

- Nigeria has the highest number of haemoglobinopathy patients with 2-3% of the total population affected and 24.7% newborn estimated carriers.
- Annually about one hundred thousand children are born with haemoglobinopathy in Nigeria, this amounts to thirty-three percent of global annual births.[13]

Prevalence of SCD in Nigeria

Author	Place	Prevalence
Kaine et al	South East	16/1000
Fleming et al	North Central	20/1000
Ernest et al	North Central	22/1000
Inusa et al	North West/Central	27/1000
Odunvbun et al	South South	30/1000
Omotade et al	South West	42/1000

NOHARM

- Novel use of Hydroxyurea in an African Region with Malaria: a trial for children with SCA by Opoka & Team in Uganda
- Domesticated at the Department of Paed and Child Health Makerere University, Uganda
- Key Points included:
  - 1. HU provided significant clinical and laboratory benefits which suggested that it would be safe and effective across SSA
  - 2. HU did not increase the incidence or severity of Malaria events in SSA Children

NOHARM

- Research that gave hope for recommendation of HU for children was done in high-resource and Malaria free environment
- BUT we do not know its safety and efficacy in Malaria-endemic SSA with high SCA burden
- However, in vitro studies suggests:
  - 1. HU could increase malaria severity
  - 2. SCA patients may have HU-associated neutropenia that could worsen infections

NOHARM

- The Study: NOHARM was a Randomized, Double-blinded Placebo-controlled trial in malaria-endemic Uganda
- HU dose : 20 ± 2.5mg daily for 12months
- Outcomes:
  - 1º Incidence of clinical malaria
  - 2º SCA-related Adverse Events (AEs)
    Clinical /Laboratory effects
    Haematologic toxicities

Randomization:

HU Arm – 104 children
Placebo Arm - 103 children

NOHARM

Outcome

- 1. Malaria incidence - No difference
- 2. Time to infection - No difference
- 3. SCA complication: Less in HU arm 45% Vs Placebo 69% P= 0.001
  - **VOC,**
  - **Dactylitis,**
  - **ACS,**
  - **Splenic sequestration and**
  - **Blood transfusion**

NOHARM

Outcome

- 4. Haematologic for HU group
  - Haemoglobin ↑
  - Fetal Hb ↑
  - Leukocytes ↓
  - Reticulocytes ↓
- 5. SAE, Sepsis episodes, Dose-limited toxicities- Similar
- 6. Deaths - 3 (HU 2, Placebo 1 and Malaria 0)

NOHARM Conclusions

- HU provided significant clinical and laboratory benefits which suggested that it would be safe and effective across SSA
- HU did not increase the incidence or severity of Malaria events in SSA Children

Realizing Effectiveness across Continents with Hydroxyurea (REACH)

- By Tshilolo and Team in 4 African Countries: Angola, DRC, Kenya & Uganda published by NEJM January 2019
- Assumption: Malnutrition and Malaria may affect the feasibility, safety and benefits of the use HU in low-resource settings.
- Methods:
  - Age: 1 – 10 years
  - HU Dose: 15-20mg/kg/day for 6months
  - Outcome:
    - **Safety;** Dose, Toxic effects and Malaria
    - **Benefit**; Lab variables, SCD related events, Transfusion and Survival

REACH

Outcomes:

- Dose limiting laboratory variables occurred in 5.1% of participants
- HU resulted into **reduction** in clinical adverse events compared with pre-treatment period
  - VOC
  - Non-malaria infections
  - Malaria
  - Transfusion
  - Death

REACH

- Conclusions:
  - HU treatment was feasible and safe in children with SCA in SSA
  - HU use reduced clinical events
  - HU recommended for wider access and use (especially in SSA)

ILORIN ANECDOTA

- Age 6mo -16 years
- Very stringent conditions especially severe complications
- Dose: 10 -15mg/ kg/day (6 monthly labs)
- Outcome:
  - Reduced frequent of crises
  - Reduced school absenteeism
  - Rapid growth (increase heights)
  - Increase appetite
  - Increase self-worth/ self-esteem
  - Increase enthusiasm to come for follow-up clinics
  - Increase Haemoglobin and Fetal Hb.

CONCLUSION

- HU is good for children with SCA in SSA in spite of the presence of both Malaria and Non-Malaria infection and Malnutrition.

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