Sustaining the efficacy of existing treatment in the shadow of increasing drug resistance

(Rise and Spread of Multi-drug resistant Malaria)

Francine NTOUMI, PhD, HDR, PvDz, FRCP
Fondation Congolaise pour la Recherche Médicale &
University M. Ngouabi, Rep. Congo

Addis-Ababa l 12.03.2018
1. Malaria burden in sub-Saharan
2. Sustain current treatment for uncomplicated malaria
3. Antimalarial drug challenges
4. Conclusion
What causes malaria?

Life cycle of *P. falciparum*
1. Malaria situation today

[Map showing countries endemic for malaria in 2016 and those not endemic in 2000.]
1. Malaria cases incidence

- Malaria cases: 216 million
  90% African region

- 15 countries carried 80% of global malaria burden

- Decline of 20% case incidence since 2010 in African region vs 48% in South East Asia.
1. Malaria deaths in African region

- 445,000 deaths
- 91% in African region
- 15 countries accounted for 80% global deaths
- 37% mortality decrease.
1. Funding for malaria (2010-2016)

increased from 65 million to 2.7 billion in 2016.
1. Funding for malaria (2010-2016) cont’

1. Drugs
2. Basic research
3. Vaccines
2. Sustain current effective antimalarial drugs
2. Manage resistance spread/emergence

Pradines et al., 2010
2. WHO’s recommendations

• 2001, WHO recommendation for Artemisinin combination therapies (ACTs) for the treatment of uncomplicated malaria.

• From 2004 many African countries change policy for malaria treatment
  • Artemether-lumefantrine
  • Amodiaquine-artesunate (1st / 2nd line)

Efficacy of ACTs reported about 85-98%
(WWARN data)
2009 (first verified cases)
Artemisin resistance

Definition: a delayed clearance of malaria parasites.

Artemisinin resistance containment project for the Greater Mekong Subregion established since 2009 by WHO and partners
Crucial steps for surveillance of drug resistance

a) Monitor regularly efficacy of existing drugs
   1) Artemisinin derivatives (severe malaria)
   2) Partner drugs

b) Adopt adequate behaviour to protect existing efficient antimalarials.
Monitor regularly efficacy of existing drugs (cont’)

Monitoring partners drugs:
- Amodiaquine
- Lumefantrine
- Mefloquine
- Sulfadoxine- pyrimethamine
- Pyronaridine
Monitor regularly efficacy of existing drugs (2)

Available tools:
Gold standard = therapeutic studies + molecular markers
- *In vivo*: Parasite clearance
- *In vitro* assays (IC 50)
- Resistance molecular markers for *P. falciparum*: pfcrt, pfmdr1, K13 propeller, dhfr, dhps,
Molecular analysis - risks to ACT efficacy?

AL
66 studies
15,000

AS-AQ
24 Studies
5,400
Molecular markers of AL and AQ are the same 2 genes

- *pfcr* and *pfmdr1*
- Resistant alleles differ
  - Parasites resistant to Amodiaquine
    - *pfcr K76*  
      - *pfmdr1 N86*
  - Parasites resistant to Lumefantrine
    - *pfcr 76T*  
      - *pfmdr1 86Y*

Copy number >1 at even higher risk of AL failure
Molecular Surveyor - *pfcr* and *pfmdr1*

http://www.wwarn.org/molecular/surveyor/#0
3. Antimalarial drug challenges

A. Poor community engagement on antimalarial drug use

A. Poor quality of drugs
   - Sub-standard, incorrect dosage
   - Falsified
A- To adopt appropriate behaviour

Confirmation of presence of malaria parasites before treating.

Necessity to better communicate and engage the population

Figure 4.3 Proportion of suspected malaria cases attending public health facilities who receive a diagnostic test, by WHO region, 2010–2015. Source: National malaria control programme reports
• Drug quality reports are lacking for 63 (60.3%) of 104 malaria endemic countries
• It may represent >50% of pharmaceuticals in several African countries
  Ex Lumbumbashi, 31.7% counterfeit (Tshilumba et al., 2014)
B- Challenges of fake and counterfeit drugs

Poor-quality including subtherapeutic drugs in malaria-endemic countries may increase the risk of artemisinin resistance
Capacities strengthening

- **Human resources**
  Molecular biologists, epidemiologist, statisticians, etc..
- **Infrastructure**
  Equipped laboratory for molecular and *in vitro* investigations

*Necessity to strengthen collaboration between researchers and National Malaria Control Programme Manager.*
Conclusions

• Generate reliable data from malaria areas is key
• Data sharing
• Importance of collaboration between community, stakeholders, researchers, health workers
• Information sharing to the population is crucial.
Acknowledgement

FCRM and Central African Network on Tuberculosis, HIV/AIDS and Malaria (CANTAM)
PANDORA
EDCTP
IDDO /WWARN
AFRICA-CDC
Thank you for your attention