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MEETING REPORT

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Research activities to improve the utilization of antibiotics in Africa

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ABSTRACT

There is a need to improve the rational use of antibiotics across continents including Africa. This has resulted in initiatives in Botswana including treatment guidelines and the instigation of Antibiotic Stewardship Programs (ASPs). The next steps involve a greater understanding of current antibiotic utilization and resistance patterns (AMR). This resulted in a 2-day meeting involving key stakeholders principally from Botswana to discuss key issues including AMR rates as well as ASPs in both the public and private sectors. Following this, the findings will be used to plan future studies across Africa including point prevalence studies. The findings will be presented in July 2016 at the next Medicines Utilization Research in Africa meeting will ideally serve as a basis for planning future pertinent interventional studies to enhance the rational use of antibiotics in Botswana and wider.

Meeting

Greater accessibility to antibiotics has contributed to their irrational and excessive use [1–3], leading to increasing antimicrobial resistance (AMR), a decline in their effectiveness, and a strain on health-care systems [4]. Irrational use is not helped by self-purchasing of antibiotics, which is common in many countries including African countries across a wide range of infections [5,6].

It is estimated that AMR infections currently cause approximately 50,000 deaths a year in Europe and the US alone, increasing to several hundred thousand when other countries are included [7,8]. The continual rise in AMR could result in infections that are resistant to antibiotics, becoming a leading cause of death by 2050, with a clear link between overuse of antibiotics and AMR. This will significantly impact on the wealth of nations, potentially costing up to US$100 trillion/year by 2050 [1,7,9–11].

These concerns have resulted in strategies across countries to reduce inappropriate use, including the instigation of multifaceted approaches in the community as well as antibiotic stewardship programs (ASPs) especially in hospitals, where antibiotics can account for up to 35% of medicine expenditure, with the World Health Organization (WHO) playing a leading role [3,5,8,11–14]. The prevalence of HIV-related opportunistic infections including TB, malaria, and sexually transmitted infections have also increased the demand and cost of antibiotics prescribed within hospitals.

There have been combined activities in Botswana to improve the use of antibiotics, including the development of antibiotic guidelines and other measures; however, research has shown that guidelines are not always followed and there are concerns with the extent of empiric use and limited use of sensitivity analyses in some hospitals [5,15]. These concerns resulted in initiatives in both public and private sectors in Botswana to document current activities, including resistance patterns, as well as plan future research activities in both ambulatory and hospital care. This was the basis of this 2-day meeting, which also included representatives from the WHO as well as other African countries.

The meeting was opened by the University of Botswana's Dean of the Faculty of Medicine, followed by Brian Godman (Karolinska University Hospital, Sweden) giving a brief introduction to drug utilization research, including the Anatomical Therapeutic Chemical/ Defined Daily Dose (ATC/DDD) classification as a standard means for collecting and comparing drug utilization patterns within and between countries [16]. In addition, Godman introduced the Medicines Utilization Research in Africa (MURIA) group. MURIA activities to-date include two meetings in 2015 to develop and progress drug utilization capabilities [5,17]. National and cross-national studies allied to health policies pave the way to plan future measures since without such studies planning is difficult. This strategy has worked well across Europe and beyond involving multiple classes of medicines [13,18–20].

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Abayneh Desta (WHO Regional Office for Africa, Republic of Congo) discussed concerns and issues with antibiotic prescribing in Africa. These included weak laboratory capacity, poor compliance to prescribed medicines—not helped by the high cost of some treatments, considerable self-medication, and poor health information systems. These factors influence the development of AMR, jeopardizing the health of individuals and society. The WHO has undertaken a number of activities to address this, including guidelines for establishing Drugs and Therapeutic Committees (DTCs) as well as strategies, policies, and other documents to reduce AMR [8,11,21]. Ways forward include strengthening the knowledge and evidence base, and optimizing the use of antibiotics. The latter includes implementing targeted strategies to reduce inappropriate use of antibiotics informed by AMR surveillance data. These include well-functioning DTCs and ASPs as well as evaluating current utilization patterns. Arno Muller emphasized the ATC/DDD methodology for comparing utilization across countries, and discussed projects comparing antimicrobial consumption in both ambulatory care and hospitals [22]. Muller also discussed current Point Prevalence Studies (PPS) as a basis for potential studies in Botswana and other African countries [23]. Advantages of PPS include greater knowledge of current antibiotic use in individual hospitals, which can subsequently provide a baseline to assess different targeted interventions, which could be part of ASPs. PPS also enable comparisons nationally and cross-nationally if standardized protocols are used to improve future antibiotic use. Challenges include resource requirements and the inherent heterogeneity between hospitals.

Celda Tiroyakosi (Ministry of Health, Botswana) discussed ongoing activities in Botswana to enhance appropriate antibiotic use through the National Standing Committee on Drugs, hospital DTCs, and the revision and implementation of the Botswana Antimicrobial Therapy Guidelines in 2012. The second edition of the guideline was divided into 12 chapters and 5 appendices including suggested antibiotic regimes for a range of infections to guide prescribers on the most cost-effective option. It also suggested second-line options such as Clarithromycin for *H. pylori* as well as comments on their side effects, resulting in a promotion of consistency in the treatment of infections. The guideline also places restrictions on the use of certain antibiotics to reduce inappropriate use, for example, amikacin and fluoroquinolones for multi-drug resistant-TB; however, there is concern that the guidelines are not regularly used, which needs to be addressed.

Bene Paramadhas (University of South Africa, South Africa) discussed microbial prevalence and antibiotic sensitivities from 2012 to 2015 in Nyangabgwe Hospital. The most common isolates included *E. coli, Staphylococcus aureus*, and *Klebsiella pneumoniae*. Prevalence rates were greater in adults and differences were observed in males and females. Resistance of *S. aureus* and *Streptococci spp* to penicillin-G was 99% and 70%, respectively; *E. coli* to ampicillin, 77%; *K. pneumonia* and *E. coli* to cefotaxime 62% and 47%, respectively; *K. pneumonia* and *E. coli* to amoxicillin plus clavulanic acid 52% and 24%, respectively. *Methicillin-resistant Staphylococcus aureus* rates declined from 55% to 2.9%, whilst *extended spectrum ß-Lactamase-producing Klebsiella* and *E. coli* increased from 15.38% to 26.92% and 0% to 16.53%, respectively. The use of guidelines, restrictive antibiotic policies, and antibiograms has improved the empiric use of antibiotics. Most microbiology products were available in 2015, enhanced by a local emergency procurement fund. The hospital Infection Prevention and Control Committee meets regularly, develops policies, guidelines, and procedures as well as oversees implementation. The results of a survey and action plan to improve hand hygiene were also discussed.

Brighid Malone and Gobuiwang Kurusa (Bokamoso Private Hospital, Botswana) discussed ongoing activities in Bokamoso Hospital to improve antibiotic utilization. These include the development of an Infection Control Committee, biannual antibiograms focusing more recently on ESKAPE organisms, an active multidisciplinary DTC with the ASP as a subcommittee meeting once-monthly, as well as the development of treatment guidelines based on the Botswana Antibiotic Guidelines, the WHO, the South Africa ASP, and other guidelines where necessary. The function of antibiograms is to guide empiric use as well as monitor the emergence of resistant strains. They also help gain closer collaboration between clinicians and microbiology staff, especially for managing difficult and unusual infections. The ASP in Bokamoso is led by an Infectious Disease (ID) Specialist and a Clinical Pharmacist, with close collaboration between ID specialist/pharmacists with Infection Control as well as with the Hospital administration under quality assurance and patient safety. As part of the program, antimicrobial use can be measured and tracked, with the potential for prospective interventions and feedback. Areas of focus include dose optimization, parenteral to oral switch, as well as time to first antibiotic dose.

Thatayaone Didimalang (Gaborone Private Hospital, Botswana) discussed current ASPs at Gaborone Private Hospital. The ASP consists of a multidisciplinary team with active participation involving all key stakeholder groups. Materials and guidance, including issues such as the duration of therapy, are prominently displayed. Roles and responsibilities are clearly defined for hospital managers, nursing staff, infection prevention specialists, unit managers, pharmacists, and physicians. Implementation is centered on four pillars: Phase 1—establishing a framework, Phase 2—pharmacy and nursing, Phase 3—progress evaluation, and Phase 4—clinical guidelines. There are ongoing audits and feedback to improve the use of antibiotics and this will continue. Mosana Moyo (Gaborone Private Hospital, Botswana) subsequently discussed current antibiotic sensitivities, which feed into any ASP. Summary of gram-negative bacteria revealed the following: (i) amoxacillin and cotrimoxazole cannot be used as first-line therapy; (ii) cephalosporins exhibited a high degree of sensitivity although the first generation should only be used to treat cystitis; (iii) fluoroquinolones demonstrated high levels of resistance; and (iv) carbapenems and aminoglycosides showed good sensitivity. No vancomycin-resistant *Enterococci* were found and only 11% *Staphylococcus aureus* isolates showed methicillin resistance.

The remainder of the meeting was devoted to developing a draft protocol with a PPS design in both private and hospital sectors in Botswana and possibly widening the scope into

Tanzania and Zimbabwe. The draft data-collection form had a set of instructions and thereafter was divided into several parts. Part one includes basic data on the hospital or study setting (completed only once) with part two including data relating to the ward, specialty, and census. Part three includes patient demographic information, diagnosis, risk factors, antibiotic history, a review of current antibiotic prescriptions, and WHO core drug-use indicators. Part four includes data to assess current microbiology services and capacity, the functioning of DTCs, Infection Prevention and Control committees, ASPs, and guideline dissemination. The variables were mostly aligned to that of the European Centre for Disease Prevention and Control PPS study [23] to enable comparisons to be drawn.

The next steps include refining the protocol, seeking ethical approval, piloting the study, and subsequently undertaking the study among hospitals in Botswana. The intention is to present the findings at the next MURIA meeting in Botswana in July 2016 as a basis for developing future pertinent interventions. Consequently, further enhance the appropriate use of antibiotics in Botswana and further afield in Africa.

Conclusion

The 2-day meeting drew together key personnel and expertise from the WHO and Botswana, as well as representatives from Tanzania and Zimbabwe, to debate and plan research activities in Africa to help enhance the rational use of antibiotics. The first step in the process is to gain a better understanding of current antibiotic utilization patterns alongside resistance patterns. This is now ongoing.

Acknowledgements

Declaration of interest

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