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MEETING REPORT

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Antimicrobial utilization research and activities in Botswana, the past, present and the future

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ABSTRACT

A number of activities are ongoing to reduce AMR in Botswana by improving antimicrobial utilization across all sectors. However, there is a need to share experiences. With the objective of sharing these, the second one day symposium was held in the University of Botswana in October 2018 involving both private and public hospitals. In Lenmed Bokamoso hospital, ESKAPE organisms were associated with 50-90% of clinical infections; however, there was no correlation between healthcare associated infections (HAIs) and admission swab positivity with ESKAPE or ESBL isolates. Hang times, the time between a prescription and IV administration, were also discussed. At Nyangabwe Hospital, the prevalence of HAIs was 13.54%, 48.9% were laboratory confirmed of which 8.5% were blood stream infections (BSIs). The prevalence of different bacteria causing neonatal BSIs was also investigated. At Princess Marina Hospital, positive cultures were seen in 22.4% of blood cultures with contaminants comprising the majority. Several activities are ongoing in Botswana across sectors as a result of the findings and will be periodically reported to further improve antibiotic utilization.

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1. Introduction

There is recognition in Botswana that the inappropriate prescribing of antibiotics increases antimicrobial resistance rates (AMR), increasing morbidity, mortality and costs [1–4], with a number of ongoing activities across sectors to improve antimicrobial utilization as part of the National Action Plan (NAP) of Botswana [5]. These include undertaking a national point prevalence study (PPS) in hospitals to guide future antibiotic prescribing, initiatives to reduce healthcare associated infections (HAIs) as well as surgical site infections (SSIs), evaluating the extent of prescribing of antibiotics for upper respiratory tract infections among private GPs, and appraising prescribing practices among primary health care facilities in Botswana with an emphasis on antibiotics [1,4,6–8]. These activities are already leading to improvements in antibiotic use and surveillance of HAIs in Botswana.

This second national antibiotic symposium in Botswana was undertaken to build on these activities. This was achieved through sharing new research findings across sectors regarding antibiotic utilization and resistance patterns, local bacterial prevalence rates and infection prevention and control (IPC) practices. The outputs would be used to inform future activities in Botswana as well as be part of the implementation of the ongoing NAP to reduce AMR rates.

2. Objectives and rationale

The theme of the symposium was 'Antimicrobial Utilization Research and Activities in Botswana, the Past, Present and the Future' held at the University of Botswana, 24 October 2018. The objectives were to sensitize the participants on developments in the areas of AMR and to share initiatives, experiences, and the findings from current activities. The outputs were aimed particularly at improving antibiotic utilization in both public and private hospitals, and to subsequently use the findings as a basis for improving future antibiotic utilization as part of the ongoing NAP. This one day symposium was followed by a training session for new researchers interested in conducting PPS in Botswana, building on the initial training sessions and ongoing lessons from the first comprehensive PPS in Botswana [1,4,5].

The meeting was chaired by Professor Amos Massele and opened by the Dean of the Faculty of Medicine, University of Botswana. This was followed by an update by Dr. Celda

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Tiroyakgosi on current initiatives in the development and implementation of the Botswana NAP to contain AMR.

3. Plenary session

Dr Brighid Malone started the session by discussing factors that may influence the development of HAIs in Lenmed-Bokamoso Private Hospital, with HAIs known to increase morbidity, mortality and costs [8,9]. Risk factors for HAIs include hand and environmental hygiene as well as surgical and critical care instrumentation involving invasive procedures [9,10]. In a prospective study conducted between July 2017 – September 2018, the rate of HAIs ranged from 0–6 per 1000 in-patient days, with ESKAPE (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter* species) organisms associated with 50-90% of clinical infections and the extended spectrum beta-lactamase (ESBL) producing bacteria with 0-25% of clinical infections. Admission swab positivity rates ranged from 0-7% of all admissions with ESKAPE bacteria constituting 80−100% of these and ESBL producing bacteria constituting 0−50% of bacteria isolates. However, no correlation was found between HAIs and admission swab positivity with ESKAPE or ESBL isolates. Overall, HAIs are not associated with bacterial colonization during admission in Lenmed-Bokamoso hospital. There was, however, a correlation between HAI rates and locally prevalent bacteria causing clinical infections in hospitalized patients in this hospital. In view of the findings, surveillance is ongoing in the hospital with admission swabs now being taken from the groins of all high risk patients. All admission swabs and all clinical infection isolates found to be positive for ESKAPE and ESBL bacteria are notified immediately by the microbiologist to key medical staff, the ward manager and the infection, prevention and control team. Appropriate contact precautions are promptly instituted. Monthly HAI and admission statistics are also now reported to all clinicians, ward managers, pharmacy and hospital management to increase general awareness of the issue of resistant bacteria, and this is being followed up.

HAIs and its potential risk factors were also the subject of research undertaken by Pinkie Mpinda-Joseph and colleagues at Nyangabgwe Hospital as a substantially higher prevalence of HAIs is often seen in developing countries [9]. This is a concern as HAIs are preventable through good IPC practices [9,10]. This is particularly important in countries such as Botswana with high rates of HIV (human immunodeficiency virus) among in-patients [1,11]. Current HAI prevalence rates are unknown among public hospitals in Botswana. To address this, in November 2017, a one-day PPS was undertaken in this public tertiary hospital in the northern part of the country through sampling the medical records of all in-patients. Three hundred and forty seven medical records were studied with a HAI prevalence rate of 13.54%. 48.9% were laboratory confirmed HAIs of which 8.5% were blood stream infections and 19.1% were SSIs. Ventilator associated pneumonia/complications were 17%, and 10.6% were decubitus ulcers [8]. Risk factors included a high injectable antibiotic use (79.2% of the patients were on antibiotics) with 32.5% (n = 58) receiving more than two antibiotics during their admission. Patients on indwelling urinary catheters were 10%, and 9% were previously hospitalized in the past 90 days. The promotion of IPC activities in the hospital are ongoing and include training, encouraging compliance with hand hygiene protocols and capacity improvements as well as improved surveillance and monitoring of activities to reduce HAI rates [8].

Pinkie Mpinda-Joseph also discussed trends in the prevalence of neonatal bloodstream infections (BSIs) and AMR rates in Nyangabgwe hospital. This is because up to 71% or more of neonates are prone to BSIs during intensive care [12], and indiscriminate antibiotic use coupled with poor IPC practices increases infection rates and AMR. This study was undertaken to assess BSI rates by conducting a retrospective review of neonatal blood culture and sensitivity test results from January 2014 to December 2017 which involved 366 isolates. The prevalence of bacteria causing neonatal BSIs were: Coagulase Negative Staphylococcus species (CoNS) – 31.97%, *Enterococcus spp*. – 18.03%, *Klebsiella pneumoniae* – 10.93% and *Staphylococcus aureus* – 8.47%. There was an increased prevalence of CoNS, *Klebsiella spp., Staphylococcus aureus* and *Acinetobacter spp*. from 2016 with a decrease in the prevalence of *Enterococcus spp*. and *Escherichia coli*. Regarding AMR, the extent of ESBL producing *K. pneumoniae, Enterobacter spp*. and *E. coli* were 55%, 15.38%, and 11.11% respectively, with *K. pneumoniae* and *E. coli* showing an increasing trend of ESBL producing strains. Of the *S. aureus* isolates, 19.35% were methicillin resistant while 6.06% of *Enterococcus spp*. were resistant to vancomycin. *Acinetobacter spp*. showed 100% resistance to meropenem, cephalosporins, aminoglycosides and the fluoroquinolones. Interventions are ongoing to reduce BSI rates among neonates in this hospital including initiatives to reduce the use of third generation cephalosporins and missed antibiotic doses [8].

Godfrey Mutashambara Rwegerera subsequently discussed BSIs at Princess Marina Hospital with early diagnosis and appropriate treatment seen as the best approaches to improve prognosis and prevent AMR. A retrospective laboratory study of all blood cultures from 1 January 2011 to 31 December 2015 showed out of 16,824 blood cultures, a positive blood culture was seen in 22.4%. CoNS, which were most probably contaminants, comprised the majority (43.0%). Of the remaining isolates, 45.8% were Gram-positive bacteria and 54.2% Gram-negative bacteria. The predominant bacteria species isolated included *Klebisella pneumoniae* – 18.3%, *Staphylococcus aureus* – 13.6%, *Streptococcus spp*. – 11.3%, *Escherichia coli* – 10.3% and *Pseudomonas aeruginosa* – 5.3%. *Enterococcus spp*. were sensitive to vancomycin, ampicillin and penicillin at 88.2%, 56.3% and 50.9% respectively. For common Gram negative isolates, moderate to high resistance patterns were observed for most antibiotics. There was, however, low resistance to gentamycin, ciprofloxacin, cefotaxime, amoxycillin with clavulanic acid, piperacillin-tazobactam and amikacin among *Escherichia coli* at 12.9%, 11.8%, 13.7%, 14.0%, 5.2% and 0% respectively. There was also low resistance for the majority of commonly tested antibiotics including amikacin, ciprofloxacin, piperacillin-tazobactam, gentamycin and ceftazidime for *Pseudomonas aeruginosa*. In addition, low to moderate resistance for amikacin, ciprofloxacin, piperacillin-tazobactam, gentamycin and cefotaxime against *Enterobacter spp*. These local resistance patterns necessitate

careful selection of antibiotics for empiric use as well as an urgent need to improve adherence to aseptic techniques during blood culture collection. These activities are already occurring in this hospital and will be reported on in the future.

Pharmacists are typically involved with improving antimicrobial use in hospitals as part of antimicrobial stewardship programmes (ASPs) and Drug and Therapeutics Committees (DTCs) [13,14], although there are concerns with the lack of ASPs in some African countries and hospitals in Botswana [1,15,16]. It is widely known that delays in administration of the initiated antibiotic is associated with poor prognosis [17]. Keamogetse Maika discussed the role of pharmacists with improving antimicrobial utilization in Bokamoso Hospital by focusing on the timeliness in administration of the first dose of intravenous (IV) antibiotics through measuring 'hang times' [18]. 'Hang time' is defined as the time interval from writing an antibiotic prescription on the patient's chart to the actual administration of the first dose of the antibiotic [18]. A prospective study was conducted to identify potential barriers that contribute to any delay in achieving the desired administration of the first dose in less than one hour following a prescription. A specific antibiotic prescription chart was introduced into the neonatal, pediatric, and adult intensive care units (NICU, PICU and ICU) as well as pediatric wards with a baseline assessment carried out over 3 weeks in June 2018. The pharmacist made ward visits to capture the times of the prescriptions and subsequent antibiotic administration, with only the first dose considered. The baseline compliance to hang time < 1 hour was 18.4% in June 2018. Various interventions were instigated in July 2018 to address this including training of staff, regular interactions with physicians, and revising the hang time monitoring tool. Improvement in hang time compliance to < 1 hour occurred by August 2018, but there was a subsequent reversal after this. The monthly hang time compliance reports from the various wards were subsequently repeatedly discussed with ward unit managers to improve times. Several challenges were encountered which led to suboptimal times. These included patient records with missing times of the initiation of prescriptions and the administration of the first antibiotic dose, absence of an IV cannulation kit on admission (NICU, Pediatric wards), and the use of non-antimicrobial prescription charts to prescribe antibiotics. These issues are currently being addressed through renewed initiatives and we will be reporting the results in the future.

4. Conclusion and next steps

Several next steps were agreed following this interactive symposium including progressing with further PPS studies. Several other activities are ongoing to improve antibiotic utilization including initiatives to reduce HAIs, SSIs, BSIs, and hang-times and these have been documented. The outcome of these activities will also be reported in the future providing exemplars to other sub-Saharan African countries. There will also be future training and initiation of ASPs in Botswana to further reduce the overuse of antibiotics.

5. Expert opinion

There is a need to share activities across sectors within countries to improve the future use of antibiotics as countries implement and refine their NAPs to reduce AMR. Botswana is no exception. The sharing of research findings and discussions is already resulting in a number of planned activities to improve future antibiotic prescribing in Botswana. These include always taking admission swabs in high risk patients and all isolates subsequently found to be positive for ESKAPE and ESBL bacteria should be immediately notified to all key personnel to instigate appropriate contact precautions. There are also ongoing activities to reduce HAIs within hospitals especially around patients with identified risk factors, and this will continue including reducing the use of third generation cephalosporins and addressing missed antibiotic doses. Identification of local resistance patterns will also grow across hospitals to improve future empiric use of antibiotics. It is also likely that hang times will be reduced in the future with increasing focus on these.

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Declaration of interest

C Tiroyakgosi is employed by the Ministry of Health and Wellness in Botswana. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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