PHARMACOVIGILANCE
NEWSLETTER

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Best practices for disposal of antimicrobials amidst the escalating threat of Antimicrobial Resistance

Content

Health professionals and patients are encouraged to **report adverse events** or **quality problems** experienced with the use of **vaccines and medicines** to the nearest NAFDAC office or via pharmacovigilance@nafdac.gov.ng or via eReporting platform available on the NAFDAC website www.nafdac.gov.ng or via Med Safety Application available for download on Android and IOS stores.

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EDITOR'S NOTE...

We wish to thank our numerous stakeholders who have been working tirelessly with the National Pharmacovigilance Centre (NPC) to ensure the safe use of medicines in Nigeria. The NPC is committed to sending out the quarterly newsletter to its stakeholders. The objectives of the Newsletter are to disseminate information on Pharmacovigilance activities nationally and globally, to educate stakeholders on medicine safety issues, to promote rational use of drugs and to promote reporting of Adverse Drugs Reactions (ADRs) and AEFIs. This edition of the newsletter focuses on: **Best practices for disposal of antimicrobials amidst the escalating threat of Antimicrobial Resistance**

We encourage Health care Professionals and other stakeholders to continue to report all adverse drug events and AEFIs. Your valued comments and acknowledgement of receipt of this issue through our email addresses (nafdac_npc@yahoo.com; pharmacovigilance@nafdac.gov.ng, fdic@nafdac.gov.ng) would be most appreciated.

Thank you for your relentless efforts in strengthening Pharmacovigilance System in Nigeria.

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Introduction

Antimicrobial medicines are the cornerstone of modern medicine. The emergence and spread of drug-resistant pathogens threatens our ability to treat common infections and to perform life-saving procedures including cancer chemotherapy and caesarean section, hip replacements, organ transplantation and other surgeries. In addition, drug-resistant infections impact the health of animals and plants, reduce productivity in farms, and threaten food security (WHO, 2023). The term antimicrobial is a broad name for all ant infectives including antifungal, antiretroviral, and antibacterial among others. Antibiotics are commonly used pharmaceutical compounds in human and veterinary medicine for treating microbial infections. They are also used as growth promoters in agriculture and aquaculture. The total amount of antibiotics used per year, including medical and veterinary uses, is 100,000–200,000 tons worldwide. By 2030, 67% global rise in livestock antibiotics consumption from 63,151 ± 1560 to 105,596 ± 3605 tons is estimated. Eventually, every antibiotic pill ends up in nature, and approximately 95% of the antibiotics is excreted in unaltered form in the environment. Large amounts of antibiotics are discharged into the environment in their original form through medical waste, pharma-industry wastewater, and sewage effluent. Antibiotics are detected in varying concentrations depending upon the source in the aquatic systems such as rivers, lakes, and even in groundwater. These antibiotics and their residues pose a great threat to the nontarget organisms and ultimately rise of resistant strains resulting in the disruption of the ecosystem. The presence of antibiotics and residuals thereof in the environment is a serious concern and results in antimicrobial resistance (AMR),

which even causes difficulty in the treatment of illnesses like typhoid, gonorrhoea, tuberculosis, and malaria, which were curable few years back (Sharma, M. et al, 2021). Antimicrobial Resistance (AMR) occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines meant to control them, making infections harder to treat and increasing the risk of disease spread, severe illness and death. Microorganisms that develop antimicrobial resistance are sometimes referred to as "superbugs" (WHO, 2024).

Antimicrobial resistance (AMR) is one of the top global public health and development threats. It is estimated that bacterial AMR was directly responsible for 1.27 million global deaths in 2019 and contributed to 4.95 million deaths. The misuse and overuse of antimicrobials in humans, animals and plants are the main drivers in the development of drug-resistant pathogens. AMR affects countries in all regions and at various income levels and the low- and middle-income countries are most affected (Sharma, M. et al, 2021). The World Bank estimates that AMR could result in US$ 1 trillion additional healthcare costs by 2050, and US$ 1 trillion to US$ 3.4 trillion gross domestic product (GDP) losses per year by 2030 (WHO, 2024).

AMR has significant costs for both health systems and national economies overall. For example, it creates need for more expensive and intensive care, affects productivity of patients or their caregivers through prolonged hospital stays, and harms

agricultural productivity. AMR is a problem for all countries at all income levels. Its spread does not recognize country borders. Contributing factors include lack of access to clean water, sanitation, and hygiene (WASH) for both humans and animals; poor infection and disease prevention and control in homes, healthcare facilities and farms; poor access to quality and affordable vaccines & relevant legislation. People living in low-resource settings and vulnerable populations are especially impacted by both the drivers and consequences of AMR (WHO, 2023).

The Key Strategies to address AMR in human health include preventing all infections, which may result in inappropriate use of antimicrobials; ensuring universal access to quality diagnosis and appropriate treatment of infections; and strategic information and innovation, for example surveillance of AMR and antimicrobial consumption/use, and research & development for novel vaccines, diagnostics and medicines (WHO, 2023).

The most common generic antibiotics include amoxicillin, doxycycline, floxacins, metronidazole, azithromycin, gentamycin, and cefixime. In India, almost all isolates of cholera were found to be resistant to the first line of drugs and ampicillin was on the top of the antibiotics list against which more than 50% of isolates showed resistance and it was followed by the group floxacin and tetracyclines. Antibiotics' consumption has become a global concern needing immediate attention. Unused and expired antibiotics are continuously disposed of as household waste in sewage wastewater, and this acts as social driver of antimicrobial resistance (AMR).

A study titled "Disposal of unused antibiotics as household waste: a social driver of antimicrobial resistance" suggests that public awareness regarding the use of prescribed antibiotics, completion of the course, and knowledge of the safe disposal of unused/expired antibiotics will be a good strategy to combat AMR. Indeed, the unethical use of antibiotics has become a worldwide concern in developed as well as in developing countries (Sharma, M. et al, 2021).

Disposal of unused Antibiotics

The Disposal of Unwanted Medication Properly program in New Zealand and the ENVIRx disposal program in Canada were initiated to ensure the suitable disposal of pharmaceutical products. While addressing quality use of medications, the improper disposal of unused, stored or expired pharmaceuticals is a major concern. Many medication users are unaware of proper disposing methods and thus opt to flush or throw away their unwanted and expired medicines. This inappropriate disposal ends up in landfills, water supplies and drains that lead to contamination of the environment and a wide range of toxicities to humans, animals and marine life. (Anwar, M. et al, 2020). Unused and expired antibiotics are categorized as the hazardous waste and they should be collected separately from other household waste and disposed of by using the incineration method at high temperature, but this not always adhered to and in general the public is not aware about these rules and regulations. Moreover, the irrational use of antibiotics and their disposal as municipal solid waste is becoming a serious concern to achieve sustain able development goals (SDGs). For example, SDGs state that local engagement in water and sanitation should be supported (SDG 6.a) and expanded water and sanitation

support to developing countries (SDG 6.b). Careless disposal of unused and expired antibiotics leads to the presence of antibiotics in the aquatic environment (Sharma, M. et al, 2021).

The NAFDAC Good Distribution Practices Guidelines for Pharmaceutical Products 2023 stipulates that the destruction of pharmaceutical products should be done in accordance with the requirements of the Agency and other national and international requirements regarding disposal of such products, and with due consideration to protection of the environment. In Nigeria, the Association of Community Pharmacists receives expired antibiotics & other medicines from its members and submits them to NAFDAC for destruction.

A study conducted in Anambra by Michael, I. et al, (2019) assessed disposal practices of expired and unused medications by pharmacists in the State and compared them to the NAFDAC guideline on disposal of expired drugs. Questionnaires and key informant interview (KII) were used for the survey. The study was aimed at assessing the methods and protocols used by community pharmacists in the disposal of expired drugs. From the results of the study, 17.0 (22.1%) of the respondents reported that NAFDAC uses incineration or other forms of heat to dispose of expired drugs, but 19.0 (24.7%) reported they do not know how NAFDAC dispose of their expired drugs. Majority of the respondents, 55.0 (71.4%) suggested that the state-run disposal system was in operation. The study concluded that poor compliance with the NAFDAC guideline for medication disposal increases the potential risk of contamination of our environment and the possibility of ingesting toxic pharmaceutical wastes by humans and animals. This underscores the need for improvement on the management protocols for expired drugs to prevent contamination and other health hazards (Michael, I. et al, 2019).

Antimicrobial Resistance

Antimicrobial resistance (AMR) is one of the greatest threats to public health globally. In 2019 alone, an estimated 4.95 million deaths associated with bacterial AMR was recorded. This is more deaths than caused by HIV/AIDS or malaria. The WHO postulates that Antimicrobial Resistance (AMR) occurs when bacteria, viruses, fungi and parasites no longer respond to antimicrobial agents. As a result of drug resistance, antibiotics and other antimicrobial agents become ineffective and infections become difficult or impossible to treat, increasing the risk of disease spread, severe illness and death. It is a threat to humans, animals, plants and the environment.

The increase in antibiotic consumption is repeatedly associated with the free availability, accessibility, and incongruous use of antibiotics and the reason for developing antibiotic resistance. However, leftover, unused and expired antibiotics, and their improper disposal as a potential driver of antimicrobial resistance is not commonly discussed in literature. Appropriate disposal of unused and expired antibiotics is of great importance because of the impending environmental hazards and public health risks. The disposed antibiotics when not degraded or eliminated during wastewater treatment reach surface water or are passed into the aquatic environment. Even though the concentration of such disposed

antibiotics is negligible, such concentrations are equally capable of promoting resistance either by horizontal gene transfer or by modifying targets. This repositions the host genomes and act as vehicles for resistance acquisition and their consecutive transmission. Hence, this indiscriminate release into the environment compromises the effectiveness of antibiotics and augments resistance as harmless microbes mutate to deadly and resistant pathogens. Consequently, the very bacteria when transmitted to humans are already resistant to the available antibiotics leading to increased morbidity and mortality as well as an increased economic burden to the health care system (Anwar, M. et al, 2020).

With neglected tropical dideases (NTDs), the emergence of AMR is a significant threat to programmes which control, eliminate and eradicate NTDs, which especially affect vulnerable and marginalized populations. Resistance has been reported in leprosy medicines (dapsone, rifampicine and clofazimine) in several countries, in several anti-helminthics (while resistance has so far only been observed in use in animals, which is a serious concern for the veterinary sector, some of these medicines are also used in humans), in medicines used to treat human African trypanosomiasis (melarsoprol) and leishmaniasis (pentavalent antimonials, miltefosine), and others. It is important to monitor resistance and drug efficacy, put in place strategies to delay or curb resistance, and strengthen the pipeline of second-line medicines for NTDs. The WHO provides guidance for surveillance of resistance for the global leprosy elimination programme, and support to control distribution and monitor the standardized use, safety and efficacy of medicines, including donated medicines, in NTD programmes. Drug resistance has also emerged in other areas including in bacteria, fungi, HIV, tuberculosis and malaria (WHO, 2023).

The various factors driving antibiotic resistance in India include unnecessary high consumption of broad-spectrum antibiotics; antibiotic fixed-dose combinations prescription even without the knowledge of a proven advantage over single compounds; social factors like self-medication, access to antibiotics without prescription, use of informal healthcare providers as sources of healthcare; lack of knowledge about when to use antibiotics, etc. and cultural activities like mass bathing in pilgrimage season (high resistance than any other time), overuse of antibiotics in food animals (fifth largest consumer), poor environmental sanitation facilities, and pharmaceutical industry pollution (Sharma, M. et al, 2021).

Global action to address AMR

Some of the recommended global actions to address AMR include the One health approach, Global action plan (GAP) on AMR, World AMR Awareness Week (WAAW), the Antimicrobial stewardship & AWaRe (WHO, 2023) as well as other novel approaches.

One health approach

AMR is a complex problem that requires both sector-specific actions in the human health, food production, animal and environmental sectors, and a coordinated approach across these sectors. One Health refers to an integrated, unifying approach that aims to achieve optimal and sustainable health outcomes for people, animals, and ecosystems. Indeed, it recognizes that the health of humans, domestic and wild animals, plants and the wider environment are closely linked and inter-dependent. The

One Health approach to preventing and controlling AMR brings together stakeholders from relevant sectors to communicate and work together in the design, implementation and monitoring of programmes, policies, legislation, and research to mitigate AMR and attain better health and economic outcomes. Cross-sectoral collaboration is important to preserve the effectiveness of antimicrobials. To effectively reduce AMR, all sectors must use antimicrobials prudently and appropriately, take preventive measures to decrease the incidence of infections and follow good practices in disposal of antimicrobial contaminated waste (WHO, 2023).

Global action plan (GAP) on AMR

To address AMR globally, countries adopted the Global action plan (GAP) on AMR during the 2015 World Health Assembly and committed to the development and implementation of multisectoral national action plans with a One Health approach to tackle AMR.

World AMR Awareness Week

The World AMR Awareness Week (WAAW) is celebrated from 18-24 November every year; it is one of WHO's official health campaigns since 2015. This is a campaign to raise awareness and understanding of AMR and promote best practices among One Health stakeholders to reduce the emergence and spread of drug-resistant infections. The theme for WAAW 2023 was "***Preventing antimicrobial resistance together***". As part of activities for the WAAW 2023 week, VMAP Directorate of NAFDAC led the celebration in NAFDAC at Lagos; a training was organised for staff of the Agency and stakeholders to create awareness and build capacity on the control of Antimicrobial resistance in the country. It was also aimed at disseminating clear messages and understanding the best practices to fight AMR in Nigeria.

Antimicrobial stewardship and AWaRe

Antimicrobial stewardship is a systematic approach to educate and support health care professionals to follow evidence-based guidelines for prescribing and administering antimicrobials. The education of the health workforce is of crucial importance, as they form the front line in safeguarding the effectiveness of antimicrobial medicines. Antimicrobial Stewardship Programmes are one of the most cost-effective interventions to optimize the use of antimicrobial medicines, improve patient outcomes and reduce AMR and health care-associated infections. To improve access to appropriate treatment and reduce inappropriate use of antibiotics, WHO developed the AWaRe (Access, Watch, Reserve) classification of antibiotics. The National Action Plan (NAP 2.0) is in place which includes Awareness & education, surveillance, antimicrobial stewardship, Infection, prevention and Control as well as Research & Development.

Novel approaches

Although improper disposal of antibiotics is now recognized as a critical concern, strategies to control and reduce this phenomenon have seen poor progress. There have been several awareness programs focusing on proper disposal of antibiotics for the community members through healthcare professionals and policymakers, but these are yet to yield the expected results. Based on the available evidence, both individualized and collective programs seem to have less effect in improving the proper disposal of antibiotics. There may be need to employ new initiatives to improve the understanding of proper disposal of antibiotics and the potential complications and contamination related to their improper disposal (Anwar, M. et al, 2020). Members of the society are usually impressed by celebrities and certain individuals have a colossal influence on their societal members. The same influence can

be utilized to change attitudes and practices regarding the improper disposal of antibiotics. The cascade-training approach has proven helpful where influencers from the society are selected, trained and appointed by healthcare authorities and professionals to educate community members about knowledge, activities, and skills related to proper disposal of antibiotics. This option may prove to be helpful in the current scenario where other interventions are yet to yield the desired success. The employment of novel approaches to address improper disposal of antimicrobials by the public is needed and the sustainability of useful interventions will play a key role in our fight against antibiotic misuse and resistance (Anwar, M. et al, 2020).

Conclusion

Appropriate disposal of unused and expired antibiotics is of great importance because of the impending environmental hazards and public health risks (Anwar, M. et al, 2020). AMR is a complex problem that requires both sector-specific actions in the human health, food production, animal and environmental sectors, and a coordinated approach across these sectors; fighting AMR is truly a global endeavor and must be addressed through a One Health approach (WHO, 2023). Creating & sustaining public awareness regarding the use of prescribed antibiotics, completion of the course, and knowledge of the safe disposal of unused/expired antibiotics is a crucial strategy to combat AMR (Sharma, M. et al, 2021).

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