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Editorial

Multidrug Therapy and Risk of Adverse Drug Reactions in Africa: The Need to Step up Pharmacovigillance to Improve Patient Health and Safety

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Background

Many chronic disorders are often managed with diverse pharmacological agents or fixed dose combination due to the complementary mechanism of the drugs which have additive or synergistic effects. In the face of different co-morbidities, combination therapy with two or more agents often adequately control the multifactorial risk factors associated with such diseases. Multidrug therapy also permits lower doses of each agent to be utilized and attenuates the side effects associated with higher doses in monotherapy [1].

Despite the benefits gained with combination therapy, the use of diverse agents may be associated with challenges as well. Complexity of most dosage regimen are known to result in discontinuation or non-adherence to therapy in some patients. Some combined drugs offer a great economic burden as well to the patients and relations. The probability of adverse drug reactions and drug-drug interactions occurring increases when drugs are combined. The diversity of pharmacological profile of medicines involved in combination therapy, involve continuous monitoring of patients on therapy for improved outcomes [2,3].

Stepping up Pharmacovigillance to Identify Adverse Reactions Associated with Multidrug Therapy in Patients with Chronic Diseases

According to WHO [4], an Adverse Drug Reaction (ADR) is defined as a drug response which is noxious and unintended, and occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function. Adverse drug reactions have limited the use or led to the withdrawal of a number of drugs from the market due to congenital defects, disabilities, hospitalizations and deaths [5,6]. They are the fourth leading cause of death in the Unites States, claiming about 100 000 to 2,00,000 lives [7, 8]. Enormous economic implications of adverse effects is estimated to be about US $ 130 billion yearly (8).

Elderly people are more susceptible to ADRs as a result of physiological changes accompanying old age (reduced efficiency of vital organs), multiplicity of co-morbidities, polypharmacy, greater admission rates, prolonged hospital stay, etc.[9]. Children (particularly neonates) experience high incidence of untoward reactions because of reduced drug organ capacity and integrity especially in metabolizing or eliminating drugs [10]. Research has shown that women have higher propensity of adverse reaction incidence compared to men [9]. Some gender related differences attributed to this observation are diversity of pharmacokinetic, immunological and hormonal factors which may require the use of difference classes of medicines [11]. Incidence of ADRs also increases with higher number of medicines taken [9]. Renal, hepatic and cardiac diseases are known to increase susceptibility of patients to adverse events because of changes in pharmacokinetic properties of drugs.

Diseases like HIV/AIDS and cancers predispose individuals to adverse events as a result of immunocompromised state [9,10]. Ethnic diversity and genetic factors such as Glucose-6-Phosphate (G6PD) Deficiency and porphyria predispose people to haemolysis and cutaneous reactions respectively [10,11]. Pharmaceutical errors in manufacturing lead to degradation of products, presence of drug contaminants, changes in quantity of drug and drug release properties. These anomalies can induce adverse drug reactions in some individuals [9]. There are drugs which are toxic by nature and others with narrow therapeutic indexes and hence increase the risk of inducing unwanted drug effects [9].

Antiretrovirals, antibiotics and ACEI are the common medicines implicated in adverse reactions in Africa with skin or Cutaneous Disorders frequently reported [12]. In other parts of the world, tumour necrosis factor, NonSteroidal Anti-Inflammatory Drugs and immunosuppressants are major causes of ADRs, with general disorders and administration site reactions among the commonest reports which incriminates tumour necrosis factor, often reported [12].

Many adverse reactions remain undetected during clinical trials until post marketing surveillance. Adverse reactions in pregnant women, children and the elderly are rarely detected as these categories of people are often excluded in clinical studies [13]. A number of approaches that reduce risk of untoward drug effects in patients include monitoring of susceptible patients, maintenance of high standards of operations in industries to reduce drug contamination, premarketing and post marketing surveillance, patient counselling on prescribed and over the counter medicines, monitoring of drug history of patients for allergies, addressing early signs and symptoms of adverse effects immediately to avoid fatalities and risk and benefit assessment of drugs for each patient [9].

Pharmacovigilance is paramount in the identification of ADRs through spontaneous and voluntary reports. World Health Organization recommends a minimum of 200 reports per year/million inhabitants for any Optimal National Centre [13]. The prime source of adverse drug reports are generated from healthcare practitioners and consumers. There is widespread assertion that ADRs are under reported in many nations and sometimes these adverse effects are not recognized as they occur [8]. A study undertaken in Mulango National Referral and Teaching hospital revealed that inadequate time and training of health personnel, additional workload to healthworkers, lack of feedback after reporting, fear of legal consequences, trivializing of reports and unavailability of ADR forms were some challenges associated with ADR reporting [14].

Approaches that have been devised to heighten adverse drug reporting include educational interventions (workshops, presentations, etc), technology strategies (telephone interviews, online reporting and phone alert systems), routine visit to health facilitiesbypersonnel ofpharmacovigilance units (protocol approach) and public education [13].

Findings gathered in a meeting on the safety of medicines in sub-Saharan Africa revealed the existence of pharmacovigilance units in most countries including Ghana, Nigeria, Kenya, Uganda and South Africa [12,15, 16, 17]. However about 50% of sub-Saharan countries lacked comprehensive data on pharmacovigilance and spontaneous reporting on ADRs [16]. Pharmacovigilance units have in Africa have increased from two in 1992 to thirty-five in 2015 with resultant cumulative increase in adverse drug reports. In a study by [12], less than 1% of global ADR reports can be attributed to Africa.

Apart from health workers and consumers, one vital source of ADR reporting which is often underutilized is pharmaceutical companies. Manufacturing companies mostly fail to carry out post-marketing of pharmaceuticals as directed by regulatory authorities [16]. Regulatory actions taken after ADR reports are known to increase confidence in institutions.

Looking at the implications of ADRs, obstacles to ADR reporting and the current avenues identified to improve pharmacovigilance, it behooves on governments in Africa to implement policies that safeguards patients with regards to medication use and safety. Education of healthcare providers on the need to identify, appropriately report and address patient concerns on ADRs is also paramount to reduce untoward effects of medications. The era in which the responsibility of ADR reporting was the sole responsibility of health professionals is fast retreating as the customer or patient has also emerged to be an essential source of information on drug usage and reactions. Active communication in addition to safety studies by African institutions would increase awareness and improve information on ADRs on the continent. These recommendations among others, if implemented effectively in Africa would enhance healthcare delivery, minimize fatalities, enhance patient trust in healthcare system and increase awareness on drug utilization and safety.

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