The impact of pharmacovigilance on the Nigerian healthcare system

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Abstract

Introduction

Pharmacovigilance (PV) is the science and activities relating to the detection, assessment, understanding and prevention of adverse drug reaction or any other drug- related problems such as drug abuse and misuse, medication errors, lack of efficacy and counterfeit or substandard medicines. PV also encompasses surveillance of side effects after short-term and long-term use of medicines. The experiences from the thalidomide tragedy which occurred from 1956 to 1962 resulting in the births of about 10,000 severely malformed infants , have influenced the World Health Organization (WHO) to initiate an international programme called pharmacovigilance in the year 1968 for the sole purpose of monitoring the safety of medicines use by the general population. Since year 2004, several African countries have been actively involved in PV including Nigeria, Ghana, South Africa, Kenya, Morrocco, Botswana, Cameroon, Mozambique, Sierra Leone,Tanzania, Togo, Uganda, Zambia and Zimbabwe.

Methodology/Results

This paper highlights the pharmacovigilance activities in Nigeria The activities include training and capacity building for healthcare providers, cohort event monitoring study, incorporating PV in public health programmes, public enlightenment, assessment of the National pharmacovigilance system, development of data tools for capturing of Adverse Events Following Immunizations (AEFIs), quality assurance through PV, research, safety of herbal medicines and the recent launch of the National PV policy

Conclusion

These activities have no doubt contributed to safety awareness and generated evidence-based safety data for the benefit of the health systems. Consequently, the risks that are associated with the use of medicines are significantly reduced.

Keywords: Pharmacovigilance, adverse drug reactions, Nigerian PV policy

Introduction

Pharmacovigilance (PV) is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug related problem.[1] Adverse Drug Reactions (ADRs) happen all over the world despite the expertise of the health care provider and it is unique to different populations. It has been estimated that ADRs are the 4th to 6th largest cause of mortality in the USA resulting in the death of several thousands of patients annually and leaving several others to suffer morbidities related to ADRs.[2]. The percentage of hospital admissions due to ADRs

vary from one country to another. It was 11.5% in Norway, 13% in France and 16% in the UK.[3]

In Nigeria, the situation may be worse due to wide spread irrational use of medicines including preference for injections, misuse of antibiotics and other prescription drugs, unstandardized use of orthodox and traditional/herbal medicines and extensive self-medication[4]. The gross inadequacy of research and paucity of data on safety of medicines in Nigeria are matters of serious concerns in Nigeria. It is therefore difficult to estimate the number of people that have died or disabled in our hospitals from unsuspected adverse drug reactions.

The past incidence in Nigeria, of contamination of teething mixture with diethylene glycol resulting in several deaths readily come to mind.[4] Pharmacovigilance therefore, is a critical component for the risk-benefit assessment of treatment. The potential for drug toxicity is continuously determined throughout the period of use of a drug or biological agent, including the development cycle.

The pharmacovigilance (PV) system safeguards the public through efficient and timely identification, collection, assessment, and communication of medicine-related adverse events. A comprehensive PV system includes both active and passive surveillance methods, effective mechanisms to communicate medicine safety information to health care professionals and the public, collaboration among a wide range of partners and organizations, and incorporation of PV activities into the various levels of the health system, from the facility to the national levels.

Methodology

This review examines the various PV activities and their impact on the Nigerian healthcare system including, incorporating PV into public health programmes, awareness creation and capacity building, cohort event monitoring, assessment of the National Pharmacovigilance System, development of data tools for capturing of Adverse Events Following Immunizations (AEFIs), PV research, safety of herbal medicines and the recent launch of the National PV policy. It also highlights the gaps and potential strategies for moving PV forward in Nigeria.

Results/Discussion

Pharmacovigilance in Africa

The experiences from the thalidomide tragedy which occurred from 1956 to 1962 resulting in the births of about 10,000 severely malformed infants , have influenced the World Health Organization (WHO) to initiate an international programme called pharmacovigilance in the year 1968 for the sole purpose of monitoring the safety of medicines use by the general population.

In recent times, a lot of activities have taken place in order to develop pharmacovigilance in Africa. As a result of these activities some African countries have become members of the WHO Programme for International Drug Monitoring being coordinated at the Uppsala

Monitoring Centre (UMC) in Sweden, As at December 2013, the UMC had 115 full member countries of which 31 are African countries. These African countries include Nigeria, Ghana, Egypt, Morocco, South Africa, Benin,Tunisia, Tanzania, Mozambique, Zimbabwe, Cote de´Ivoire, Burkina Faso, Botswana, Democratic Republic of Congo, Erithrea, Ethiopia, Madagascar, Sierra Leone, Uganda, Sudan, Zambia, Burundi, Liberia, Mauritius, Gambia, Cape Verde, Guinea, Guinea bisau, Rwanda, Zanzibar, and Niger.[5]

However, many African countries still require more training and support to establish effective pharmacovigilance. To facilitate this, a centre was established in Accra, Ghana to assist the Uppsala Monitoring Centre in developing pharmacovigilance in Africa. In October 2010, WHO designated the University of Ghana Medical School as a WHO Collaborating Centre for Advocacy and Training in Pharmacovigilance. The centre, also known as UMC-Africa (UMC-A) had aims and objectives similar to those of the UMC, which include the provision of technical support to National Pharmacovigilance Centres in Africa, training in various aspects of pharmacovigilance for health professionals and disease control managers in Africa and provision of pharmacovigilance tools and aids to countries.

Though the infrastructure for PV is beginning to be deployed more widely in Africa, the actual performance from a system's perspective is still very limited. To contribute to the efforts at improving pharmacovigilance systems' performance, USAID in collaboration with Strengthening Pharmaceutical Systems-Management Sciences for Health conducted an assessment of the pharmacovigilance system in 46 Sub-Saharan African countries with detailed investigation and interview conducted in nine countries including Nigeria.[6]

The result of the assessment showed that the PV system that is in place in most of the Sub-Saharan African countries, including Nigeria did not meet systems capacity and performance indicators.

The assessment also revealed that public health programmes made little efforts to routinely collate and aggregate adverse events and treatment modification data and share same with PV centres. These public health programmes are usually adequately funded and focus on mass distribution of medicines with inadequate systems in place to monitor the safety of the medicines they distribute.

Another study showed that most of the PV centres were not adequately staffed and had very limited resources.[7]

Preliminary information from PV Assessment has helped the Nigerian National PV centre to identify gaps in the PV system in Nigeria and efforts are being made to strengthen those areas of deficiencies

This minimum requirement formed the basis for systems classification and development of indicators for evaluation of PV systems. The National PV Center has keyed into this indicator

based pharmacovigilance assessment tool to effect self audit and develop strategies for developing effective platform for pharmacovigilance in Nigeria.

Evolution of PV in Nigeria

Pharmacovigilance began in Nigeria in the year 1981 following the training of a staff of the Federal Ministry of Health (FMOH) for one month in Uppsala, Sweden. NAFDAC was established in 1993 (Decree 15 of 1993, Act Cap N1 law of FRN 2004) and charged with the responsibilities of ensuring the quality, safety and efficacy of Food, drugs, cosmetics, chemicals/detergents, medical devices and all drinks including packaged water.

In 1996, the second attempt at PV was carried out through the distribution of ADR reporting forms (yellow forms) to private and public hospitals in Nigeria and this effort was followed up with the distribution of circulars (to serve as reminders) to the same health facilities. The collation of the filled yellow forms was done and it was observed that health care providers have responded poorly to the art and science of ADR reporting

In 2003, a review of the previous attempt at PV was done and it was decided that the poor reporting response was due to low level of PV awareness and that more FMOH staffs would have to be trained. The training took place at the UMC in May 2003. By November 2003, Nigeria had applied to WHO for membership of countries participating in WHO International Drug Monitoring Programme (pharmacovigilance) in Uppsala, Sweden and was rewarded with associate membership in December 2003. However, the full membership was not granted until September 2004, after Nigeria had developed working documents such as the yellow forms and guide for safe Monitoring of medicines in Nigeria, the setting up of a National Pharmacovigilance Centre in Abuja and organizing series of training workshops to improve the knowledge, attitudes and practices of PV among health care providers in the country[8]. Nigeria is the 74th member country of the UMC.

Pharmacovigilance activities in Nigeria

The National Pharmacovigilance Centre was established with the following broad objectives: to ensure the safety and quality of medicines and other regulated products in Nigeria; to entrench good PV practice in all aspects of healthcare delivery in Nigeria; to foster effective collaboration on PV activities amongst healthcare providers; and to create and sustain awareness amongst the healthcare providers and public on the need to detect and report ADR's and other medicine related problems.

Keeping its vision of promoting patient safety in mind and the above aims and objectives, the NPC, despite very limited funding, has made a significant progress. The Centre has since established a database on ADRs. It also has been a building capacity of healthcare workers across the nation as well as strengthening the structure and system of PV as highlighted below.

Incorporating PV In public health programmes

The rationale for this was to leverage resources for PV activities from public health programs. PV system is instituted into public health programs involved in mass distribution of medicines and other consumables. It also involves monitoring and helping to ensure safety of medicines used in public health programs. PV Focal Point officers were designated for each of the four major public health programs in Nigeria i .e. Malaria, HIV/AIDs, Immunization, Tuberculosis and Leprosy Control Programs.

Several advocacy visits were then conducted to the management of these public health programs as well as their major partners. Proposals for incorporation of PV into the different public health program were written and submitted. Written memorandum of understanding (MOU) was endorsed by some of these programs and this led to listing of and adequately budgeting for PV activities in these MOUs. In collaboration with the programs, health care practitioners were identified from public and private sectors for training.

The result is that resources have been leveraged from these public health programs which had contributed positively to strengthening the Nigerian PV system. For example the development of the final draft of a comprehensive pharmacovigilance training curriculum for in-service training of healthcare professionals was made through support from Management Sciences for Health, and National Tuberculosis and Leprosy Control Programme. Also, another training manual for healthcare professionals was developed for facilities supported by GHAIN in collaboration with the Howard University, Pharmacists and Continuing Education (HU-PACE). It can be stated that sensitization of Public health workforce on PV is gradually improving public consciousness in reporting of ADR to the PV center.

Awareness creation and capacity building for healthcare providers

Awareness and capacity building for healthcare professionals (HCPs) is facilitated through conferences, training workshops, seminars and electronic distribution of quarterly PV newsletters. The objectives of the newsletter are to disseminate information on pharmacovigilance activities nationally and globally, to educate stakeholders on drug safety issues and to promote spontaneous reporting and rational use of drugs.[9]

The NPC has distributed over 80,000 individual case safety reports (ICSR) forms and 6,000 Guides for detecting and reporting ADRs to healthcare professionals nationwide. Over 12,000 healthcare practitioners have been trained through train the trainer (TOT) workshops while many more have received PV quarterly newsletters. The National pharmacovigilance center has also recently introduced a Pharmacovigilance Rapid Alert System for Consumer Reporting (PRASCOR) to stimulate enhanced consumer reporting. These credible inputs, notwithstanding, the output and impact in terms of actual ADRs reported fall far short of the WHO's recommendation.

Over 11,000 completed ICSR forms have so far been received at the NPC from inception till date translating to approximately 8.1 reports/million inhabitants/year. The WHO has indicated that adequate reporting had translated to 200 reports/million inhabitants/year.[5]

In July and October 2012, the National Pharmacovigilance Centre organized the first mandatory PV training workshop for Marketing Authorization Holders (MAHs) in Lagos, Nigeria involving one hundred and twenty three company PV responsible persons.

Cohort event monitoring (CEM) study of patients treated for malaria with artemisinin combination therapy in Nigeria.

Following the change in the antimalarial treatment policy from Chloroquine to artemesinin-based combination therapies (ACTs) as first line drugs in the treatment of uncomplicated malaria, the need for proper understanding of the safety profile of the use of Artemisinin and its derivatives in Nigeria became necessary in the interest of patient safety. Consequently, the National Pharmacovigilance Centre (NPC) in conjunction with the National Malaria Control Programme (NMCP), Federal Ministry of Health (FMOH) and the World Health Organzation (WHO) deemed it expedient to embark on a CEM study of ACTs recommended by the FMOH viz: 20mg Artemeter + 120mg Lumefantrine {AL} and 10mg/kg Amodiaquine + 4mg/kg Artesunate {AA}.

Although spontaneous reporting, currently the mainstay of safety reporting of medicines in Nigeria, has been providing useful information on the safety of ACTs, some important safety information might be omitted by the spontaneous reporting system due to its voluntary and passive nature. This underscores the need for active monitoring of patients treated with ACTs and it informed the adoption of the CEM research approach, which has been proven to offer a better advantage in early information generation and also helps in overcoming the shortcomings of spontaneous reporting., The main objectives of the CEM programme were to proactively determine the adverse event (AE) profile of artesunate/amodiaquine (AA) and artemether/lumefantrine (AL) in real-life settings in the Nigerian population, and to find out the factors predisposing to AEs.

The CEM pilot study of 3000 subjects commenced in the second week of January 2009. The report has been published.[10] The study has been scaled up to 10,000 subjects in 2012 and the findings are currently being analyzed.

Adverse Events Following Immunizations (AEFIs)

There is no doubt that pediatric immunization prevents serious diseases, but the administration of these vaccines to healthy children also involves risks of Adverse Events following Immunization (AEFI), some of which are potentially serious. An adverse event following immunization is a medical incident that takes

place within one month after an immunization and is believed to be caused by the immunization.[11]

In Nigeria, AEFI Surveillance is in place. There is an AEFI Causality Expert committee and AEFI Review Committee who work in collaboration with the National Primary Health Care Development Agency (NPHCDA) and then forward reports of AEFI to the NPC. The AEFI reporting form is called a Case Investigation form. The NPC centre has facilitated a training of trainers (TOT) on AEFI monitoring. The NPC has also collaborated with the NPHCDA to monitor deployment of H1N1 pandemic flu vaccine on healthcare providers in some States in Nigeria. A local database was developed by the NPC for documenting AEFIs - from MenAfriVac Conjugate Vaccine this will be included in the Vigiflow software to facilitate upload to UMC database and local management of the AEFI data.

Research

Studies on PV have been majorly formative research dealing with baseline knowledge, attitudes and practice (KAP) of health professionals in general[12-15] Others have explored KAP of specific groups of health professionals like the doctors,[16-17] nurses,[18] community pharmacists[19] and patent medicine vendors.[20]

The focus of researchers should be on evaluating training interventions and their impact with a view to understanding the best strategies for effective interventions that would improve ADR reporting. Some studies in this direction are ongoing [21] Other ongoing studies include intensive monitoring of ADRs using mobile technology [22] and medication error studies in selected Nigerian tertiary health facilities and pharmacovigilance of herbal medicines.

Safety of herbal medicines

There is extensive use of herbal remedies in Nigeria, with an estimated 80% of the population taking herbal remedies.[22] As the use of herbal medicines increased, so too have the reports of suspected toxicity and adverse events and since many herbal products in the market have not been thoroughly tested for their pharmacology and toxicology, proper monitoring of these products is of paramount importance in detecting unwanted reactions.[23,24]

In order to properly monitor the safety of these herbal medicines, it is important that the practitioners who produce and use these products have adequate knowledge about post-marketing safety monitoring of their products and realize the need for and importance of this monitoring. The NPC has commenced training and re-orientation of TMPs with respect to herbal medicine safety.

Challenges

Some identified gaps include inadequate funding, inadequate political will and support, intellectual property rights issues, none or slow implementation of the National PV policy, under detection/reporting of ADRs and dearth of active surveillance studies.

Recommendations for improving PV in Nigeria

For PV to achieve its goal of protecting public health the collaboration between the National Pharmacovigilance Center and public health programs is holistically beneficial and should be sustained. More partnerships could also be established with relevant stakeholders and drug access campaigners through these partnerships data can be obtained from a range of studies of large populations in a structured and systematic fashion, and these data could then be used to identify warning signals.

Government should provide statutory budget lines for PV activities. Also public health programs should continue to make budget provisions to fill up identified funding gaps in PV activities in their programs.

Health systems research on PV should be encouraged by all stakeholders. Finally donor agencies must integrate in their planning phase, functional medicine safety systems to monitor effects of their donated products. Each state should be encouraged to establish PV in their health systems and liaise with the NPC. Lagos State has set the pace in this regard.

Conclusion

An effective PV system in Nigeria is key to preventing drug related morbidity and mortality especially those associated with mass distribution of medicines within PHPs. Leveraging of resources through effective collaboration with relevant stakeholders/partners would strengthen medicine safety systems, enhance the impact of PV and ultimately improve quality of care and patient safety.

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