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Review Article

Providing safe medicines for children in Nigeria: The impediments and remedies

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Abstract

Promoting safety of medicines for children is a global concern which has prompted the World Health Organization (WHO) to launch a campaign of "Making Medicines Child Size". Children in Nigeria were once victims of unethical clinical medicine trials and repeated victims of use of fake and adulterated medicines. Considering the magnitude of harms children had suffered in Nigeria from the use of medicines, there is a need for literature review to identify the factors preventing children from accessing safe medicines and to suggest remedies to the problems. Lack of access to up- to- date medicine information, lack of training and research in pediatric clinical pharmacology, deficiencies in undergraduate and postgraduate teaching of medicine risk management and clinical pharmacology and therapeutics, irrational medicine use due to lack of pediatric focus on essential medicine list and inappropriate home storage of medicines by parents, lack of evidence- based medicine (EBM) practice, lack of national adverse drug reaction surveillance among children, and weak national drug policies were the major problems identified. It is to be hoped that development and provision of a pediatric national drug formulary for health professionals in Nigeria, creating a comprehensive national pediatric drug research network in collaborations with developed countries, reviewing the undergraduate and postgraduate curriculum in pediatrics to include teaching of basic elements of rational prescribing, drug dose calculations, adverse drug reactions and pharmacovigilance, increasing access to essential medicines for children, postgraduate teaching of EBM, and strengthening of the national drug policies would improve children's access to safe medicines in Nigeria.

Keywords: Children, medicine, Nigeria, safe

Résumé

Promotion de la sécurité des médicaments pour enfants est un problème mondial qui a incité l'Organisation mondiale de la santé (OMS) pour lancer une campagne de "Faire de la taille d'enfants médicaments". Enfants au Nigeria ont été une fois victimes des essais de médecine clinique éthique et répétées aux victimes d'utilisation des médicaments de contrefaçon et adultérés. Compte tenu de que l'ampleur des dommages enfants avait subi au Nigeria, de l'utilisation de médicaments, il faut une revue de la littérature pour identifier les facteurs empêchant les enfants d'accéder aux médicaments sûrs et de suggérer des solutions aux problèmes. Le manque d'accès à l'information de haut-de-date de médecine, de manque de formation et de recherche en pharmacologie clinique pédiatrique, lacunes dans le cycle et postdoctorale d'enseignement de la gestion des risques de médecine de pharmacologie clinique et thérapeutique, utilisation irrationnelle de médecine en raison d'un manque de PEDIATRIQUE mettant l'accent sur la liste des médicaments essentiels et inapproprié de stockage domestique de médicaments par les parents, manque de preuve - fonction pratique de la médecine (MFP), manque de surveillance de réaction nationale antidrogue néfastes chez les enfants, et les politiques antidrogue faibles ont été les principaux problèmes identifiés. Il est à espérer que développement et la fourniture d'un formulaire PEDIATRIQUE antidrogue pour les professionnels de la santé au Nigéria, création d'un réseau de recherche globale antidrogue pédiatrique de collaborations avec des pays développés, en examinant le premier cycle et études postgrades en pédiatrie à inclure l'enseignement des éléments de base de rationnelle prescrire, calculs de dose de drogue, sur les effets indésirables et pharmacovigilance, accroître

l'accès aux médicaments essentiels pour les enfants, troisième cycle d'enseignement de la MFP et le renforcement des politiques antidrogue améliorerait l'accès des enfants aux médicaments sécuritaires au Nigeria.

Mots-clés: Enfants, médecine, Nigéria, coffre-fort

Providing safe medicines for children is a complex task that has received considerable global attention in recent times.[1] An international alliance for better medicines for children was established by a declaration affirmed to unanimously by pediatricians, pediatric clinical pharmacologists and pharmacists present at the International Paediatric Pharmacology Workshop in Shanghai 2006.[2] This declaration expressed concerns about providing essential medicines for children and suggested possible ways of achieving it. The World Health Organization (WHO) has recently recognized the importance of children's medicines and has published a special report on "Promoting safety of medicines for children", which was concerned with problems associated with formulations and medication errors.[3] The WHO, in collaboration with United Nations Children's Fund (UNICEF), Save the Children, Médecins Sans Frontières and the International Paediatric Association, has also launched a major campaign entitled "Make Medicines Child Size", which is concerned with improving availability and access to safe, child-specific medicines for children throughout the world.[4]

The key areas for providing safe medicines for children in developing countries have been identified as promotion of rational use of medicines, including guidelines for appropriate medicine choice and use in pediatrics; development of appropriate formulations for children, and where such formulations are not available, provision of guidelines for preparation of extemporaneous formulations; and improvement in the methods by which medications are purchased and distributed within a country.[5] It is important to recognize that these interventions are individualized to the needs of every country or specific regions within a country. The effective methods used to maintain compliance with drug administration in children may be specific to the culture and belief system in a country.

The burden of childhood disease of a country is a determinant of her drug use pattern for children. The under five mortality in Nigeria is mostly due to birth asphyxia, malaria, severe anemia, septicemia and malnutrition.[6,7] This probably explains why the use of antimalarials and antibiotics for under five children in Nigeria was very high.[8-10] These medicines are frequently associated with severe adverse reactions.[10] Adverse drug reactions (ADRs) have been reported as a cause of death in children;[10] yet, medicine has not been recognized as a cause of death in the various studies that reported childhood mortality in Nigeria.[6,7] There is abundant evidence on medicine- related childhood morbidity and mortality in Nigeria. Eleven children died and many others suffered brain damage, paralysis or deafness from the use of Trovan antibiotics in an unethical clinical trial study performed by Pfizer pharmaceutical company in 1996.[11] Forty-seven children also died in Nigeria in 1992 following a deliberate use of diethylene glycol as a solvent for paracetamol instead of propylene glycol,[12] and very recently, another 25 children died from the use of a teething mixture called "My Pikin Teething Mixture" which had been erroneously tainted with diethylene glycol.[13] Before the strengthening of policies on importation and indigenous manufacturing of medicines in Nigeria, thousands of children had died from the use of counterfeit and fake medicines.[14]

Considering the magnitude of harms suffered by children in Nigeria from medicine use, there is a need for literature review to identify the factors that may prevent children from receiving safe medicines and to suggest remedies to the identified problems. The identified factors are summarized in Table 1.

Impediments to Providing Safe Medicines for Children

Lack of evidence-based practice

Evidence-based medicine (EBM) is the process of systematically reviewing, appraising and using clinical research findings to aid delivery of optimum clinical care to patients.[15] The practice of EBM entails obtaining the best available information about therapies and combining this with the physician's own clinical experience and patient-specific factors and preferences.[16]

Clinical trial of drugs is a major component of EBM, which provides good evidence about drug safety and efficacy.[17] Unfortunately, there is lack of pediatric randomized clinical trial (RCT) studies globally which has contributed to the scarcity of knowledge about drug safety and efficacy in children.[18] In spite of the highest global burden of childhood disease and deaths in developing countries,[19] only a very few RCT studies have been performed in children of

Table 1: Impediments and remedies to providing safe medicines for children in Nigeria

Impediments	Remedies
Lack of EBM for children population	Teaching and accessing information on EBM
Lack of access to up-to-date medicine information to doctors	Increased access to up-to-date medicine information to doctors
Lack of training and research in pediatric clinical pharmacology	Encouraging research and training in pediatric clinical pharmacology
Inadequate training of doctors in clinical pharmacology and therapeutics	Reviewing undergraduate and postgraduate teaching of clinical pharmacology and therapeutics
Irrational use of medicines for children by parents and health professionals	Promoting rational use of medicines
Lack of pediatric focus on pharmacovigilance and awareness for ADRs reporting	Education of parents and their access to information on medicine for children
Weak national drug policies	Strengthening national drug policies

developing countries,[20,21] especially in sub-Saharan African countries.[22] A majority of the reported pediatric RCTs in developing countries is focused on medicines for infectious and parasitic diseases, with little or no attention paid to other relevant childhood diseases.[21] Many of the studies lacked information on safety and tolerability of the medicines that were evaluated. In addition, ethical approval for the studies was not reported in many cases.[21]

Lack of access to up-to-date medicine information to doctors

Health information is asymmetrically distributed between the developed and developing countries[23,24] and efforts have been made to narrow this gap through provision of free or highly subsided online publications to the poorest countries, mostly in Africa.[25-28] In spite of this gesture, there are barriers preventing health professionals from accessing health information. Some of these barriers have been identified by the International Network for the Availability of Scientific Publications (INASP).[29]

The asymmetrical information distribution includes medicine information, which has an important bearing to therapeutic outcomes. Medicines are a salient and cost-effective element of health care and a key factor for success of a healthcare system.[30] Optimal medicine use requires that healthcare professionals are well informed about clinically relevant aspects of medicines. Due to the large number of medicines in the market, rapid developmental changes occurring in the pharmaceutical industry and increase in medicine-related publications, it is essential that health professionals have access to unbiased and up-to-date medicine information.

A study in Nigeria has shown that doctors rely on medicine information from pharmaceutical sales representatives and medicine advertisements in medical journals,[31] which are unreliable sources of information for safe prescribing. Evaluation of some prominent Nigerian and other African medical journals for pharmaceuticals advertisement has shown that none adequately provided the basic information required by the WHO for appropriate prescribing for children.[32]

Many hospitals in Nigeria do not have accessible internet facilities to allow healthcare professionals quick reference on new medicine before prescribing. Many peer reviewed journals such as *Paediatric Drugs*,[33] *Journal of Pharmacy and Pharmacology*[34] and many others that specifically publish issues relating to safe medicine use in children require subscription for online access. Irregular power supply and lack of time are other barriers that can impair medicine information sourcing from the internet. Consultation with pediatric clinical pharmacists and clinical pharmacologists when doctors are in doubt about safety of medicines for a child would have been a more appropriate alternative, but scarcity of these specialists in the teaching and general hospitals would make this seemingly impossible. Many of the private hospitals and clinics in Nigeria hardly employ the services of a clinical pharmacist in their practice, yet new medicines are indiscriminately prescribed to children in private practices. In Uganda, all cadres of doctors in private, district, general and teaching hospitals were found to lack access to current medicine information due to their lack of time to consult standard pharmacology textbooks.[35] Alternative reference materials that were available for consultation such as the Monthly Index of Medical Specialists (MIMS) Africa, British National Formulary (BNF) and National Standard Treatment Guidelines were found outdated.[35] Such problems are not uncommon in Nigeria.

Lack of training and research in pediatric clinical pharmacology

The scientific study of medicines in children is

known as pediatric clinical pharmacology and is recognized as a subspecialty of pediatrics in both North America[36] and Europe.[37,38] The International Alliance for Better Medicines for Children[2] and the WHO[3] have long recognized the need to increase the numbers of pediatric clinical pharmacologists throughout the world. Just as the formal training in this specialty is increasing in America[36] and Europe,[37, 38] it is yet to see the light of the day in Africa. By international standard, there are no pediatric clinical pharmacologists in Nigeria and researches in pediatric clinical pharmacology are scarce. Pediatric clinical pharmacologists have significantly contributed to providing evidence base for medicine therapy in children.[39] Their leading roles in reducing drug fetotoxicity[40] and performing randomized clinical trials to provide information on efficacy and safety of medicines in children[41-43] are well recognized globally.

Inadequate training in undergraduate and postgraduate clinical pharmacology and therapeutics

Clinical Pharmacology and Therapeutics (CPT) is the speciality responsible for training doctors in the safe, rational and efficacious use of medicines. CPT is not taught in the entire medical schools in Nigeria,[44] and where it is taught, the knowledge imparted is only theoretical.[44,45] Drug dose calculation for children is rarely formally taught in both pharmacology and pediatric lectures during undergraduate medical training.[46] Thus, medical students tend to have a poor understanding of different ways of expressing concentrations of drugs in the various formulations for pediatrics.[44,46] The house officers are the highest prescribers in a teaching hospital and are often left to fend for themselves during their training. Their prescriptions are hardly supervised;[44] therefore, these young doctors who are ill-equipped in rational prescribing will continue to make medication errors. Prescribing errors are the most common cause of preventable adverse drug events.[47] Errors in the use of dosage equations account for more than 15% of all prescribing errors in the United States, with a significant potential for producing adverse effects.[48]

Irrational use of medicines

Irrational use of medicines is a significant problem in Nigeria.[49-51] Antibiotics and antimalarials are the leading cause of ADRs among children in Nigeria, yet these medicines are indiscriminately prescribed by doctors and non-medical personnel.[10] Over half of the world's 15 billion injections per year are considered unsafe for human use,[52] yet they are prescribed to children in Nigeria as intramuscular administration even when it is unnecessary or on the request of parents with little regard for their potential hazards.[9,50,53]

Lack of pediatric focus on essential medicine list

The rational use of medicine starts with choosing appropriate medicine for a patient. The WHO model essential medicine list (EML) helps countries to develop their own EML with the aim of improving medicine use through rational choice.[5] The EML has been in existence for more than 25 years and has proven to be a very successful public health initiative, with over 156 countries adopting the concept and developing their own EML.[52] The current edition of the Nigerian EML/National Formulary was produced about 6 years ago.[54] In spite of newer medicines being developed and widely available in the market for pediatric use, the Nigerian EML has not been updated. Unlike the WHO model EML for children,[55] the Nigerian EML and formulary lack a pediatric focus. Despite there being over a hundred medication listings in the current WHO model EML for children, the Nigerian EML did not provide any information on the use of caffeine, ibuprofen, prostaglandin E and surfactant in neonates. In addition, newer medicines for children such as ondansetron (antiemetics) and ciprofloxacin and fourth generation cephalosporins-imipenem (antibiotics) were not included in the Nigerian EML.

Lack of access to pediatric essential medicines

Access to essential medicines begins with access to quality and essential health services. A larger percentage of children in Nigeria live in the rural areas where quality health care is lacking.[56] Even in the urban areas where quality health care is rendered in the government hospitals, parents are involved in self-medication because of longer waiting hours.[56]

The cost of medications is another key barrier to their full access.[5] In most parts of Nigeria, the cost of medications for children is borne by the parents. The implication of this is that health care is either not sought or delayed, leading to under-treated morbidity and mortality. Poverty is a common trend in developing countries with transitional economies and has been recognized by the WHO as one of the key barriers to accessing essential medicines.[57]

Drug formulation and storage

The majority of medications worldwide are not formulated for easy or accurate administration to children.[5] This has led to the use of some medicines as off label and unlicensed medicines.[58] The lack of appropriate formulations for children makes dosing of medications in them less precise and less safe than in adults.[5] Several studies have confirmed that off label medicine prescribing was a problem in hospitalized children,[59] in neonates,[60] and in

primary health care.[61] The younger the child, the less likely is the availability of an appropriate formulation.[62] Artemether with lumefantrine antimalarial (Coartem®) has been recommended as first-line treatment for malaria in both children and adults in Nigeria.[63] Before the generics of Coartem were manufactured, only the tablet forms were available for use in both children and adults, despite the fact that malaria predominantly affects young children, with most of the deaths each year occurring in the under five children.[63] The danger of use of tablet formulations in children has been recognized by the WHO reports that highlighted deaths of four Ethiopian children from choking on albendazole tablets.[64]

Most indigenous pharmaceutical industries in Nigeria market generic medicines which are usually imported. The multinational pharmaceutical industry has historically shown little interest in developing medicines for diseases affecting people of developing countries.[65] Even when the medicines are developed, they are unlikely to be produced in different formulations for adults and children.

Medicines used for both adults and children contain both the active drug and a variety of excipients that ensure that the active drug is soluble, stable and palatable. Error in a drug formulation is very common in Nigeria and children have experienced significant harms from the use of inappropriate excipients.[66]

Lack of good storage facilities for medicines is a major problem of developing African countries, especially Nigeria, where electric power supply is very erratic. Most children live in the rural areas where there is no access to electricity. Mothers are fond of storing antimalarials and antibiotics at home in anticipation of febrile illness in their child.[67] The shelf life and stability of medicines kept at home, especially on a warm climate, are known to decrease over time, thereby increasing treatment failure from loss of potency and possible toxicity.[68]

Lack of pediatric pharmacovigilance and awareness for adverse drug reactions reporting

Pharmacovigilance is an area of pharmacology that is concerned with post marketing medicine surveillance. It is very important in analyzing and managing the risks associated with medicines, once they are available for the use of the general population.[69] Spontaneous reporting of ADRs has contributed significantly to successful pharmacovigilance. The contribution of health professionals, in this respect, to ADRs databases is enormously significant and has encouraged ongoing ascertainment of the benefit–risk ratio of medicines,[70] as well as contributed to signal detection of unsuspected and unusual ADRs previously undetected during the initial evaluation of a medicine.[71] Unfortunately, in spite of the efforts of the National Pharmacovigilance Center to increase awareness on ADRs reporting, Nigerian doctors are unable to demonstrate a good knowledge of ADRs recognition and reporting,[72] which reflects the deficiency in their undergraduate and postgraduate training in pharmacovigilance and medicine risks management.[44]

Pediatric pharmacoepidemiology and pharmacovigilance has gained much international recognition and has significantly contributed to safe medicine use in children.[73] Most of the studies on pediatric pharmacoepidemiology and pharmacovigilance were conducted in developed countries where disease pattern, access to medicines, drug use patterns and patient management pattern with drugs differ significantly from those of developing countries.[74] Therefore, epidemiological studies of medicines used for children, as well as their surveillance for adverse reactions, are very necessary in Nigeria.

Weak national drug policies

The National Agency for Food and Drug Administration and Control (NAFDAC) is responsible for regulating local manufacturing, importation, exportation, advertisement, sales and distribution of processed foods and drugs in Nigeria. These processes are done in accordance with Decree 19 of 1993 as amended by food, drugs and related products Decree 20 of 1999.[75] In spite of the holistic and multidimensional approach of NAFDAC to fight against the prevalence of fake, substandard and expired drugs and food items, counterfeit drugs continue to proliferate in the Nigerian markets[76] and children have been major victims.[77] The use of counterfeit medicines has significantly contributed to increased disease burden of children and increased child morbidity and mortality.[78]

Direct-to-consumer advertisement (DTCA) of medicines, through newsprint, radio and television, is practiced in Nigeria.[79] However, this may not be limited to over-the-counter medicines only. DTCA is a method by which pharmaceutical companies inform the "consumer" about a disease and about prescription medicines that are now available for treatment of that condition.[80] Such information is addressed to consumers without having to go through the normal channel of doctors, pharmacists and other healthcare professionals.[80] In a society where the majority of the general population is

illiterate, the possibility of parents misinterpreting or misunderstanding the pharmacological information of the advertised medicines is high. This can eventually promote inappropriate and irrational medicine use for children.

Complementary and alternative medicines (CAMs) are often used by parents to treat their children for common self-limiting ailments[56,67,81] and medically treatable health conditions.[82] The CAMs may be beneficial, but nevertheless are not harmless. Adverse reactions to CAMs and their potential to interact with prescription medicines have been previously reported.[82,83] Herbal medicines as a cause of childhood death had been reported in Nigeria.[10] Many Nigerians patronize traditional medicine because of disillusionment with conventional medical care.[84] Among the multitude of herbal medicines in circulation in Nigeria, only about 20 have been registered by the NAFDAC and most of them are imported,[14] yet these products are freely and aggressively advertised in the media and are freely obtainable on the open market.[85] Misleading information is often given about CAMs and self-medication is encouraged, thus potentially endangering the lives of many children and adults.

How to Achieve Safe Medicine Use for Children

Increasing access to up-to-date medicine information to doctors

A national drug formulary, similar to the BNF for children, is required in Nigeria to guide prescribers for children in selecting appropriate drug, dosages, and appropriate route and frequency of administration. The Paediatric Association of Nigeria, West African Society for Pharmacology and Pharmacist Council of Nigeria should come together to initiate this idea and pursue it to an accomplishment. The document should, however, be updated periodically and circulated throughout the country to all healthcare professionals.

Encouraging research and training in pediatric clinical pharmacology

There is a need for and creation of a comprehensive pediatric drug research network in Nigeria, which has to collaborate with developed countries. This network would seamlessly coordinate research that spans the spectrum from bench to bedside to implementation, and from drug development in the laboratory to clinical trials to outcomes research that assesses long-term safety and effectiveness of medications used in children.[86] The scope and vision of the network should be very comprehensive, especially now that more than ever newer medicines are developed on a daily basis and children are prescribed an increasing number of medications.

The postgraduate medical colleges should look into the possibility of including pediatric clinical pharmacology into their training programs. Expertise can be drawn from pediatrics, clinical pharmacology, and anaesthesia at the early design of the program and its curriculum. Expert opinions should be sought from other postgraduate medical colleges in Europe and America where pediatric clinical pharmacology training is well grounded. However, absolute transparency should guide expertise selection both locally and internationally.

Reviewing undergraduate and postgraduate teaching of clinical pharmacology and therapeutics

Considering the dearth of expertise in clinical pharmacology in Nigeria, focal persons should be identified in each medical school to teach basic topics in clinical pharmacology and therapeutics. The Nigerian Medical and Dental Council, Paediatric Association of Nigeria, West African Society for Pharmacology and Pharmacist Council of Nigeria should jointly organize workshops on training the focal persons on what to teach. Rationale for prescribing for children; guidelines for prescribing medicines for children with special conditions such as protein-energy malnutrition, HIV/AIDS, and renal failure; drug dosage calculations; sourcing references for pediatric drug dosages; and pediatric pharmacoepidemiology and pharmacovigilance should form the core areas of the training. Medical students should begin the training in pharmacology class and continue throughout their pediatric training and internship training in pediatrics. Teaching should be both theoretical and practical and the ability to demonstrate competence in these areas of clinical pharmacology should form part of the criteria for pre-registration of the newly qualified doctors with the Nigerian Dental and Medical Council, as practiced in the UK.[87]

Clinical pharmacology should form the core curriculum of postgraduate residency training in pediatrics in Nigeria, as practiced in the developed countries.[36-38] Core topics should include mechanism of drugs in relation to their ability to correct pathophysiologic state; pharmacokinetics in infants and children; pharmacogenomics and pharmacogenetics in children; placenta transfer and breast milk excretion of drugs; drug interactions; modification of drug dosages required in altered pathophysiologic states (renal failure, liver failure, and protein-energy malnutrition); medication

errors; pediatric drug dose calculations; therapeutic drug monitoring; cost of commonly used drugs; choice of drugs with respect to availability of drug plans; issues related to drug compliance; clinical trials of drugs in children; systematic review of studies on drug therapy and EBM in children; adverse drug reactions and drug surveillance in children; and drug poisoning, overdose and toxicity in children. Teaching should be both theoretical and practical, and residents should be able to demonstrate competence in these topics before and during the postgraduate examinations.

Promoting rational use of medicines

Access to essential medicines for children needs to be increased. Government needs to subsidise the prices of medicines through taxes, duties and fees reduction. Importation of essential medicines for children should not be monopolized by a few companies, so as to reduce the market prices. Manufacturing of essential medicines for children should be encouraged through appropriate legislation. Regional and local monitoring system on prices of selected essential medicines for children should be established.

Teaching and accessing information on evidence-based medicine

Pediatric trainees and pediatricians should be able to demonstrate ability to critically appraise papers on child health and pediatric drug therapy. This should be mandated as a key skill for trainees and practising pediatricians in Nigeria and made a component of postgraduate pediatric trainings. The Paediatric Association of Nigeria should educate their members on how to practice and teach EBM through workshops. Critical appraisal of literature is being taught to trainees and consultants in journal clubs in the UK[88] and America[89] and has yielded a very good result. The existing journal clubs in Nigerian postgraduate training institutions should be re-activated and focus on teaching EBM. Trainees should be frequently assessed and, if possible, the assessment should contribute toward their final postgraduate examinations.

The Cochrane library is probably the most valuable single access point for EBM. It contains high-quality information on drug therapy to independently inform healthcare decision making. It includes databases of systematic reviews, abstracts of reviews of effects of drug therapy, the Cochrane central register of controlled trials, the health technology assessment databases, and economic evaluation databases,[90] all of which can be searched simultaneously from a single user interface. Physicians and other healthcare professionals should endeavor to visit the website regularly for updates on current drug therapy for children.

Strengthening national drug policies

The loopholes in drug policies governing the control of medicine administration in Nigeria need to be adequately redressed. The existing laws and regulation relating to quality assurance of medicines should be strengthened and implemented to the latter. Stiff penalties should be meted out to perpetrators to serve as deterrent to manufacturers of adulterated medicines. Although NAFDAC has achieved a lot in fighting against importation, sales and use of counterfeit medicines in Nigeria,[14] it appears that the effort is not enough. NAFDAC should therefore increase their collaboration with health officials and health institutions to jointly fight the course. More public awareness and workshops on how to identify fake and counterfeit medicines are required. This should focus more on the illiterate parents and those living in the rural and remote areas where quality health care is scarce.

Unlicensed private pharmacies are proliferating and are involved in selling prescription medicines without prescription. This act has promoted irresponsible self-medication for children.[10,53,56,67,82] The Pharmacist Council of Nigeria, NAFDAC and stakeholders should come together to fight this illegal business through concerted efforts.

Irresponsible self-medication for children is on the increase in Nigeria due to decreased health coverage, increase in the use of alternative remedies, availability of over-the-counter health products, and an increasing presence of pharmaceutical and CAM products in the media.[53,56,67,82] Appropriate laws and regulation guiding the advertisement, sales and use of these products should be enacted and implemented.

Education of parents and their access to information on medicine for children

Parents need transparent information on the benefits and risks of medicines used for their children. This information should be provided in regulatory information such as product information (summary of product characteristics, labeling and the package leaflet), public assessment report and product safety announcements. Previous studies have shown that adolescents and adults obtain information about medicines from a variety of sources such as friends, family members, healthcare professionals, the media and medicine package leaflet.[91]

Given the increasing communication on medicine through various media channels, the physicians, nurses, community pharmacists and NAFDAC remain primary sources of information on medicines in Nigeria. A UK study showed that healthcare professionals are the most trusted source of information on benefits and risks of medicines to patients.[92] It is therefore suggested that healthcare professionals in Nigeria should include communication on the benefits and risks of medicines prescribed to children in their routine pediatric consultation. Education campaigns in the media and public and private hospitals should be organized so as to help parents on how to use medicines appropriately for their children. Public enlightenment campaigns on fake and adulterated medicines, as frequently practiced by the NAFDAC, should be intensified and extended to parents in the rural and remote areas.

References

1. Sweis D, Wong IC. Giving medicines to children: Understanding the parents' views. Pediatr Drugs 2004; 6:67-9.
2. The International Alliance for Better Medicines for Children: The Alliance Declaration. Available from: http://www.ppag.org/en/art/?348 [last accessed on 2008 Jan].
3. WHO. Promoting safety of medicines. Geneva: WHO, 2007. Available from: http://www.who.int/medicines/publications/essentialmedicines/Promotion_safe_med_childrens.pdf [last accessed on 2008 Jan].
4. WHO. Make medicines child size. Available from: http://www.who.int/childmedicines/en/index.html [last accessed on 2008 July].
5. Beggs SA, Cranswick NE, Reed MD. Improving drug use for children in the developing world. Arch Dis Child 2005;90:1091-3.
6. Fetuga B, Ogunlesi T, Adekanbi F, Olanrewaju D, Olowu A. Comparative analyses of childhood deaths in Sagamu, Nigeria: Implications for the fourth MDG. SAJCH 2007; 1:106-11.
7. Eke FU, Frank- Briggs A, Ottor J. Childhood mortality in Port Harcourt, Nigeria. Anil Aggrawal's Internet Journal of Forensic Medicine and Toxicology, 2001;2: Available from: http://www.geradts.com/anil/ij/vol_002_no_002/papers/paper003.html [last accessed on 2008 Dec].
8. Nwolisa CE, Erinaugha EU, Ofoleta SI. Prescribing practices of doctors attending to under fives in a children's outpatient clinic in Owerri, Nigeria. J Trop Pediatr 2005;52:197-200.
9. Oshikoya KA, Chukwura HA, Ojo OI. Evaluation of outpatient paediatric drug prescriptions in a teaching hospital in Nigeria for rational prescribing. Paediatr Perinat Drug Ther 2006;7:183-8.
10. Oshikoya KA, Njokanma OF, Chukwura HA, Ojo OI. Adverse drug reactions in Nigerian children. Paediatr Perinat Drug Ther 2007;8:81-8.
11. Levin T. Families sue Pfizer on test of antibiotics. NY Times. Available from: http://www.mindfully.org/Industry/Pfizer-Trovan-Nigerian-Suit.htm [last accessed on 2008 Dec].
12. Okuonghae HO, Igbogboja IS, Lawson JO, Nwana EJ. Diethylene glycol poisoning in Nigerian children. Ann Trop Paediatr 1992;12:235-8.
13. Uzendu M, Udoh F. Nigeria: Paracetamol kills 25 kids. Available from: http://www.allafrica.com/stories/printable/200811260698.html [last accessed on 2008 Nov].
14. NAFDAC NIGERIA. Journey: Some administrative guidelines. Available from: http://www.nafdacnigera.org/journey.html [last accessed on 2008 Oct].
15. Rosenberg W, Donald A. Evidence based medicine: An approach to clinical problem-solving. BMJ 1995;310: 1122-6.
16. Kleinke JD, Malone DC, Urick P. Shift toward evidence-based medicine: The role of community-based guidelines. J Manag Care Pharm 2005;11:S1-24.
17. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: What it is and what it isn't. BMJ 1996;312:71-2.
18. Bonati M, Pandolfini C. Pediatric clinical trials registry. CMAJ 2005;172:1159-60.
19. Murray CL, Lopez AD. The global burden of disease: A comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. Cambridge: Harvard University Press; 1996.
20. Campbell H, Surry SA, Royle E. A review of randomised control trials published in archives of disease in childhood from 1982-96. Arch Dis Child 1998; 79: 192- 7.
21. Nor Aripin KN, Sammons HM, Choonara I. Published paediatric randomised drug trials in developing countries, 1996-2002. Pediatr Drugs 2010; 12: 99- 103.
22. Isaakidis P, Swingler GH, Pienaar E, Volmink J, Ioannidis JP. Relation between burden of disease and randomised evidence in sub-Saharan Africa: Survey of research. BMJ 2002;324:702.
23. Kale R. Health information for the developing world. Br Med J 1994;309:939-42.
24. McConnell H, Haile-Mariam T, Rangerajan S. The world health channel: An innovation for health and development. World Hosp Health Serv 2004; 40: 36- 9.
25. Crawford BD. Open-access publishing: Where is the value? Lancet 2003;362:1578-80.
26. Katikireddi SV. HINARI: Bridging the global information divide. Br Med J 2004;328:1190-3.
27. Aroson B. Improving online access to medical information for low-income countries. N Engl J Med 2004;350:966-8.
28. Smith R, Williamson A. BMJ journals free to the developing world. Br Med J 2002;324:380.
29. International Network for the Availability Scientific Publications. INASP infobrief 6. Journal Access Programmes in African University Libraries 2005. http://www.inasp.info/uploaded/documents/INASP%20infobrief%206-web.pdf [last accessed on 2009 Aug].
30. Falkenberg T, Tomson G. The World Bank and pharmaceuticals. Health Policy Plan 2000;15:52-8.
31. Akande TM, Aderibigbe SA. Influence of drug promotion on prescribing habits of doctors in a teaching hospital. Afr J Med Med Sci 2007;36:207-11.
32. Oshikoya KA, Senbanjo IO, Soipe A. Adequacy of pharmacological information provided in pharmaceutical drug advertisements in African medical journals. Pharm Pract 2009;7:100-7.
33. Pediatric Drugs. The official journal of the International Alliance for Better Medicine for Children, Pediatric Drugs is dedicated to improving the effective and safe use of drugs in pediatrics. Available from: http://www.ovid.com/site/catalog/Journal/293.pdf [last accessed on 2009 Aug].
34. Journal of Pharmacy and Pharmacology. An internationally recognised research publishing multidisciplinary research on the latest development in the pharmaceutical

sciences. Available from: http://www.pharmpress.com/shop/editorial/docs/JPP_2009_factsheet.pdf [last accessed on 2009 Aug].
35. Tumwikirize WA, Ogwal-Okeng JW, Vernby A, Anokbonggo WW, Gustafsson LL, Lundborg CS. Access to up-to-date drug information in developing countries continues to pose problems: The case of Uganda. Pharmacoepidemiol Drug Saf 2007;16:1177-9.
36. Anderson M, Choonara I, Ito S, Koren G, Reider M. Paediatric clinical pharmacology training programmes in Canada and UK: A comparison. Paediatr Perinat Drug Ther 2007;8:26-30.
37. Choonara I, Dewit O, Harrop E, Haworth S, Helms P, Kanabar D, *et al*. Training in paediatric clinical pharmacology in the UK. Br J Clin Pharmacol 2004;58: 217-8.
38. Bonati M, Breitkreutz J, Choonara I, Hoppu K, Jacqz-Aigrain E, Langhendries J, *et al*. Paediatric clinical pharmacology in Europe. Paediatr Perinat Drug Ther 2006;7:134-7.
39. Bonati M, Choonara I, Hoppu K, Pons G, Seyberth H. Closing the gap in drug therapy. Lancet 1999;353:1625.
40. Loebstein R, Addis A, Ho E, Andreou R, Sage S, Donnenfeld AE, *et al*. Pregnancy outcome following gestational exposure to fluoroquinolones: A multicentre prospective controlled study. Antimcrob Agents Chemother 1998;42:1336-9.
41. McIntyre J, Robertson S, Norris E, Appleton R, Whitehouse WP, Phillips B, *et al*. Safety and efficacy of buccal midazolam versus rectal diazepam for emergency treatment of seizures in children: A randomised controlled trial. Lancet 2005;366:205-10.
42. Impicciatore P, Choonara I, Clarkson A, Provasi D, Pandolfini C, Bonati M. Incidence of adverse drug reactions in paediatric in/out-patients: A systematic review and meta-analysis of prospective studies. Br J Clin Pharmacol 2001;52:77-83.
43. Sammons HM, Gray C, Hudson H, Cherrill J, Choonara I. Safety in paediatric clinical trials: A 7 year reviews. Acta Paediatr 2008;97:474-7.
44. Oshikoya KA, Senbanjo IO, Amole OO. Interns' knowledge of clinical pharmacology and therapeutics after undergraduate and on-going internship training in Nigeria: A pilot study. BMC Med Educ 2009;9:50.
45. Oshikoya KA, Bello JA, Ayorinde EO. Prescribing knowledge and skills of final year medical students in Nigeria. Indian J Pharmacol 2008;40:251-5.
46. Oshikoya KA, Senbanjo IO, Soipe A. Ability of medical students to calculate drug doses in children after their paediatric attachment. Pharm Pract 2008; 6: 191- 6.
47. Bates DW, Cullen DJ, Laird N, Petersen LA, Small SD, Servi D, *et al*. Incidence of adverse drug events and potential adverse drug events: Implications for prevention. ADE Prevention Study Group. JAMA 1995;274:29-34.
48. LesarTS, Briceland LL, Stein DS. Factors related to errors in medication prescribing. JAMA 1997;277:312-7.
49. Ohaju- Obodo JO, Isah AO, Mabadeje AF. Prescribing patterns of clinicians in private health institutions in Edo and Delta States of Nigeria. Nig Q J Hosp Med 1998;8:91-4.
50. Odusanya OO, Oyediran MA. Rational drug use at the primary health care centres in Lagos, Nigeria. Nig Q J Hosp Med 2000;10:4-7.
51. Oshikoya KA, Senbanjo IO. Cefixime-induced dystonia and hypothermia in a 12-year old boy: A need for safe prescribing. Int J Pharmacol 2008;4:233-6.
52. Quick JD, Hogerzeil HV, Velasquez G, Rago L. Twenty-five years of essential medicines. Bull World Health Organ 2002;80:913-4.
53. Oshikoya KA, Senbanjo IO, Njokanma OF. Parental reporting of suspected adverse drug reactions in children in Lagos, Nigeria. Arch Dis Child 2009;94:469-73.
54. Federal Ministry of Health. Essential drug list in Nigeria. 4th Revision, Lagos, 2003.
55. WHO model list of essential medicines for children. 2nd ed, March 2010. Available from: http://www.who.int/medicines/publications/essentialmedicines/Updated_second_children_list_en.pdf [last accessed on 2010 May].
56. Oshikoya KA, Njokanma OF, Bello JA, Ayorinde EO. The use of prescribed and non-prescribed drugs in infants in Lagos, Nigeria. J Med Sci 2008;8:111-7.
57. WHO. Selected topics in health reform and drug financing. Geneva: WHO, 1998. Available from: http://www.who.int/medicines/library/dap/who-dap98-3/who-dap-98-3.pdf [last accessed on 2008 Apr].
58. Choonara I, Conroy S. Unlicensed and off-label drug use in children: Implications for safety. Drug Saf 2002;25:1-5.
59. Turner S, Longworth A, Nunn AJ, Choonara I. Unlicensed drug use on paediatric wards. BMJ 1998;316:343-5.
60. Conroy S, McIntyre J, Choonara I. Unlicensed and off-label drug use in neonates. Arch Dis Child Fetal Neonatal Ed 1999;80:F142-4.
61. McIntyre J, Conroy S, Avery A, Corns H, Choonara I. Unlicensed and off-label prescribing of drugs in general practice. Arch Dis Child 2000;83:498-501.
62. Tan E, Cranswick NE, Rayner CR, Chapman CB. Dosing information for paediatric patients: Are they really "therapeutic orphans"? Med J Aust 2003;179:195-8.
63. Oshikoya KA. Antimalarial prescription for children presenting with uncomplicated malaria to a teaching hospital in Nigeria after the change of national guidelines for malaria treatment. World J Med Sci 2007;2:49-53.
64. Choonara I. WHO wants safer medicines for children. Arch Dis Child 2008;93:456-7.
65. Anabwani GM. Drug development: A new perspective from Africa. Paediatr Perinat Drug Ther 2002;5:4-11.
66. Choonara I, Reider MJ. Drug toxicity and adverse reactions in children: A brief historical review. Peadiatr Perinat Drug Ther 2002;5:12-8.
67. Oshikoya KA, Njokanma OF, Bello JA, Ayorinde EO. Family self-medication for children in an urban area of Nigeria. Paediatr Perinat Drug Ther 2007;8:124-30.
68. Taketomo CK, Hodding JH, Kraus DM. Pediatric Dosage Handbook. 11th ed. Ohio: Lexi-Comp Inc.;2004.
69. Edwards I, Olsson S. WHO: Global monitoring. In: Mann RD, Andrew E, editors. Pharmacovigilance. Chichester: Blackwell Publishing: Oxford; 2003. p. 169-82.
70. Ahmad SR. Adverse drug event monitoring at the food and drug administration. J Gen Intern Med 2003;285: 437-43.
71. Lexchin J. Is there a role for spontaneous reporting of adverse drug reactions? CMAJ 2006;174:191-2.
72. Oshikoya KA, Awobusuyi JO. Perceptions of doctors to adverse drug reaction reporting in a teaching hospital in Lagos, Nigeria. BMC Clin Pharmacol 2009;9:14.
73. Luo X, Doherty J, Cappelleri JC, Frush K. Role of pharmacoepidemiology in evaluating prescription drug safety in pediatrics. Curr Med Res Opin 2007;23: 2607-15.
74. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: Systematic analysis of population health data. Lancet 2006;367:1747-57.
75. National Agency for Food and Drug Administration and Control. Drugs-general guidelines. Available from: http://www.nafdacnigeria.org/drugs.html [last accessed on 2008 May].
76. Ibekwe J. Artemesinim resistant malaria on the horizon (editorial). Int J Med Sci 2009;1:1-2.

77. Bonati M. Once again, children are the main victims of fake drugs. Arch Dis Child 2009;94:468.
78. World Health Organization. Combating counterfeit drugs: A concept paper for effective international collaboration. WHO (Health Technology and Pharmaceuticals) 2005. Available from: http://www.who.int/medicines/services/counterfeit/CombatingCounterfeitDrugs_Conceptpaper.pdf [last accessed on 2009 Nov].
79. Yusuff KB, Yusuf A. Advertising of OTC products in a Nigerian urban setting: Content analysis for indications, targets, and advertising appeal. J Am Pharm Assoc 2009;49:432-5.
80. Vitry A. Is Australia free from direct-to-customer advertising? Australian Prescriber (Aust Prescr). 2004; 27:4-6.
81. Oshikoya KA, Senbanjo IO, Njokanma OF. Self-medication for infants with colic in Lagos, Nigeria. BMC Pediatr 2009;9:9.
82. Oshikoya KA, Senbanjo IO, Njokanma OF, Soipe A. Use of complementary and alternative medicines for children with chronic health conditions in Lagos, Nigeria. BMC Complement Altern Med 2008;8:66.
83. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs: A systematic review. Drugs 2001; 61:2163-75.
84. Adesina SK. Traditional medical care in Nigeria. Available from: http://www.onlinenigeria.com/links/LinksReadPrint.asp?blurb=574 [last accessed on 2009 Mar].
85. Obi E, Agbasi PU, Ezejiofor NA, Maduagwuna C, Orisakwe OE. Safety warnings and first aid instructions on Nigerian traditional herbal remedies: Are they adequate. World J Med Sci 2006;1:108-11.
86. Yoon EY, Freed GL. The need for creation of comprehensive pediatric research network. Pediatr Drug 2008;10:279-80.
87. General Medical Council. Tomorrow's doctors. London: General Medical Council; 2002. Available from: http://www.gmc-uk.org/med_ed/tomdoc.htm [last accessed on 2009 Nov].
88. Khan KS, Dwarakanath LS, Pakkal M, Brace V, Awonuga A. Postgraduate journal club as a means of promoting evidence- based obstetrics and gynaecology. J Obstet Gynaecol 1999;19:231-4.
89. Yew KS, Reid A. Teaching evidence-based medicine skills: An exploratory study of residency graduates' practice habits. Fam Med 2008;40:24-31.
90. The Cochrane Library. Cochrane Central Register of Controlled Trials. Available from http://www.mrw.interscience.wiley.com/cochrane/cochrane_clcentral_articles_fs.html [last accessed on 2009 Nov].
91. Darmanin Ellul R, Cordina M, Buhagiar A, Fenech A, Mifsud J. Knowledge and sources of information about medicines among adolescents in Malta. Pharm Pract 2008;6:176-86.
92. MHRA. Risks and benefits of medicines and medical devices: Perceptions, communication and regulation-overview of IPSoS MORI Research Conducted for The Medicines and Healthcare Products Regulatory Agency (MHRA). Available from: www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE...Latest [last accessed on 2010 May].

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