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Promoting Patient Safety - Medication without Harm

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EDITORIAL

A commentary on Pharmacovigilance from a healthcare setting

Mirfin Mpundu
Executive Director, Ecumenical Pharmaceutical Network and Head, React Africa, Kenya

Today, worldwide, medication errors cost an estimated US$42 billion annually. This is 0·7% of the total global health expenditure. Of course, this dollar amount is nothing compared to the millions of undocumented lives lost due to medication errors in low- and middle-income countries (LMICs) where, by and large, we do not keep such records. According to the WHO, unsafe medication practices and medication errors are a leading cause of injury and avoidable harm in health systems. These facts compel us to explore the thin paradoxical line between medicines that cause harm and medicines that heal. How do we, as healthcare providers remain diligent in navigating this line?

In this special edition of the Pharmalink, we learn, share and participate in meaningful practical discussion that dives deeper into the causes of medication errors. What are the synergies between medication harm and the roles of health care workers and relevant stakeholders (e.g. government ministries of health, international NGOs). We explore how faith-based health facilities can be positioned to reduce the effects of medication errors.

In March 2017, the World Health Organization (WHO) launched its third Global Patient Safety Challenge, Medication without Harm, with the ambitious goal of reducing avoidable medication-related harm by 50% worldwide over the next five years. Third Global Patient Safety Challenge seeks the commitment of health ministers, health-system leaders, and a range of stakeholders, including educational institutions, experts, medicines regulators, researchers, pharmaceutical companies, patient representative bodies, and professional organizations. Therefore, it is no coincidence that the themes of the Pharmalink and the EPN Forum 2018 are dedicated to the concept of Patient Safety, Medication without Harm.

A medicine error is described as:

"[…] any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing, order communication, product labeling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use" (WHO)

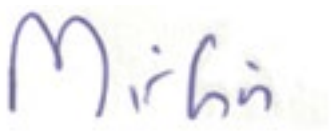
In 1960 Alphonso Chapanis, an engineer, conducted a health study on medication-related errors in 1100-bed hospital that identified seven sources of such errors potentially leading to harm to a patient: medicine omitted, or given to the wrong patient, at the wrong dose, as an unintended extra dose, by the wrong route, at the wrong time, or as the wrong drug entirely. We know that these errors arise during prescription, dispensing or administration mainly because healthcare facilities may have poor alert systems and unimplemented/unmonitored standard guidelines or inadequate communications systems. Further, health care providers (physician, nurse, pharmacist, etc) also tend to be overwhelmed, tired or simply do not enjoy the administrative side of healthcare. Thus, even when systems and standard guidelines are in place, medication errors tend to occur, however, it is best to be aware of the situations where medications errors occur most frequently.

This brings us back to Chapanis. Logically, after his initial study, Chapanis later provided the following four key recommendations to limit the alarming medication errors observed in his 1960 study, namely: written communication, medication procedures, the working environment, training, and education. These were the guiding principles to the global steps being taken on medication error, and ultimately adopted and expanded by the WHO Global Patient Safety Challenge.

Both this Pharmalink edition and the EPN Forum 2018, offer an unprecedented occasion for faith-based health facilities, their stakeholders and the global health community to engage on how best to avoid medication errors within the African context and causing no harm to patients.

It is our hope that the contributors to this publication will simplify the intricate complexity that this topic demands and allow everyone to better serve the patients in our respective communities. Patient safety and strategies to achieve minimum medication errors should be one 'big breath of life' into our health care institutions. We are incredibly grateful to all the authors and the editors for taking time to contribute to this Pharmalink on patient safety; medication without harm.

God bless,



Mirfin Mpundu, PharmD, MBA, MPH

MEDICATION SAFETY: HOW FAR IS THE TARGET?

Heber Rew Bright, M.Pharm

Christian Medical College & Hospital, India

Summary

Medication safety has been a topic of discussion for many years. More than the harm introduced by medicines themselves, the harm caused by medication errors is often more threatening. Hypothetically, achieving absolute medication safety is conceivable in all healthcare settings. Reaching the target of absolute medication safety will cost our commitment, care, determination and bringing forth innovative interventions towards the cause of medication safety. WHO's latest global challenge launched in March 2017 on patient safety – "medication without harm" is a giant leap towards that target. Its primary goal is to globally reduce medication errors by 50% over five years, is a noble objective and pragmatic, with respect to its proposed strategies and plans. Accordingly, countries and stakeholders are asked to focus on three early priorities of action which includes: high-risk situations, polypharmacy, and transitions of care. Also to be considered, is that medication safety has a "cultural" component to it, implying one size does not fit all.

Introduction

If safety and efficacy of a medicine are compared, safety would inevitably gain the priority and significance. Regulatory authorities approve medicines to be used in humans only if medicine related harm does not exceed its benefits. Nevertheless, medicines often induce harm when inadvertently administered, and this is perhaps preventable. Medicines are generally intended to be safe, improve quality of life, increase the duration of our lives and protect us, although the contrary can often result(1). Though the impact of medication errors and need for medication safety endeavours has been realized for decades, the problem still remains vibrant.

The Institute for Safe Medication Practices (ISMP), defines medication safety as freedom from preventable harm with medication use(2). Although there is no universally accepted definition of medication safety, the above definition sounds more pragmatic. Adverse events due to medication errors are preventable and hence are encompassed within the definition. However, adverse events occurring at the recommended dosage of medicines are often not preventable and are usually precluded by the term medication safety.

There was a period when patients graded the performance of medical professionals as perfect(3). The truth is medication errors were underreported and not measured in those days. This situation is no more in existence. Patients are increasingly becoming skeptical about the healthcare industry owing to the abounding reports of numbers and statistics on medication errors and their consequences. Today, patients seem to search and check on their symptoms or disease conditions, anticipated medications, their effects, side-effects, and dosage before consulting a doctor. 'Pharmacophobia' a term representing fear of medicines, is increasingly appearing in medical literature recently. Pharmacophobia and skepticism together can not only affect medication adherence(4), they are also contagious and has enough potential to infiltrate a group, community or even a country as a whole(4).

Eradication of pharmacophobia and skepticism on medication safety is a must. We are in an age that primarily requires building faith amongst those whom we serve by setting a target and bringing down the medication error rate to modest. For those of us who ask if it is an attainable target, I would say yes; at least hypothetically, because medication safety ensures freedom from preventable harm which literally means the possibility of attaining the target. Yes, I agree it's not an easy task but at the cost of commitment, care, determination, bringing forth innovative interventions, the target can be materialized.

There are technologies and systems to avert a bullet from penetrating the president's vest, technology to cease missile in the blue, to predict the power of tornados well in advance and it's humiliating that we have no technology to ensure what we prescribe, dispense or administer is precise. The cost of today's pharmacovigilance system in 1960's was thousands of limbs of innocent infants(5). The infants were born with malformed limbs (phocomelia) because their mothers consumed thalidomide which was available over-the-counter to treat morning sickness while they were pregnant. Thalidomide-induced phocomelia was only later understood and withdrawn from the market immediately.

By then, there were already 10,000 children who were harmed(6) which led to the development and implementation of modern pharmacovigilance(7). Since then the system of

practicing pharmacovigilance has been on a mission of saving thousands of lives by rapidly disseminating safety information throughout the world(8). Nevertheless, we continue to spend hundreds of lives every year but haven't yet designed an efficient system that could save lives, health and money being squandered, due partly to our mistakes. Clinicians inadvertently prescribe a wrong medicine or dose, the pharmacists dispense another medicine that looks similar to the intended one while in a hurry, nurses push the unfamiliar injection instead of infusing it over half an hour, patients skip a dose of warfarin not knowing its repercussions, stockists put their hoard of vaccines outside the cold-chain long enough to compromise their potency, regulators grant green signal to new medicines without comprehensive evidence and the list goes on and on. Yes, the medication error could possibly spike anywhere on its way beginning from the regulator's approval via the premises of its manufacturer till it is administered. Stakeholders of medication safety are many; disregarding one stakeholder would impede us reaching the target.

WHO global challenge

WHO has been in the forefront in culminating undying plights of medication errors and associated patient harms. The latest challenge(9) by WHO towards global patient safety was launched last year (March 2017). The primary goal of the challenge themed under "medication without harm" is to reduce the level of severe, avoidable harm related to medications by 50% over five years globally. The challenge aims to make improvements at each stage of the medication process, including prescribing, dispensing, administering, monitoring and use and have prioritized three key areas namely high-risk situations, polypharmacy, and transitions of care to protect patients from harm. Each area is associated with a substantial burden of harm and therefore, if appropriately managed, could reduce the risk of harm to many patients. Further, WHO has identified four key domains to the medication error challenge: patients and the public, medicines as products, healthcare professionals and systems, and practices of medication.

The ambitious challenge seeks support from a range of stakeholders including health ministers, health-system leaders, educational institutions, experts, medicines regulators, researchers, pharmaceutical companies, patient representative bodies, and professional organizations. Countries and organizations are already on their toes. To give an instance, in September 2017, the National Health Service (NHS) of England established a Short Life Working Group (SLWG) in support of the latest WHO challenge. The purpose of SLWG is to advise the Department of Health and Social Care on how to reduce medication errors and best ways to measure progress(10).

In New Zealand, during the fall of 2017, the Health Quality and Safety Commission hosted a series of medication safety workshops facilitated by experts on the subject in order to support participants to meeting today's medication safety challenges(11).

With diligence, this challenge is usually surmountable in any given setting. We can make significant progress towards the Medication Without Harm goal, but only if the governments and other stakeholders live up to the aspirations embodied in the WHO's intention proposed via the challenge.

Need for measuring medication safety

The magnitude and pattern of medication safety problems widely vary with respect to geographic location, patient care set-up and economic status of countries. Few countries have already implemented systems in place to report, track and analyze medication errors at respective national levels. For example, the Institute of Safe Medication Practices (ISMP) in Canada, The European Foundation for the Advancement of Healthcare Practitioners (EFAHP) in Europe, Medication Error Reporting Program (MERP) in the US were all established quite recently considering the significant mortality rate and healthcare costs associated with medication errors(12). However, all these available systems encourage only voluntary and spontaneous medication error reports and hence estimation of absolute medication error rate may not be feasible with these systems. Prospective studies or well-designed retrospective studies could probably provide the estimates of the true prevalence of medication errors. Nevertheless, such medication error monitoring systems are available mostly in developed countries but are scarce among developing- and under-developed countries. Measuring the extent of prevailing medicines safety issues and categorizing them geographically and further patternization helps scheming comprehensive strategic plans to tackle these issues globally.

A recent study report(13) has trigged many swift actions to curb the existing menace of medication errors in England. The study reported an overwhelming 237 million errors per year and a quarter of those causing patient harm. The study estimated 700 deaths per year due to drug errors and could also be a factor in another 1,700 to 22,300 deaths. The common mistakes causing patient harm as reported in the study included wrong medicines being given to patients, incorrect doses dispensed and delays in medicine being administered. Another paper recently published in the Journal of Antimicrobial Chemotherapy(14) has shown that up to 23.1% of prescriptions for antibiotics made in primary care may be inappropriate. These are only two hand-picked examples from the database to highlight the importance of measurement. Measuring medication errors would explore areas of pitfalls, the magnitude of specific errors, identify contributing factors and above all, would change our perceptions.

Systems in healthcare

Since the Institute of Medicine's famous report titled To Err is Human which was published in 2000(3) few other reports also revealed that medication safety issues are rooted in system failures. 'Systems' in healthcare means linking people, processes, structures, and technology in an integrated and interdependent whole,' which can work both to lower the cost of

care and to improve patient outcomes(15). 'Systems thinking' is a way of better understanding complex workplace issues and exploring relationships between system elements to inform efforts to improve(16). However, this approach is not routinely practiced in healthcare. The healthcare industry usually zeroes in on a single individual for any given medication error not taking into account the many confounding factors including stress that equally contributed to the error(17). Vosper.H et.al. (16) believes that real safety improvements require healthcare staff, leaders and decision-makers at all levels to develop systems-thinking competencies and behaviours.

A recent study(18) by Lawes S, found the poor implementation of health IT can result in medication errors and higher risks of patient harm. The researchers found that 889 medication errors in provider reports submitted between January 1 and June 30 of 2016 cited health IT as a contributing cause of the problem. Of these reported medication errors, the most frequently cited problems were dose omission, dosage errors and extra doses

Access to medicines

According to a previous UN report, nearly 2 billion people all over the world do not have sufficient access to essential medicines(19). Access to medicines is a human right; however, access without safety monitoring is an injustice as it may do more harm than good to public health. The problem with access is that lack of medicines would naturally promote off-label uses of medicines. But, off-label medicine use has an increased risk for preventable adverse reactions(20). It has been estimated that more than 70% of the drugs used in children have not been studied scientifically in these groups to assess safety(21). This is in congruence with many studies which reported infants and children as the most vulnerable groups for medication errors(21). Often children are excluded from clinical studies due to ethical issues and hence the prescribing information of many medicines for children has been rooted from adult data. Regulatory authorities have been more stringent recently in producing safety data pertaining vulnerable groups including children.

The reasons for inadequate access to medicines are many including the term of the medicine patent, scant resources, and poverty. The international medication safety stakeholders could probably connect with health systems of nations, especially developing countries to strengthen medicines access by financing, making medicines more affordable, and investing in the development of new medicines for those diseases affecting people of developing countries.

Pharmacists as medication safety stewards

Though health and patient care are being delivered by teams consisting of multi-professionals, the pharmacy is a point where all patients stop to purchase their medicines and could also be a point where pragmatic medication safety efforts can begin. The pharmaceutical care concept equips pharmacists to enhance medication safety. In spite of this, the concept hasn't gained enough momentum in many countries due to established inter-professional dynamics(22). However, health administrators are progressively realizing the potential roles of pharmacists in promoting medication safety in all settings ranging from community pharmacy to specialized clinics. In March 2018, NHS England recruited and deployed hundreds of pharmacists into care homes to help reduce overmedication and cut unnecessary hospital stays(23).

A school of pharmacy in Scotland has recently launched a training programme(24) for 8- and 9-year old school kids in the local area on medicines safety. The programme has been named as "pill school project". The programme involves training on how to accurately count and label tablets, how to measure medicinal liquids using different pieces of pharmaceutical apparatus, medicines safety while at home and getting help from adults. The pupils undergoing this training are certified as medicines safety champions. I completely concur with the prime concern of the programme to discipline children from a young age to stay safe around medicine.

Cultural differences and medication safety

Though there are differences in ethnicity, beliefs, food habits, languages and religions, the same aspirin tablet is used by all. However, these differences can affect attitudes towards health, diseases, and medications. Some are typically intolerant to pain while others consider pain as part of their lives; some believe that their disease would respond to medications while others do not rely on medications; some are more concerned about the effectiveness of medicines while others on its safety; some are open about their problems while others are reluctant etc. People from a different cultural background, therefore, may have a difference in opinions regarding the type of medicine prescribed, dosages and side-effects.

A patient's race or ethnic background can influence how medicines are metabolized(25). Genetic polymorphisms of liver enzymes are common among different ethnic groups. These differences could potentially contribute to significant differences in effectiveness as well as occurrence and severity of side-effects.

Discussing cultural differences and relating them to medication safety would be a sensitive subject, because it may offend people. However, the intention of the author is only to highlight culture as an important entity when we talk about medication safety. A holistic approach including culture is ideal and essential to tackle medication safety issues.

Discussion

Medication safety is a broad term encompassing various entities and stakeholders. Given the recent rapid advances in information, technology, and other sectors, it appears that medication safety in healthcare is one area which lacks sophistication. Like other high-reliability organizations (HROs), it's high time that healthcare being recognized as one of those

bests. Creating a vision, developing missions and setting rational targets would drag healthcare towards this dignified recognition. The WHO's third global patient safety challenge Medication Without Harm is a welcome initiative to reduce medication errors by up to 50% over five years.

Reaching the target necessitates multi-faceted approach concurrently. All stakeholders need to be identified and all possible medication safety entities including access, systems, and culture should be embraced.

Pharmacists could be a vital force in bringing the medication safety efforts to fruition.

As part of the health profession, we are inherently part of the fight; a fight to free our community from the preventable harm caused by adverse medication use. Let's ignite the spirit of this fight at the individual, institutional and community level to accomplish the goal Medication Without Harm. Even teeny-weeny efforts will contribute to us playing a role that will positively impact this healthy cause.e.

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ROLE OF HEALTH PROFESSIONALS

Picture courtesy of Christian Health Association of Zambia

TIPS FOR PRESCRIBERS IN MEDICATION SAFETY

Nzou Chidzewere

Programme Manager, Zimbabwe Association of Church related Hospitals, Zimbabwe

Introduction

The ultimate goal prescribing is to help each client to receive optimum and to ensure the acceptance and effectiveness of treatment plan. Prescribers must collect and report on evidence of medicine-related problems including treatment failure, counterfeit medicines, and poor quality medicines to generate the evidence that will inspire public confidence and trust in the use of medicines.Prescribers are health personnel who are allowed by law to give directions, either orally or in writing, for the preparation and administration of a remedy to be used in the treatment of any disease. Independent prescribers are healthcare professionals who are responsible for: assessing the health of a client and making clinical decisions about how to manage the condition, including prescribing medication and these includes doctors, nurses, pharmacists, physiotherapists, therapeutic radiologists, optometrist and dentists. Supplementary prescribers are responsible for continuing the care after an independent prescriber has assessed the client's health to fulfil a clinical management plan agreed between the prescriber and the client. Supplementary prescribers include: nurses/midwives, pharmacists, diagnostic radiographers, therapeutic radiographers, optometrists and dieticians.

It is important to note that significant harm to a few patients can destroy the credibility, adherence to and success of most public health programmes hence the need for prescribers to follow "safe prescribing" tips outlined below.

Safe Prescribing: Hippocrates' advice "Primum non nocere- first do no harm" is still valid today and prescribers must prescribe only when it's necessary considering benefits versus risk. Un-safe prescribing is becoming an important issue as this is associated with the increase Antimicrobial Resistance (AMR) world-wide and high mortality and morbidity among patients with chronic conditions as well as various infections[1].Safe prescribing needs to consider the following issues; Prescribing within ones limit of competency, evidence based prescribing, drug to drug interactions, tolerability, friendly formulations, adverse effects, correct dosing and the use of standard treatment guidelines.[2].

1. Have a deeper understanding of patient's problem

The prescriber must get as much information about the patient problem through taking a good history of the illness as well as thorough a medical examination and the prescriber should remember issues listed under 'Safe Prescribing" above to avoid causing any harm.[3]

2.Concordance relationships

Patients with chronic conditions have challenges to take their medicines as prescribed due to fatigue.[4] The prescriber and patients relationship where the prescribers gives compulsory instructions to the patient to be compliant in taking medicines is no longer working.[5] The prescriber and patient should enter into a concordance partnership on the use of medicines. Concordance relationship includes empowering of the patients with information on; the use of medicines, effectiveness, how to take the medicines, the cost of medicines, side effects and lifestyle modifications. [5]

3. Set a realistic therapeutic objective

This allow prescribers to prescribe for an intended purpose and to reach desired outcomes e.g. to obtain a blood pressure reading of less than 130/80mmHg in a hypertensive patient.

4. Select appropriate therapy

The selection of an appropriate therapy can be guided by national or WHO treatment guidelines which takes into consideration the issues of: Safety, Tolerability, Effectiveness, Price, and Simplicity (STEPS)[6]

5. Give information, instructions and warnings

Prescribers should educate patients about their conditions, the intended use of prescribed medicines, expected outcomes, potential adverse effects and what to do if these occur, how the medication should be administered, relationship with food and other medications being taken by the patient and dosage in relation to the time of the day.[7]

6.Regular reviews

Set a review date to check on the progress and this also give an opportunity to revisit diagnosis, evaluate adverse effects or drug interactions, stopping unnecessary medications and helps avoid the Prescribing Cascade where the prescriber adds new medicines to treat adverse effects of other medicines.[8][9]

7. Consider the cost of medicines

Prescribers should consider the cost of medicines and the patient ability to pay as patients comes from diverse economic backgrounds. [10]Cost can be a big factor in the delay to start medication among patients'.[11]

8. Simplified guidance on writing prescriptions

A well written prescription allows the dispensing personnel to issue the right medicine, in right dosage, to the right patients with clear instructions for use. [2] The prescribers should observe the following instructions;[2]

- Write legibly as the prescription is hand written
- All prescriptions should have full legible names and signature of the prescriber
- Prescribe generic medicines instead of branded products to avoid expense
- Avoid unnecessary use of decimals (e.g. 10 mg , not 10.0 mg)
- For quantities less than 1gram write in milligrams (e.g. 500 mg, not 0,5 g)
- For quantities less than 1 milligram write in micrograms (e.g. 100 micrograms, not 0,1 mg
- Use Millilitres (ml or mL, not cubic centimetres or cc)
- Information on the prescription should include the following; date, full names, age (under 5 should be written in years and months),
- Supplementary warnings, advice and instructions must be written in full
- Unused space on the prescription pad must be counselled
- Schedules should be written in English and the following Latin Abbreviations are acceptable

Stat =immediately

p.r.n = pro re nata = when required (state minimum dosage, interval and maximum total amount)

o.d = omni die = every day

o.n = omni nocte = every night

b.d = bis die = twice daily

t.d.s = ter die sumendum = three times daily

q.d.s = quarter die sumendum = four times daily

Conclusion

Prescribers must always abide with the international, national medicines regulatory authorities code of conduct and safe prescribing tips outlined above to protect the public from the escalating drug safety and reliability crisis. We urge the prescriber to take just a few minutes in making sure that the client fully understands directions for useto get the full benefit of the treatment plan.

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THE ROLE OF PHARMACISTS IN MEDICATION SAFETY

Susan A. Mutua | Chief Pharmacist

Gertrude's Children's Hospital, Kenya

Summary

Medications are the most common treatment intervention used in healthcare. When used safely and appropriately, they contribute to significant improvement in the health and well-being of patients. However, despite the best intentions of healthcare providers and the design of healthcare systems, medications can cause patient safety incidents.

Even though medication safety is the responsibility of all involved in medication management and use,pharmacy professionals are expected to play a key role in reducing medication errors by ensuring that safety is considered in medication organization and management, as well as by making appropriate interventions in the medication use processes.

Pharmacists as the medication experts are required to take a leadership role in ensuring that possible sources of medication-related harm are addressed in all the medication management and medication use processes.

Medication Safety

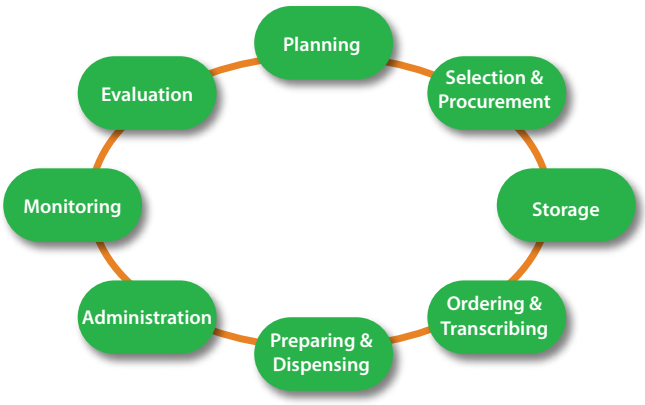
Medications constitute a significant part of the care provided to patients and are used for diagnostic, symptomatic, preventive, curative, and palliative treatment. Medication safety is defined as freedom from preventable harm with medication use1.

Safety concerns with regard to medication use were brought to the fore by the 1999 US report by the Institute of Medicine (IOM) titled, To Err is Human: Building a Safer Health System2. The report described the costs of medical errors to the US economy and how medical errors numbered higher than deaths due to AIDS, motor-vehicle accidents, and breast cancer, combined. The report also described how errors could be minimized. Medication-related errors were reported to occur frequently in hospitals and although not all result in actual harm, those that do are costly. It was estimated that at the time, generalization of findings from a certain study indicated that, the increased hospital costs alone of preventable adverse drug events affecting inpatients were about $2 billion for the nation as a whole. Further to these findings, the IOM presented another report in 2007 on Medication Safety, Preventing Medication Errors3, which emphasized the importance of continuous monitoring of medication errors, providing clinicians with decision-support tools, and improving and standardizing medication labeling and medication-related information.

Medication-related errors contribute a significant proportion of preventable adverse events resulting in patient harm and increased direct and indirect hospital costs4,5,6,7. Though grossly under-reported, medication errors are considered one of the most common types of error, and account for a sizable increase in health care costs. They affect large numbers of persons due to the extensive use of medicines both out-of-hospital and in hospital settings. Numerous factors, both human and systemic, have been found to contribute to the errors[8,9,10].

Potential harm from medication use should be prevented at each point of medication management and use processes described below 11:

The medication managment process

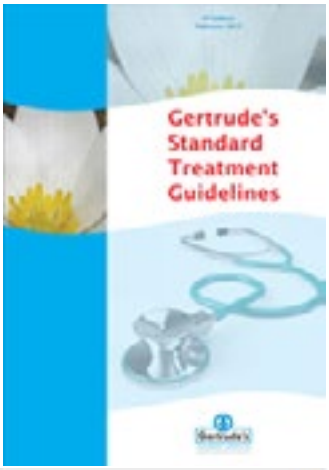


The above processes involve professionals from various disciplines. Similarly, medication safety is the responsibility of all involved in medication management and use – from the procurement officers, store personnel, prescribers, pharmacy staff and nurses. However, the Pharmacist is recognised as the custodian and authority on medication, and therefore is required to take the lead in ensuring avoidance of preventable harm with medication use.

Safe medication practices are anchored on the "five rights" of medication use: the right drug, the right patient, the right time, the right dose, and the right route12,13. These rights have however been described as a "destination without a map" as they are broadly stated goals or desired outcomes of safe medication practices that offer no procedural guidance on how to achieve these goals14. The Pharmacist is expected to spearhead safety considerations at each stage of the Medication Management Process in order to achieve the five rights and patient safety.

Right Drug: Product-centred Safety

Ensuring that the medicinal product is safe is the first step in preventing harm. The pharmacist should guide the selection and procurement of safe, efficacious and high quality medicines. In light of the wide range of medicines available, standard treatment guidelines and a formulary (list) enable selection of preferred agents based on the institution's mission, patient needs and types of services provided. See examples below.



The process of selection should be a collaborative process that considers patient need and safety as well as economics. All those who are involved in prescribing and managing medications should participate in the process. The team charged with this responsibility is usually known as the Medicines (or Pharmacy) and Therapeutics Committee. .

The medication (formulary) list should also be maintained and monitored by a multidisciplinary team comprising of those involved in the prescribing, dispensing, administering, and monitoring processes for medications. Criteria for addition or removal of medications from the list should be defined and these include the indication for use, efficacy, risks, and cost-effectiveness.

A pharmacist should monitor use of any newly added medication with regard to appropriateness of indication, how the medicine is prescribed (dosage or route, for example), and any unanticipated adverse events or conditions associated with the new medicine during the introductory period. They should also ensure that the formulary list is reviewed at least annually based on emerging safety and efficacy information and information on usage and adverse events.

Selection also involves considering the packaging, child safety caps and information leaflet as well as avoiding look-alike packs that may cause mix-up. High-risk (high alert) medications should be identified and necessary precautions taken to prevent unsafe use15. High-alert medications bear a heightened risk of causing significant patient harm when they are used in error. Although mistakes may or may not be more common with these drugs, the consequences of an error are clearly more devastating to patients.[16] Examples of lists of high-alert medications are available from organizations such as the Institute for Safe Medication Practices (ISMP) and the World Health Organization (WHO) but each institution needs to develop their own list of medications which in their setting require special safeguards to reduce the risk of errors and minimize harm. Precautions for high-risk (high alert) medication may include[16]:

1. Standardizing the storage, ordering, preparation, and administration of these medications
2. Improving access to information about these drugs
3. Limiting access to high-alert medications
4. Automated alerts
5. Use of auxiliary labels (as shown below)

Procurement system should ensure avoidance of counterfeit and substandard medications. This requires liaison with relevant regulatory bodies and sourcing from reputable organizations. It is also important to regularly evaluate the supply chain and put mechanisms to track supplies identified as "at most risk" of falsification as well as damage during storage or transport.

The Pharmacist should be a source of Medicine Information to advice on appropriate use of medications. Pharmacists should always be available for consultation and have access to up-to-date user-friendly medication information resources that facilitate quick search of necessary information. These could be hard copy or electronic e.g. BNF®, Martindale®, Medicines Complete®.

Storage requirements should be observed to maintain the potency, stability and safety of procured medications. Regular inspections of all medication storage areas should be conducted to ensure good storage practices. Appropriate safe storage practices such as segregation, limitation of access and labelling of storage areas should be applied. Medicines that look-alike should be stored separately. Expiry management and monitoring is important to avoid inadvertent dispensing of expired medicines. The practice of First Expiry First Out (FEFO) minimizes loss due to expiry.

Preparation and Dispensing processes should also ensure that the medication remains safe. Medications should be prepared and dispensed in a clean, safe and uncluttered environment that complies with laws, regulations, and professional practice.

Hand hygiene and aseptic technique should be practiced as required to prevent contamination of medications.

Appropriate auxiliary labels should be used to support safe use of medication e.g. contraindications, shaking of suspensions, special storage requirements, to enhance alertness when handling high risk medications[15] .

Clean, uncluttered dispensing environment

Medication use counselling should always be provided to patients and their families.

Right Patient: Patient-centred Safety

Correct patient identification is critical to ensure the right medication is prescribed and given to the correct patient. Special patient-specific precautions should be noted e.g. in case of allergies, comorbidities and concurrent medication.

Pharmacists have an important role in intercepting and preventing prescribing/ordering errors. One study found that while dispensing errors were 14 percent of the total adverse drug events, pharmacists intercepted 70 percent of all physician ordering errors17. All prescriptions should be reviewed before dispensing happens. The pharmacist should establish suitability and appropriateness of the medications for the particular patient. The process to conduct an appropriateness review for an order or prescription prior to dispensing includes evaluation by a trained professional of[11]:

1. the appropriateness of the medicine, dose, frequency, and route of administration;
2. variation from hospital criteria for use
3. therapeutic duplication;
4. real or potential allergies or sensitivities;

5. real or potential interactions between the medication and other medications or food;
6. patient's weight and other physiological information; and
7. other contraindications

The Pharmacist may thus facilitate safe prescribing and dispensing by ensuring:

1. Patients are identified appropriately
2. Patient-specific factors are considered in choice of medications
3. Only prescriptions from eligible approved prescribers are processed
4. Legible prescribing is practiced and clarifications are sought from the prescriber where required
5. Avoidance of abbreviations
6. Completeness and appropriateness of prescribed medicines – the pharmacist should contact the prescriber in case of any queries
7. Verbal, telephone, and text medication orders are handled correctly
8. Uniform and standardized dispensing system that ensures accurate and timely dispensing of medications
9. Proper labelling which should include the name of the medication, dosage/concentration, date prepared, expiration date and two patient identifiers.

Right Dosage, Time and Route: Administration-centred Safety

Medication should always be administered in the right dose at the right time through the right route12,13. This should only be done by those individuals with the requisite knowledge and experience and who are also permitted by licensure, certification, laws, or regulations to administer medications.

The pharmacist should provide necessary information and tools to support correct administration e.g. reference charts such as Dosing Charts, Dilution and Stability Charts, Side Effects for Common Medications or medication counselling checklists.

An additional role that may be considered by pharmacists is surveillance/audit of medicine administration to check correctness of administration by nurses and doctors.

Pharmacists have a critical role in monitoring effects of medications. This includes observing and documenting the desired therapeutic effects as well as adverse effects. Where possible, pharmacists should conduct regular treatment reviews to evaluate any changes of signs and symptoms following administration of medication. They should work together with patients, their physicians, nurses, and other health care practitioners to monitor patients on medications. Based on the findings, they may recommend adjustments where needed. It is important that Pharmacists identify and report adverse effects, medication errors and near misses for necessary preventive and corrective measures to be taken.

Conclusion

It is important that medication safety measures are in-built in the medication management and use processes. The measures should be evaluated periodically for effectiveness and efficiency and improvements made where gaps are noted.

Medication errors or adverse effects should be routinely monitored and reported for corrective and preventive actions to be taken.

Medication errors are often preventable, but reducing error rates significantly requires interventions at all stages of medication management and use.

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PHARMACOVIGILANCE

A COMMENTARY ON PHARMACOVIGILANCE FROM A HEALTHCARE SETTING

Mirfin Mpundu

Executive Director, Ecumenical Pharmaceutical Network and Head, React Africa (Kenya)

Introduction

When patients enter our hospitals with any condition they come in with, the last thing they expect are adverse drug events (ADEs) occurring, following administration of medicines that compromise their safety. Many times patients are not cautioned or counseled on possible side effects or adverse drug reactions (ADRs) that might occur while taking their prescriptions. This is a common practice in both in-patients and out-patients. Patients are simply given medication with written instructions on the packaging – where sometimes the name of the drug is not included. The pharmacist or pharmacy technician's role including doctors/ clinical officers, is considered finished with writing, filling and dispensing of a prescription. In most healthcare settings in Low and Middle Income Countries (LMICs) including EPN member facilities tracking-of ADRs is not a common practice yet is so fundamental in assuring patient safety.

Pharmacy staff need to consider the medicine profiles of the medicines that patients are taking - including looking at any duplication of treatments – and counsel the patients on expected possible interactions and possible ADRs. Examples may include retinal detachment associated with the use of fluoroquinolones for example, toxic necrolysis associated with drug exposure and sudden death that might occur associated with attention deficit hyperactivity disorder (ADHD) treatment. Other drug related problems that might occur include weakness or drowsiness, biochemical or haematological derangements (such as acute kidney injury, electrolyte imbalance or anaemia), bleeding, gastrointestinal disturbances, hypoglycaemia or healthcare-associated infections such as Clostridium difficile.

One important role of the pharmacists is to always look out for adverse events that might occur to patients following administration, beyond simply looking out only for side effects. Patient counseling on medications being taken is thus of uttermost importance. Some of these activities fall under what is called pharmacovigilance (PV) and one would argue that PV is part of pharmaceutical care.

PV ensures medications effectiveness and safety. Thus, pharmacists and pharmacy technicians need should always take their role as medicine dispensers seriously and should be consistently diligent in following standard guidelines principals. Negligence of this responsibility may cause severe morbidity following administering of medications, which could lead to mortality. Understanding and monitoring of adverse events i.e. adverse drug reactions (ADRs) has many benefits. Despite the benefits however, ADRs continue to cause preventable injury, illness, disability and death, most of which are not recorded in many health facilities.

Important definitions

What is pharmacovigilance (PV)?

PV is defined by WHO as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine - related problem (2004). The aim of PV is to assure safety and effectiveness of medicines and treatment. Medicines have the potential to bring about healing, control a patient's chronic condition such as hypertension and diabetes but can also cause adverse events, such as heart conditions etc. Drug events can occur immediately leading to severe conditions or death e.g. heart attacks and other times, to not so immediate reactions such as a deteriorating cardio vascular system.

Adverse Drug Event

An ADR is a type of ADE whose cause can be directly attributed to a drug and its physiologic properties. A main distinction between ADRs and ADEs is that ADRs occur despite appropriate prescribing and dosing, whereas ADEs may also be associated with inappropriate use of the drug or other confounders that occur during drug therapy but are not necessarily caused by the pharmacology of the drug itself.

Adverse Drug Reaction

An adverse drug reaction (ADR) can be defined as 'an appreciably harmful or unpleasant reaction resulting from an intervention directly related to the use of a medicinal product; adverse effects usually predict hazard from future administration and warrant prevention, or specific treatment, or alteration of the dosage regimen, or withdrawal of the product'.

Box 1-1. Adverse Drug Reaction Terms and Definitions

Adverse Drug Reaction (ADR)

- A response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease or for modification of physiological function (WHO)[a]
- An appreciably harmful or unpleasant reaction, caused by an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product (Edwards)[b]
- Any unexpected, unintended, undesired, or excessive response to a drug that requires discontinuing the drug (therapeutic or diagnostic), requires changing the drug therapy, requires modifying the dose (except for minor dosage adjustments), necessitates admission to a hospital, prolongs stay in a health care facility, necessitates supportive treatment, significantly complicates diagnosis, negatively affects prognosis, or results in temporary or permanent harm, disability, or death (ASHP)[c]
- Harm directly caused by a drug at normal doses (Edwards)[b]

Adverse Drug Event (ADE)

- Any untoward occurrence that may present during treatment with a pharmaceutical product but that does not necessarily have a causal relation to the treatment (WHO)[a]
- Injuries caused by medical interventions related to a drug. Adverse drug events may result from medication errors or from ADRs in which there was no error (Bates)[d]

Unexpected Adverse Reaction

- An adverse reaction, the nature or severity of which is not consistent with domestic labeling or market authorization, or expected from characteristics of the drug (Cobert)[e]

Serious Adverse Effect

- Any untoward medical occurrence that at any dose results in death, requires hospital admission or prolongation of existing hospital stay, results in persistent or significant disability/incapacity, or is life threatening (Edwards)[b]

Signal

- Reported information on a possible causal relation between an adverse event and a drug, the relation being previously unknown or incompletely documented (Edwards)[b]

Medication Error

- Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer (NCC MERP)[f]
- Errors in the process of ordering or delivering a medication, regardless of whether an injury occurred or the potential for injury was present (Bates)[d]
- Inappropriate use of a drug that may or may not result in harm (Nebeker)[g]

[a]WHO: International Drug Monitoring: The Role of the Hospital. Technical Report Series No. 425. Geneva: WHO, 1969.
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Side effects

A side effect is usually defined as 'an unintended effect occurring at normal doses related to the pharmacological properties'. Some common side effects go away in a short time and these might differ from drug to drug and may typically include diarrhea, nausea, constipation, weight gain, headache, disruption of sleep or disruption of desire or ability to have sex.

It is thus important to understand these differences and use the correct terms and be vigilant to look out for ADRs especially and alerting the relevant authorities. A number of recalls occur because of ADRs being reported. Role of pharmacists in PV

Both community and hospital pharmacists can play a major role in PV. Hospital pharmacists play a significant role in ADR reporting because the most serious adverse drug events occur in hospitals, and ADRs account for a substantial proportion of hospital admissions. Community pharmacists also play an important role in ADR through reporting of ADRs to regulatory authorities or governing bodies.Generally premarket surveys may not reveal ADRs because of the small sample size, the simple set-up and short duration of trials. However once a drug is on the market ADRs can be observed because of a larger population on the medication and the duration of treatment may be longer.

To promote PV, a pharmacist may perform the following activities:

- Monitoring of any ADRs
- Reporting of ADRs within the hospital and to regulatory agencies
- Utilize a risk-benefit profile assessment that might include;
- Ensuring risks are minimized by; encouraging reporting of adverse events, restricting access to a particular prescriber/patient group, educating patients and health professionals of specific risks including warnings/ precautions/contraindications on product information/ packaging.

Table 1-1. Classification of Adverse Drug Reactions

Type of Reaction (Mnemonic)	Features	Examples	Management
A: Dose related (Augmented)	Common Related to the pharmacologic action of the drug – exaggerated pharmacologic response Predictable Low mortality	Dry mouth with tricyclic antidepressants, respiratory depression with opioids, bleeding with warfarin, serotonin syndrome with SSRIs, digoxin toxicity	Reduce dose or withhold drug Consider effects of concomitant therapy
B: Non–dose related (Bizarre)	Uncommon Not related to the pharmacologic action of the drug Unpredictable High mortality	Immunologic reactions: anaphylaxis to penicillin Idiosyncratic reactions: malignant hyperthermia with general anesthetics	Withhold and avoid in future
C: Dose related and time related (Chronic)	Uncommon Related to the cumulative dose	Hypothalamic-pituitary-adrenal axis suppression by corticosteroids, osteonecrosis of the jaw with bisphosphonates	Reduce dose or withhold; withdrawal may have to be prolonged
D: Time related (Delayed)	Uncommon Usually dose related Occurs or becomes apparent sometime after use of the drug	Carcinogenesis Tardive dyskinesia Teratogenesis Leucopenia with lomustine	Often intractable
E: Withdrawal (End of use)	Uncommon Occurs soon after withdrawal of the drug	Withdrawal syndrome with opiates or benzodiazepines (e.g., insomnia, anxiety)	Reintroduce drug and withdraw slowly
F: Unexpected failure of therapy (Failure)	Common Dose related Often caused by drug interactions	Inadequate dosage of an oral contraceptive when used with an enzyme inducer Resistance to antimicrobial agents	Increase dosage Consider effects of concomitant therapy

SSRI = selective serotonin reuptake inhibitor.

Adapted with permission from Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. Lancet 2000;356:1255-9.

Conclusion

Pharmacists and pharmacy technicians have a central role in ensuring patient and medication safety. We need to fully unpack the significance of understanding the medicines we dispense to our patients, provide information that include the indication, dosage, possible side effects and ADRs and that, crucially, ADRs should be reported immediately. ADRs or any ADE should be discussed within the hospital through the Drugs & Therapeutic Committee (DTC), administrators and reported to regulatory authorities so they may be tracked. After all PV is all about harnessing good patient outcomes through assuring effectiveness and safety of medicines we dispense to our patients.

MEDICATION SAFETY IN DONOR-SPONSORED PUBLIC HEALTH PROGRAMMES

Slobbe Richard

Chairman GIMS foundation, Netherlands

Abstract

Medication safety has been a major topic among pharmacists and other healthcare professionals throughout the world, both pharmaceutical care (PC) as pharmacovigilance (PV). While PV consists of passive retrospective analysis, PC is considered to be an active engagement at the dispensing level including checks on interactions, contra-indications, allergies and improving patients' adherence. However, not much is known about the quality of medication safety at the level of the individual patient in the developing world. The aim was to find out about the currentefforts to improve medication safety in donor-sponsored public health programmes (PHPs). The research was an initiative of the Global Initiative on Medication Safety (GIMS) Foundation. This is an organisation which emphasises the importance ofminimizing health risks originated by the global use of medication, with a focus on the developing world.

To collect the data required on this matter, some of the biggest organizations involved in the financing and distribution of medication through public health programs were studied. The websites of the organizations were studied along with direct contact through e-mailing, telephone calls and meetups.

The main organisations who responded or were of the biggest interest were the WHO, The Global Fund, Médecins sans Frontières, SIAPS programme and Healthy Entrepeneurs. The WHO has issued more focus on PV and the importance of medication safety and follows up with funding. The Global Fund funds many PHPs, but since changing the funding system it is unclear how involved they are in medication safety. MSF and SIAPS have developed tools to improve PV, while MSF is also focusing on PC through its field workers. Healthy Entrepeneurs works in a different way by using a socially commercial way of operating with a focus on access to medicines, but less on medication safety.

Our findings seem to show that although PV has received proper attention, individual medication safety in the form of PC, also in donor-sponsored programs, is still in its infancy, underreported or completely absent.

Introduction

Through the years there has been much attention for medication safety on a global scale. Medication safety is however a wide term and includes several factors. One of them is PC, the term used for pharmacists acting as a health care provider who can actively participate in illness prevention and health promotion [1]. The pharmacist does this on a patient level by checking dosages, contra-indications, allergies, interactions, improve adherence and inform the patient to ensure a safe and effective treatment. Another factor of medication safety, consists of PV which is defined by the WHO as "the science and activities related to the detection, assessment, understanding and prevention of adverse drug effects or any other possible drug-related problems" [2]. However, the definition of the WHO also includes the detection and collection of medication errors, lack of efficacy and counterfeit or substandard medicines. Therefore, a shift to a more broadened view has been noticed in recent years, stressing the importance of PV [3, 4].

In 2006, the WHO published a report to stress the importance of PV in PHPs in order to improve medication safety in developing countries. In this report it was claimed that "the idea that PV is a luxury, affordable only in the developed world, should be replaced by the realization that a reliable system of PV is essential for the rational, safe and cost-effective use of medicines in all countries and consequently for public health, and should produce clear advantages in relation to cost" [5].PV became of apparent importance due to the improved access to medicines which put many more individuals consequently at risk of treatment-related adverse effects. Therefore, The Global Fund (GF) introduced PV as a requirement in the proposals for the 10th round of grant applications back in 2010. GF is one of the main parties responsible for providing medication in developing countries on a widespread level [3]. However, since 2011 GF has changed its ways of funding and now uses a network of country coordinating mechanisms (CCMs) to distribute grants [6]. It is unclear what effect this change of funding has had on the medication safety agenda.

The focus on the importance of medication safety and thus PV, has led to many countries starting up national PV systems

between 2000 and 2010. However, there is a clear lack of resources and staff to support these [7]. Recently the PV agenda in these countries has become very much donor-driven, with most efforts going into setting up PV programs for medicines used in PHPs, such as malaria and HIV[7]. The need for adequate medication safety activities is growing as non-communicable diseases (diabetes, cardiovascular disease) are becoming more prevalent in developing countries. Therefore, the main point in this project was to find out what the current situation is of efforts to improve medication safety in donor-sponsored PHPs, ten years after the WHO emphasized its importance?

Method

This project was initiated by the Global Initiative on Medication Safety (GIMS) Foundation in conjunction with the University of Utrecht. The GIMS Foundation's main objective is to minimize health risks originated by the global use of medication. The writer is a student who is at the end of his Master's degree in Pharmacy at the University of Utrecht.

To collect the data required for this project, some of the biggest organizations involved in the financing and distribution of medication through PHPs were studied. To achieve this the websites of the organizations were studied along with any files detailing their incorporation of medication safety. Direct contact was initiated by e-mailing, followed up by calling through telephone in case of a lack of response. The collected information was discussed and analysed and in some cases summarized in short abstracts. These proved to be the basis of this article.

Results

Table 1 summarises the findings of the different organisations studied for this project. Detailed information is found further up this section.

World Health Organization (WHO)

The WHO plays a big part in supporting developing countries to improve their healthcare. Their main aim is to direct international health within the United Nations community. Next to providing financial aid, the WHO sets up policies, norms, standards and guidelines, such as how to start and maintain functional national PV centres, but also how to perform PV for medicines against malaria, HIV/AIDS and tuberculosis[8,9]. They keep a watchful eye over developments in medication safety throughout the world and publish scientific articles to keep the scientific world aware and updated [3,5,7]. The WHO also has close bonds with the Global Fund and these two parties collaborate on many fronts

Table 1: Overview of results of the studied organisations.

Organisation	Response?	Policy on PV	Actions towards PV	Actions towards PC
WHO: several departments	No or not helpful	Yes	• Setting up guidelines, standards, etc. • Drug Monitoring Programme • Financing	Unclear
The Global Fund	Yes, not helpful	Unclear	• Financing	Unclear
MSF	Yes	Yes	• Field work • Electronic tools • Training	• MSF Clinical guidelines • Training
SIAPS	Yes	Yes	• Electronic tools • Financing	Unclear
HE	Yes	No		Awareness through applications on tablets
ISMP	No	Unclear	Unclear	Unclear
AMREF Flying Doctors	No	Unclear	Unclear	Unclear
Aidspan, GF Watchdog	No	Unclear	Unclear	Unclear
Cordaid	No	Unclear	Unclear	Unclear
Bill and Melinda Gates Foundation	No	Unclear	Unclear	Unclear

One of the WHO biggest accomplishments on medication safety is the creation of the WHO Programme for International Drug Monitoring. This programme was set up after the thalidomide tragedy and saw the appointment of the Uppsala Monitoring Centre in Sweden as WHO Collaborating Centre for Drug Monitoring to internationally collect individual case safety reports in their database 'VigiBase™'. This database comprises of over 10 million entries, which allow the detection of potential medicinal safety hazards. [10]

On a more local level, the WHO has created a WHO Collaborating Centre for Advocacy and Training in PV at the University of Ghana. This institution is focused on training healthcare professionals and supporting national PV centres as well as performing research in PV like cohort event monitoring of specific medicines [11]. The centre has been involved in the introduction of several modules of MedSpina, a longitudinal safety data management system, into the clinical field of Ghana. It consists of software for a healthcare situation which supports patient data records and prescribing software[12, 13]. The intention was to improve the PC by adding health technology. However, it is not known what effect this software has had in practice.

The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM)

GFATM raises and invests resources to support programs run by local experts in countries and communities most in need. Its existence started through some of the Millennium Development Goals set by the United Nations at a G8 summit in 2000. As its name indicates, GFATM focuses on the three major diseases and invests the money of the largest developed nations to improve the healthcare in developing countries [14]. Through process-indicators they monitor and evaluate their funded projects in order to reach pre-set goals [15].

Although it is described that The Global Fund has made PV a requirement since the Round 10 proposals, not much is known about how individual medication safety is put into practice. It is to be expected that due to the local nature of the proposals much variation will exist in the execution of medication safety by healthcare professionals.

Médecins sans frontiers (MSF)

Through the help of M. Serrano, section pharmacist at MSF Holland, we received information on the MSF activities and way of working. MSF works principally to assist populations caught up in humanitarian crises where there is a high level of medical need. MSF Holland (Artsen zonder Grenzen) is present in about 23 countries.In 2015,it spent 34 million euros of which roughly 50% was spent on pharmaceuticals. MSF is frequently perceived as an organization fully committed to emergencies, but the organization has very long standing interventions as well. Non-communicable diseases have received increased focus in recent years, like hypertension and diabetes. MSF aims to provide these treatments integrated in their programs as well.

The pharmacists in MSF do various kinds of jobs, some of these comprise of approving manufacturer or supplier couples for the procurement lists; investigating markets, prices, prescription protocols, together with other healthcare professionals and there are periods where they do field work as well. [16]

As for medication safety during general practice, when patients are treated their data is collected in patient files to keep track of the clinical history, medical and pharmaceutical information. MSF provides standard therapeutic protocols to prescribers which take patient's age and weight into account and are adjusted, where appropriate to national protocols. The most general is called "MSF clinical guidelines", which is published once a year. Contra-indications and interactions are further explained in disease specific training. For instance, doctors attending training to work on anti-tuberculoticcenters re-learn that rifampicin interacts with about everything. Known allergies are investigated during the clinical history, however it is often impossible to retrieve such data in the contexts where MSF works. Additionally, MSF provides field teams with updated versions of the 'British National Formulary'. MSF also owns a formulary, a rationalized and restrictive assortment list of products, which is updated once a year with new available products and special considerations. However, MSF does not have a standard ICT system for prescribing and dispensing, as most locations rely on paper based systems to date. [16]

Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program

Management sciences for health (MSH) started the Strengthening Pharmaceutical Systems (SPS) Program which over time evolved into the SIAPS Program. Nowadays this program is funded by USAID and has many influential partners, such as Harvard University and the University of Washington. The SIAPS approach to pharmaceutical systems strengthening has been implemented in over 50 countries since the program began in 2011. [17]

The program enhances countries' capacity to procure and distribute high-quality medicines and health technologies, but also works with local partners to develop strong systems for health financing, human resources, governance, information, service delivery, and PV [18]. By promoting local ownership of wide-ranging initiatives, stronger, more sustainable health systems overall are fostered. As part of this, they have developed several electronic tools, such as an electronic dispensing tool (EDT) and a web-based application for PV data capturing (PViMS). Other applications consist of disease-specific software (e-TB manager, QuanTB) or for quantification and distribution purposes (Quantimed, RxSolution) [19]. RxSolution is a tool on which a small facility or hospital could function in order to manage patient information, appointments, prescribing, ordering and dispensing. New modules could be added to support prescribing decisions.

SIAPS focuses on improving pharmaceutical systems, mostly through sponsors who determine the needs of the systems to be

implemented. Therefore, they don't have a generic approach to work on individual medication safety. They are however actively working on setting up PV systems in countries and developing a PV automated information system (PAIS) to be used in PV centres to manage the data entries [17].

Healthy Entrepreneurs (HE)

HE is a small business set up by two Dutch businessmen who apply a financially sustainable micro-franchise formula to a network of local entrepreneurs. Their aim is to reach and provide basic care to people in remote villages whom are isolated from standard care and are often not included in major vertical medication programmes. HE works with micro entrepreneurs who offer essential health products, like painkillers, contraceptives, sanitary pads, antibiotics, soap, vitamins and health information. They have set up an education application on tablets to raise awareness people about topics such as sexual and reproductive health, nutrition and hygiene. Some of the medication requires a prescription, through use of the tablet information is supplied about correct dosing. HE is focused on logistics and therefore does not provide information about medication safety. The entrepreneurs are not pharmacists, although HE has national pharmacists employed in the areas where they are active. [20]

Discussion

The WHO is heavily active in the area of PV through their International Drug Monitoring Programme. Health care professionals get trained to help improve PV reporting. Yet it is not known if the WHO directly acts on medication errors through training pharmacists to perform proper PC. Analysing PV data is one step to improve medication safety through rational use of medicine and setting up standards and policies. The other is to improve the practice, although this might be harder to measure through indicators. Efforts have been made to include health technology to this cause, such as MedSpina and the electronic tools of the SIAPS programme.

Funded vertical medication programs by the WHO or The Global Fund focus on one disease and therefore only provide medication safety for the respective medicines. Next to this, it is not clear if pharmacists (or other medical professionals) perform PC as in checking dosages, interactions, contra-indications, allergies, conform to prescribing guidelines and more activities. The focus in most PHPs still seems to be focused on logistics, to reach the patients in order to be able to treat them. Another option is that there could be a severe underreporting of PC efforts in developing countries in scientific literature. Just like PV at first, PC might be seen as a luxury, affordable only in the developed world. However, proper PC by pharmacists fuelled by knowledge and tools might save more lives than one could imagine.

Despite being started up in many countries by medical professionals, national PV centres currently lack the resources and staff to function normally. The efforts that are put in setting up PV programs in PHPs could be integrated into national PV centres to support the development of PV and eventually individual medication safety in the long run. A shift of efforts towards national or regional PV centres is of great importance to cover these issues in the near future.

Another point is the use of electronic prescribing tools and other supporting software for healthcare purposes. The SIAPS programme is one program that has started developing and spreading electronic tools to aid local healthcare. Many of these tools are focused on the distribution, logistics and patient management, while one performs basic pharmaceutical care (e-TB manager).PViMS is a tool which they created to collect PV data. Another company consisting of staff of the WHO Collaborating Centre in Ghanacreated an electronic pharmaceutical system called MedSpina. Software like MedSpina is exciting because it consists of several functions combined into one system, such as patient records, logistics, management and prescribing tools. Health technology is a helpful tool in improving medication safety through advancements, like addition of decision-supporting prescribing software.

Most organizations seem hesitant in releasing any information about medication safety not described on the websites. Nor do they respond to e-mails when asked about the topic. Therefore, it has proven to be somewhat of a struggle, in the given time frame, for an outsider to perform a proper analysis of the current situation of medication safety in donor-sponsored PHPs. There is not much scientific literature available on the topic of practical medication safety in developing countries. Most hits concern PV and not the level of PC.

Much of the medical slang surrounding medication safety has been standardized by the WHO. However, in the (scientific) field there seems to be a lot of confusion [21]. For instance, PV is a much wider meaning than many people in the field seem to realise. It comprises of all the issues drug-related, which like put forward in the introduction includes medication error, lack of efficacy and substandard or fake medicines. Another example is medication safety, which is often directly linked to PV. However, medication safety comprises not only of detection and reporting of many different drug-related problems. Medication safety also consists of the direct consequences of a medication error to the individual patient and is therefore tied to the practical work of pharmacists: PC. Perhaps this confusion in medical slang is one of the reasons why not much is reported about the level of PC in developing countries or the funding or training concerning this matter.

Conclusion

Although medication safety in developing countries has received much attention from funding organisations in recent years, the efforts seem to have mainly gone to introducing PV in the form of PV centres and integrating PV into PHPs. Individual medication safety in the form of PC, also in donor-sponsored programs, is still in its infancy, underreported or completely absent. This surely imposes a (serious) health risk.

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ROLE OF OTHER STAKEHOLDERS

Left to Right Bottom Role: Susan Githii (National Public Health Laboratories), Evelyn Wasangula (WHO), Mirfin Mpundu (EPN), Kem Muma (Kijabe), Marc Sprenger (WHO), Franklin Njagi (Kijabe Hospital)

Left to Right Top Role: Samuel Shangu (EPN), Helle Aagaard (React), Dusan Jasovsky (React), Jarred Nyakiba (MoH- Kenya), Peter Yeboah (Christian Health Association of Ghana), Ginny Barnetter (IPC Consultant Kijabe), Salome Gathoni (Kijabe Hospital).

QUALITY OF MEDICINES AND MEDICATION SAFETY – THE EPN DIFAEM MINILAB NETWORK

Christine Häfele-Abah

German Institute for Medical Mission, Germany

Executive summary

The recent WHO report on "Public health and socioeconomic impact of substandard and falsified medical products" established a failure rate of 10.5% for medicines in low and middle-income countries. The quality of medicines is of major concern especially in African countries where regulation is still insufficient. Poor-quality medicines directly affect medication safety and have tremendous negative health and socioeconomic effects. In order to support faith-based Drug Supply Organizations (DSOs) and further partners to assure the quality of medicines, the DIFAM EPN Minilab project was started in 2010. Until today, 17 "Minilab Network" members in 11 countries screened 4000 samples - of their own supply chain but also from private markets - with the easy-to-use GPHF Minilab (based on thin layer chromatography). Out of these, 40 products were detected and confirmed as falsified products. Activities of the network have led to increased quality awareness within the faith-based health sectors, and cooperation with local authorities and international partners was enhanced.

Background and introduction

The recently published WHO report "Public health and socioeconomic impact of substandard and falsified medical products" established a failure rate of tested products in low and middle-income countries of 10.5 % [1]. This means that 1 in 10 products in many of the EPN member countries are either substandard or falsified, whereby substandard products are responsible for the largest portion of all poor quality products. In May 2017, WHO adopted new clear definitions: "Falsified" refers to medical products that "deliberately/fraudulently misrepresent their identity, composition or source", whereas "substandard" refers to "authorized medical products that fail to meet either their quality standards or their specifications, or both" – these later products are also called "out of specification" [1].

The negative impact of substandard and falsified medicines for the population is significant and is displayed in figure 1. It is evident that poor quality medical products affect medication safety, especially through increased morbidity and mortality (in case of no active pharmaceutical ingredient (API), underdosed API or even wrong API) and progression of antimicrobial

Fig. 1: Impact of substandard and falsified medical products [1]

resistance (in case of underdosed antibiotic and antimalarial), but also by causing loss of confidence in the health sector. WHO estimates that these products cause an economic loss of 30.5 billion USD annually worldwide.Antimalarials and antibiotics still seem to be the product groups most affected, especially through falsifications. Notably, a majority of studies in the past were focusing on these products groups [1].

The Ecumenical Pharmaceutical Network's (EPN) mission and vision focuses on "quality pharmaceutical services for all" [11]. According to WHO, essential medicines save lives and improve health when they are available, affordable, of assured quality and properly used [2]. Thus, the task of Drug Supply Organizations (DSOs) within EPN is to have essential medicines continuously available at reasonable prices and especially in good quality.

But how to assure the quality of medicines?

Today, most products on the African market originate from India, China or Africa itself. Regulatory authorities are in charge of registering the medicines entering their markets, performing quality control and post-marketing surveillance and inspecting the manufacturing sites. Even though progressive improvement can be seen in a number of countries and regions [3], many regulatory systems in Africa still have very limited capacity and markets are not regulated to a sufficient extent [4].

Therefore, applying appropriate quality assurance systems is crucial for DSOs operating in this context. The WHO "Model Quality Assurance System for Procurement Agencies" [5] provides guidance on establishing standard operating procedures (SOPs) and checklists focusing on supplier qualification, product qualification, good storage and distribution practices. When procuring medicines, DSOs should look at the product specifications (e.g. BP or USP standard), request further quality-related information like appropriate stability studies (e.g. climatic zone IV), product registration status and API quality. They should request manufacturing license/ GMP certificates and find out whether the company distributes medicines to regulated markets and to international organizations like UNICEF and MSF (from the same manufacturing site!). Provision of a batch-specific Certificate of Analysis (CoA) should be a MUST.

Strong procurement organizations (like Joint Medical Stores(JMS) in Uganda and Mission for Essential Drugs and Supplies (MEDS) in Kenya for example) are able to perform own GMP audits at the suppliers´ manufacturing sites. Joint audits with different participating DSOs were piloted some years ago and could be further pursued as a promising (but still quite expensive) option [6].MEDS in Kenya is running a WHO prequalified Quality Control laboratory – this prequalification process was actively supported by EPN and DIFAEM. However, to install such a lab needs big investment (of at least 1 million USD) and well trained and experienced lab staff. This is far from reality for most DSOs. Governmental laboratories exist in a number of countries, but they are often expensive, with limited capacity or focusing on the analysis of their own products only.

EPN DIFAEM Minilab Network

This situation led to the project that EPN member DIFAEM developed in 2010: To offer a small scale system, the so-called "Minilab", developed by the Global Pharma Health Fund (GPHF), to all EPN DSOs that wanted to screen their own products on quality. The GPHF Minilab provides relatively simple methods on visual inspection, colour reaction, disintegration and especially on thin layer chromatography for qualitative and semi-quantitative detection of currently about 100 pharmaceutical ingredients. According to GPHF, medicines with an API content of 80% or less can be detected, even though in reality sensitivity may be less. There is no need for a fully equipped lab on the ground – the Minilab comes in two suitcases with an additional pallet of all needed chemicals [7].

Fig. 2: The GPHF Minilab [7]. Picture credit: GPHF

'GPHF Minilab' using thin layer chromatography, developed and distributed by Global Pharma Health Fund (supported by Merck, Darmstadt)

- Reasonably cheap
- Reasonably simple and reasonably fast
- Qualitative (and semi-quantitative) determination of about 100 pharmaceutical ingredients
- + simple test for disintegration of tablets
- Reference medicines with correct type and quantity of ingredients supplied with Minilab®

In 2010, JMS in Kampala received the first Minilab and a five-days-training, moreDSOs joined, and until today, 17 partners in 11 countries were equipped and trained to test the quality of medicines used.

In 2013, DIFAEM started to network these Minilab users by circulating "Minilab Newsletters", organizing workshops in Kampala/Uganda and Limbe/Cameroon, with the goal that users were able to share their own experiences and results. The members formed three regional Minilab groups and in 2016/17 these regional groups met for the first time in Nairobi, Ghana, and DRCrespectively.

Table 1: DIFAEM EPN Minilab Network members (2018)

Country	Partner	Minilab Partner since
Burundi	Life Net	2015
Cameroon	Cameroon Baptist Convention Health Services(CBC)	2010
Cameroon	Presbyterian Church Cameroon (PCC)	2011
Cameroon	Organisation Catholique pour la Santé au Cameroun (OCASC)	2015
Chad	Association Evangelique pour la Santé au Tchad(AEST)	2017
DR_Congo	DépôtCentral Medico-Pharmaceutique(DCMP)	2013
DR_Congo	Centrale d'Approvisionnement et de Distribution des MedicamentsEssentiels de Bunia et Uele (CADIMEBU)	2013
DR_Congo	Centrale d'Approvisionnement et de Distribution des MedicamentsEssentiels de Bunia et Uele (CADIMEBU) Isiro	2017
Ghana	National Catholic Health Services (NCHS)	2012
India	Community Development Medical Unit(CDMU)	2013
India	Tezpur Hospital	2014
Kenya	Mission for Essential Drugs and Supplies(MEDS)	2013
Malawi	Nkhoma Hospital	2013
Nigeria	Christian Health Association of Nigeria (CHAN) Medi-Pharm	2012
Nigeria	Daughters of Divine Love (DDL) FBO-MSD Enugu	2017
Tanzania	Kilimatinde Hospital	2015
Uganda	Joint Medical Store(JMS)	2010

Since 1998 the Global Pharma Health Fund in Germany distributed about 800 Minilab kits to 97 different countries. They are used by governments, international institutions, NGOs and others[7].But according to GPHF, the DIFAEM EPN Minilab Network is the only group actively presenting the results. Dr. Richard Jaehnke, "father" of the Minilab and winner of the 2017 "Humanity in Sciences" award, states in an article "Taking down Goliath": "I find with church groups, there is more of a rapport – […] and it´s more transparent. […] They track fake medicines down even more effectively than the police – because in their eyes, delivering counterfeit medicine with nothing inside is ´like cheating God´ "[8].

The DIFAEM EPN Minilab Network applies the following testing and reporting scheme:

Minilab test if positive (product suspicious):

- 2nd test for confirmation (at the same institution)
- If still positive:
- Repeating the test by 2nd Minilab Network partner If still positive:
- Confirmation test (High-Performance Liquid Chromatography (HPLC)) by WHO prequalified laboratory (e.g. MEDS in Kenya)

Reporting of confirmed cases (falsified or substandard):

- By DIFAEM: immediate information to concerned local partner and to the network for warning the health facilities and informing the local authorities
- By DIFAEM: sharing details with WHO in Geneva (anonymous to protect the partner from violence e.g. by local traders)
- By WHO (and/or DIFAEM) to contact the original manufacturer about the "case" and request statement
- By WHO: to share results and inform local regulatory authorities through "Medical Product Alerts"

Since the beginning in 2010,a total of 4000 samples were tested by the network members, most of them collected out of the DSO warehouses, some were bought from local markets, and a few collected from health facilities. Forty "cases" were discovered and confirmed as falsified products, medicines without any or with very little active ingredient only. And in addition,manysubstandard products were documented that failed for example visual test (e.g. important information not written on the label or different on package and blister respectively) or failed disintegration test.

The three most recent cases of falsified medicines were detected at theend of 2017 by a network partner in Eastern DRC and concerned two antibiotics (Cefixime tabs) and one antimalarial medicine (Quinine tabs). These three products were collected in faith-based health facilities during supervision visits of a DSO pharmacist. They had not been procured from the DSO but from the private market - and even through governmental and local NGO supply chains. Based on information from the network partner, confirmatory results from MEDS laboratory and the declarations of the stated manufacturers, the WHO issued a medical product alert for the two Cefixime products in early 2018 [9].

Figure 3: Falsified Cefixime products from DRC [9], Picture credits: MEDS, Kenya and DSO, DRC

The Minilab testing results from 2015 were published in 2017 in cooperation with the University of Tuebingen in the international journal PLOS ONE:"Surveillance for falsified and substandard medicines in Africa and Asia by local organizations using the low-cost GPHF Minilab", authored by Albert Petersen, Nadja Held, Lutz Heide – on behalf of the DIFAEM-EPN-Minilab Survey Group [10].

The results showed that in total, 35 of 869 products failed the Minilab test, and subsequently, 21 (equivalent to 2.4% of all products) were confirmed as being substandard or falsified through pharmacopeial tests at MEDS. 1.4% did not contain the declared API and were considered as falsified.

The sampled medicines in this study originated mainly from private uncontrolled markets. There were substantial differences in the prevalence of poor quality products among the various countries; the highest prevalence was seen in Cameroon (7.1%) and Eastern DRC (2.7%), whereas in Kenya, Uganda, Ghana and India, there were no suspicious products detected. Due to low sensitivity of the Minilab testing, the actual numbers especially of substandard medicines might have been higher than the reported results. Part of the results are displayed in table 2.

Table 2: Results of the Minilab Network study 2015 [10]

Number of Minilab Network partners and countries involved in the 2015 study		Number of:			% of samplesfailing pharmacopeial tests
		samples included	samples failing 1st TLC test	samples failing pharmacopeial tests(at MEDS)	
1	Cameroon	106	12	9	8.5%
2	Cameroon	106	11	6	5.7%
3	DR Congo	85	8	4	4.7%
4	DR Congo	98	1	1	1.0%
5	Nigeria	95	3	1	1.1%
6	Kenya	94	0	0	0%
7	Uganda	31	0	0	0%
8	Ghana	89	0	0	0%
9	India	101	0	0	0%
10	India	64	0	0	0%
Total		869	35	21	2.4%

Effects within and beyond the network

In 2015, the network started an "Awareness campaign": Two posters, one flyer and one little training session (powerpoint) were developed and financed by DIFAEM and distributed to all members (all in English and French – to be downloaded on EPN webpage)[12,13]. They were used to raise awareness on quality of medicines and safe procurement in health facilities.

Discussion

The Minilab network has been effective in collecting and analyzing large numbers of medicines in countries that often do not have functional testing facilities. The rates of substandard and falsified medicines detected within the Minilab network are considerably lower than recent WHO estimates.

The reasons being twofold: First, most products tested within the Minilab network were sampled from the DSO warehouses. These EPN procurement organizations apply good procurement practices, they try to source from qualified suppliers only and thus ensure the quality of the products procured. Secondly, the Minilab testing is limited to detecting poor quality products with an API content of 80% or less. Substandard products with higher API content (but not meeting pharmacopeial standards) and products e.g. with dissolution problems can hardly be detected – even though poor disintegration may provide some hint. This means that only a certain percentage of substandard products can be detected with the Minilab. Therefore, the main focus of the Minilab is on detecting falsified medicines with a low API content. For EPN partners, the Minilab is especially useful in countries where the prevalence of falsified medicines is comparably high, like in Cameroon and DRC, and where falsified medicines are even found in regular supply chains and not only on the illegal markets.

So far, Minilab network members applied their own sampling approaches, however each member was asked to test at least 75 products per year and sample part of these products from private markets. It needs to be discussed whether a standardized and rather risk-based sampling approach would be more efficient in detecting falsified and substandard medicines through Minilab testing in the future. Furthermore, the DSOs should be encouraged and supported to strengthen their overall QA systems, with the Minilab testing being one component wherever relevant. Strengthening and building the network will have positive benefits both for EPN member organizations but also more broadly for the countries where this testing occurs.

Participants of the Minilab Network workshop in Limbe/ Cameroon, August 2017. Picture credit: PCC/DIFAEM

Minilab analysis at PCC in Cameroon performed by pharmacy technician Ms Manyi Patinora Dohnji (in charge of quality control) and MsTarsa Jenny (registered nurse). Picture credit: PCC/DIFAEM

CONCLUSION

A number of positive effects of the Minilab network activities were seen within and beyond the network so far:

1. Delivery of tested poorquality products was stopped by the DSO and/or the respective Ministry of Healthso patients were “saved” from being exposed to substandard or falsified medicines.
2. More and more local authorities are aware about this Minilab network of faith-based organizations and are open for close cooperation (at least in some of the countries concerned). Minilab network members are respected and are now “known” by the government for good services, shown by a recent case where the government asked the Minilab partner to test a product on their behalf.
3. As “cases” are made transparent e.g. through distribution by WHO, governments are forced to start activities. This can be seene.g. in Eastern part of DRC, in Cameroon and Malawi.
4. Minilab network members gain experience in quick identification of suspect products in the health facilities, e.g. in DRC where this led three times already to a confirmation of falsified products.
5. Personnel in health facilities become aware about this service run by the DSO and start utilizing it.Theyalso become aware of the importance to introduce and actively implement standards of procurement to avoid buying medicines from unreliable sources.

The DIFAEM EPN Minilab Network today is recognized and appreciated by national and international stakeholders like the WHO for its active communication and quick action. Furthermore, there is close cooperation on several research projects with the University of Tuebingen -currently, two studies on 12 selected essential medicines with a random sampling design are ongoing with four network partners in Cameroon and DRC. In May 2018, Minilab network partners will gather in Kampala to discuss the achievements but also challenges of the network and its testing activities and will prepare a strategy for future cooperation.

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GIMS MODEL FOR THE SCREENING AND RATING OF MEDICATION SAFETY IN COUNTRY.

Slobbe Richard

Chairman GIMS foundation, Netherlands

Abstract

Qualitative research with the aim of creating a concept of an international applicable model (to be used as an analytical tool) for the very broad screening and rating of the status of Medication Safety (MS) in a country.

The results obtained can be used to realize a helicopter view to get insights and will/can give direction towards area's of attention and desired or needed improvements.

Local adaptations from the original GIMS model are likely to be expected but need not to be a real problem.

Introduction

Medication is used on a global level. However, there has always been a safety aspect when using medication.

Paracelsus already stated it quite clearly about 500 years ago with his famous phrase 'The dose makes the poison'.

For example, the World Health Organization estimates that more than half of all medication is inappropriately prescribed, dispensed or used. Furthermore, half of all patients fails to take them correctly. Also medication errors are still the leading cause of harm to patients in hospitals.

With the ever-increasing consumption of medicines, also in the LMIC's, increasing health risks there are also to be expected. Especially when the circumstances are (far) less favorable when compared to HIC's.1,2,3,4

So, the much desired and realized improvement of the 'Access' to medication is accompanied unfortunately by a, until now, fairly neglected awareness considering increased health risks due to increased medicine use.

WHO's present campaign for 'Medication without Harm' is hopefully an accelerator and catalyst for rising awareness and serious improvements.

Pharmacovigilance has been introduced the last decades to also reduce medicine adverse effects and error rates.

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine related problem.

GIMS is a pharmacovigilance (PV) organization with a focus on the last part of the WHO definition; '….and all other medicine related problems'.

GIMS drafted from this specific part its own definition: 'Medication Safety (MS); minimize health risks originated by the global use of medicine'.

To minimize these health risks, GIMS aims at creating awareness, insights, responsibility and practical IT-tools in the whole of the medical chain. This also includes industry, healthcare governance and patients worldwide.

Academic research into the theme helps in creating insights and data. In order to get better insight in the actual situation in a country, for all the stakeholders, a structured scientific analysis is needed, which is the main purpose of the model. By realising a valued research model GIMS hopes to contribute. Finally, by identifying the situation of each of the stakeholders' strengths and weaknesses, possibilities and focus for improvements regarding MS can be identified.

Goals of the GIMS model:

1. Facilitate countries to identify the situation of all of the stakeholders regarding Medication Safety in their owncountry.
2. Identify strengths and weaknesses and with that good practices and room for improvements regarding Medication Safety in a country.

Material & Methods

To create the GIMS model, the visual representation of groups of all actors and factors concerning Medication Safety in a country, created by the GIMS foundation, is used as base for the model (see Figure 1).

Actors and factors

The main structure or frame work of the GIMS model is constructed out of actors and factors.

An actor is an entity which can have influence on a situation. Examples are a company, an organization or an individual.

A factor is a circumstance which has influence, but is of course not a true entity with corresponding possibilities of making choices. Examples are culture, religion and politics.

They are sorted in the GIMS model on the amount of direct influence on the patients and consumers regarding MS (see Figure 1). They are called Alpha, Beta and Gamma actors and Delta factors. Alpha actors have the most direct influence on patients and consumers regarding MS, therefore they are the nearest to patients and consumers in the model. The others are placed upon a greater distance as their influence is gradually less direct.

Figure 1: GIMS actors and factors concerning Medication Safety in a country

Alpha actors: patient and consumer, health care practitioner (doctor, pharmacist, nurse), hospital and retail.

Beta actors: professional organization of health care practitioners, national health care institute (like NICE for the UK), health care software provider, pharmaceutical retail formula, pharmaceutical wholesaler, pharmacovigilance organization.

Gamma actors: national medicines regulatory body, national inspectorate, ministry of health, academia, patient & consumer organizations, pharmaceutical industry, insurance body and/or company, international bodies like WHO, EMA, EFPIA, PGEU, Cochrane.

Delta factors: national medicines and healthcare legislation, technology, culture, religion, economics, politics, stability and prosperity of a society and media.

Critical dynamics (statements which describe a situation) were formulated for each stakeholder. The critical dynamics of each actor/facor evaluate the situation regarding MS in the country of that certain question. The critical dynamics are self-devised and the Lickert scale rating is added. It is a scale where respondents can express their strength of agreement with each of the statements; in this case the critical dynamics. Each critical dynamic can be rated on a 4 point Likert scale. If 1 is rated, the critical dynamic is not at all present or an issue in your country. If 4 is rated, it is very much present or an important issue in a country. Also there is a place to put remarks and sources.

If all critical dynamics are answered and the overall result appears, a total overview of the situation of Medication Safety in the evaluated country can be made.

When the first draft (version 0.1) of the model was completed, a panel of different stakeholders with a broad view on MS gave their feedback about the quality of the model. Based on their feedback, adaptations were made in the number of stakeholders and the number & phrasing of the critical dynamics and version 1.0 was realised. (See table 1)

Table 1

		Number of critical dynamics model 0.1	Number of critical dynamics model 1.0
Alpha actors	Patient and consumer	-	12
	Doctor	13	33
	Pharmacist	13	31
	Nurse	7	16
	Hospital board	-	8
	Retailer	4	7
Beta Actors	Healthcare practitioner organizations	8	17
	National healthcare institute	2	2
	Pharmaceutical wholesale	3	3
	Pharmacovigilance organization	6	18
	Pharmaceutical retail formula	2	5
	Healthcare software provider	3	3
Gamma actors	National medicines regulatory body	4	8
	National inspectorate	2	7
	Ministry of health	5	7
	Academia	2	7
	Patient & consumer organization	3	5
	Pharmaceutical industry	1	6
	Health insurance company/ public health insurance	1	4
	National laboratory	-	5
	International bodies	2	16
Delta factors	National medicines and healthcare legislation	1	7
	Technology	4	1
	Culture	4	4
	Religion	1	2
	Economics	8	4
	Politics	2	2
	Stability and prosperity of a society	2	1
	Media	2	3
Total		105 critical dynamics for 26 stakeholders	247 critical dynamics for 29 stakeholders

Results

As the result is a questionnaire (with corresponding user guidance) of about 250 questions it is not possible to present it here in the article. It can be found on the GIMS website.

Discussion

It is a first approach to look at MS with a helicopter view. Literature offered few clues how to formulate such a model. Therefor a lot of original thinking (and probably not yet full grown) had to be done.

As only a relatively small expert panel (6 persons) gave feedback further improvement is likely to be expected when expanding to a bigger panel.

Conclusion

The model has no absolute value and should be adapted to local situations. It is mainly an innovative concept to achieve a comprehensive overall assessment regarding Medication Safety in a country on a scientific level. Furthermore, this model has been produced in The Netherlands. Therefor there is a great possibility of the incorporation of Western-European influences in the model.

Testing the GIMS model in different countries will bring clarity wether this approach has true international applicability and i fit can be helpfull in MS improvement activities .

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MEDICATION SAFETY, HUMAN RIGHTS AND THE PHARMACEUTICAL INDUSTRY

Jennifer Sellin
Assistant Professor International and European Law at Maastricht University

Slobbe Richard
Chairman GIMS foundation, Netherlands

The term 'essential medicines' first appeared in the 1970s in the context of the WHO and is now defined as medicines that 'satisfy the priority health care needs of the population.' This definition intends that essential medicines should be 'available within a national context at all times, in all adequate amounts, in the appropriate dosage forms and with the assured quality and at an affordable price for individuals and the community.

The ever-increasing use of (essential) medicines in Low- & Middle Income Countries (LMICs) however, also introduced increased health risks due to improper handling, prescribing, dispensing, administration and patient use. Research (although only sparsely available) and common sense administration and patient use. Research (although only sparsely available) and common sense make it very likely that having physiologically (very) active products available in a country without the corresponding and crucial safety barriers, like for example, adequate legislation and policy, state enforcement power, quality and quantity of Health Care Practitioners (HCP's), professional health care IT-tools, inter HCP communication, can seriously endanger the health status of the general public. As a simple (pharmaceutical) example; HIV/TB medication is distributed widely through Global Fund programs,but is known to givemany interactions with other medicines. Is that taken into account when prescribing, distributing or using the other medication?

This problem has been recognized internationally and the WHO has taken up an active role the last twenty years, for example in promoting national pharmacovigilance (PV) centres, relevant legislation and policy development and creating an international PV network. In its definition on Pharmacovigilance the WHO states: 'Pharmacovigilance is the science and activities related to the detection, assessment, understanding and prevention of adverse effects or any other medication-related problem'. The WHO has further stressed the importance of this particular issue in its 2014 publication titled 'Reporting and learning systems for medication errors: the role of pharmacovigilance centres'; and more recently at the 69th WHA (2016) side event: 'Addressing the Global Challenge of Medication Safety to Improve Patient Safety and Quality of Care'.

Historically the pharmacovigilance focus has been especially on the adverse effects of medication, while far less so on the last part of the WHO definition '…any other medication-related problem'. In this article the term 'Medication Safety' is used instead of pharmacovigilance as it includes all health risks related to the (global) use of medicationand as such is much clearer to the general public. Medication Safety focuses on all of the aspects (including besides the HCPs, also policy, legislation, health system-analysis, stakeholders, culture) concerning the goal of minimizing health risks originating from the global use of medicines.

The provision of and access to essential medicines is protected by international (human rights) law, most obviously in the framework of the human right to health. The right to health is codified in a number of international instruments, most notably article 12 of the 1966 International Covenant on Economic, Social and Cultural Rights (ICESCR). Article 12.1 ICESCR recognises the 'right of everyone to the enjoyment of the highest attainable standard of physical and mental health', including 'the prevention, treatment and control of epidemic, endemic, occupational and other diseases' and 'the creation of conditions which would assure to all medical service and medical attention in the event of sickness'. Today the use of medicines is an essential and indispensable part of the treatment of disease.

The ICESCR is an international agreement and as such creates obligations for states party to the Covenant under international law. Article 2.1 ICESCR states that each state party undertakes to take steps, individually and through international assistance and cooperation, to the maximum of its available resource to progressively realise the rights enshrined in the Covenant, including the right to health.

The international Committee on Economic Social and Cultural Rights – a treaty body consisting of independent experts set up to monitor state compliance with the ICESCR – in its General Comment No. 14 on the Right to the Highest Attainable Standard of Health affirms that essential medicines are not only a component of the right to health but, in fact, considered part of its so-called 'minimum core content', referring to those

elements of a human right without which the right would be devoid of any meaning or relevance. It further finds that the right to health, in all its forms, needs to meet the four interrelated and essential AAAQ-requirements of availability, accessibility, acceptability and quality. These criteria therefore also apply to the provision and use of essential medicines. Consequently, essential medicines have to be available in sufficient quantity within the state party, physically and economically accessible to everyone without discrimination, respectful of medical ethics and culturally appropriate and, finally, scientifically and medically appropriate and of good quality.

The Committee finds that, like all human rights, the right to health imposes three types of obligations on state parties – to respect, protect and fulfil. Consequently, state parties must respect the right to health by abstaining from interfering with it, fulfil the right to health by actively working towards the full realisation of the right, and protect the right to health by preventing third parties from interfering with it. It is, therefore, the primary responsibility of the state to regulate the pharmaceutical industry, for example, by legislating and enforcing safety and quality regulations with regard to the manufacturing and use of medicines. In that regard, the Committee has stated that 'while only states are parties to the Covenant and thus ultimately accountable for compliance with it, all members of society – […] as well as the private business sector – have responsibilities regarding the realization of the right to health.

The process of globalisation over the past decades shows that non-state actors such as transnational corporations play an increasingly important role both internationally, but also at the national and local levels. This has given rise to a debate about the roles and responsibilities of such actors with regard to human rights.International human rights standards have traditionally been the responsibility of states. However, the increasing (global) power, reach and impact of big business and concern over human rights violations relating to business led to an international effort to identify and clarify human rights responsibilities of businesses.

In 2005 the United Nations Human Rights Commission mandated John Ruggie, as Special Representative of the Secretary-General, to undertake this task. The result was that in 2011 the United Nations Human Rights Council unanimously endorsed the UN Guiding Principles on Business and Human Rights (or also the 'Ruggie Principles'). At the same time a parallel development was taking place with regard to pharmaceutical corporations initiated by Paul Hunt, the first UN Special Rapporteur on the Right to Health. He argued that safeguarding access to medicines was a 'shared responsibility' between public and private actors and that the pharmaceutical industry had an 'indispensable role to play'. A set of draft Guidelines for Pharmaceutical Corporations in Relation to Access to Medicines (or also the 'Hunt Guidelines') was released in 2007 for public comment and finally submitted to the UN General Assembly in 2008.

Both the Ruggie Principles and the Hunt Guidelines reaffirm the primary responsibility of the state to protect human rights, also from violations by business. But in addition they recognise that companies, next to complying with national laws, have a baseline responsibility to respect human rights, meaning not to infringe on the rights of others. Besides this responsibility to respect, the Hunt Guidelines also recognise that pharmaceutical companies might have additional responsibilities beyond this baseline. These are often closely connected to the state duty to protect.

When it comes to access to medicines, much focus has been put on the pharmaceutical industry and their input on this issue; see for example the 'Access to Medication Index', in which the positive actions of different pharmaceutical companies are rated. In light of the right to health, and the Hunt Guidelines, we argue that the pharmaceutical industry has a responsibility to act upon the issue of Medication Safety. And not just from a mere technical product quality point of view, but by taking a systematic approach in which the industry accepts its role as a system player for whom other system players' activities and results have a big impact on the individual therapeutic result. In the end, medication is a (potentially dangerous) tool in reaching a desired health goal, in which numerous stakeholders have their positions, responsibilities and goals.

As a first step, the pharmaceutical industry should acknowledge and accept its role and responsibility both from a human rights, as well as a moral point of view. The second step could be to jointly start up integrated and structural discussions with organisations like the WHO, national Patient Safety Organisations and entities like the GIMS foundation, to find out how to address the global issue of Medication Safety systematically, mutually and effectively. A multi-party and multi-disciplinary 'Medication Safety Taskforce' under guidance of the WHO should be the initial objective. According to the GIMS foundation state/country oriented items which should be addressed are: national research into the theme, medicine regulation and legislation, pharmaceutical policy, academia, training of HCP's, available or desired professional health care ICT-tools, marketing guidelines, culture, advocacy on the theme, etc.

This article advocates that the right to health and access to (essential) medicines, and the subsequent issue of health risks originating from the global use of medicines, entail obligations and responsibilities for state parties as well as for the pharmaceutical industry. Consequently, the pharmaceutical industry, as a system player and according to the Hunt Guidelines, should take up this responsibility and shift to a real action modus so as to protect patients and consumers from non-desired and avoidable health effects of its products wherever in the medication-system the health risk may occur. If structural results fail to get realised by the industry in a reasonable time frame, state parties could follow the road of legislative measures in order to enforce industry.

Correspondence concerning the article: arg@gims-foundation.org

EPN

Ecumenical Pharmaceutical Network
Réseau Pharmaceutique Œcuménique

www.epnetwork.org