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Effects and Adverse Reactions of Drugs on Patients under Clinical Monitoring and Evaluation

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Abstract

In clinical practise, this entails having a well-organized Pharmacovigilance system in place. Pharmacovigilance is a crucial activity for monitoring drug-related concerns after they have been sold in the "real world." Pharmacovigilance and all drug-related concerns are critical for everybody whose life is affected in some manner by medical treatments. An organised Adverse Drug Reaction monitoring programme is one mechanism for more actively detecting ADRs and, as a result, improving patient care quality. The numerous processes for evaluating and monitoring the safety of medications in clinical use are critical for preventing or lessening damage to patients and enhancing public health. Adverse drug reactions (ADRs) have a significant influence on public health, decreasing patients' quality of life and laying a significant financial burden on health care systems at a time when many are under financial duress. All healthcare practitioners have a role to play in balancing the advantages and hazards of a drug. Once a medicine is offered to the public, determining its safety is the joint duty of all those involved in the prescription process, including patients. Healthcare practitioners play an important role in collecting and reporting suspected ADRs so that regulatory bodies are notified of potential safety issues, allowing for early and appropriate action. Pharmacovigilance is a crucial activity for monitoring drug-related concerns after they have been sold in the "real world." Pharmacovigilance and all drug-related concerns are critical for everybody whose life is affected in some manner by medical treatments. This study

discusses many issues of monitoring and evaluating adverse medication reactions in clinical settings.

Keywords: *- Drug, Adverse drug reactions, Pharmacovigilance.*

INTRODUCTION

Pharmacovigilance has grown in relevance in recent years as a discipline crucial to good clinical practise and public health research. At a time when medication safety concerns are becoming increasingly essential in public health and clinical practise, national Pharmacovigilance centres have become a key impact on drug regulatory agencies. Drug-related difficulties, such as adverse drug reactions (ADRs), contribute significantly to severe health- and quality-of-life issues. According to prevalence surveys conducted in various contexts, adverse medication responses account for 5 to 35% of hospital admissions (ADR). The World Health Organization (WHO) defines an adverse drug response (ADR) as any unpleasant, unexpected, or undesirable consequence of a medicine that occurs at dosages used in humans for prevention, diagnosis, or therapy. ADRs are ranked fourth to sixth in terms of mortality among hospitalised patients. Adverse related events cause roughly 2.9-5.6 percent of all hospitalizations, while approximately 35 percent of hospitalised patients encounter an ADR. ADRs not only increase mortality and morbidity, but they also raise health-care costs. ADR monitoring is especially important for medicines with a restricted therapeutic index. ADR research is necessary to assess the prevalence of ADRs in medical inpatients, evaluate the contribution of ADRs to hospital admissions, define the types of ADRs seen, identify predisposing risk factors, and estimate the costs of ADRs in terms of ADR-related extra hospital stay[1-3]. An structured Adverse Drug Reaction monitoring programme is one method for more actively detecting ADRs and, as a result, improving patient care quality. The numerous processes for evaluating and monitoring the safety of medications in clinical use are critical for preventing or minimising harm to patients and enhancing public health. In clinical practise, this entails having a well-organized Pharmacovigilance system in place. Pharmacovigilance is a crucial activity for monitoring drug-related concerns after they have been sold in the "real world." Pharmacovigilance and all drug-related concerns are critical for everybody whose

life is influenced in some manner by medical treatments. Pharmacovigilance has grown in prominence as a discipline crucial to good clinical practise and public health science in recent years. National Pharmacovigilance centres have had a considerable effect on drug regulatory authorities at a time when medication safety concerns have grown in importance in public health and clinical practice. Adverse drug reactions (ADRs) have a significant influence on public health, decreasing patients' quality of life and laying a significant financial burden on health care systems at a time when many are under financial duress. All healthcare practitioners have a role to play in balancing the advantages and hazards of a drug. Once a medicine is offered to the public, determining its safety is the joint duty of all those involved in the prescription process, including patients. Healthcare practitioners play an important role in collecting and reporting suspected ADRs so that regulatory bodies are notified of potential safety issues, allowing for early and appropriate action. Pharmacovigilance is a crucial activity for monitoring drug-related concerns after they have been sold in the "real world." Pharmacovigilance and all drug-related concerns are critical for everybody whose life is affected in some manner by medical treatments. Pharmacovigilance has grown in relevance in recent years as a discipline crucial to good clinical practise and public health research. At a time when medication safety issues are becoming increasingly relevant in public health and clinical practice, national Pharmacovigilance centres have been a key impact on drug regulatory bodies.

Pharmacovigilance was described in the early 1990s as the monitoring of adverse drug responses "The identification of drug effects, typically negative, in the population. Pharmacovigilance can be passive (the collecting of spontaneous reports) or active (the recruitment and surveying of patients and prescribers) '" Pharmacovigilance is defined by the World Health Organization as "the science of collecting, monitoring, researching, assessing, and evaluating information from healthcare providers and patients on the adverse effects of medications, biological products, herbalism, and traditional medicines in order to identify new information about hazards associated with medicines and prevent harm to patients". Pharmacovigilance has been defined as "the science and actions concerned with the detection, assessment, comprehension, and prevention of adverse effects or any other drug-related issue."

Pharmacovigilance is now firmly founded on sound scientific concepts and serves as the foundation for good therapeutic treatment. To fulfil public expectations and the demands of current public health, the field must evolve further.

Pharmacovigilance is aimed at;

- Improving public health and safety in relation to the use of medicines,
- Improving patient care and safety in relation to the use of medicines and all medical and paramedical interventions,
- Contributing to the assessment of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective (including cost effective) use, and
- Promotion of understanding, education and clinical training in pharmacovigilance and its effective communication to the public [16].

Need for Pharmacovigilance

Everything is not known about any medicine when it receives its license for marketing. The merits of a new drug, balancing its beneficial and its untoward effects become established only after sufficient experience has been gained from its use in real practice.The reasons for the necessity of Pharmacovigilance are:

- Clinical trials are evaluated for limited duration and limited numbers of carefully selected patients in carefully selected settings and so it is extremely difficult to accurately determine actual efficacy, adverse effects and total risk-benefit ratio under actual clinical setting
- Information on drug safety collected during drug development is incomplete as preclinical drug development processes involve the evaluation of drug safety and efficacy in animal experiments and often it may not be appropriate to extrapolate the results of animal experiments to human information is often incomplete or not available on
  - Rare but serious reactions
  - Use of drugs in vulnerable groups (pregnant women, children, geriatric)
  - Risks of long term, repeated use and drug-drug, drug-food, drug-nutritional supplement interactions
- At least 30,000 people are required to be treated with a drug to be sure not to miss at least one patient with an ADR which has an incidence of 1 in 10,000 exposed individuals [17].

- At the time of licensing, the drug is exposed to less than 5,000 human subjects. This allows only the most common ADRs to be detected

REGULATORY PHARMACOVIGILANCE

The authorities, both at the national and increasingly at the international level, have initially helped fostered the field. Various stakeholders have been integral to the development of Pharmacovigilance. Labelled as regulatory Pharmacovigilance by Waller et al., they define pharmacovigilance as 'the process of evaluating and improving the safety of marketed medicines'. They underlined the responsibilities the various governments have in the monitoring of drug safety, which task many national governments took firmly in hand following the thalidomide tragedy.

The contribution of the WHO stands out here. The flagship programme was launched under the auspices of the WHO by 10 countries in 1968, resulting in the WHO International Drug Monitoring Programme[19-21]. Strong regulatory arrangements provide the base for a national ethos of medicine safety, and for public confidence in medicines. To be effective, the scope of drug regulatory authorities needs to go further than the approval of new medicines, to encompass a wider range of issues relating to the safety of medicines, such as; Clinical trials , safe use of complementary and traditional medicines, vaccines and biological medicines and arrangement of communication between all parties which have an interest in safety of medicines, ensuring that they are able to function efficiently and ethically, particularly at times of crisis.

Pharmacovigilance program and drug regulatory authorities must be mutually supporting of each other to achieve their respective objectives. On one hand, Pharmacovigilance program need to maintain strong links with the drug regulatory authorities to ensure that the latter are well briefed on safety related problems in everyday clinical practice, whether these problems and issues are related to future regulatory action .On the other, regulators need to understand the specialized and pivotal role that Pharmacovigilance plays in ensuring the ongoing safety of medicines.

Partners in Pharmacovigilance

The people responsible should jointly anticipate, elucidate and respond to the continually enhanced demands and

expectations of the public, health administrator policy officials, politicians and health professionals. However, there is little prospect of this happening in the absence of strong and comprehensive systems which make such associations possible. Management of the issues related to the use of medicines demands close and effective association between the key stakeholders in the Pharmacovigilance. The obstacles typically encompass lack of training, resources, political support, and especially scientific infrastructure. Understanding and tackling these are a necessary prerequisite for future development of the science and practice of Pharmacovigilance [22]. Pharmacovigilance is the responsibility of everyone so that all drugs can be used safely. Furthermore, the Ministry of Health (MOH) or its equivalent in any country of the world is not only responsible for monitoring drug safety but also needs commitment and collaboration between the different Pharmacovigilance partners [23].

A comprehensive list of these 'partners' includes:-

1. **Healthcare professionals:-**

a) Prescribers
b) Nurses

2. Pharmacist
3. Patients.
4. Hospitals and academia.
5. Pharmaceutical Industry.
6. The WHO Quality Assurance and Safety (Medicines Team).
7. National Pharmacovigilance Centers (NPC).
8. Uppsala Monitoring Center (UMC).
9. Others.

1. Healthcare professionals

Protected medication use is significant for physicians, dentists, pharmacists and nurses. They have the responsibility to be vigilant of their patients of any issues related with drug therapy including,

a) Nature of the disease,
b) Purpose of medication, and
c) Any potential risks involved in its use.

They also have an additional responsibility to ensure that their patients have an adequate understanding of the nature of the treatment(s) they are taking.

Prescribers

The intention of the prescriber is to use a medicine to help the patient, not harm them, as they hope all drugs used are without any risk. It is a prerequisite that all involved in the process of prescribing of medicines have some knowledge of the potential ADRs, so that an assessment of

the balance between the beneficial and harm is considered before a drug is prescribed, dispensed and administered to a patient.

Any medication or any kind of treatment should take in consideration all these factors including, the individual patient and their predisposition to drug toxicity. This should facilitate the key recognition that if the patient develops any undesired signs and symptoms it may be drug related and eventually turn out to be due to an ADR [24]. Therefore, all the members of the healthcare team arerequired to be aware of the importance of ADR reporting and that they are competent to provide practical information for reporting of ADRs. They should have a familiarity with the policy and procedures of ADRs reporting and guidance as to how and when to report and where to actually send it.

Healthcare professionals usually consider that they have a major responsibility to be a Pharmacovigilance partner by reporting suspected ADRs. The best management of ADRs needs to involve all healthcare professionals in any type of hospital whether government or private so as to both observe and report unwanted or unexpected ADRs. Sometimes, due to inadequate information from the pharmaceutical company or industry or even a Food and Drug Administration (FDA), a healthcare professional cannot always be blamed if a patient has an ADRespecially so, if it is of an idiosyncratic type where its prediction isclearly impossible. But, even when healthcare professionals have enough safety information they may misuse it due to not having the patient's full medical history and that can lead to ADRs.

A good example is Spironolactone which is contraindicated in patients with renal dysfunction or hyperkalemia. However, some doctors are not aware of this well reported effect and yet still prescribe it .

Nurses

Some new developments for ADRs reporting have taken place for nurses and as they are now also able to prescribe drugs in some countries such as USA and the UK as such prescribers they have the responsibility to report ADRs. Traditionally nurses did not report ADRs. For example, in the UK, some nurses after October 2002 played a valuable part in the improvement of Pharmacovigilance by ADRs reporting.

A little later, in the Sweden, nurses could report ADRs and so contributedto the improvement of public health by the detection of suspected ADRs;. Currently, the contribution of nurses to the rate of reporting in some countries is quite significant, for example, Sweden 12%, Canada 16% and in the UK 21%. In contrast, the spontaneous nurse reporting in the Italian database is still lower than that in other countries . It isquite clear that nurses do represent an important and valuable sourceof reporting for ADRs.

Pharmacist

The pharmacists explicitly focus in making a contribution to ADR reporting. A pharmacist, in a dispenser of medicines, is in a "cornerstone position", he/she should be fully aware of any suspected ADRs

Patients

The reporting system for suspected ADRs by patients to the regulatory authorities started in the UK via using YCS (yellow card system) in 2005. Moreover, in 2009, ADRs reporting by patients in the UK, Sweden, Australia and the USA were in the range of 18% to 20%, submitted using three major methods: postal, internet and telephone to provide assessment awareness. These methods were found fitting for the UK‘s general population and indicated that the awareness was low and could be improved.

In the study by Van Grootheest and Berg, 2004, which examined the role of patients in reporting ADRs, they concluded that, because patients have a positive value and involvement in drug therapy, their concern regarding possible adverse effects is a major factor in possible ADR reporting. As a consequence, patients' reports on ADRs should be accepted albeit with care as is now done in the UK. The literature, as yet, does not provide any major results in relation to the detection of ADRs by patients, more recent studies are required to show their contribution worldwide.

In any system where patients have taken medicines, their views and options about their therapy can be of great knowledge for ADRs reporting. It is, however, a difficult problem to address. Often, because of the brevity of the physician's consultation process, patients have little time to understand any warnings that may be given about the potential problems of their treatment(s).

It could be argued that the inclusion of the patient's information leaflet should avoid such difficulties. However, this applies to people whose first language is English

and, when they are used in Saudi Arabia, where many people who use the medicine do not read a high level of English, their value is very difficult if not impossible to assess. On the other hand, in a study by Hughes et al. (2002) ADRs reporting by patients was not considered by Pharmacovigilance centers to be equivalent to those of the health care professionals as many of ADRs patient reports were incorrectly filled in, so increasing the overall workload for little gain. Another study by Arson et.al (2011) concluded that direct patient reporting through the YCS is viewed as important by those who have used the scheme, in order to provide the patient experience for the benefit of Pharmacovigilance, as an independent perspective from those of health professionals.

Hospital and Academia

Only a small number of medical institutions provide medical student education related to ADR during their curricula in pharmacology. So, the majority of healthcare professionals may graduate without an adequate background regarding drug ADRs. Collaborations between the pharmaceutical industry, academia and drug regulatory authorities has led to the development of Pharmacovigilance as a clinical discipline. Therefore, academic centers of pharmacology and pharmacy should provide a knowledge of ADRs to healthcare professionals and the public by; training, teaching and research. In many schools of health and medical institutions the topic is still neglected. Consequently, there is a still greater need forintegration of Pharmacovigilance by clinical practice so as to affect a system for ADR monitoring to protect public health as suggested by WHO 10 years ago.

Pharmaceutical Industry

Every company in the pharmaceutical industry has a vital role to play in the provision and supervision of drug safety and they must inspect all drug related information, from drug development to patient use, and should also consider the assessment of the safety of the drug and monitoring system. An important role exists in communication between the pharmaceutical company and drug regulatory authority that leads to an improvement by exchanged information.

The WHO Quality Assurance and Safety

Medicines Team

The purpose of the department is stated to be: "to help save lives and improve health by closing the huge gap between the

benefit that essential drugs have to offer and the reality that for millions of people– particularly the poor and disadvantaged – medicines are unavailable, unaffordable, unsafe or improperly used". Clearly, the purpose of Quality Assurance and Safety for Medicinesteam is "To ensure the quality, safety and efficacy of all medicines by strengthening and putting into practice regulatory and quality assurance standards".

The provision of guidance and support to countries regarding drug safety matters is a function of the Quality Assurance and Safety: Medicines Team within WHO.. Hence, Pharmacovigilance needs to be applied to all related health technologies, including medicines, vaccines, blood products, biotechnology, herbal medicines and traditional medicines.

Uppsala Monitoring Center (UMC)

WHO still highlights the importance of collaboration and communication at local, regional and international levels, so as to ensure Pharmacovigilance delivers the necessary protection to the public. During early 1960s, after the infamous event of 'Thalidomide disaster', various national schemes for collecting information concerning emerging drug hazards were implemented, and, in 1968, the WHO set up an international drug monitoring programme. 10 years later, in 1978, the UMC was started and was made responsible for leading and managing this programme. Working with the WHO Collaborating centre for international drug monitoring UMC, WHO promotes Pharmacovigilance at the country level, and encourages the participation in the WHO programme for international drug monitoring.

In 2004, the numbers of countries that were participating in this scheme was 86, and all these provided the necessary data for the WHO programme with the collaborating centre in Uppsala, Sweden. This contrasts with the initial established national reporting system for ADRs which was for only 10 countries. In March 2010, the number of countries had grown to 97 and in addition there were a further 33 countries as "associate members".

At the end of 2010, the number had increased to 134 countries and they were all part of the WHO Pharmacovigilance Programme. More recently, In May 2012, the number now stands at 142 countries. It can be seen that the Kingdom of Saudi Arabia (KSA) has been a member of the WHO IDMP since 2009. On 30 March 2010, new information from the Uppsala

monitoring centre website showed that the global ADR database they maintain for the WHO programme contains 5 million ADR reports from all the countries who are members of the WHO programme. In 2011, the UMC-WHO, which managed the global database of Individual Case Safety Reports (ICSRs) and consists of reports of ADRs which were received from national centers in the WHO network database, is called "VigiBase".

It currently contains over 6 million descriptions of individual cases which make a significant contribution to promoting a global ADRs awareness. This information about ADRs is extremely useful and helpful as, unfortunately, many hospital admissions are caused by drug use.

The Uppsala centre can therefore clarify any problems should they occur. The Uppsala center, to function effectively, requires constant new information about ADRs, where and when they occur.

The National Pharmacovigilance Centers (NPC)

Furthermore, during their Annual Meetings of National Pharmacovigilance, the International Conference for Drug Regulatory (ICDRA) provides a unique opportunity for the WHO initiative for International Drug Monitoring to be completely and appropriately reviewed. Furthermore, most MOHs in their respective nations can completely or partially support Pharmacovigilance National Centers by comparing drug spending with NPC policies and regulatory requirements.

Others partners of Pharmacovigilance

By cooperating and communicating with the appropriate authorities, the media, encouragement organisations, and attorneys may aid in the establishment of policies and regulations on pharmacovigilance, either directly or indirectly.

CONCLUSION

It involves the entire life-cycle management of pharmaceutical goods for human use while keeping safety in mind. As a result, we must emphasise the importance of Pharmacovigilance as a continuation and completion of the analysis conducted on medications beginning with clinical trials when the medication is delivered for the first time in humans, rather than simply after they have been launched.

Pharmacovigilance is vital for public health because it prevents, identifies, and evaluates adverse responses to human-use pharmaceuticals. To increase patient trust in the medicines they use, thereby increasing trust in the health-care system in general; to ensure that risks in drug use are predicted and managed; to provide regulatory authorities with relevant information in order to change recommendations on the rational use of medicines; and to improve communication between health-care professionals and the general public in order to educate and inform them about the efficacy or risk of medicines.

REFERENCES

1. A Dictionary of Pharmacology and Clinical Drug Evaluation: Desmond Laurence and John Carpenter (1994).

2. Mudasir Maqbool1, Mohmad Amin Dar, ShafiqaRasool ,Suhail Ahmad Mir , Ahsan Ullaha Bhat and Misba Khan. CLINICAL PHARMACY PRACTICE IN HEALTH CARE SYSTEM: A REVIEW. ejpmr, 2019,6(4), 630-633.

3. Mudasir Maqbool et al., Compatibility Issues In Blood Transfusion., Indo Am. J. P. Sci, 2019; 06(03):5410-5414.

4. Rasool S, Maqbool M, Joshi Y, Drug utilization studies among ENT patients in various clinical settings: A comprehensive review, Journal of Drug Delivery and Therapeutics.2019;9(1-s):481-485

5. Mudasir Maqbool* and Imran Gani. ANTI- EPILEPTIC DRUGS CAUSING ADVERSE DRUG REACTIONS IN CLINICAL PRACTICE. WORLD JOURNAL OF ADVANCE MEDICAL AND PHARMACEUTICAL RESEARCH. Volume: 1 Issue: 4 Page: 10-18. www.wjampr.com.

6. Mudasir Maqbool, Imran Gani , Geer Mohamed Ishaq, Misba Khan; Hemovigilance and Blood Safety: A Review; International Journal of Pharmaceutical & Biological Archives 2018; (3):122-127. Available Online at www.ijpba.info.

7. Mudasir Maqbool et al., Adverse Events of Blood Transfusion and Blood Safety in Clinical Practice.,

Indo Am. J. P. Sci, 2018; 05(08):8254- 8259. DOI: http://dx.doi.org/10.22270/jddt.v9i1- s.2354.

8. Maqbool M, Dar MA, Rasool S, Bhat AU, Geer MI, Drug safety and Pharmacovigilance: An overview, Journal of Drug Delivery and Therapeutics. 2019; 9(2-s):543-548 http://dx.doi.org/10.22270/jddt.v9i2-s.2469.

9. Mudasir Maqbool, Mohmad Amin Dar, ShafiqaRasool, Imran Gani, Misba Khan. Pharmacovigilance: A Program In Practice. Journal of research in health science. Volume 1- 2 issue 3 2019, pp. 82-86.

10. Mudasir Maqbool et al., Adverse Drug Reaction Monitoring and Occurrence in Drugs Used In Pulmonary Disorders, Indo Am. J. P. Sci, 2018; 05(08):8060-8065.

11. Lindquist A.M. Seeing and Observing in International Pharmacovigilance. Academic thesis. KatholiekeUniversiteit Nijmegen. Nijmegen 2003.

12. Olsson S. The Role of the WHO Programme on International Drug Monitoring in Coordinating Worldwide Drug Safety Efforts. Drug Saf1998;19:1-10.

13. Waller PC, Coulson RA, Wood SM. Regulatory pharmacovigilance in the United Kingdom: current principles and practice. Pharmacoepidemiol Drug Saf1996;5:363-75.

14. A short history of involvement in drug safety monitoring by World Health Organization. The importance of Pharmacovigilance, Safety monitoring of medicinal products. WHO bulletin; 2002.

15. WHO. The Importance of Pharmacovigilance, Safety Monitoring of medical products.WHO Geneva 2002.

16. Gupta R, Sheikh A, Strachan D, Anderson HR. Increasing hospital admissions for systemic allergic disorders in England: analysis of national admissions data. BMJ 2003;327(7424):1142-3.

17. Amery WK; ISPE, "Why there is a need for Pharmacovignance" Pharmacoepidemiology and Drug Safety, 1999 Jan; 8(l):61-4.

18. Meyboom RH, Egberts AC, Gribnau FW, Hekster YA. Pharmacovigilance in perspective. Drug Saf. 1999 Dec;21(6):429-47.

19. Pirmohamed M, Atuah KN, Dodoo ANO and Winstanley P. 2007. Pharmacovigilance in developing countries: Requires collaboration between stakeholders to develop novel models of funding. British Medical Journal; 335: 462.

20. The Importance of Pharmacovigilance, World Health Organization, 2002.

21. Fortnum, H., Lee, A. J., Rupnik, B. and Avery, (2011) Survey to assess public awareness of patient reporting of adverse drug reactions in Great Britain. Journal of Clinical Pharmacy and Therapeutics, 37 (2), pp. 161-165.

22. Lindquist M, Edwards IR. The WHO Programme for International Drug Monitoring, Its Database, and the Technical Suport of the Uppsala Monitoring Centre. J Rheumatol2001;28:1180-7.

23. Conforti, A., Opri, S., Dlncau, P., Sottosanti, L, Moretti, U., Ferrazin, F. et al. (2012). Adverse drug reaction reporting by nurses: analysis of Italian pharmacovigilance database.Pharmacoepidemiology and Drug Safety, 21 (6), pp. 597-602.

24. Ulfvarson, J., Mejyr, S. and Bergman, U. (2007) Nurses are increasingly involved in pharmacovigilance in Sweden. Pharmacoepidemiology and Drug Safety, 16 (5), pp. 532-537.

25. Morrison-Griffiths, S., Walley, T. J., Park, B. K, Breckenridge, A. M. and Pirmohamed, M.(2003) Reporting of adverse drug reactions by nurses. The Lancet, 361 (9366), pp.1347-1348.

26. Van Grootheest, K. and Berg, L. (2004) Patients' role in reporting adverse drug reactions.Expert Opinion on Drug Safety, 3 (4), pp. 363-368.

27. Pitt, B. (2007) Drug safety: who is responsible? International Journal of Clinical Practice, 61 (2), pp. 182-183.

28. Beard, K. and Lee, A. (2006) Introduction. In: Adverse drug reactions. 2nd ed. London:Pharmaceutical Press, pp. 1-22. http://apps.who.int/medicinedocs/en/d/Js6164e/2html, accessed on 30th November 2018.

29. WHO (2002a) Safety of Medicines: A guide to detecting and reporting adverse drug reactions; Why health professionals need to take action. World Health Organization.[cited12/10/2018].Availablefrom:http://whqlibdoc.who.int/hq/2002/WHO_EDM_Q SM_2002.2.pdf

30. WHO (2012) Safety, efficacy and utilization (Pharmacovigilance). World Health Organization. [cited 19/1/19]. Available from:http://www.who.int/medicines/areas/quality_safety/safety_efficacy/en/index.l.

31. WHO-UMC (2010) WHO Programme, WHO Programme for International Drug Monitoring. [cited 19/1/2019]. Available from: http://www.who-umc.org/DynPage.aspx?id=13140#1.

32. WHO-UMC (2009) Being a member of the WHO Programme for International Drug Monitoring. [cited 19/1/2019]. Available from: http://who-umc.org/graphics/25642.pdf

33. Hughes, M. L., Whittlesea, C. M. and Luscombe, D. K. (2002) Review of national spontaneous reporting schemes: strengths and weaknesses. Advances in Drug Reactions and Toxicology Review, 21 (4), pp. 231-41.

34. Roden, S. (1991) An introduction to drug safety surveillance. In Research international Drug Surveillance Depertment (IDSD) Glaxo Group, ed. Drug safety: a shared responsibility, pp. 1-10.

35. Anderson, C., Krska J., Murphy, E. and Avery, (2011) Assessing the usability of methods of public

reporting of adverse drug reactions to the UK Yellow Card Scheme. Health Expectations. British Journal of Clinical Pharmacology, 72 (5), pp. 806-822.

36. McLernon, D. J, Bond, C. M, Lee, A. J, Watson, M. C, Hannaford, P. C, Fortnum, H. et al. (2011) Patient views and experiences of making adverse drug reaction reports to the Yellow Card Scheme in the UK. Pharmacoepidemiology and Drug Safety, 20 (5), pp. 523-531.