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Review On Pharmacovigilance System in Use of Off-label Drug

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ABSTRACT:This review article is about to determine the avaibility of pharmacovigilance systems engrossed in the monitoring & control of off-label medicines use in allover the world. Off-label drug use ,is describe as use of drug in a way that diverge from its approved use defines by the FDA,it is critical because such type of uses have not evidence about safety and efficacy. Administering drugs outside the terms of their official labeling is called off-label use. Pharmacovigilance is the science and activities relating to the detection, assesment, understanding, and prevention of adverse effects or any other medicine/vaccine related problems.All medicines and vaccines go through rigorous testing for safety and efficacy through clinical trials before they are authorize.
KEYWORDS: ADR(adverse drug reaction), FDA, WHO, OLU(off-label use),off-label drugs, Efficacy

I. INTRODUCTION

In Unapproved use of an approved drug is often called as off-label use. Off-label use of medicines term described by stafford (2008), they described that the drug used for treatment other than the approved by regulatory authority like FDA(food and drug administration) in USA ; several medicines are used off-label without any evidence about efficacy & safety. like off-label prescribing--which have no evidence to treat certain disease. off-label use arises through many use of drugs for unapproved clinical indications (ex.tamoxifen is approved by FDA and it is used in treatment of breast cancer but, it is also prescribed off-label to treat certaincauses of infertility in females.) another example is about beta-blockers its approved use is for treating high blood pressure, angina, heart disease, migraine but,it is used as off-label to treat anxiety.there are many other examples likes this.

[1]. Off-label use of medicines is not illegal; however, it can be risky and harmful, or beneficial and innovative. the problem of this practice is the lack of systems for monitoring adverse drug reactions, since the drugs are used in a manner that is not approved by regulatory agencies.for this reason public health protection is not guaranteed. Off-label drug use neither have some advantages but, have some disadvantages also. therefore off-label drug use is not good practice..

[2].The primary purpose of pharmacovigilance is risk mitigation, prevention, and management of adverse drug reactions. a major impediment to achieving this purpose is lack of effective communication about signals , adverse drug reaction (ADRs), and drug interactions to healthcare proffesionals and patients. PVs main motto is to improve health and safety in relation to the use of medicines.

[3]. In this article we have to see the FDA(food and drug administration) roles, to market entry and use of un-proven and nonsafe drugs. according to WHO, the main focus of PV are: rational use of drug, for safety and effective. treatment and also take the patient care and their safety. In this article we also study the different category drugs which are used as off-label prescribed, and their disadvantages and their efficacy & safety. however, the off-label medicines prescribing is not always safer. there are many reasons for off-label prescribing by doctors i.e a person have consumed all other FDA approved drugsand they have no option. there are other major factors for off-label prescription of drugs. This paper presents the pharmacovigilance systems to detect the ADRs occurs due to off-label/unapproved drug use. all the medicines and vaccines were go through testing before their authorize use. but, the clinical trials process involves study of very short number of peoples for short time.some side effects may emerge once a different types of peoples use this. FDA authority and physicians may prescribed the drug as off-label.but manufacturers not encourage to this uses. In this we also highlighten the firmness and future possibility of pharacovigilance systems, in this we also enlighten different ADRs detecting methods. In this we see that different types of drugs are used with no much more evidence to their safety and efficacy, like

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azithromycin,hydroxychloroquine,clonidine, cyclizine, Methotrexate etc

[4].In this paper we study the different off-label drugs use in practices,we also rectifies their ADRs associated with the use, and the different pharmacovigilance systems to detect ADRs. We also study about FDA roles in the pharmaceutical markets. apart from this,we also study the FDA approved drugs for the different types of diseases. The main intentions of the pharmacovigilance to identify the the adverse effects of any drugs.pharmacovigilance is the key to locate new drug therapies and its safety and efficacy through the systems.

[5].The main intention of this study to overview all the systems available for the detection of ADRs,or FDA roles. ADRs are difficult to identify sometimes from the disease which we have treated. In this paper we covered all necessary information about Pharmacovigilance systems to detect ADRs and Off-label drugs which have been used by physicians. In this ,the study also highlights the importance of PV and post marketing surveillance within the use of off-label drugs. Dresser & Frader in (2009) adds information regarding labels in regulatory affairs module are; 1.Indications about drugs, 2.dosage of drugs, 3.age group of patients, 4.route of administration. The above information invoked to off-label drug use. By this, we study that management of risk regarding the use of medicines generally, is compulsory for all healthcare proffesionals.

TABLE: SOME DRUGS WHICH ARE USED AS OFF-LABEL:

FDA approved drug	FDA approved use	Off-label use
Beta-blockers	Treating high blood pressure, angina	Treating anxiety
Lisinopril	hypertension	coronary artery diseases
Montelukast	Asthma	COPD
Erythromycin	Infections	Gastroparesis
Methotrexate	Cancer,Selective autoimmune diseases	Medical abortions
Propranolol	High blood pressure,heart diseases	Stage fright
Minoxidil	Arterial vasodilator	To promote hair growth

WHAT IS PHARMACOVIGILANCE?

Pharmacovigilance described by WHO is that the detection, assessment, of any drug and its prevention from causing any certain adverse effects.The main aim of this to monitor whether a particular drug is safe or not during use.Adverse reaction is a unexpected effects of drug when administered to a patients,it is dangerous, and life threatening also.it might be fatal, and disability also occur. Adverse drug reaction is the name used to outline the unexpected responses of any of the drug in pre-clinical trial.the adverse drug reaction is devided into two subtypes i.e. Expected Adverse drug reaction and Unexpected adverse drug reaction, in this one reaction which have no evidence that drug causes adverse drug reaction, and it is unpredictable. and second have predictable but not surely.

Pharmacovigilance plays an important role in daily life.the main goal of PV is to promote the safe and effective use of health products,by providing information time to time to health care proffesionals,and to the public.the ultimate goal of pharmacovigilance is monitor the advantages and disadvantages of the medicinal product.

Pharmacovigilance main responsibility consists of collecting all the information regarding adverse effects, reports of all ADRs and then further evaluating and focus on analyzing the new ADRs, and then maintain record of its database and it give the alertness to peoples, healthcare workers and industries. Pharmacovigilance is mainly concerned with Adverse drug reaction , which is called as the reaction which is noxious and unintended and occurs at doses for function.

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FIG: Source Google

WHAT IS OFF-LABEL USE ?

It is defined as use of drug which is not approved by food and drug administration to treat certain disease,but it use to treat such disease. Off-Label use is very common and legal, upto when it can not exceeds the regulatory guidelines. example of this, is when a drug is approved at a dose of half tablet everyday but, physicians prescribed it one a day. Off-Label is often described as, an unapproved use of an approved drug.means drug which can be approved by FDA for certain disese treatment, but it is also intentionally used for another treatment by the healthcare professionals. simply it is explain as, a drug which can not be approved for cetain type of disease but, it is used to treat this disease called as off-label use. As we know , chemotherapy is used to treat certain\one type of cancer but healthcare professionals use it to treat various types of cancer.Another example of this, is when a drug is approved at a dose of half tablet everyday but,physicians prescribed it one a day. Off-Label prescribing is common.taking a drug as off-label is safe,but sometimes it is risky or fatal also. there are advantages and disadvantages of related to Off-label use. Take a another example of drug i.e Propranolol it is a beta-blocker and used to treat angina, hypertension, heart rhythm disorder but,it is also use as off-label to treat stage fright i.e nervousnes before any performance. Off-label use of drugs sometimes profitable, because the physicians exceeds prescription and they have no drug to prescribe.

II. MATERIALS & METHOD

1. Articles associated with Off-label drugs and also associated with PV were reviewed.

2. Manual and Electronic search of literature published in english was done

3. A literature including journals articles, international guidelines, and also PV websites i.e (FDA, Uppsala Monitoring Centre) were explored and so on.

4. The Articles were taken from sites such as Pubmed, Google Scholar,(Through access to the Collage library) and the internet search.

5. From the previously published articles we ccollected, and summerize and study all the necessary points regarding Off-label and PV.

6. All the literature was specially studied for Pharmacovigilance and Off-label use of drug taken in to consideration.

7. We also studied the publications books of subject pharmacovigilance for better understanding.

RECENTLY USED DRUGS AS OFF-LABEL: We all know that ,COVID-19 is an challenging task to all the health care workers, physicians etc. In this period, the drug for the treatment of COVID-19 is not available.Several publicized drug were used to treat this disease with no evidence of their safety & efficacy.Following drugs are used as off-label like hydroxychloro-quine, azithromycin or lopinavir-ritonavir in the recent COVID-19 treatment.

1. Azithromycin: It is an antibiotic and used to treat several bacterial infections such as Throat ,nose, ear,skin. Recently it is used in Covid-19 treatment, and several adverse effects are noticed, Like QT-prolongation or retinopathy.

2.Hydroxychloroquine: It is an antimalarial drug, it is used to treat malaria.but,It is recently used in

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covid-19 treatment. and some adverse effects are noticed like, loss of vision, occasional arhythmia, peripheral-neuropathy.

3.Remdesivir: It is an broad-spectrum antiviral drug, it is used to treat several viral diseases..recently it is also used in covid-19 treatment as an emergency and some ADRs are noticed such as Anemia,decreased hemoglobin.

4.Lopinavir/Ritonavir: Both drugs are belong to the class of protease inhibitor.it used to treat human immunodeficiency virus(HIV) which can cause AIDS. It it recently used in covid-19 treatment and ADRs are noticed i.e acute respirarory distress (ARDS).

III. PURPOSE OF STUDY

a) The purpose of this study is that off-label use can put people at risk of receving ineffective or even harmful treatment.

b)To avoid these risks associated with Off-label drugs.

c)To study the different types of off-label drugs used in the market

d)To reduce the upcoming ADRs in future

e)To understand the different types of Pharmacovigilance systems.

f)To study the importance of post maketing surveillance.

g) FDA roles in drug safety and efficacy.

IV. CONCLUSION

Mainly Pharmacovigilance plays an important role in detecting the ADRs related any of the drugs. looking back to this article , we conclude that how the importance of PV is for safety and efficacy of medicines. Off-label use of medicines posses a regulatory science thats a dream. it is very complicated to to the regulatory authorities to manage the marketed drugs, without any proper regulations or laws regarding drug safety.

Off-label drug also have laws and regulation for the public use, this diminished the further consequences about adverse drug reaction and will improve reporting of ADRs.

From this article we conclude that the new studies should be done on the following parameters :

1.Off-label use of all drugs

2.new regulations and laws for Off-label drugs

3. Monitoring the effect of Off-label drug PV action.

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