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DRUGS PRESCRIBED AND ADVERSE DRUG REACTION MONITORING IN SKIN DISEASES

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ABSTRACT

Background: Skin diseases are more common due to bacteria and fungi, mostly antibiotics, antifungal, NSAIDs, corticosteroids, antipsoriatics and antiacne agents are prescribed. 10% of hospital admissions are due to these ADRs that include anaphylactic shock, hypersensitivity reactions. Monitoring of ADRs associated with the use of these drugs can be monitored by various ways including spontaneous reporting, yellow card scheme, direct patient reporting, and case control and cohort studies. **Method:** It is a retrospective study conducted by reviewing research articles and journals like Journal American Medical Association, JAMA, American Society of Health System Pharmacists, MedCare etc. relating to skin diseases and ADR monitoring relating to use of drugs for treatment from 1969 to 2016. **Conclusion:** Most prevalent skin diseases are acne, microbial infections, psoriasis, hypersensitivity reactions, fungal infections and drug used for their treatment results in various adverse drug reactions which should be monitored during the therapy. These ADRs may be associated with minor to life threatening conditions.

Keywords: Drugs prescription, Adverse drug reaction, Monitoring, Skin diseases

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INTRODUCTION

Pharmacovigilance is assessment of drug related adverse effects. It is vital part in monitoring of drug therapy and in developing countries it isn't practiced **[1]**. Every patient responds to drugs differently and intensity of response depends on various physiological and pathological processes. Adverse drug reaction is harmful effect of a drug which depends on other parameters. One of major cause of mortality and morbidity reported is adverse drug reactions **[2]**. Hospital admissions up to 5% results from adverse reactions of various drugs. Pharmacokinetic and pharmacodynamic differences of patient make them prone to suffer from adverse drug reactions. Body mass index also plays markedly significant role in occurrence of adverse drug reactions, as a study proves that women with lean bodies are more prone for adverse drug reactions **[3]**. Genetic and demographic factors vary within each race and geographical area. Hepatic clearance especially role of cytochrome P450 enzyme system adversely effects plasma drug profile of drugs which require therapeutic drug monitoring **[4]**. Adverse drug reactions are of six types which are dose related, non-dose related, dose related-time related, chronic time related, delayed time relating, withdrawal of drugs **[5]**.

Adverse drug reactions are the leading causes for mortality as well as morbidity **[6]**. A group of researchers carried out a hospital based, prospective study recording various ADRs caused by dermatological drugs. About 10% admissions to hospital are due to ADRs and around 5-20% hospitalized patients experience serious ADRs **[7-8]**. ADRs reporting program is helpful as it encourages surveillance of ADRs, promotes education of health professionals related to ADRs **[9]**. Various drugs that are used to treat dermatological problems cause various adverse or side effects, severity of which may vary from itching to life threatening Stevens-Johnson-syndrome (SJS) **[10]**. Mostly used drugs for treatment of skin problems are antibiotics (penicillin, sulphonamides and cephalosporin) that are associated

with acute ADRs including Erythematous eruption, Drug-induced vasculitis, Urticaria, angioedema, and anaphylaxis. Prevalence of these ADRs by antibiotics is 20-30%. ADRs such as Drug-induced vasculitis, SJS, Pigmentary changes may occur by use of NSAIDs in 5-10% population. While excessive use of topical and inhaled steroids and tretinoins caused Drug-induced acne, hypersensitivity syndrome in almost 10% patients reporting to physicians **[11-12]**.

Hospital-based ADR monitoring aim to identify the risks associated with use of drugs **[13]**. This information is useful for the prescribers to minimize the preventable ADRs more efficiently. The involvement of pharmacist is very necessary in such programs **[14]**. The purpose of hospital ADR monitoring is to documenting and evaluating the ADRs according to set criteria. Different forms were designed for this purpose. These included a notification form, a patient and reaction details documentation form, an ADR assessment form and an ADR classification form **[15]**. Notification forms were kept in the participating wards **[16]**. All the in-patients were assessed for ADRs during the study period. In the suspected cases, past medical history of patients was collected. Patients were interviewed, monitored daily throughout their hospital stay and their medical records were reviewed **[17]**. The suspected ADRs were carefully analyzed and documented. All relevant data including all drugs the patients received prior to the onset of the reaction, their respective dosage, route of administration with frequency, date of onset of reaction and the patient allergy status (to drugs and foods) were noted **[18]**.

The complexity in the management of adverse drug reactions may cost approximately billion dollars annually. Adverse drug reactions may cause prescription cascades as the new drugs are prescribed for ailments that are the result of another drug, which is regarded as unrecognized adverse drug reaction (ADR) **[19]**. The cost for preventable adverse drug reactions was considered to be more than the cost of non-preventable adverse drug reactions **[20]**. In a hospital setting, drug surveillance studies showed that greatest economic burden was due to fever, itching, bleeding, diarrhoea and in fatal cases, the cardiac arrhythmia **[21]**. The major cause of adverse drug reaction related costs was due to the excessive use of non-steroidal anti-inflammatory drugs, anti-bacterial agents, anti-neoplastic agents, corticosteroids and cosmeceuticals **[22]**. As a result of adverse drug reactions, prolonged hospitalization and additional clinical investigations constitute the reason for financial burden **[23]**. The cost burden may be direct or indirect. The direct financial cost includes the medications, wages and disposable goods in a hospital setting while the indirect financial costs include the morbidity, like anxiety due to adverse drug reaction episodes **[24-25]**.

During prescribing the medications clinical pharmacists provide services for prescription monitoring such as reviewing the prescribed drugs including proper drug choice for specific indication, dosage, frequency, duration, if there is a need for dose adjustment, suggest the proper drug for untreated indication, consider history of drug allergy, evaluate and manage adverse drug reactions, and possible drug interactions **[26]**. After prescribing the medications: Clinical pharmacists design pharmaceutical care plan, identify problems, establish outcome goals, provide patient counseling, monitor pharmacokinetics and therapeutic drug level, report adverse drug reaction (ADRs), evaluate treatment outcome, and drug information to health care professionals **[27]**. Clinical pharmacists are responsible for taking patient history, medication reconciliation, patient counseling & education, provide educational materials and patient follow up **[28]**.

Pharmacological Classes and Respective ADRs

Antiacne

Isotretinoin belongs to the class of retinoids and used for the treatment of acne and other skin related diseases. Another name for isotretinoin is 13-cis-retinoic acid (RA). It is associated with various psychiatric adverse effects including depression and psychosis **[29]**. Various cases of suicidal attempts are reported due to depression, psychosis and aggression. As retinoids are used in teenagers for treatment of acne vulgaris so risk of depression and suicide is relatively higher in this age group **[30]**. Researches has proven that risk of psychiatric disorders are 30-50 % in ages ranges from 20-30 years and mainly female population is at higher risk **[31]**.

Antibiotics are other agents used either topically or systemically including doxycycline, azithrocycline, clindamycin and various others. Azithromycin as various other antibiotics cause allergic reactions but with statin drugs they both cause rhabdomyolysis and this risk is higher than other antibiotics that co-administer with statins **[32]**. Doxycycline is associated with over expression of Pgp (P glycoprotein) in MCF-7 breast carcinoma, researches has proven that over expression of Pgp results in resistance to antineoplastic agents **[33]**. Clindamycin rarely used systemically for the treatment of acne due to its serious adverse effect pseudomembranous colitis **[34]**. Clindamycin is also associated with stomach upset, diarrhea even gastrointestinal bleeding **[35]**.

NSAID's

Non steroidal anti-inflammatory drugs belong to the group commonest drug class that affects the skin. It is complicated to measure the frequency of side effects of skin caused by NSAIDs as these are extensively used without any prescription. In a study of almost 20,000 patients, 0.3% of the patients are prescribed with NSAIDs that developed some skin reactions including urticaria, skin rashes, serum-sickness, angioedema and erythema nodosum. An analysis on patients using NSAIDs was evaluated and skin side effects were reported in 1-2% of the total patients **[36]**

Table 1: Anti acne agents and reported ADRs.

Sr. No.	Anti-acne agents	Reported ADRs
1.	Isotretinoin	Depression, psychosis, aggression **[29]**
2.	Azithromycin	Abdominal pain, diarrhea, loose stool, swelling, blistering [**37]**
3.	Doxycycline	Tooth discoloration, hypersensitivity reactions, serum sickness **[38]**
4.	Clindamycin	Colitis, diarrhea, decrease platelet count, rashes, redness, itching. **[39]**

Table 2: NSAIDs and reported ADRs.

Sr. No.	NSAIDs	Reported ADRs
1.	Bufexamac	Contact dermatitis
2.	Ibuprofen, Indomethacin, Naproxen, Piroxicam	Alopecia
3.	Oxicam derivatives	Stevens Johnson syndrome
4.	Naproxen	Pseudoporphyria, necrotising fasciitis
5.	Aspirin	mast cell degranulation

Photo contact dermatitis has been reported by the use of topical Non steroidal anti-inflammatory drugs (NSAIDs). This side effect was most commonly occurring by the use of Bufexamac gel with an occurrence of 0.013-0.028/1000. This reaction was supposed to appear after stopping the use of the gel when the skin is next exposed to UV-radiations. So, the chances of the reaction are more seen in summer season. Depending on the severity of the reaction, hospitalization may be required **[40]**.

Pseudoporphyria matches with the cutaneous porphyria tarda. It was first reported by the prolonged use of naproxen. Pseudoporphyria appears with skin fragility and blisters formation, sun sensitivity and scarring, therefore, clinically presents as cutaneous porphyria tarda. But no abnormality is detected when a specific biochemical testing is done. Skin problems were not solved even after the cessation of drug naproxen **[41]**. Another side effect associated with naproxen is necrotizing fasciitis. Delay in diagnosis is seen when the masking of signs and symptoms of an infection is done. Some researchers have mentioned that in certain skin and soft tissue infections, especially by a group of beta-haemolytic streptococci, delay in diagnosis leads a simple infection to necrotizing fasciitis **[42]**. Aspirin is related with the degranulation of mast cells and more complexity in patients having urticaria pigmentosa **[43]**.

CORTICOSTEROIDS

Topical corticosteroid's availability of formulations and potency gives flexibility to treat all groups of patients in different phases of disease and at different anatomic sites **[44]**. However, the rapid rise in incidence of improper use of these drugs increases the incidence of adverse drug events reporting. Responsibility to provide proper knowledge regarding the use of topical corticosteroids benefits to rational and ethical use and decrease the adverse drug reporting **[45]**. Simultaneous efforts to use political, legal, and other institutions to prevent misuse of these drugs by rationing their availability only through proper prescriptions will greatly help the cause **[46]**. Topical corticosteroids are frequently used for the treatment of eczema, psoriasis and other skin diseases. Contact hypersensitivity reactions are recognized by the use of topical corticosteroids in about 2-5% of the patients complaining contact dermatitis **[47]**. These corticosteroids are often related to worsening of a pre-existing skin infection. Betamethasone and clobetasol as the topical steroid ointments were mainly associated to cause skin rash, skin irritation, skin atrophy, freckles, melasma,

itching, red patches, erosion, rosacea, hyperpigmentation and dry skin **[48]**.

Prednisolone, a commonly used corticosteroid is associated with the delayed (type IV) hypersensitivity reactions in which a person becomes immune to the allergens and susceptible to other disorders. Undesirable consequences of delayed-type hypersensitivity include illness such as contact dermatitis and allograft's rejection **[49]**. Fluticasone propionate as a topical corticosteroid used to treat fungal infections like dandruff is often related to the skin irritation

(local effect) or burning sensation when applied to the skin **[50]**. Dexamethasone induces Stevens-Johnson syndrome which is a life threating skin infection; in which death of the epidermal cells occur. It mostly affects the skin and mucous membrane **[51]**.

ANTI-PSORIATIC

A wide variety of therapies are available to treat psoriasis. Management of psoriasis can be done by using corticosteroids, vitamin D analogues, retinoids, anthralin, antihistamines, anti-metabolites, immune modulators and monoclonal antibodies **[52]**.

Acitretin, a severe retinoid, is drug of choice in pustular and erythrodermic psoriasis and can also be for the treatment of plaque type psoriasis in combination with other systemic and topical agents **[53]**. Frequent side effects caused while using acitretin include cheilitis (inflammation of lips), peeling of palms and soles, alopecia etc. along with the elevation in the levels of serum triglycerides, serum cholesterol and trans-aminase **[54]**. Cyclosporine, an immune-modulator is effective in serious and resistant psoriasis. As the side effects depend upon dose so they can be controlled at doses below 5 mg/kg **[55]**. Most common adverse events reported include gastrointestinal complaints, followed by common cold and other viral infections along with increase in serum level **56]**. Efalizumab, a monoclonal antibody, is used for the treatment of moderate to severe psoriasis. Adverse reactions associated include headache, chills, fever, nausea myalgia, serious hematological side effects, thrombocytopenia, hemolytic anemia, hypersensitivity reactions (e.g., dyspnea, asthma, urticaria, angioedema etc.) as well as reversible increase in lymphocyte count and total white blood cell count **[57]**. Calcipotriene an analogue of vitamin D3 was approved in early 1990's in Europe for the treatment of psoriasis with the name calcipotriol having more efficacy than class II corticosteroids and anthralin **[58]**. Calcipotriene treatment caused common side effect that is the development of irritant contact dermatitis (burning and itching) at the site of application among 20% of patients **[59]**. Patients also reported hypercalcemia on excessive use **[60]**. Methotrexate, an anti-metabolite is effective in psoriatic arthritis as well as psoriatic erythroderma and pustular psoriasis. Methotrexate caused short term bone marrow toxicity and long-term hepatotoxicity **[61]**. Other side effects include mucosal ulcerations or stomatitis, nausea in a daily dose of 1 to 5mg **[62]**. Miscarriages and birth defects have also been reported in pregnancy during its use **[63].**

ANTIBIOTICS

Although antibiotics use is common practice but may cause few adverse effects **[64]**. Commonly prescribed antibiotics are; azithromycin, doxycycline, ceftriaxone, cefixime, amoxicillin, cephradine, clindamycin, lidocaine, fusidic acid, metronidazole.

The primary indication for oral antibiotic therapy in acne is moderate to severe inflammatory involvement on the face or trunk **[65]**. A serious problem with the extended use of oralantibiotic therapy is emergence of strains of bacteria that cause resistant to oral antibiotics e.g. tetracycline and erythromycin **[66]**. To overcome this rising problem, various researchers recommend optimal use of oralantibiotics **[67]**. Among the conventionally prescribed oral antibiotics the greatest resistance has been documented with minocycline, followed in order by doxycycline, tetracycline, and erythromycin. Alternative oral antibiotics useful in the treatment of skin diseases are trimethoprim sulfamethoxazole, azithromycin, clarithromycin, cephalosporin and fluoroquinolones **[68]**. Oral antibiotics may cause side effects that may be mild i.e. gastrointestinal upset or life threatening for example Stevens-Johnson syndrome, epidermal necrolysis and hypersensitivity syndrome **[69]**.

Table 3. Corticosteroids and reported ADRs

Sr. No.	Corticosteroids	Reported ADRs
1.	Prednisolone	Delayed hypersensitivity reactions **[70]**
2.	Betamethasone	Facial edema, skin irritation **[71] [72]**
3.	Fluticasone propionate	Skin irritation
4.	Clobetasol propionate	Skin rash, Disturbed adrenal functions **[73]**
5.	Dexamethasone	Drug-induced Stevens-Johnson syndrome (SJS)

Table 4: Antipsoriatcis and reported ADRs

Sr. No.	Antipsoriatics	Reported ADRs
1.	Acitretin	Cheilitis (inflammation of lips), peeling of palms and soles, alopecia, increased level of serum triglycerides, cholesterol and transaminase **[48]**
2.	Cyclosporine	Gastrointestinal complaints, followed by common cold and other viral infections **[50]**
3.	Efalizumab	Headache, chills, fever, nausea myalgia, thrombocytopenia, hemolytic anemia, hypersensitivity reactions (e.g., dyspnea, asthma, urticaria, angioedema etc.), increase in lymphocyte count and total white blood cell count **[51]**
4.	Calcipotriene	Irritant contact dermatitis (burning, itching), hypercalcemia **[53, 54]**
5.	Methotrexate	Bone marrow toxicity, hepatotoxicity, mucosal ulcerations or stomatitis, nausea, miscarriages and birth defects **[55-57]**

Table 5: Antibiotics and reported ADRs.

Sr. No.	Antibiotics	Reported ADRs
1.	Fusidic acid	Allergic reactions, stomach upset, yellowing eye **[74]**
2.	Ceftriaxone	Black stools, chills, shortness of breath, white spot on lips or around mouth **[75]**
3.	Amoxicillin	Diarrhea, hives, itching, cramps, decrease blood platelet, Steven Johnson syndrome, erythema **[76]**
4.	Lidocaine	Flushing, itching, purple spots on skin **[67]**
5.	Metronidazole	Back pain, blurred vision, hallucinations, convulsions, blindness, drowsiness, stiff neck **[67]**
6.	Cephradine	Pseudo membranous colitis, hypersensitivity reaction, hematological reactions, hepatic insufficiency, nephritis **[66]**
7.	Cefixime	Diarrhea, abdominal pain, bleeding gums, joint inflammation **[66]**

ANTIFUNGALS

Antifungal therapy reduces the number of yeasts on the skin, leading to an improvement in disease condition. With a wide availability of preparations, including creams, shampoos, and oral formulations, antifungal agents are safe and effective in the treatment **[77]**. Amphotericin B (Fungizone) remains the standard therapy for many invasive or life-threatening mycoses, this polyene drug is associated with significant toxicity, including infusion-related events, such as chills, fever, headache, nausea and vomiting, and dose-limiting nephrotoxicity **[78]**.

Among the pyrimidine class of antifungal drugs, only flucytosine is approved. However, this drug's utility has somewhat limited spectrum of activity (Candida species, Cryptococcus neoformans, and some molds), and its significant potential for toxic effects (skin rash, nausea, vomiting, diarrhea, liver dysfunction, and bone marrow suppression) **[79]**. In addition, emergence of resistance during flucytosine therapy, especially among Candida species, is a troublesome feature **[80]**.

The azole antifungal agents represent a major advance in the management of systemic fungal infections **[81]**. Miconazole, the first azole drug to be approved and now recently withdrawn from the market, was available only as a highly toxic IV formulation. By contrast, the 3 oral azoles, ketoconazole, an imidazole, and, especially, itraconazole and fluconazole (both triazoles), have become frequently used therapeutic alternatives to amphotericin B **[82]**.

Azole-drug interaction may lead to an unexpected toxicity of the co-administered drug, relating to the ability of the azoles to increase plasma concentrations of other drugs by altering hepatic metabolism via the cytochrome P-450 system **[83]**. Available data indicate that the annual incidence of fluconazole resistant oropharyngeal candidiasis in AIDS patients is ~5% **[84]**.

Table 6: Antifungals and reported ADRs.

Sr. No.	Antifungals	Reported ADRs
1.	Amphotericin B	Chills, fever, headache, nausea and vomiting, and dose-limiting nephrotoxicity **[85]**
2.	Flucytosine	Skin rash, nausea, vomiting, diarrhea, liver dysfunction, and bone marrow suppression **[86]**
3.	Fluconazole	Immunosuppression and Bloodstream infections with increased use of fluconazole for both prophylactic and therapeutic purposes **[87]**
4.	Itraconazole	Rash, hives, itching, swollen, blistered, peeling skin, ringing in the ears, sensitivity to sunlight **[88]**
5.	Ketoconazole	Headedness, fainting, fast or irregular heartbeat, fever, chills, or persistent sore throat, swelling of the hands, ankles, or feet, swollen or tender abdomen **[89]**

A broth dilution method has emerged as a reproducible tool for testing yeasts. By correlating results obtained by this method with outcome of therapy in both mucosal and bloodstream Candida infections, data-driven interpretive breakpoints for fluconazole, itraconazole, and flucytosine have recently been proposed **[90]**. Susceptibility testing of mucosal Candida isolates from patients who have failed conventional therapy may be used to assist in determining the cause of the therapeutic failure **[91]**.

Adverse Drug Reaction Monitoring

The aim of ADR monitoring involves the detection of unknown safety issues at the initial stage and increment in their frequencies, identification and quantification of risk factors, and the prevention from being affected **[92]**. This can be done by collecting data on ADRs by the general public and by the pharmacovigilance study. Based on these data, regulatory authorities can change or banned the use of drugs or withdraw drugs **[93]**.

Objectives of ADRs Monitoring

To detect the nature and frequency of ADRs including a periodic reevaluation of the benefit-risk ratio of medicinal products in order to assist the drug regulatory authority **[94]**. Pharmacist take appropriate action to minimize risks of ADRs to consumers by providing drug safety information to health care professionals, design appropriate package insert information. To identify risk factors that may predispose, severity and incidence of adverse reactions in the population **[95]**.

Cutaneous Adverse Drug Reactions (CADRs)

Cutaneous adverse drug reactions (CADRs) are a frequent problem in dermatology, because patients are often on multiple drug regimes. Besides clinical parameters, there is no widely usable complementary test to help establishing the definite cause of the CADR. Skin testing (patch testing and also prick and intradermal (IDT) testing), with the suspected compound, has been reported to be helpful in determining the cause of a CADR and in studying the pathophysiological mechanisms involved in these reactions **[96.]** The results of drug skin tests mainly depend on the drug tested and the clinical features of the CADR but there are, at present, a few extensive studies that determine the sensitivity and specificity of these drugs against skin tests. Many isolated reports of positive drug skin tests in investigating CADR are published, but without detailed information concerning the clinical features of the CADR, the imputability of the suspected drug, the methods used in performing drug skin tests, namely the concentrations and vehicles used for testing the suspected drugs, this data is not always very informative **[97]**. Moreover, there are undoubtedly many negative results that are not published, which make it still more difficult to ascertain the sensitivity and specificity of such tests in the study of CADR. **[98]**.

Data Collection

Patient demographic information includes

- Presenting complaints
- Past medication history
- Drug therapy details including over the counter, current medications, medication on admission
- Lab data such as hematological, liver and renal function test **[99]**.

Methods for Monitoring of ADRs

Spontaneous Reporting

Individual reporting is also known as spontaneous monitoring in which reports are either sent directly by practicing physicians and doctors **[100]**.

Causality Assessment

Causality assessment of ADRs is done by Naranjo's probability scale **[101]**. This uses a questionnaire and points are added based on the responses to each question.

Hartwig Severity Scale

The severity of the ADR is analyzed by using adapted Hartwig severity scale.

The Scale is classified as: **[102]**

1. Mild: A reaction that does not require hospital stay.
2. Moderate: A reaction that needs treatment.
3. Severe**:** A life threatening reaction that contributes to the death of patient and requires intensive medical care.

Yellow Card Scheme

Health care professionals can submit reports of ADRs by using an on-line form named as yellow card scheme. A suspected ADR is reported in the form, even if minor events occur **[103]**.

Direct Patient Reporting

Direct patient reporting system is more oriented and detailed reporting **[104]**. Despite the limited awareness of direct patient reporting, in the main people find it relatively easy to report suspected ADRs **[105]**.

Cohort Studies

Cohort studies are expected pharmaco-epidemiological studies that observed a large group of patients taking a particular drug over a specific period of time **[106]**.

Case-control Studies

Case-control studies compare the extent of drug usage in a group of patients who have experienced the adverse event with the extent of usage among a matched control group who are similar in factors, but have not experienced the adverse events **[105]**.

Under Reporting

- Maintain records of ADRs
- Disseminate useful information

Every drug has its own adverse effects associated with therapy, the risk associated with such ADRs can be minimized through proper monitoring, and patient oriented prescribing decisions.

Skin diseases are commonly caused by genetic factors, microbes, pollutants, radiations etc. susceptibility to adverse reactions is variable depending on host factors and drug related factors. Severity of the reaction also varies among individuals depending upon duration of therapy and dosage regimen. Dose of drug need to be modulated by considering patient disease related as well as drug's pharmacokinetics.

- Anti acne agents are commonly prescribed to teenagers and adults, without calculating the risk-benefit ratio.
- ADR monitoring is insufficient in case of drugs belongs to retinoids class.
- NSAIDs are commonly used class of drugs and can be easily purchased in bulk quantities without any prescription.
- Patients may use these medications without the knowledge of physician that may harm

Under reporting may be due to various reasons including reporting higher for new drugs than for old, serious reactions are reported to a higher degree, type B reactions are reported more commonly than their share of events in practice **[107]**. Adverse reactions reporting is affected by promotional claims of the drug sponsor, reporting is affected by general publicity around the ADR reporting scheme **[108]**. The reasons more often by health professionals for not reporting are: Lack of time, Lack of knowledge on what, how or where to report, reaction is already well known, Belief that all registered medicines are safe and Non-availability of reporting forms **[109]**.

Role of Pharmacist in Monitoring

American society of health system pharmacist established the role of pharmacist in monitoring of ADRs. Pharmacist can lead such programs in hospital setting with previous approval of P&TC **[110]**. Pharmacist involve in following activities;

- Analyze already reported ADR
- Identify patients who are at high risk of ADRs against prescribed drugs
- Develop policies and procedures for monitoring of ADR
- Description of Interaction of health professionals in monitoring programs
- Use ADR programs for educating the patients and prescribers

Report ADRs of serious nature to FDA **[111-112]**.

CONCLUSION

- Their current therapy and cause adverse effects.
- Patients receiving NSAIDs may have higher risks of cardiovascular diseases and gastrointestinal problems.
- Topical corticosteroids are intended to be used in the management of most patients but need careful management to minimise the risk of adverse effects.
- Topical corticosteroids may cause local side effects as well as systemic side effects depending upon the dose taken.
- The unrestricted over the counter (OTC) sale of topical corticosteroids is the main concern for the adverse effects. Since a large number of topical corticosteroids are sold as OTC products like Fluticasone, Betamethsone etc.
- A chain of awareness campaign programmes or the adverse drug monitoring may halt the progress of topical corticosteroid's adverse effects
- Antibiotics are extensively used in our society, mostly without any prescription.

- Frequent usage of antibiotics may cause several side effects or adverse effects which may be moderate to life threatening.
- Another problem with extensive use of antibiotics is the emergence of resistance as mainly in case of minocycline, doxycycline, tetracycline, and erythromycin.
- The extensive use of antifugal drugs cause emergence of resistance and toxic effects like in case of miconazole and flucytosine.
- Azole-drug interaction may lead to an unexpected toxicity of the coadministered drug, relating to the ability of the azoles to increase plasma concentrations of other drugs
- Some oral antifungals may interact with other medicines that you might take. This may cause reactions, or reduce the effectiveness of one or other of the treatments. So, when take prescribed an antifungal, tell doctor if you take other medicines.

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