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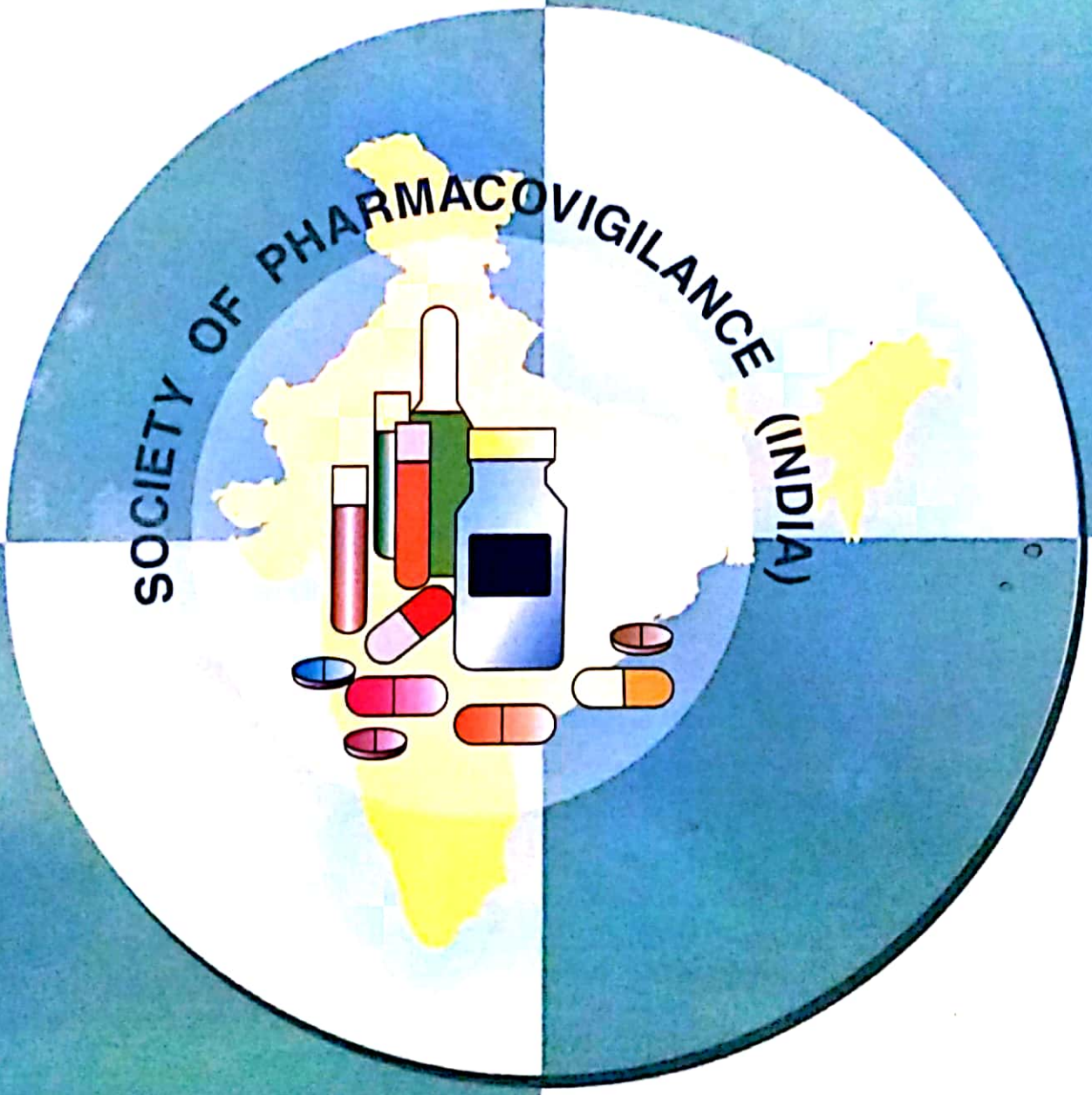

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EDITORIAL...

About 30 Years ago the WHO set up an International Program for Adverse Drug Reaction Monitoring to identify rare adverse drug reactions (ADRs) that could not be found through clinical trials. Maintaining an international database of ADR case reports and a network of institutions and scientists concerned with drug safety issues provide great additional gains when compared with operating in isolation. This activity is now often named "Pharmacovigilance". The WHO collaborating centre for International Drug Monitoring in Uppsala maintains the international database and serves the national centers of more than 60 Countries. India became a collaborator in this program in 1998. Within a year after this under the leadership of Prof. K. C. Singhal the Society of Pharmacovigilance (India) was formed and registered under the Act of 1950 at Ahmedabad (No F 7199/ Ahmedabad dated 27th Sept. 1999).

Although the WHO program is going on in 60 countries the work is not getting published widely. Only two journals are published in the world devoted to the subject of pharmacovigilance. One is "The International Journal of Risk and Safety in Medicine" from The Netherlands. Other is that of ours "Journal of Pharmacovigilance and Drug Safety". The journal is in infancy and only three volumes have come up so far. There has been a delay in third volume. However, it will be a long way before it becomes a popular journal.

It will be a pleasure of the Editorial Board if journal receives more articles as well as suggestions for the improvement.

Dr. Ramesh K. Goyal
Chief Editor

THE IMPORTANCE AND NEED FOR PHARMACOVIGILANCE

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Modern medicines have changed the way in which diseases are managed and controlled. However, despite all their benefits, evidence continues to mount that adverse reactions to medicines are a common, yet often preventable, cause of illness, disability and even death.

The Thalidomide tragedy is now well known. Thalidomide was introduced in 1957 and widely prescribed as an allegedly harmless treatment for morning sickness and nausea. It was soon linked to a congenital abnormality, which caused severe birth defects in children of women who had been prescribed this medicine during pregnancy[1]. The Sixteenth World Health Assembly (1963) adopted a resolution that reaffirmed the need for early action in regard to rapid dissemination of information on adverse drug reactions and led later, to creation of the WHO Pilot Research Project for International Drug Monitoring in1968[2]. The purpose of this was to develop a system, applicable internationally, for detecting previously unknown or poorly understood adverse effects of medicines. By 1965, thalidomide had been removed from the market in most countries. A WHO technical report followed based on a consultation meeting held in 1971[3].

Adverse drug reactions (ADRs) rank among the top 10 leading causes of mortality. Aside from the intrinsic dangers associated with the products themselves, individual patients may exhibit particular and unpredictable sensitivities to certain medicines. The selection and use of the best and safest medicine(s) for a given individual out of the many choices available thus requires considerable skill on behalf of the prescribing practitioner.

In order to prevent or reduce harm to patients and thus improve public health, mechanisms for evaluating and monitoring the safety of medicines in clinical use are vital. In practice this means having in place a well-organized pharmacovigilance system. Pharmacovigilance is a key component of effective drug regulation systems, clinical practice and public health programmes.

What is pharmacovigilance?

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

Major aims of pharmacovigilance are:

1. Early detection of hitherto unknown adverse reactions and interactions
2. Detection of increases in frequency of (known) adverse reactions
3. Identification of risk factors and possible mechanisms underlying adverse reactions
4. Estimation of quantitative aspects of benefit/risk analysis and dissemination of information needed to improve drug prescribing and regulation.

The ultimate goals of pharmacovigilance are:

- The rational and safe use of medicinal drugs.
- The assessment and communication of the risks and benefits of drugs on the market .
- Educating and informing patients.

Why is Pharmacovigilance is needed?

The information collected during the pre-marketing phase of a medical drug is incomplete with regard to possible adverse reactions. The reasons for this are:

- Preclinical toxicity studies in animals do not predict human safety sufficiently.

Safety and efficacy studies in humans are carried out in controlled conditions in a selected and limited number of patients. The conditions of use differ from those in clinical practice. The duration of trials is limited.

Information about rare but serious adverse reactions, chronic toxicity, use in special groups or drug interactions is incomplete or unavailable.

Therefore, it is essential that new treatments be monitored for their effectiveness and safety under real-life conditions. More information is generally needed about use in specific population groups, notably children, pregnant women and the elderly, and about the efficacy and safety of chronic use, especially in combination with other medicines. Many adverse effects, interactions (i.e. with food or other medicines) and risk factors come to light only during the years after the release of a medicine.

Pharmacovigilance is needed in every country. This is because differences exist between countries in the incidence and patterns of adverse drug reactions and other drug related problems. This is primarily due to differences in drug production, distribution and use. Regional differences also exist in the genetic makeup, diet, traditions and food habits of the people. The other factors that contribute to these differences include pharmaceutical quality and composition of locally produced pharmaceutical products and the use of alternative systems of medicine that may produce special toxicological problems.

The key partners in monitoring the safety of medicines include the Government, industry, hospitals and academia, medical and pharmaceutical associations, poisons and medicines information centers, health professionals, patients, consumers, the media and the World Health Organization[4]. Globalization, consumerism, the explosion in free trade and communication across borders, and increasing use of the Internet have resulted in a change in access to all medicinal products and information on them. These changes have given rise to new kinds of safety concerns such as:

- illegal sale of medicines and drugs of abuse over the Internet
- increasing self-medication practices
- irrational and potentially unsafe drug donation practices
- widespread manufacture and sale of counterfeit and substandard medicines
- increasing use of traditional medicines and herbal medicines

In view of this it is increasingly being felt that the scope of pharmacovigilance should be extended beyond the strict confines of detecting new signals.

Recently, the scope of safety concerns have been widened to include:

Herbals, traditional and complementary medicines, blood products, biologicals, medical devices and vaccines[5].

The scope of pharmacovigilance continues to broaden as the array of medicinal products grows. Nowadays drug safety is more than the monitoring, detection and assessment of ADRs occurring under clearly defined conditions and within a specific dose range. Rather, it is closely linked to the patterns of drug use within society. Problems resulting from irrational drug use, overdoses, polypharmacy and interactions, use of traditional and herbal medicines with other medicines, illegal sale of medicines and drugs of abuse over the Internet, increasing self medication practices, substandard medicines, medication errors and lack of efficacy are all within the domain of pharmacovigilance. The risk of harm by medicines is less when medicines are used by an informed health professional and by patients who themselves understand and share responsibility for their drugs.

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ADVERSE DRUG REACTIONS: AN OVERVIEW

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In recent years, advances in modern medicine have changed the way in which diseases are treated and prevented. The widespread and extensive use of drugs while providing disease-alleviating effects on the one hand has also resulted in the precipitation of some undesirable effects, and in some instances these unwanted drug effects have overshadowed their benefits. Such untoward effects, which are regulated by both drug-related and drug-unrelated factors, have assumed alarming dimensions, ranging from mild inconveniences to permanent disability and even mortality.

The severity of the problem can be assessed from the fact that adverse drug reactions (ADRs) now rank among the top 10 leading causes of morbidity and mortality all over the world. Over 2 million people across the globe suffer from serious ADRs and nearly 1,00,000 deaths are reported annually. ADRs are the fourth leading cause of death ahead of pulmonary disease, diabetes mellitus, AIDS and accidents/trauma. Studies have shown that nearly 7% of hospitalized patients have serious ADRs with a mortality rate of 0.3%. It is estimated that annual ADR related health care costs is around 136 billion US dollars. Further, multiple drug therapy regimens, increasing indulgence in self medication by over the counter (OTC) drugs, intentional use of drugs of addiction, and unintentional exposure to environmental pollutants through food, water and air, have merely compounded the extent of the problem.

Adverse drug reaction is defined as "a response to a drug which is noxious and unintended & which occurs at doses normally used in man for prophylaxis, diagnosis, or for modification of physiological functions, excluding failure to accomplish the intended purpose" (WHO Technical Report Series No, 498, 1972).

Classically, ADRs are of the following types:

Type-A: Dose related and extension / exaggeration of therapeutic effects. These account for 70-80% of all ADRs. The onset is gradual, may remain undetected for long and may induce mortality, e.g.: digoxin induced bradycardia

Type-B: Unusual or bizarre responses, appearing at very low doses/concentrations. The onset is insidious, can be quickly detected and could be fatal, e.g.: drug induced anaphylaxis (penicillin)

Type-C: Result from long-term drug use. Tolerance development to drugs of abuse (e.g. opiates) and the resultant withdrawal reactions (abstinence syndromes) fall in this category.

Type-D: Drug induced reproductive effects and carcinogenesis qualify in this category.

Several complex factors and their interactions could contribute to the aetiopathogenesis of adverse drug reactions. These could be:

1. Factors intrinsic to the drug or formulation: the use of drugs and drug interactions
2. Factors intrinsic to the patient viz. age, sex, genetic factors, tendency to allergy, personality, habits
3. Factors extrinsic to the patient: the prescriber and the environment

ADRs due to drug-drug interactions: This is of great clinical relevance with drugs with narrow therapeutic indices and steep dose-response curves, wherein, a small change in blood levels or at target sites may precipitate toxicity, eg. digoxin and lithium. This is also prevalently seen with (a) microsomal enzyme

inducers and inhibitors (rifampicin, fluconazole, cimetidine), (b) drugs following zero order kinetics where interference with kinetic may lead to enhanced plasma concentrations (phenytoin, theophylline), (c) drugs used over long periods and where precise plasma concentrations are required, eg. oral contraceptives, antiepileptics, cardiac antiarrhythmics, lithium, (d) use of multiple drug combinations with special risk, eg. salbutamol and theophylline in asthma can precipitate cardiac arrhythmias, (e) drug use in extremes of age, etc. In addition, drug interactions could also result from pharmacodynamic factors, eg. Alcohol + bezodiazepine (sedation), morphine+naloxone (reversal of overdose), rifampicin+isoniazid (effective tuberculocidal combination). It is also noteworthy to mention that such interactions could occur inside as well as outside the body (eg. two incompatible drugs added to the same I/V fluid reservoir may cause inactivation of one another). Classical examples of the latter category are: precipitation of phenytoin in dextrose, amphotericin in saline, and physical/chemical incompatibility of gentamicin with beta-lactams.

ADRs due to drug-disease interactions: Liver disease, renal disease, cardiac disease, acute viral infections, endocrinal disorders are conditions where a drug effect could be modified. For example, heart failure reduces hepatic blood flow and thus decreases clearance of drugs that are primarily excreted by the liver, eg. lidocaine and propranolol. Acute viral infections and changes in thyroid function have been associated with altered clearance of drugs like theophylline and warfarin. Pharmacodynamic examples include, beta-blocker induced aggravation of asthma, digoxin induced cardiac dysrrythmias in myocardial infarction, aggravation of myasthenia gravis by quinine/quinidine, aminoglycoside antibiotics, increased sensitivity of the respiratory center to opioids in patients with increased intracranial pressure and respiratory insufficiency.

ADRs due to drug-food interactions: The presence of food can also influence drug concentrations and result in ADRs. Grapefruit juice contains a bioflavinoid, which inhibits CYP3A and blocks the metabolism of many drugs, eg. felodipine. Tetracycline absorption is inhibited when taken with milk products, and absorption of vital antimicrobials like ampicillin and rifampicin may be reduced when taken in a full stomach. Alcohol and methylxanthines (present in tea, coffee, cola drinks) can inhibit metabolism of other drugs.

ADRs due to herbal drug usage: Treatment with drugs of alternative systems of medicine alone or in combination with modern medicine can result in ADRs. For example, St. John's Wort, a drug commonly used in depression is known to decrease the bioavailability of the indinavir, cyclosporin and digoxin. This is due the induction of CYP1A2 by the herbal drug. It is therefore extremely important to detect and confirm the presence of ADRs in order to deal with this rapidly emerging global health problem. Specific laboratory and clinical methods to assess ADRs are few, and uncertainties regarding the various factors contributing to the incidence of ADRs are manifold, and it is absolutely crucial to extract meaningful information from such host-substance interactions. Accordingly, the experience of the evaluator/professional in recognizing the presence of an ADR is of paramount importance. In order to prevent or reduce ADR related harm to patients and improve public health, mechanisms for evaluating and monitoring the safe use of medicines are vital.

Pharmacovigilance is the term used to describe the processes for monitoring and evaluating ADRs. This is a key component in effective drug regulation system, clinical practice and

public health. WHO defines pharmacovigilance as the selective activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine related problems. Historical events like the thalidomide disaster led to the realization of the need for a system to monitor adverse drug reactions.

The WHO took a lead in this matter set up its own programme in 1978 and we now have an International Drug Monitoring Centre at Uppsala, Sweden, for this purpose. The Uppsala Monitoring Centre (UMC), as it is commonly known, is an independent center of scientific excellence and is responsible for collection of ADR data from all over the world, especially countries who are members of the WHO, and generation of signals from potentially problematic drugs. Using this database the WHO provides resources for regulatory authorities, health professionals and prescribing physicians, the primary emphasis being on minimizing ADRs by rational prescribing and usage. They have taken the initiative to spread the concept in various countries, and in India we have today a National Pharmacovigilance Programme in collaboration with the WHO to oversee ADR monitoring activities in the country in an organized manner.

The primary objective of this programme is to foster, amongst participants of this programme, an ADR reporting culture. Before a product is marketed, knowledge on its safety and efficacy is limited to its use in clinical trials. The conditions of such studies are highly controlled and limited to a handful of patients, which does not necessarily reflect the effects of the drug in the general population. Studies during the pre-marketing phase do not necessarily apply to the way in which the drug will be used in general or hospital practice and so, information about rare and serious adverse effects may not be detected until a vary large number of people have been observed over a prolonged period of time.

Pharmacovigilance is therefore an important post-marketing tool for ensuring safety of pharmaceutical and other health related products. ADR information generated in this way can be transmitted /communicated to health care professionals, and such a system has helped to detect ADRs with drugs like terfenadine, cisapride, COX-2 inhibitors and nimesulide. It is also important that both the academia and the industry have an important role to play in the implementation of this programme. In order to detect/discover an ADR, several steps are followed. Viz. signal generation (detection), Signal strengthening and signal follow-up. Some of the methods used in pharmacovigilance include: spontaneous reporting, stimulated reporting, active surveillance, comparative observational studies and descriptive studies. Subsequent to collection of data, an important aspect is to assess causality in order to be able to attribute a particular effect to a specific drug. Causality assessment, which is an important aspect of pharmacovigilance, can be done in many ways, and conclusions can be drawn as to whether the ADRs association with the drug is certain, probable/likely, possible, unclassified, unlikely or inaccessible/ unclassifiable.

The bottom line is that ADRs are preventable, and the following precautions can be taken:

1. Rich knowledge base about drug actions and interactions
2. History from patient about prior allergies
3. History about concomitant use of herbal drugs
4. Preventing irrational use of multiple drugs by rationalizing prescribing
5. Foster a culture of ADR reporting amongst health professionals, physicians and academia-industry interactions in this regard.

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PHARMACOVIGILANCE - ROLE OF THE INDUSTRY

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INTRODUCTION

During the last decade it has been demonstrated by a number of studies that illness and death due to medicine is one of the major health problems which is beginning to be recognized by health professionals and the public.

Almost any article on Pharmacovigilance starts with its definition – here are a few more views on what "pharmacovigilance" is all about:

(a) All medicines have side effects and, hence, should be followed up after they are introduced into the market.

(b) "First, do no harm", a principle first put forward by Hippocrates and followed through the centuries.

(c) Absence of evidence is not evidence of absence.

BACKGROUND

In the Pharmacovigilance Workshop at La Baule, France, it was concluded that misuse concerns every step of the drug process — prescription, dispensing and administration — and all health professionals as well as the patient. "Ref: Therapie. 2002 May-Jun; 57(3): 283-8".

It has been estimated that Adverse Drug Reactions (ADRs) are the 4th to 6th largest cause of death in the USA (we need Indian figures, but don't have them). They result in the death of several thousands of patients each year, and many more suffer from ADRs. The percentage of hospital admissions due to Adverse Drug Reactions in some countries is more than 10%. In addition to the sufferings of the patients, the treatment of Adverse Drug Reactions imposes a high financial burden on healthcare. Some countries spend 15-20 % of their hospital budget dealing with drug complications.

Nowadays, quite frequently, questions concerning drug policy and post marketing surveillance are being raised. In September 2004, Merck & Co. announced the voluntary withdrawal from the market of rofecoxib (Vioxx®), a widely used non-steroidal anti-inflammatory drug, due to safety concerns.

David Graham, Scientist, USFDA (Safety of Medicines), testified in front of the Senate's Finance Committee to explain VIOXX withdrawal circumstances and had two very terse comments to make:

(a) "FDA overvalues the benefits and seriously undervalues, disregards and disrespects drug safety".

(b) The FDA has become too chummy with the industry it regulates.

An uncomfortable consequence of this episode was the erosion of the public confidence in the development, approval, and follow-up of medicines. Not only the pharmaceutical industry, but also the FDA, as well as the investigators who participated in the studies - none of them have escaped criticism. The final question, which will not go away, is how public trust can be recovered.

We, including our health authorities, feel that since we are mostly into generic drug marketing, there is no need for "Pharmacovigilance" here. We can withdraw a drug when it is withdrawn abroad and allow others to be marketed as long as they are being marketed in other countries.

Therefore, there is no guideline from our health

authorities on Pharmacovigilance. And everybody expects the Drug Industry to keep a vigil on this topic all by itself. Such an expectation may be misplaced. The guidelines must come from the health authorities and they must ensure its implementation. This is what is followed in the countries where the pharma industry is strictly regulated.

An outline of what most multinational companies already do is described below:

(a) Drug Safety Governance Framework

(b) Benefit-Risk Management

(c) Collecting and Reporting Safety Data

Drug Safety Governance Framework – (i) Systems in place to collect adverse events of products, (ii) Follow-up with the reporter, (iii) Transmit the adverse event data to the Central Safety Departments, (iv) Forward appropriate reports to the regulatory authorities and evaluate the safety data.

Benefit-Risk Management – (i) Evaluate and document all available safety information to build a detailed benefit-risk profile of each product, (ii) Use this to develop a Benefit-Risk Management Plan, which identifies ways to improve a product's benefits and minimize any risks, (iii) Plans are reviewed and updated regularly during clinical development and for a period after a product is approved for marketing.

Collecting and Reporting Safety Data - Receive information on adverse events from several sources such as:

- Unsolicited reports from health professionals and patients
- Post-marketing trials or observational studies
- Investigators who submit clinical study reports
- Regulatory authorities
- Medical and scientific literature
- Newspapers and other media

The U.S. Department of Health and Human Services, Food and Drug Administration Center for Drug Evaluation and Research (CDER) & Center for Biologics Evaluation and Research (CBER) published in March 2005, a "Guidance for Industry - Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment," which is summarized below:

(A) FROM CASE REPORTS TO CASE SERIES

Good pharmacovigilance practice is generally based on acquiring complete data from spontaneous adverse event reports, also known as case reports. The reports should be used to develop case series for interpretation.

In the event that one or more cases suggest a safety signal warranting additional investigation, a case series should be assembled and descriptive clinical information be summarized to characterize the potential safety risk and, if possible, to identify risk factors.

(B) INVESTIGATING A SIGNAL THROUGH OBSERVATIONAL STUDIES

There are a variety of methods for investigating a safety signal. Signals warranting additional investigation can be further evaluated through carefully designed non-randomized observational studies of the product's use in the "real world" and randomized trials.

There are three types of non-randomized observational studies:

(i) Pharmacoepidemiologic studies, (ii) registries, and (iii) surveys.

i. Pharmacoepidemiologic Studies:

Pharmacoepidemiologic studies can allow for the estimation of the relative risk of an outcome associated with a product, and some (e.g., cohort studies) can also provide estimates of risk (incidence rate) for an adverse event.

ii. Registries:

A registry is "an organized system for the collection, storage, retrieval, analysis, and dissemination of information on individual persons exposed to a specific medical intervention who have either a particular disease, a condition (e.g., a risk factor) that predisposes [them] to the occurrence of a health-related event, or prior exposure to substances (or circumstances) known or suspected to cause adverse health effects."

iii. Surveys:

Surveys can gather information to assess, for example:

A safety signal; knowledge about labeled adverse events; use of a product as labeled, particularly when the indicated use is for a restricted population or numerous contraindications exist; confusion in the practicing community over sound-alike or look-alike trade (or proprietary) names.

Maker/marketer of drugs should choose the method best suited to the particular signal and research question of interest.

(C) INTERPRETING SAFETY SIGNALS

After identifying a safety signal, a maker/ marketer of a drug should conduct a careful case level review and summarize the resulting case series descriptively.

A maker/marketer of a drug should consider further study (e.g., observational studies) to establish whether or not a potential safety risk exists.

When evaluation of a safety signal suggests that it may represent a potential safety risk, a maker/marketer of a drug should submit a synthesis of all available safety information and analyses performed, ranging from preclinical findings to current observations to the health authorities.

(D) DEVELOPING A PHARMACOVIGILANCE PLAN

For most products, routine pharmacovigilance (i.e., compliance with applicable post market requirements under the Drug and Cosmetics Act) should suffice for post marketing risk assessment.

A pharmacovigilance plan should be developed by a maker/marketer of a drug that is focused on detecting new safety risks and/or evaluating already identified safety risks. Specially, a pharmacovigilance plan should describe pharmacovigilance efforts above and beyond routine post marketing spontaneous reporting, and should design to enhance and expedite the safety of a drug being reported to the manufacturer also.

Following is a suggestion for the contents of a Summary of Pharmacovigilance Systems **(SPS), based on the first recommendations from Medicines and Healthcare products Regulatory Agency, UK (MHRA) :**

(1) Prepare a SPS dossier - Essentially, a summary of the organization, processes, procedures etc.

(2) Will be used for a Regulatory Audit as well as a useful reference for internal purposes

Another suggestion is to "USE BAR CODES" to reduce medication errors. At minimum, they could contain -

(1) The drug's National Code Number.

(2) Its strength.

(3) Its dosage form eg. 10 mg capsule.

The industry can take the initiative to "EDUCATE" the:

(1) Public - of the potential for drugs to cause adverse reactions.

(2) Doctors - to be more aware of the very preliminary nature of data, both in terms

of safety and efficacy, which come with newly licensed drugs.

(3) And explain the therapeutic strategies already available, and the perceived benefit-risk balance.

The industry can inform about concomitants (Concomitant products include OTC products, dietary supplements, and herbals). These are very important potential confounders, and, a high proportion of the population considers these "safe" despite their great potential for toxicity and interactions.

The industry can request through, "Dear Doctor" letters and ask every member of the medical profession to report promptly, details of any untoward condition in a patient which might be the result of drug treatment.

CONCLUSIONS:

Even if we don't have a guideline from them right now, the concerned Health Authorities must always be informed of each and every development, and corrective measures, as advised, must be implemented. What is really needed is a culture that encourages the sharing rather than the hiding of errors.

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CAUSALITY ASSESSMENT IN ADR MONITORING

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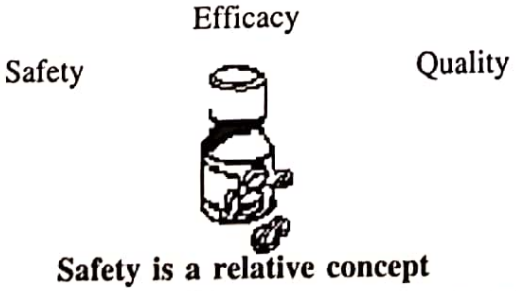
Pharmacovigilance is the science of collecting, monitoring, researching, assessing, and evaluating of current safety drug information from healthcare providers (primarily from spontaneous reporting), aiming the early identification of drug safety problems, their quantitative (frequency) and qualitative characterization (seriousness, severity, reversibility, mechanism and public health implications) and prevention of harm to patients (through the identification of risk factors and groups of risk and the implementation of regulatory actions toward risk management). Effective and open communication of safety information, supporting health education, is the final and challenging goal of pharmacovigilance.

No drug, which is pharmacologically effective, is entirely without hazard. There is no such thing as a safe drug. Safety is a relative concept, concerning the disease, the therapeutic alternatives and the individual perception and acceptance of risk.

Causality assessment of reported adverse drug events is crucial in pharmacovigilance due to its implications in benefit-risk evaluation of medicines.

No drug which is pharmacologically effective is entirely without hazard



Safety is a relative concept

One of the most difficult components of safety monitoring is the causality assessment of reported adverse events, named "imputation". Imputation does not prove a causal relation. It's a dynamic process of causal inference thorough continuous assessment of information considered on the differential diagnosis of an adverse drug reaction.

Why is causality assessment difficult?

It is a difficult process due to the complex nature of adverse event, multiple therapy and individual clinical variability. Additionally, the retrospective process of spontaneous report and its context of suspicion might be difficult and /or bias follow up and information collection.

Therefore one has to consider possible alternative explanations, and to weigh the probabilities of the AE being caused by them. The important alternative explanations include; a pretreatment condition, a new manifestation of the diseases being treated; a new interim disease, and any other drug(s) given concomitantly.

The following are associations that support causation linking a drug and suspected adverse reaction (adapted from Gehlbach 1993):

- Strength of the association
- Consistency of the observed evidence
- Temporality of the relationship
- Dose-response relationship
- Confounding factors

Strength of Association

If the odds are known and are very high for an observed event, e.g. gastrointestinal upset with aspirin, then the case is strengthened for causation.

Consistency of the Observed Evidence

When association between a drug & an adverse reaction has been demonstrated consistently over years of clinical practice, causality becomes more likely.

The closer the relationship of the administration

of the drug and the occurrence of the ADR, the more likely that the drug may be the actual cause of the reaction. However some adverse events may occur several weeks after the administration of the offending drug.

Dose –Response Relationship

Frequently, adverse events occur in relation to the dose being administered. The higher the dose of the drug, the more likely an ADR is a result of the administered agent. However, this is not always true as very low doses of some drugs, e.g., penicillin, can elicit serious anaphylactic responses.

Confounding factors

The minimization of confounding factors is important in determining causality. Confounding factors such as the administration of the other drugs, food, beverages can account for observed events. The existence of concurrent diseases and infections can also cause certain effects., making it difficult to distinguish them from the suspected drug . Environmental factors, such as air pollutants, weather conditions & exposure to allergens may play a role.

To examine the role of alternative explanations in a manner that would yield consistent conclusions with different evaluators, various algorithms have been proposed. None of the available systems has been validated, i.e. that they consistently and reproducibly give a reasonable approximation of the truth.

Algorithms are all supported by the combination of five common major criteria for causality assessment:

i) Previous general experience with the drug
ii) Any alternative cause
iii) An appropriate time sequence between administration of the drug and the onset of event
iv) Effect of withdrawal or decreasing the dose -dechallenge
v) Rechallenge if possible

WHO Causality Categories

(All points should be reasonably complied with)

Definite / Certain :

- Event or laboratory test abnormality with plausible time relationship to drug intake
- Cannot be explained by disease or other drugs
- Response to withdrawal plausible (pharmacologically, pathologically)
- Event definitive pharmacologically or phenomenologically
  (An objective and specific medical disorder or recognized pharmacological phenomenon)
- Rechallenge (if necessary)
- Probable / likely event or laboratory test abnormality with reasonable time relationship to drug intake
- Unlikely to be attributed to disease or other drugs
- Response to withdrawal clinically reasonable
- Rechallenge not necessary
- Possible event or laboratory test abnormality with reasonable time relationship to drug intake
- Could also be explained by disease or other drugs
- Information on drug withdrawal lacking or unclear
- Unlikely event or laboratory test abnormality with a time relationship to drug intake that makes a connection improbable (but not impossible)
- Diseases or other drugs provide plausible explanations
- Conditional / Unclassified event or laboratory test abnormality
- More data for proper assessment needed
- Or additional data under examination Unassessible / unclassified
  The database is not sufficient for evaluation and not available.

Three key questions relating to uncertainty:

- Can the drug cause the adverse reaction?

- Has the drug caused the adverse reaction?
- Will the drug cause the adverse reaction?

Four assessment criteria:

- The association in time (and place) between drug administration and event
- Pharmacology (features, previous knowledge of side effects)
- Medical plausibility (characteristic signs and symptoms, laboratory tests, pathological findings)
- Likelihood or exclusion of other causes

What causality assessment can do?

When there are several reports of adverse reactions to particular drug, causality assessment may lead to signal generation - a notice of the need for increased awareness of a possible safety problem communicated to countries.

This report may serve as a basis for decision-making by the regulator and the pharmaceutical company, for communication between national centers, and for the preparation of information for practitioners and in the published literature.

What causality assessment cannot do?

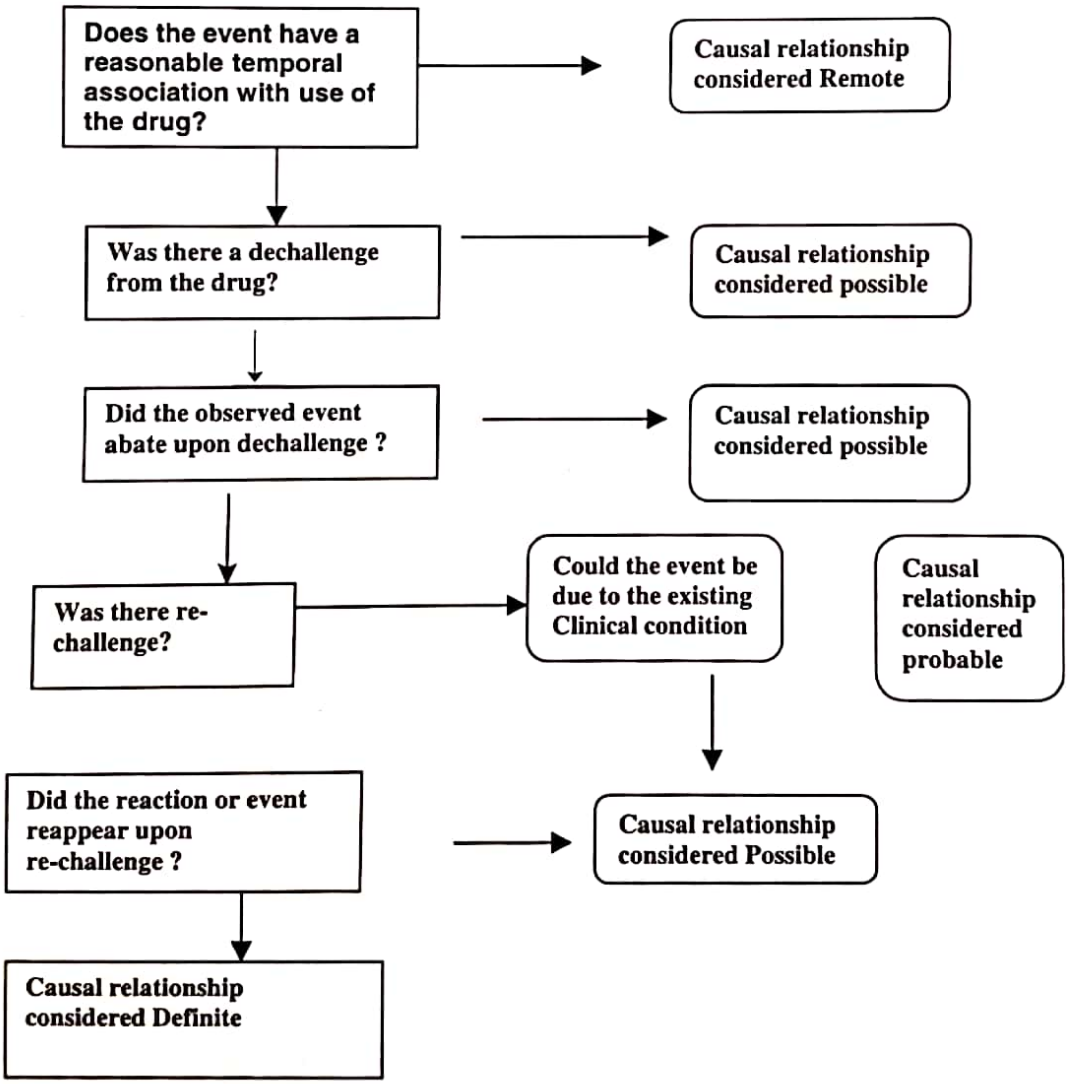
i.) Exact quantitative measurement of relationship likelihood

ii) Distinguish valid from invalid cases

iii) Prove the connection between drug and event

iv) Quantify contribution of a drug to the development of an adverse event

vi) Change uncertainty into certainty



ABSTRACTS OF THE RESEARCH PAPERS PRESENTED AT THE FIFTH ANNUAL CONFERENCE OF SOPI, AHMEDABAD

PZ1

A STUDY ON HERBAL DRUG INTERACTION INFORMATION: PHARMACOVIGILANCE IS NEED OF THE HOUR

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Objective: The aim of our present study is to assess the published clinical literature regarding interactions between conventional drugs and herbal medicinal products for appraisal of herbal drug interaction information available [From 1998-2005].

Method: An exhaustive search on Medline, Cam-PubMed, google search engine and J-gate.informindia was conducted using the search terms "herbal drug interactions, side effects, herb toxicities, adverse drug reactions, herbal medicine and clinical assessment. Almost all major reference texts, review articles and the bibliographies of all articles used were also searched. A 10-point scoring system assessed interaction probability. The scoring system, while not validated, helped to determine whether reports of herb-drug interactions contained reliable information. Reports received one point for each of the point marked as considered significant.

Results: The search of all listed sources produced about 100 cases of suspected, which were tabulated and categorized by herb, drug, other medications, signs or symptoms of interaction, mechanism, and report reliability score. While many, though not all, drug-drug interactions are well defined, it was stated that herb-drug interactions might occur more frequently due to the many pharmacologically active compounds present in most herbal products.Seventy-four cases (74 percent) were considered to contain insufficient information to evaluate (unevaluable), 14 % were classified as well-documented (likely), and 20% as possible.St. John's Wort was the herb most commonly implicated in interactions having major number of cases reported, of which the highest number of the cases were with the drug cyclosporine. Other Reports involving St. Jon's Wort were with oral contraceptives, warfarin, antidepressants, theophylline and loperamide. Warfarin was found to be the most common drug involved responsible for interaction with various herbs.

Conclusions: Despite a widespread use, Herb / drug interactions are a stark reality today. It is a world where much is still unknown. Knowing, that millions of patients take herbal and conventional medicine concomitantly, often without the knowledge of their physicians, and considering our present lack of understanding of herb-drug interactions, further systematic research in this area seems to be a matter of urgent concern and pharmacovigilance, a dire need of the hour.

PZ2

BANNED AND RESTRICTED DRUGS: WHAT DO THE PRACTITIONERS KNOW?

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Objective: In India National Pharmacovigilance Programme has been launched recently. Presently several banned or restricted use drugs are freely available and also prescribed by medical practitioners in India. Hence it was decided to undertake a study to assess medical practitioners knowledge regarding banned and

restricted use drugs.

Method: A questionnaire based study of practitioners belonging to different specialties was carried out in Ahmedabad to assess their knowledge and prescribing practices of banned and restricted use drugs.

Results: Of the 200 practitioners, 113 responded. Practitioners reported use of medical journals, print media, medical representatives and internet in descending order of frequency as sources of information regarding banned or restricted use drugs. Nimesulide and rofecoxib were the most frequently mentioned drugs as banned or restricted .The average number of banned drugs known to a doctor was 2.18.In response to the question regarding status of ban in Western countries and India, only 62% and 46% answered correctly for Nimesulide and rofecoxib respectively. The banned or restricted use drugs regularly prescribed by practitioners were nimesulide, phenylpropanolamine containing cough mixtures, loperamide, metamizol (Analgin) and iodochlor in descending order.

Conclusion: The study shows poor knowledge among medical practitioners regarding the status of banned and restricted use drugs. This could be due to lack of availability of sources providing such information. This ignorance can lead to their widespread use in general population.

PZ3

PHARMACOENONOMIC IMPACT OF CUTANEOUS ADVERSE DRUG REACTIONS RESULTS FROM THE REGIONAL PHARMACOVIGILANCE CENTER, WESTERN NEPAL.

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Introduction: The high mortality, morbidity and cost associated with adverse drug reactions (ADRs) represent an important public health concern. Cutaneous ADRs are the most common among ADRs with an incidence of 15 to 30% of total ADRs. The economic impact of cutaneous ADRs is unknown.

Objectives: To analyze the cutaneous ADRs reported to the Regional Pharmacovigilance Center, Manipal Teaching Hospital, to establish the causality, severity, preventability and to calculate their economic impact.

Methods: The filled ADR reporting forms received by the center from September 2004 till August 2005 were analyzed. Additional patient details were obtained from the medical records department.

Results: Fifty seven ADRs were reported (men 22 and women 35). The mean ± SD age distribution was 30.21 ± 17.89 years. Department of Dermatology encountered 22 (38.59%) of the total ADRs followed by Medicine 14 (24.56%). Antibiotics were responsible for 18 (31.57%) of the ADRs, followed by non-steroidal anti-inflammatory drugs [6 (10.52%)] and antiepileptics 4 (7.01%). Maculopapular rashes were reported in 18 (31.57%) of the cases followed by contact dermatitis [9 (15.78%)]. The causality assessment (Naranjo algorithm) revealed 47 (82.45%) ADRs were probably attributed to the suspected drugs. Fifty (87.71%) of the ADRs were Moderate (Level 3) [Modified Hartwig and Siegel scale]. Two (3.5%) of the ADRs could be definitely preventable (Schumock and Thornton scale). Fifty four (94.73%) patients were prescribed drugs for managing the ADRs with a total of 181 drugs (average 3.17 per patient). Antihistamines were used commonly [56 (30.93%)] followed by corticosteroids 53 (29.28%). The average treatment duration was 13±7 days with an average cost burden of 110.49 ± 99.16 Nepalese rupees (US $ 1.58 ±1.41) for drug therapy.

Conclusion: The cutaneous ADRs were associated with increased economic impact and early detection and prevention may be beneficial in minimizing the economic implications of the cutaneous ADRs.

PZ4

CONTRIBUTION OF MEDICATION COUNSELING CENTER TOWARDS CONSUMER SAFETY: EXPERIENCES FROM WESTERN NEPAL

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Introduction: Adverse drug reaction (ADR) results in increased health care costs, diminished quality of life, increased hospitalization and even death. The fundamental role of the pharmacist is to monitor, identify, resolve and prevent potential and actual drug related problems. Medication counseling deals with providing information to patients in layman's language with the ultimate goal of encouraging them towards safe and appropriate use of medications.

Objectives: To describe the contribution of the Medication Counseling Center (MCC) in Manipal Teaching Hospital (MTH), Pokhara, Nepal towards consumer drug safety.

Methods: The MCC of MTH provides counseling to patients as per the Omnibus Budget Reconciliation Act-1990. The details of counseling were documented in a self-developed medication counseling documentation form and the data of final quarter of 2004 were analyzed.

Results: Totally 229 patients were counseled, among which more than half were women and nearly one quarter of age groups 21-30 years. Majority (79%) were directed for counseling by the dispensing pharmacists. Patients from department of Otorhinolaryngology accounted for 57.2% of the total followed by medicine (32.3%), dermatology (5.2%), and eye (3.1%) departments and so on. The counseling pharmacist emphasized on the description of the medication in nearly all the patients (96.55%) followed by dosage form (96.1%), dosage (95.2%), routes of administration (94.3%), duration of therapy (90.4%), storage (78.6%), special direction (71.2%), refill information (63.8%), action to be taken in case of missed dose (61.6%), common side effects(44.5%), techniques and self monitoring (41.5%), respectively. About 6-10 minutes was dedicated while counseling 41.9% of patients. Nasal sprays were found to be mostly used (52%) counseling aids and nasal congestion (27.8%) was the major presumed diagnosis. Drugs related to respiratory system (38%) were counseled frequently.

Conclusion: MCC in hospital setup can play an active role to ensure consumer safety by imparting counseling to the patients.

PZ5

A STUDY OF EFFECTS OF ANTIHISTAMINIC DRUGS ON PSYCHOMOTOR FUNCTIONS AND MEMORY IN PATIENTS WITH SKIN DISORDERS.

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Conventional and newer antihistaminic drugs are widely used for various skin disorders. The cognitive and psychomotor adverse effects of these drugs have however been ignored. This study evaluates the effect of chlorpheniramine maleale (4mg BD). Cetirizine (10 mg OD) and desloratadine on psychomotor function and memory in patients suffering from skin disorders, using a simple battery of tests. Baseline (pretreatment) scores for psychomotor function using digit letter substitution test

(DLST), six letter cancellation test (SLCT), Finger tapping test (FTT) were determined. The P.G.I. memory scale was used to evaluate the memory. Patients (n=59) were reevaluated at seven days, one month and three months of treatment with antihistaminic drugs. It was observed that total scores on psychomotor functions and P.G.I. memory scale were decreased in the chlorpheniramine group as compared to the baseline scores. Significant decrease in mental balance, attention and concentration, immediate recall, visual retention, total memory score, DLST, SLCT and FTT ($p<0.01$) was observed during the study period. Patients in cetirizine group showed mild and transient decrease in scores for mental balance, attention and concentration; immediate recall ($p<0.01$) at the end of seven days, mental balance and attention and concentration ($p<0.05$) at the end of one month. Cetirizine also showed transient decrease in FTT at seven days and at 3 months of treatment. Patients in desloratadine group showed no significant change in scores for memory and psychomotor function during the study period.

Hence desloratadine produces no effect on psychomotor functions and memory, cetirizine produces mild and transient effects while chlorpheniramine produces impairment of memory and psychomotor functions.

PZ6

COMPARATIVE EVALUATION OF VARIOUS DEVICES USED DURING PERCUTANEOUS CORONARY INTERVENTIONS

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Objective: Distal embolism and restenosis are the phenomena that complicate the otherwise successful percutaneous transluminal coronary angioplasty (PTCA). In the present study we evaluated the usefulness of distal protection device (DPD) and the efficacy of sirolimus coated stent versus S_7 stent after acute coronary syndrome (ACS) in patients undergoing PTCA.

Methodology: 109 patients with ACS were divided into two groups: PTCA done using DPD and PTCA done without DPD. Patients having active significant bleeding, major surgery within previous six weeks or those having current participation in other trials using investigational drugs or devices were excluded. All patients without DPD required the administration of intracoronary (IC) adenosine and sodium nitroprusside to avoid no-reflow but in patients with DPD only 7.7% patients required IC vasodilators. In patients with DPD only 29% patients required the additional use of glycoprotein IIb/IIIa (Gp IIb/IIIa) receptor antagonists as compared to 100% usage in patients without DPD. On studying the MACE data it was found that amongst the patients with DPD no patient had either dysnea or needed repeat revascularization or urgent CABG. Amongst the patients without DPD four patients had angina and one had dyspnoea.

In another set of experiment 138 patients amendable for PTCA were divided into two groups. The conventional stent (S_7 stent) was used in 68 patients and the drug coated (CYPHER-sirolimus eluting) was used in 70 patients. Patients having active significant bleeding, major surgery within previous six weeks or current participation in other trials using investigational drugs or devices were excluded.

Results: In patients with cypher stent 40% patients required the usage of Gp IIb/IIIa receptor antagonists. Whereas, in patients with S_7 stent 45.7% patients required the usage of Gp IIb/IIIa receptor antagonists. On studying the MACE data it was found that amongst the patients with S_7 stent one patient had angina

and one patient expired due to cardiac reasons. Amongst the patients with cypher stent none of the patients had either angina or required revascularization but one patient died due to cardiac reasons.

Conclusion: We suggest that the use of DPD, although safe, effective and expensive modality, we however did not find any difference between S_7 and Cypher stent with respect to MACE.

PZ7

AN ANALYSIS OF SPONTANEOUS ADVERSE DRUG REACTIONS - REPORTED FROM CIVIL HOSPITAL, AHMEDABAD-

A THREE MONTHS' EXPERIENCE.

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Adverse drug reactions(ADRs) are responsible for 3-5% of hospital admissions and occur in 10-20% of hospital inpatients. They also contribute to morbidity and sometimes mortality. Some ADRs necessitate withdrawal of drug therapy. A continuous prospective ongoing Adverse Ddrug Event (ADE) monitoring is being carried at the Department of Pharmacology, B.J.Medical College. During a period of 3 months, 105 cases of ADEs were reported. The age of affected patients varied from 8 years to 80 years with mean age of 39.5 years. Male to female ratio was 7:8. The common causal groups of drugs in decreasing order of occurrence were antimicrobials, antiepileptics, antihypertensives, analgesics, antipsychotics, antidepressants, sedative and hypnotics, antiemetics and antidiabetic agents. Out of 151 suspected medications, 118 were oral medications while 33 were parenteral medications. The common reactions observed were skin rashes and pruritus, GIAE, giddiness, tremors, dystonia, headache and weakness. Altered laboratory tests were found in 13 patients. 48 patients required withdrawal of the drugs or their dose reduction. The adverse events abated completely in 40 patients. In 3 patients, the adverse event reappeared after reintroduction of the drug. 47 events were serious, requiring hospitalization or prolongation of hospital stay or were life threatening. Monitoring of ADRs and pharmacovigilance helps in early detection and management of ADRs. It also gives information about the incidence and prevalence of ADRs to a particular drug in the community.

OPA1

DRUG UTILISATION IN PEDIATRIC OUTPATIENT DEPARTMENT OF A TEACHING HOSPITAL.

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Objectives: To study the drug use pattern in pediatric outpatient department of a teaching hospital. To evaluate drug utilization based on W.H.O. Drug prescribing indicators.

Materials and methods: A prospective study was conducted for one year in pediatric outpatient department at Sheth V.S. General Hospital, Ahmedabad. The data was analyzed for drug use pattern with help of Anatomical Therapeutic Chemical (ATC) classification of drugs. W.H.O. core drug prescribing indicators were calculated.

Results:A total of 400 patients have received 1744 drugs. The average number of drugs per prescription was 4.36. Only 9% of the drugs were prescribed by generic names. Ten percent of the drugs were prescribed from hospital drugs list. About 46.5% of patients have received antibiotics. Vitamins (24%) was the most commonly prescribed drug group followed by antibacterials (11%), analgesics (11%) and antihistamines (10%). The diseases of respiratory system (57.5%) were most common

followed by infectious diseases (27%), nutritional diseases (8%), diseases involving genitourinary (2.5%) and digestive system (1.75%).

Conclusion: This study shows high incidence of polypharmacy in pediatric outpatient department, major contributors being vitamins and antibiotics. Moreover, greater tendency to prescribe drugs by brand names and outside the hospital drugs list is observed. Interventional measures to increase awareness of prescribers are desirable to promote rational prescribing.

OPA2

ASSESSMENT OF POTENTIAL DRUG-DRUG INTERACTIONS IN PRESCRIPTIONS RECEIVED AT COMMUNITY PHARMACY

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Potential drug-drug interactions (PDDIs) may be significant factors responsible for inpatient morbidity and mortality. PDDIs not only present a danger to the patient but may also have an influence on the health care costs. The assessment as well as prevention of PDDI is an important component in pharmaceutical care. Certain patient populations and patients with polypharmacy are at higher risk in developing PDDIs. The main objective of the study is to assess the frequency and severity of PDDIs in prescriptions prospectively collected at community pharmacy in Mysore city. All the prescriptions with two or more drugs were included in the study and reviewed for drug interactions using drug interaction software and standard text books. An effort is made to prepare PDDI guidelines with management strategies for the benefit of practicing community pharmacists. A total of 1686 prescriptions were reviewed and assessed for the PDDIs. 676 PDDIs were observed in 385 (22.83%) prescriptions analyzed, with frequency rate of 40.09%. Patients with one or more PDDIs used a significantly larger number of drugs than those without PDDIs, on average 4.56±1.29 versus 3.82±1.05 (ranged from 2-9 drugs). Among the prescriptions having 2-4 drugs about 15.28% prescriptions shown PDDIs, where as prescriptions having 8 or more drugs shown maximum incidence rate of PDDIs (94.44%). Among the total number of prescriptions with PDDIs, 55.82% prescriptions containing more than 4 drugs suggesting direct relationship between the number of drugs prescribed and the PDDIs (r=0.39). Out of 676 PDDIs, 13.90% were severe in nature. The results of present study showed a high frequency rate of PDDIs in prescriptions received at community pharmacy. Thus the study suggests that the community pharmacist shall be cognizant about commonly occurring, clinically significant PDDIs, and the skills to advise suitable management strategies when interactions occur.

OPA3

ROLE OF PRESCRIPTION AUDIT IN PROMITING RATIONAL DRUG USE AMONG HEALTH PROFESSIONALS

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Introduction: The assessment of drug utilization is important for clinical educational and economical purpose. The study of prescribing pattern is a component of medical audit which seeks monitoring, evaluation and necessary modification in the prescribing practices of prescribers to achieve rational and cost effective medical care. A very important and useful work of prescription audit has been taken up by department of pharmacology, Dr. Sampurananad medical college, jodhpur to

assess the present status of prescribing trends in tertiary care centers and to determine whether prescribing is pattern is based on the concept of rational therapeutics and to utilize the results in a evolving strategies for cost effective drug use.

Materials and Methods: Every month 50 randomly selected prescriptions were analyzed. In order to provide broad base to the cross section, prescriptions were collected from different hospitals attach to Dr. S.N. Medical college, Jodhpur. Prescriptions were obtained from different O.P.Ds and wards of main hospitals.

Each prescription was analyzed under following heads:-

1. Prescription format including number of drugs, doses, dosage forms, and duration of treatment.
2. Various drugs were classified according to the systems.
3. Antimicrobials were analyzed according to number single or fixed dose combination, nature and whether rational or irrational.
4. Prescriptions were segregated as single or multiingredient, oral versus parentral.
5. Analgesics and cough preparations were segregated as single or fixed dose combination and whether rational or irrational.

Observations : On analysis of prescriptions, many short coming were detected (eg. Unclear diagnosis, no mention of duration of treatment and dose and chances of interactions were noticed in some preparations. Most of the prescriptions had more than five drugs and most of the drug combinations prescribed were approved.

Conclusions: This campaign has left an impact and has helped the physicians to improve their prescription habits.

OPA4

TRENDS IN THE TREATMENT OF UPPER RESPIRATORY TRACT INFECTIONS: A SURVEY IN HISAR.

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In the present study, a survey was undertaken to determine the trends in the treatment of Upper Respiratory Tract Infections in infants and children. Considering the economic status of the patients and different geographical localities, 50 physicians (General practitioner- 38, pediatric consultants-12) in Hisar region of Haryana state were recruited for the survey. General practitioners were consulted because of less number of pediatric practitioners in the concerned region. A questionnaire was prepared on the line of treatment and the choice of drugs for the URTI. It was seen that most of the physicians initially start with cough and cold remedies for 2-3 days. If the disease still persists they prescribe antibiotics in majority of the cases. Amoxycillin and ampicillin were the most commonly prescribed drugs as 1st line therapy. The 2nd line therapy includes Cefadroxil and other antibiotics. Though certain toxic effects were associated with chloramphenicol but because of its good effects in URTI, the drug is being recommended by the physician in around 11% of cases. Sulfonamides were also prescribed but to a lesser extent because of the risk of hypersensitivity reactions. In case of viral infections antibiotics were prescribed to a lesser extent and the patient was treated with the antiallergics, decongestants etc. Multivitamin products were also prescribed in 90% cases along with antibiotic or antiallergic compounds. One group of physicians (about 58% of total), use to fair therapy for 3-5 days but other group of physicians (42% of total) extends the therapy upto 7 days. Use of corticosteroids was found

to be around 46% in all the cases. During the survey one point was also stated by number of physicians that the choice of drugs or dosage form in case of age group under consideration also depends on some additional factors along with the efficacy of drug. Among these are its palatability, ease of administration and the dosing frequency required for a particular drug.

OPA5

A STUDY OF PHARMACOECONOMICS OF ANTI-INFECTIVES IN AN INTENSIVE CARE UNIT IN A MEDICAL COLLEGE HOSPITAL OF NORTH INDIA

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Objective: The study was conducted to study Pharmacoeconomics of anti-infectives in an Intensive Care Unit (ICU), Department of Medicine of a Medical College.

Methods: Patients (n=54) admitted to ICU from November 2004 to January 2005 were included. Anti–infective agents were tabulated in a structured proforma and were analyzed to assess their pattern of use, rationale for start and subsequent stoppage, relationship to culture and sensitivity reports, investigations required as per recommendations and documentation of adverse drug reactions (if any).

Results: We reported as total encounters with anti-infective agent =184

Total no. of days anti-infectives administered = 8917

Total expenditure of all anti-infectives = 766681.58/-

Empirical use: 52

Evidence Based Medicine: 17

Adverse effects: 5 episodes (n=3)

The expenditure per patient for the use of each anti-infective agent was calculated to be Rs. 6807.24 for the use of cephalosporins, Rs. 2940.48 for the use of miscellaneous group of anti-infective agents (mainly teicoplanin), Rs. 2290.17 for the use of penicillins. The expenditure per day for the use of each anti-infective agent was also calculated to be Rs. 2400 for meropenam, Rs. 1011.37 for the use of miscellaneous group of anti-infective agents mainly Teicoplanin, Rs. 640.40 for the use of cephalosporins. Nitroimidazoles were administered for 2757 patient days, quinolones for 2175 patient days, penicillins for 1753 patient days.

Conclusions: The anti-infectives most commonly prescribed were from nitroimidazole, quinolone and penicillin groups. The expenditure per patient for all these anti-infectives was less as compared to the other group of anti-infective agents like meropenam. Meropenam was the most expensive drug among the anti-infectives and was minimally prescribed.

OPA6

PRESCRIBING PATTERN FOR MALARIA IN A TEACHING HOSPITAL: NEED FOR A CHANGE IN RECOMMENDATION OF NATIONAL ANTI-MALARIA PROGRAM?

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Objective: To evaluate prescribing pattern and cost-effectiveness of anti-malarial therapy used for indoor patients of a tertiary care hospital for clinically diagnosed cases of malaria and its comparison with National Anti-malaria Program recommendation.

Materials and Methods: All clinically diagnosed cases of malaria admitted in G.G.Hospital Jamnagar, during the period July

to December 2004 were subjected to peripheral smear examination. All smear positive cases were included in the study. Those smear negative cases responding to antimalarial therapy without additions of any other drug were also included. Patients were followed up till discharged from the hospital. All clinical finding were recorded in a pre-designed case record form (CRF). Analysis was carried out at the end of the study period using these CRF.

Observations and Results: 214 cases of clinically diagnosed malaria included in the study. Of these 112(52.33%) were smear negative and 102(47.27%) were smear positive. All smear negative cases responded to anti-malarial therapy only. They were afebrile within 24 hours. Of the 102 smear positive cases, 72 (70.59%) were of falciparum, 24(23.53%) were vivax and 6(5.88%) of mixed variety. Complications were noted (32.35%) only in cases falciparum or mixed infection. The commonest drugs prescribed for complicated falciparum malaria were quinine alone or its combination with other anti-malarial (41.81%). While in uncomplicated falciparum malaria chloroquine alone or its combination with other antimalarial were most common (67.46%). Among vivax and smear negative malaria intravenous infusion of chloroquine was found most common treatment which had not shown any better effect on afebrile day, average hospital stay and cost effective compared to oral chloroquine.

Conclusions: Complication are quite frequent in cases of falciparum malaria and since resistance in given cases cannot be assessed. A use of intravenous quinine or combination therapy appears justified.

Excessive use of intravenous chloroquine in vivax malaria and uncomplicated falciparum malaria does not seem justified. In an endemic zone smear negative malaria should be considered as an important disease entity.

OPV1

ADVERSE DRUG REACTION RELATED QUERIES RECEIVED BY THE DRUG INFORMATION CENTRE OF A TERTIARY CARE TEACHING HOSPITAL

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Objective: Accurate information about safety of drugs is very essential for health care professionals in identifying, preventing and managing Adverse Drug Reactions (ADRs), which thereby ensure safe use of medications. The objective of the present study was to assess the nature of queries related to ADRs received over a period of one year by the Drug Information Center (DIC) of Kasturba hospital, Manipal.

Methodology: Retrospective evaluation of the drug information (DI) queries received in the DIC over a period of one year (August 2004 – July 2005) was done for various parameters such as purpose and type of query, references used, drugs involved and incidence of the ADRs for which query was asked.

Results: Out of 724 DI queries received, 210 (29%) were related to ADRs. In majority (71.9%), the enquirer wanted the information immediately and was from Department of Medicine (73.3%). The information was sought for better patient care in 64.2% of queries followed by for updating knowledge of the enquirer (35.23%). MICROMEDEX system was used as the reference in answering most (69.04%) of the queries. Considering the type of query, majority (65.71%) were asked on identification of an ADR, followed by queries on incidence of a specific reaction to a drug (18.57%). Upon evaluation more number of queries was regarding common reactions (36.8 %) followed by rare (32.8 %). Drug class for which more number of queries was asked was

antiretrovirals (11.42%) followed by antimycobacterials (8.1%) and individual drug was cotrimoxazole (2.8%). Health care professionals utilized the information related to ADRs for better patient care and most for the queries were related to identification of an ADR.

Conclusions: Accurate and unbiased information on ADRs is very essential for health care professionals in rational prescribing and safe drug use.

OPV2

RETROSPECTIVE EVALUATION OF ADVERSE DRUG REACTIONS REPORTED OVER A PERIOD OF 12 MONTHS IN A TERTIARY CARE TEACHING HOSPITAL

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Objective: Pharmacovigilance is gaining lot of importance in clinical practice and is becoming an integral part of the same. Periodic evaluation of the pattern and incidence of ADRs occurring in hospitals is essential to improve safe use of medications. Present study was conducted to evaluate the pattern of ADRs reported in the ADR reporting unit of Kasturba Hospital, Manipal over a period of 12 months.

Methodology: Retrospective evaluation of the ADRs reported over a period of 12 months (March 2004 –February 2005) was done. Evaluation of the data for various parameters such as demographics of the patients, drugs involved, types of ADRs, etc was done. Individual ADRs were analysed for their causality, severity, preventability and predictability using standard scales.

Results: A total of 408 ADR reports were received during one year period. More number of ADR reports were in males (57.5%) and patients in the age group of 41-60 (34%). Greater number of reports for an individual drug was with phenytoin (6.3%) and the drug class was antibacterials (21.56%). Most common reaction observed was skin rash (7.84%) and the organ system most commonly involved was dermatologic system (18.62%). On causality assessment, 47.5% of ADRs were probably drug induced and most of them were of mild nature on assessment of severity. Majority (75.24%) of the ADRs were predictable and 24% were preventable. Drug dechallenge was done in majority (64.7%), while rechallenge was done only in 9%. Multiple drug therapy was a predisposing factor in 46.5% of reports.

Conclusions: Antibacterials were the drug class and dermatologic system was the organ system most commonly involved. Many of the ADRs were potentially preventable. Periodic evaluation and dissemination of ADR related data to the health care professionals helps in promoting safer use of medications in hospitals.

OPV3

CNS DEPRESSANTS/MOOD ELEVATORS INCREASE SODIUM RETENTION IN THE BODY.

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Objective: Most CNS depressants/mood elevators are associated with the adverse effects like constipation, oedema and weight-gain that lead to hypertension, obesity, restricted movements and confusion. The therapy with these drugs is usually long duration and most patients suffer from above symptoms and to avoid these, require co-therapy to reduce the above adverse effects. The co-therapy includes diuretics like *furosemide*, pro-thalidones, thiazides, potassium channel blockers etc.

Methodology: Experiment was carried out on 20 patients suffering from oedema, hypertension, obesity and restricted movements because of

long term use of CNS depressants/mood elevators. They were taken for observation: "Leg oedema was taken into consideration for virtual observation and loss of body weight was considered for the loss of total water from the body. Patients were given 20-40mg SOS *furosemide* daily at 8 am along with prescribed CNS depressants/mood elevators for 1 month and subsequent oedema and body weight were observed for the changes that have occurred due to subsequent treatments".

Results: It was observed that this produced as much as 80% improvement in body movement, correction of Blood Pressure and no oedema in legs. *Furosemide* is a well known diuretic that acts by lowering sodium in the body.

It may be concluded from the above findings that CNS depressants/mood elevators increase Sodium retention in body.

OPV4

INCIDENCE AND PATTERNS OF ADRS DUE ANTICANCER DRUGS IN CANCER PATIENTS OF A SPECIALIZED TEACHING CANCER HOSPITAL IN A SOUTH INDIAN DISTRICT

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Introduction: Shri Sridi Sai Baba cancer hospital and research center ia a 150 bedded teaching hospital of K.M.C. Manipal, this study was conducted in the medical oncology department. 145 patients received treatment with anticancer drugs, 95 patients received a total 495 cycles of chemotherapy, 50 patients received daily dosing anticancer drugs.

Objectives: The main objective of the study was to know the incidence and pattern of ADRs due to anticancer drugs in the patients of medical oncology department by evaluation of ADRs for causality, severity, preventability, predictability and predisposing factors.

Methodology: The data was collected by the investigator during ward round participation and attending at the out-patient department of medical oncology along with the oncologist and from patient's medical records by chart reviews and patient interview.

Results: A total of 385 ADRs were observed in 145 patients, total no. of patients who had atleast one ADRs were 114, 360 ADRs were seen in patients on cyclic chemotherapy. 25 ADRs were seen in patients on daily dosing medications. The average number of ADRs per visit was 0.74. ADRs per patient on cyclic chemotherapy was 3.7 while that on daily dosing was 0.5. A total number of 26 different anticancer drugs were used during the study. Females and the patient in age group 21-40 had more no. of ADRs Neutropenia was the commonest ADR followed by alopecia. The incidence of nausea, vomiting, Mucositis and constipation was low, Doxorubicin, cyclophosphamide and cisplatin were the commonest drugs involved in ADRs. NonHodgkin Lymphoma patients had the maximum no. of ADRs. Majority of the ADRs were of Type-A and Mild in severity. The majority of the ADRs were classified as probable according to Naranjo's acale and possible, by WHO scale. Majority of ADRs were predictable, 29% of ADRs were preventable, and in majority of ADRs multuiple drug therapy was a predisposing factor.

Conclusion: Anticancer drugs can lead to serious ADRs, 29% of ADRs were preventable and a clinical pharmacist needs to play an important role in management of ADRs for better and safer use of anticancer drugs.

OPV5

ANTICOLD FORMULATIONS ARE BENEFICIAL OR TROUBLESOME TO SOCIETY?

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Symptoms of common cold are treated symptomatically with existing rational combinations, that include anti-allergic agents (antihistaminic), antitussive, anti-inflammatory, antipyretic, bronchodilators and cough suppressants. Most favoured agents are chlorpheniramine maleate, cetrizine, phenylpropanolamine, pseudoephedrine, diphenhydramine HCl that are given alone or along with triprolidine, dextromethorphan, codeine phosphate, ambroxol and bromhexine HCl. For cough and cold, mixture of above agents with some bronchodilators like salbutamol, terbutaline etc., are usually prescribed. It is observed that most patients suffer from drying of nose and throat including thickening of sputum. This lead to increase in frequency of cough, inflammation in throat, congestion in chest, sedation, constipation and depression in motion.The selected combinations for experimental work were *chlorpheiramine meleate, dextromethorphan, ammonium chloride and menthol*. It was observed that out of 50 patients, 90% patients got relieved from cold, but 60% suffered from dry cough while 80% from dry nose, 62% dry throat, 35% lead to increase in frequency of cough, 28% inflammation in throat, 5% congestion in chest, 98% sedation, 24% constipation, 45% depression in motion. Out of them, 23% shifted to Ayurveda and Homeopathy.When Atarax (Hydroxyzine HCl) was given to 20 patients having common cold, the percent relief was 94%. Out of them, 34% suffered from dry cough, 23% dry nose, 34% dry throat, 22% increase in frequency of cough, 12% inflammation of throat, no complain of congestion in chest, 78% sedation, 23% constipation, 28% depression in motion whereas 15% patients shifted to Ayurveda and Homeopathy. Addition of Bromhexine HCl to Atarax was found to be more beneficial in treatment of cold and cough than chlorpheniramine maleate. It reduced the thickening of sputum and inflammation of throat by 12% and 8% respectively.Advertisement based self-medication and attitude of manufacturers to cover all symptoms in one formulation are hazardous to patients. Separate, need based medications are well tolerated by patients and having less side effects. So less shifting of modern medicine are more beneficial having minimal adverse drug reactions.

OPV6

ALTERED RESPONSIVENESS TO ATORVASTATIN DUE TO THE GENETIC POLYMORPHISM OF HUMAN LIVER CYP3A4 IN GUJARAT POPULATION

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Introduction: Cytochrome P450 (CYP) enzymes are important catalysts for oxidative biotransformation of both endogenous and exogenous compounds,including drugs.Genetic polymorphism of CYPs can lead to severe toxicity or therapeutic failure of medications. The subfamily CYP3A consists of four isoforms, CYP3A4, CYP3A5, CYP3A7 and CYP3A43. In man the CYP3A isoforms are the most abundant in the liver and accounting for about 30% of total hepatic P450s It is involved in the metabolism of more than 50% of clinically used drugs and also in the metabolism of endogenous compounds.The range of substrate specificity is broad and covers drugs from different therapeutic categories.

Material and method: Fourty-three subjects,were enrolled for the study. They were considered healthy according to standard physical examination and routine laboratory tests. They were not allowed to take any medications 1 week before or during the study

period. Alcohol, grapefruit and/or grapefruit juice were not allowed 2 days before or during the study period. They had to abstain from intake of a caffeine-containing diet from 16 h before drug intake and throughout the study. The Institutional ethics committee approved the study design. An oral dose of one tablet of Atorvastatin 40mg was administered to the subjects on the dosing day along with 240 mL of drinking water under the supervision of trained personnel.Samples were collected by a fresh clean venipuncture using a disposable, sterilised, syringe and needle from forearm vein.The post-dose samples were collected at 2 hr of the scheduled time and was stored at -20°C until analysed for atrovastatin and its metabolite ortho hydroxyatorvastatin and Drug: Metabolite ratio was estimated.

Result: The mean concentration of drug atrovastatin in blood after 2hr was 8.08ng/ml with SD of 4.19 and %CV of 51.8. The mean concentration of Ortho hydroxyl atorvastatatin in blood after 2hr was 9.20ng/ml with SD of 5.34 and %CV of 58 .Log drug: metabolite was estimated and it was plotted against frequency. It gave a curve which was not normal, signifying a polymorphism in the metabolizing capacity of the enzymes.

Conclusions: The population showed genetic polymorphism for Human CYP 3A4.

OPV7

LIPODYSTROPHY AN ADVERSE DRUG REACTION OF INDINAVIR

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One of reasons to withdraw drug treatment is the development of an adverse drug reaction. Highly active antiretroviral therapy (HAART) is no exception to this. Protease inhibitors (PI) based regimen of HAART is very effective in treatment of HIV infected patients. Lipodystrophy is a one of the adverse effects of PI. Indinavir was the first PI used in treatment of HIV. Lipodystrophy or fat maldistribution includes both fat accumulation and fat atrophy. Fat accumulation can occur within the truncal region leading to protruded abdomen known either "Crix belly" or "Protease Paunch", over the cervicodorsal fat pad region (Buffallo hump) and in breast tissues. Some patients show facial atrophy due to buccal fat loss and thin limbs. Laboratory investigations show increase in total cholesterol and triglyceride. Management of this patient is either a change to non-nucleoside reverse transcriptase inhibitor (NNRTI) based regimen of HAART or continuing same regimen but managing hyperlipidemia. A 41 years old HIV positive patient was on PI based regimen of HAART (Indinavir + stavudine + lamivudine) since last 3 years. Since last 12 months she noticed change in her body structure. On examination there was presence of buffalo hump, truncal obesity, facial atrophy and thinning of limbs. Investigations showed significant hypertriglyceridemia (448 mg %). Since the patient responded very well to HAART same treatment was continued including Indinavir with added fenofibrate for hypertriglyceridemia. The triglyceride levels decreased to 200 mg% after treatment but lipodystrophy was persistent. Lipodystrophy is an important adverse drug reaction due to use of Indinavir in long term management of HIV infection.

OPV8

STEVENS-JOHNSON SYNDROME: A SERIOUS ADVERSE DRUG REACTION WITH PRESCRIPTION AND NON-PRESCRIPTION DRUGS.

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Pharmacovigilance is intended to provide early detection of warning signals to minimize the occurrence and impact of adverse drug reactions. For the system to be effective, there must be early reporting of adverse drug events to minimize the morbidity and mortality associated with them. Stevens-Johnson syndrome is a life threatening adverse drug reaction (type B) caused by many drugs and needs to be reported immediately.In a prospective study being carried out over a period of 3 months, to report ADEs occurring in Civil Hospital, Ahmedabad; nine cases of SJ syndrome due to various drugs were detected. The sex ratio was 4:5 (M: F) and patients belonged to age group of 20 to 40 years. The patients presented with the complains of macules, papules and vesicles all over the body associated with fever, malaise and joint pain .The causal drug groups that were identified were antiepileptic drugs, cephalosporins, fluoroquinolones, antiretroviral drugs and co-trimoxazole. In two cases causative agents were not known, as they were OTC products. Though all the cases were severe enough to require hospitalization, no mortality occurred. Early detection of such ADRs can help to prevent the mortality and morbidity associated with them.

OPV9

PHARMACOEPIDEMIOLOGY AND ITS IMPACT ON THE ENVIRONMENT

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Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. Development of the system for ADRs reporting led to the development of science of pharmacoepidemiology. Pharmaco-epidemiology is the study of use and effects of drugs in terms of benefit & risk in large number of population. It is based on the application of the principles of epidemiology to drug use and effect. Modern pharmacoepidemiology as a science truly develop after sedative drug thalidomide disaster in early 1990s when several case reports of limb malformations (phocomelia) in offsprings of women were reported. The importance of pharmacoepidemiology is evaluated more so when we see the problem of ADRs. It occurs in 10-20% of hospital inpatients, accounts for 5% of all hospital admissions and 0.1% death of surgical inpatients. They adversely affect patient's quality of life, negative impact in the socio-economic environment and increases the costs of patients' care. Morever, it also causes patients to loose confidence in their doctors. The purpose of pharmacoepidemiological studies is signal generation, risk quantification and hypothesis testing. The present paper delved into the relation of ADRs and environment.

OPV10

ADVERSE DRUG EVENTS TO ANTIMICROBIAL AGENTS REPORTED AT B.J. MEDICAL COLLEGE AND CIVIL HOSPITAL, AHMEDABAD.

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Antimicrobial agents are the most commonly prescribed group of drugs followed by anti-inflammatory and analgesic drugs. About 100 million courses of antimicrobials are prescribed each year. On an out patient basis, more than 50% of these are prescribed for upper respiratory tract infections and lower urinary tract infections. Ampicillin, cloxacillin, ciprofloxacin and metronidazole are the most frequently used antimicrobial agents in the out patient departments. We report 46 Adverse Drug Events

(ADEs) from an ongoing Adverse Drug Events monitoring programme conducted by Department of Pharmacology, B.J. Medical College, Ahmedabad. These ADEs were reported over a period of 4 months. These adverse drug events occurred with anti retroviral agents, fluoroquinolones, cephalosporins, ampicillin, antimalarial agents, AKT and aminoglycosides indecreasing order of frequency. Commonly encountered ADEs were skin reactions (rash and itching) and GIAE (nausea, vomiting, diarrhoea, decreased appetite). Stevens Johnson Syndrome was reported in 3 patients. The common indications for prescribing antimicrobial agents in these cases were HIV infections, pyrexia of unknown origin, malaria, secondary infections after surgery, tuberculosis, urinary tract infections andasthma. Serious ADEs were reported in 16 cases. Early detection and reporting of ADEs helps to decrease their incidence and decreases the morbidity and mortality in the patients.

OPV11

TO COMPARE THE PATTERN OF DRUG RELATED PROBLEMS (DRPs) AND DRUG RELATED HOSPITAL ADMISSIONS (DRHAs) OF OUT-PATIENTS AND IN-PATIENTS WARDS OF THE MEDICINE DEPARTMNET IN KIMS HOSPITAL AND RESEARCH CENTER (BANGALORE)

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Objective: To compare the pattern of Drug Related Problems (DRPs) and Drug related hospital admissions (DRHAs) of out-Patients and In-Patients wards of the Medicine Department in KIMS Hospital and Research Center (Bangalore).

Material and Methods: Fifty subjects of DRHA and DRP aged between 18-80 yrs who had orally consented to participate in the study and had fulfilled inclusion and exclusion criteria from the department of medicine in-patients and out-patients were interviewed, their case sheets were studied and discussed in detail with respective physicians. The data was assessed by causality scales.

Results: DRPs (52%) were among age group of 40-60 whereas DRHAs (56%) were more in the age group of 50-80. 40% of DRHAs and 48% DRPs were having single diagnosis. DRHAs had 38% dose related therapeutic failure (DTF) and 50% of adverse drug reactions (ADRs). In case of DRHAs 68% were due to DTF & only 30% were due to ADRs. The reason for DTF for both DRHAs and DRPs was mostly noncompliance and normal side effects of the drug. The severity of the problem in DRHA was 68% where for DRPs it was only 14%. 100% of DRPs were predictable whereas 84% of DRHAs were predictable. 64% of DRHAs were preventable whereas 52% of DRPs were preventable. Multiple drug therapy was the main predisposing factor for DRHAs (52%) and DRPs (62%). Dose altered was most common given management for both DRHAs and DRPs.

POP1

ADVERSE EFFECT OF ARSENIC IN DRINKING WATER

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Arsenic has been recognized as a poison since ancient times. Understandably, the public may have concerns about low levels of arsenic found in some municipal water supplies and in some private wells. Arsenic is a natural element widely found in the earth's crust. There are trace amounts of it in all living matter. Arsenic may enter lakes, rivers or underground water naturally, when mineral deposits or rocks

containing arsenic dissolve. Arsenic may also get into water through the discharge of industrial wastes and by the deposition of arsenic particles in dust or dissolved in rain or snow. Data collected indicate that the levels of arsenic in Indian drinking water are generally less than 0.005 milligrams per liter, although concentrations may be higher in some areas.Arsenic in drinking water is absorbed by the body, with the bloodstream taking it to various organs. The highest levels are found in nails and hair, which accumulate arsenic over time. Your body gets rid of arsenic mostly through the urine with smaller amounts removed from the body through the skin, hair, nails and sweat.The International Agency for Research on Cancer considers arsenic a human carcinogen. Consuming drinking water that contains arsenic higher than the over a period of years has been found to increase the risk of skin cancer and tumors of the bladder, kidney, liver and lung.The present work reveals the adverse effect of arsenic containing drinking water, estimated of arsenic and steps taken to reduce the arsenic level in drinking water.

POP2

ACUTE AND SUBACUTE HEPATO-TOXOCOTY OF NIMESULIDE IN RAT

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Objective: Assessment of acute and and subacute hepatotoxicity of Nimesulide in growing and adult rats and its comparison with Ibuprofen.

Materials and methods: For evaluating acute hepatotoxicity, Nimesulide was fed as a single dose of 50mg/kg to growing rats (3 wk old). For evaluating subacute hepatotoxicity, Nimesulide was fed orally with dose of 50mg/kg to adult rats (3 month old No. 20) once a day for consecutively for 21 days to the same rats who were exposed to Nimesulide earlier. Extent of damage was studied by assessing biochemical parameters such as alanine aminotransferase (ALT), alkaline phosphatase, S. protein, S. albumin. Histopathological studies of the liver of the experimental animals were also done. Above parameters were further compared with a Ibuprofen (150mg/kg orally NO.20) treated group.

Results: In acute hepatotoxicity study of Nimesulide, S. protein level was decreased, no significant changes of other liver functions were noted in growing rats. Histopathological examination of liver shows congestion, degeneration, necrosis and fatty changes in few of the animals. In subacute hepatotoxicity study of Nimesulide, S. protein was raised and S. alkaline phosphatase was decreased, no significant changes of other liver functions were noted in adult rats. Histopathological examination of liver showed fatty change, degeneration, congestion, and fibrosis in few of the animals. During recovery phase, no significant changes on liver function in adult rats and histopathological examination of liver showed normal histological structure in 50% of the animals. When effect of Nimesulide was compared with Ibuprofen, there was no significant difference on liver functions during acute and subacute hepatotoxicity study. Histopathological examination of liver shows that Nimesulide produce more congestion, degeneration and fatty changes as compared to Ibuprofen in few of the animals.

Conclusion: If Nimesulide is used repeatedly and for longer period of time it may produce irreversible liver injury in few of the animals which is not reversed at least in 50% of animals even after stoppage of the drug for 10 days. As compared to Ibuprofen, Nimesulide produced more hepatic damage so Ibuprofen appears safer than Nimesulide. However more extensive studies will be needed to corroborate these findings.

POP3

LIPID & GLYCEMIC PROFILE OF TWO GROUPS OF DIFFERENT AWARENESS LEVEL – A COMPARATIVE STUDY

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Objective: Hyperlipidemia and hyperglycemia are an emerging risk factor for the development of coronary artery disease (CAD). This study was conducted to see the lipid profile and blood sugar level into two different healthy professionals viz. Engineering college staff and Primary school staff.

Design and Methods: Subjects were selected in a range of 35-55 years of age. Subjects were divided into two groups. Group1- Subjects working in Engineering college; Group2- Subjects working in primary school. Various parameters for lipid levels viz. total cholesterol (TC), triglycerides (TG), LDL-C, HDL-C, VLDL-C, atherogenic index (AI), fasting blood sugar (FBS) level were estimated.

Results: Group1 subjects showed TC (154 mg/dl), TG (93.5 mg/dl), HDL-C (95.6 mg/dl), LDL-C (60 mg/dl), VLDL-C (22.7 mg/dl), AI (0.865), FBS (82.6 mg/dl). Group2 subjects showed TC (145 mg/dl), TG (178.5 mg/dl), HDL-C (61 mg/dl), LDL-C (71.6 mg/dl), VLDL-C (33.5 mg/dl), AI (1.72), FBS (66 mg/dl).

Conclusion: It can be concluded from the present study that awareness towards health in terms of blood sugar level and lipid level is more in Engineering staff as compared to the Primary school staff.

POP4

PSORIASIS:-AN EPIDEMIC DISEASE

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Psoriasis is chronic, genetic, noncontiguous skin disorder that appears in much different form and can affect any part of the body including nail and scalp. Multiple genes are involved in producing the sequence of events those results in expression of disease. Complicating the picture still further is the probability that genes found to be associated with psoriasis may or may not cause psoriasis in the individual person depending on the activity of genes in relation to one another. Psoriasis may be of several types: plaque, pustular, erythrodermic, guttae psoriasis. It is also associated with psoriatic arthritis. Its treatment falls in the three categories: topical, phototherapy, systemic. Topical steroids are the mainstay of treatment for localized psoriasis. In the phototherapy the dermatologist are concerned with the regions of UV radiations 100-290nm. The systemic medication may be indicated by the extent or severity of the disease .The selection of therapy for the psoriasis is multi factorial. Psoriasis treatment also includes moisturizing creams and ointments, herbal extract, homeopathic treatment etc. The data collected by asking question from skin specialist doctors of several districts of Haryana, Uttar Pradesh, and Rajasthan.

The result shows that there is no sexual specification for disease to occur and number if patients are 5-7 per month. The only prescribed drugs are coal tar, salicylic acid preparations, topical steroids, psoralens and UVA and emollients. Winter is supportive for this disease to occur. The duration of therapy to suppress is 2-3 months as it is life long disease. This preview provides the suppression of psoriasis with treatments and therapies and future finding are greatly awaited.

POP5

AYURVEDA Vs ALLOPATHY

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Ayurveda "The science of life" is the oldest holistic alternative medicinal system from India in existence. It is said to be the world of medicine which include knowledge of herbs, foods, aromas, gems, colors, yoga, mantra, life style and surgery. Ayurveda is no longer just about jadi-bootis and obscure voids .It's big business with classy spas that cost a bomb. Bhasma's made of metal are very much useful and shows drastic effects . Ayurveda also include various aspects of medical sciences like month by month development of fetus and an entire section is devoted to discussion of the medicinal aspects of herbs diet and reversal of aging without any latest diagnostic equipments. It also offers methods of finding out early stages of disease that are undetectable by modern medical investigation. Ayurveda is spiritual science which suggests true health as healthy functioning of physical health, mental health, career, life purpose and spiritual relationship where as allopathic an approach is more physical and chemical. People are moving towards alternative measures for relief because it cheaper, natural, safe, general sold, and with absolutely no side effects. Allopathic medicines mainly consist of isolated herb ingredients which have potentially dangerous side effects unknown but in Ayurveda whole plant/herb is taken for the treatment. If an ealchi (cardamom) is given as it is then it is considered as Auyurvedic or unani medicine, but if it's tincture is prepared than it is called allopathic medicine. Ayurveda is important because it offers rejuvenation program and treatment for basic functioning of the body for e.g. panchkarma. It is concluded that in present era allopathy sometimes fail to recognize the outside situation and factors influencing the health leading to incomplete treatment of health hazards. Ayurveda in real sense offers complete cure and can be continued for longer time, which is restricted in modern medicinal system. The goal of Ayurveda is to balance body mind and emotion, so that spirit can express through outlines with this standardizations of Ayurveda is also necessary which should be in reach of common man and easy to use with full satisfaction. Ayurveda has to go in this direction to make health and peace available for every person.

POP6

RESIDENTIAL TREATMENT PROGRAMME FOR SUBSTANCE ABUSE AND PSYCHO-EMOTIONAL IN A STRESS FREE TROPICAL SETTING

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Residential treatment program for a small group of 12 clients, middle class, was conducted in a center situated in an urban area. Clients with either chemical dependency/alcohol abuse of average age 25 yrs were chosen for the workshop. Is the depression causing the addictive behavior or is the addiction causing the depression? We need to find out the root cause of their problem by uncovering & resolving it by opening up to therapeutic techniques designed to help them move on in their life in a positive, healthy and productive way. It's important to remove oneself from your addictive or destructive lifestyle and environment and focus on creating stress free environment. Drug and alcohol use can be extremely costly and take a negative effect on personal and family finances. This cycle must be stopped. Most people struggle in recovery with relapse, which unfortunately is a common occurrence. Preventing relapse is one of the most important aspects in the recovery. Why do so many people suffering from alcoholism, substance abuse relapse? This is the question that we have been asking ourselves for the last 40-50 yrs, with no concrete answers being provided. Focused measures such as Individual

Psychotherapy, Small Group Therapy, Spiritual Enlightment, Psychiatrist Consultation, Physical Examination and Laboratory Work, Reinforcement of Individual Talents & Abilities, Weekly Yoga & Daily Meditation, Self-Esteem building, Nutritional Counseling. The tropical setting rehabilitations center should have infrastructure facilities such as Comfortable living, Peaceful environment, Internet to communicate with family or business, outdoor sports like Swimming, Tennis, ability to prepare your own meals, Cable TV, a fully equipped work out room. While you are in treatment you will have time to focus on rebuilding your self-esteem and rediscovering your true nature. Scheduled aftercare program was conducted online, 24-hour supervision was provided for complete safety, seclusion and anonymity.

POP7

ADVANTAGES OF SOFT GELATIN FORMULATIONS OVER OTHER DOSAGE FORMS LIKE TABLETS OR HARD GELATIN

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CAPSULES IN TERMS OF ONSET OF ACTION AND BIOAVAILABILITY:

1. In a tablet formulation the number of excipients are numerous due to which the release of the active ingredients from the tablet matrix is hampered which ultimately affects the dissolution of the active ingredients in the body fluid and thereby affects bioavailability. In Soft Gelatin Formulation the number of excipients which are used are few in number and the active ingredients are present in a dissolved or slurry form which gives rise to quick dissolution in the body fluid and therefore faster onset of action and better bioavailability.
2. Clinical trials have also proved that when an active ingredient like Artemether (Antimalarial) is formulated with several excipients and filled into a hard gelatin capsule in powder form, its cure rate is only 35 %, Whereas the same Artemether when it is dissolved in oil and then encapsulated in soft gelatin capsule gives a cure rate of 95%.
3. For those active ingredients which are liquids at room temperature like Vitamin E, Cod Liver Oil, Vitamin A etc., the soft gelatin dosage form is so convenient that direct encapsulation is possible without adding any excipients.
4. For herbal extract which are semi solid in nature, soft gelatin is the preferred dosage form since they can be encapsulated directly without adding excipients and therefore the purity of the herbal extract is maintained.
5. The disintegration time of a tablet or hard gelatin capsule becomes more and more along with aging of the formulation. Therefore, the release of the active ingredient from a tablet or a hard gelatin capsule just prior to expiry is always less compared to a soft gelatin capsule, which has also undergone similar aging.
6. The gelatin which is used in soft gelatin formulation is of a special type which helps the capsule to disintegrate in the body fluid quickly and immediately release the active ingredients. Since the active ingredients are in a dissolved condition or semi dissolved condition, they quickly become soluble in the body fluid and thereby have a complete absorption.

POP8

SIGNIFICANCE OF VALIDATION IN PHARMACEUTICAL INDUSTRIES

Atul gupta[1], Navneet Kaur[2], Naveen Goyal[1], S.K. Shing[1] and D.N. Mishra[3]

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Validation is a process to establish by documented evidence to provide a high degree of assurance that a planned process will consistently perform according to the intended specified outcomes. Validation consists of Design Validation, Installation Validation, Operational Validation, and Performance Validation. Design validation ensures that the components selected will have adequate capacity to function for the intended purposes where as Installation Validation ensures that the selected components match with the desired specifications. Operational Validation provides evidences that all the components of a system or equipment operates as specified and it involves testing of all interacting controls and any other indications of operation and functions. Performance Validation describes the procedures for demonstrating that a system or pieces of equipment can consistently perform and meet required specifications under routine operations and where appropriate under worst case situations. For Validation in pharmaceutical industries, run the process according to standard operating procedures three times and record all the required data and compare this data with the accepted criteria and deviation if any, must be recorded and justification for acceptance, if any, must be mentioned. Conclusion should take into account individual as well as the results of three consecutive validation runs. Approval and acceptance of the report by Quality Assurance (QA) must meet all specification.

POP9

ANALYSIS OF BLOOD TRANSFUSION REACTION

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Transfusion reactions are the main complications of blood transfusion, which could negate the effects of transfusions and their benefits. By minimizing the risk of reactions occurring during blood transfusion, one can improve quality of life of the recipient. This study is a small step in the direction. The objective of this study was to find out the indications of blood transfusion, analysis of blood transfusion reactions, their management and methods suggested to minimize the reactions. It was a retrospective study conducted in KIMS hospital Bangalore over a period of one year from April 2004 to March 2005, based on data"s of blood bank statistics and transfusion reaction forms. Out of 2486 recipients, 31(1.2%) cases if transfusion reactions were reported. Maximum was from age group of 36-50(29%) years with a slight preponderance in females (67%). Who were found to be suffering from anaemia (68%) and operative (32%). These reactions were non hemolytic febrile type of reactions (58%) and allergic/anaphylactic reaction (42%), which was controlled by using antihistamine, antipyretic, diuretic and hydrocortisone. The majority of patients were receiving blood for the first time (93%) and type of blood given was whole blood (97%). Blood groups commonly affected were O group (42%), B group (39%), A group (16%) and AB group (3%). Maximum cases of reactions were observed after 30 min to 6 hours (94%) of the blood transfusion. As the majority of blood transfusion reactions were found in females suffering from anaemia this can be prevented by decreasing the blood transfusion and going for treatment with drugs, if not responding then go for blood components supplements.

POP10

PHARMACOVIGILANCE IN INDIA: AN URGE TO IMPLEMENT SPONTANEOUS ADR REPORTING SYSTEM – WITH SPECIAL REFERENCE TO YELLOW CARD SCHEME.

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Objective: Protecting and Promoting public health and safety by implementing schemes like Yellow card Scheme for reporting of Adverse Drug Reactions (ADR) in India.

Pharmacovigilance deals with early detection of rare Adverse Drug Reactions and responding risk benefit issues arising with newly marketed drugs. Adverse Drug Reactions account for 5% of hospital admissions & as per recent study, most of them are predictable but rare types are unpredictable. For example, it is necessary to collect data from 6,000 patients in order to detect an ADR with an incidence of 1 in 2,000.Clinical trials are usually limited predictability for such rare and unexpected ADR reporting. After thalidomide tragedy, in 1965 United Kingdom's CSM(Committee on Safety of medicines) established Yellow card scheme and since then it has become one of the major International Pharmacovigilance resources. It involves reporting of suspicions drugs from General physicians, Pharmacists and even from patients and all suspected reactions to newer product are marked with "Inverted Black Triangle symbol in British National Formulary". Thus it is helpful for generating "SIGNALS"— hypotheses that particular drug may cause particular ADR. This scheme has been found to be extremely useful in detecting both rare and common ADRs, also it is relatively inexpensive compared to all other Post Marketing Surviellence tools— using ADROIT (Adverse Drug Reaction Online Information Tracking)

Conclusion: Seeing the present Indian Scenario its certain that Pharmacovigilance has just touched the stage of infancy & there's a desperate need for its extensive growth, so that it can reach to every corner of the Health Care System. And that will be a very difficult task especially in a country like India. But we have to start now and shoulder the responsibilities if we aspire a bright future of Indian Health Care.

POP11

ORPHAN DRUGS – VISION OF CLINICAL PHARMACIST

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Orphan drugs, essential for the treatment of persons with rare diseases, generally are unprofitable for manufacturers to develop and market. People with orphan diseases are often the victims of triple trouble. First the disease is often so rare, it takes a very long time before a proper diagnosis can be made & might also be misdiagnosed as common similar diseases. Secondly, even after a proper diagnosis has been reached, probably the physician in charge has not enough knowledge about the effects of or experience in treating it according to the state of art. Finally if a patient is lucky enough to find physicians with the specific knowledge, they often do not have the means to treat the disease because of the lack of proper medication. Even if the area of concern for orphan diseases can be identified by the pharmaceutical industry, they are very hesitant to invest in research and development (R&D) of orphan drugs as the chances of recovery of the invested amount is questionable. Most of the time, the demand for such drugs is so slight that the R&D costs will never be recovered, let alone the impossibility of realizing any profit from it. Post-marketing surveillance systems for detecting rare, serious, unexpected ADRs are helpful in reducing medical errors but in this case it is much difficult

because of lack of epidemic data. Answers to above difficulties are feasible task. One possibility is making Government policies for encouraging development & manufacturing orphan drugs. The Orphan Drug Act, 1983 in U.S.A. has worked very well. Such amendments must be made for every country for welfare of mankind. Institutions like National Bureau of Economic Research & private organizations like Institute for OneWorld Health are turning accessible therapy dreams for rare diseases into reality. Secondly, introduction of home-testing kits has made easier diagnosis for rare diseases, like phenylketonuria as that in case of diabetics & hypertensive patients. Computerised physician order entry (POE) with decision support has been successful in reducing medication errors such as dose errors, frequency errors, route errors, substitution errors and allergies. We don't need ideas but the right attitude which will make our implementation of plans regarding an affordable & accessible orphan drug therapy in a positive way so that we can come with flying colours.

POP12

POLYPHARMACY: TOO MUCH OF GOOD INTENTIONS

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Objective: Reducing the unnecessary polypharmacy in elderly patients by better councelling.Polypharmacy is the unwanted duplication of drugs, and often results when patients go to multiple physicians or pharmacies. Typically, polypharmacy occurs when prescribed medications duplicate or interact with each other. However, it may also include:

- Ø Dosages that are too high or too low
- Ø Medications incorrectly prescribed or filled
- Ø Herbal medications interacting with physician-prescribed medications.

Polypharmacy can lead to adverse reactions and drug interactions, hospitalisations and other adverse outcomes. It is a particular concern for older adults, who make up 13% of the population but account for almost 30% of all prescribed drugs. Studies indicate that more than one third of older patients had experienced adverse reactions to their medications, resulting in clinic or emergency room visits.

In many conditions, especially in the common area of cardiovascular diseases, we are realising that polypharmacy is becoming a part of management. Patients with ischaemic heart disease, heart failure, or diabetes may well end up on an antiplatelet agent, statin, ACE inhibitor, and other antihypertensives as well as agents specific to their primary condition. Also in the treatment of psychopharmacological disorders polypharmacy has been proven to be more effective than single drug therapy.

Conclusion: Polypharmacy is many times beneficial but often results in fatality. so, the issue is not how to reduce it ,but how to reduce unnecessary polypharmacy. That can be done with the active participation of clinical pharmacist and the physician.

POV1

EFFECT OF BRAND ON THERAPEUTIC EFFICACY: A SURVEY IN HISAR REGION.

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A survey was conducted on personal contact with different prescribers, patients and retailers from district Hisar, Haryana with the help of selected questionnaire to study their views about effect of different brands of therapeutic efficacy

of a drug. Total study was done with 32 prescribers, 145 patients and 30 retailers. 81% prescribers agreed with concept that reputed brand has better efficacy. Almost all (91%) agreed with the concept that there is no difference in therapeutic efficacy amongst the brands of reputed companies. However, 34% prescribers change the brand only to satisfy the patient's psychology. About 41% prescribers select the brand because of the reputation and services provided by the pharmaceutical company while 78% prescribers select the brand on the basis of experience with particular brand. 93% of patients consider that brand has effect on therapeutic efficacy while only 7% patients were ready to take other brands at economical prices. The study on retailers shows that 53% of retailers consider importance of brands while other has opinion that there is no difference of therapeutic efficacy between brands of same drug. The study thus highlights the view of people about the different brands of same drug.

POV2

FODR: A NEW PAPER AND PENCIL TEST FOR PSYCHOMOTOR PERFORMANCE IN HUMAN BEINGS

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Aim: To evaluate Four Option Digit Response (FODR) – a new mathematical test of psychomotor performance in normal human volunteers.

Material & methods: The study was carried out in 22 normal human volunteers of either sex. Reliability was evaluated by test-retest method on short term (24 hours) as well as long term (2 months) basis. To test the validity, the volunteers were randomly divided into three groups. Drugs used were placebo (PLC) Po, Chlorphrniramine maleate (CPM) 4 mg PO and Caffeine (CAF) 250 mg PO. All the three groups received all the three treatments at 2 months intervals in a cross over fashion e.g. Group A received PLC after control session on Day 1 followed by 2 test sessions at 90 and 150 minutes. The same group received CPM at 2 months and CAF at 4 months. The results were pooled and the data analysed to evaluate the validity of the test.

Statistical methods used: Short term and long term reliabilities were computed by using Pearson's coefficient of correlation (r). To compare the pre-drug and post-drug sessions, paired t-test was used.

Results: The test demonstrated good short term as well as long term reliability. CPM significantly increased mean FODR scores at 150 minutes. PLC and CAF significantly increased mean FODR scores both at 90 and 150 minutes.

Conclusion: FODR differentiated between PLC and CPM. It appears to be a promising addition to paper & pencil tests of psychomotor performance. If the results are duplicated, it can also be utilized to study the effects of CNS depressants on normal human volunteers as well as patients receiving CNS depressant drugs.

POV3

PROPER SELECTION OF DRUG FORMULATION CAN AVOID ADVERSE DRUG REACTIONS.

A. Roy, A. P. Mehere, M. K. Kale, D. K. Vithalani, S. M. Bhattacharya.

The case study is presented here. Aspirin is prescribed as anti-clotting agent in some cardiac and paralytic disorders. The oesophageal paralytic patients were selected as subjects for experimentation. These patients had main complication of engulfing. The patients were treated with *Ecosprin (an enteric coated Aspirin)* from last few days, which was administered in

the crushed form through rile's tube.During the case study patients were complaining of severe stomachache and blackish abnormal stool colorations. The authors after monitoring the patients advice the physician, and ask the physician to shift treatment from *Ecosprin (An enteric coated Aspirin)* to *Dispersible tablets Aspirin.* The further examination after few days revealed that the stool was of normal colour and the patients were relieved of gastric pain and irritation (stomachache).Thus, the proper selection of drug formulations and sound consultation of pharmacists can prevent Adverse Drug Reactions.

POV4

PHARMACOVIGILANCE AND CLINICAL STUDY OF SOME POLYHERBAL ANTIDIABETIC FORMULATIONS IN NIDDM PATIENTS.

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Objective: A large numbers of polyherbal formulations (PHFs) are available and being prescribed Nation wide even by registered doctors for diabetes mellitus. The objective of the present investigation was to evaluate various polyherbal formulations available in the market and study the effect of Mersina.

Design and Methods: Pharmacovigilance study was done using pretested questionnaires and interviews with patients (100), physicians (100) and pharmacists (35). Four districts Sabarkantha, Banaskantha, Mehsana and Gandhinagar in the north Gujarat region were selected for the study. Questionnaires forms for physicians included questions like whether they would like to prescribe herbal drugs with allopathic drugs or herbal drugs alone, which ayurvedic preparation would they like to prescribe more. Clinical study was conducted in 30 NIDDM patients. It was an open, multicentric clinical study based on parallel group design. 15 non-diabetic healthy persons were selected as control they were not taking any kind of herbal or allopathic drugs. 15 diabetic patients patents taking only allopathic drugs were selected as standard. Patients of either sex with mild to moderated diabetes mellitus were selected as test for the study. Patents were excluded from the study if their age was above 70 years, had complicated hypertension, severe diabetes (> 450 mg / dl). All the patients were randomized to PHFs (1gm/ day) for 3 months.

Results: Data revealed that 70 % doctors prescribed PHFs as an add-on therapy with allopathic drugs due to minimum adverse effects. It was found that 65 % patients were taking herbal antidiabetics with out prescription due to less control by allopathic drugs alone in the disease. Patients were taking frequently herbal products as home remedies in more than 80 % of total sales of PHFs were without prescriptions.Treatment with PHFs add-on produced a significant decrease in blood sugar level ($p < 0.05$) as compare with the changes indicate in patients groups taking allopathic alone. However, PHFs did not produce any significant change in triglycerides, LDL, HDL.

Conclusion: This study reveals that ayurvedic antidiabetics are being used more as add-on drugs with little scientific basis. Most of PHFs of antidiabetics are sold with out physicians' prescriptions from the ayurvedic or general medical stores.Mersina study was found to produce beneficial effects on blood sugar.

POV5

A REVIEW ON THE CONCEPT OF PHARMACOVIGILLANCE –ADVERSE DRUG REACTIONS DISCUSSION IN AYURVEDA.

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In the presentation author has tried to introduce the learned gathering about the less spoken

aspect of ADR discussion & concept of Pharmacovigillance as discussed in Ayurveda. Author has taken efforts to discuss concepts about the aspects regarding ideal drug, ideal therapy as discussed in Ayurveda. Also gives examples of certain known side effects of wrongly processed, ill-purified herbomineral drugs. Author also mentions certain common side effects of certain commonly used herbomineral formulations, tentative reasonings for getting these kinds of ADRs, possibility of safety or otherwise regarding usage of Ayurvedic drugs along with Modern medicines. As we are aware Ayurveda can be considered to be the most ancient traditional system of medicine. There are lots of myths about the safety of Ayurvedic drugs. It has been thoghtover that they are completely safe, no work or references are available on their adverse effects. There are question in the minds of modern medical practisioners with regards to their safety profile. Contamination with heavy metals & many related aspects. Aspect regarding starting co therapy of Ayurvedic drugs with modern drugs, about their possible drug interactions. All these aspects will be discussed in the said paper.

POV6

PRESCRIBING TRENDS IN PAEDIATRIC PATIENTS

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Objective: To analyze current trends of prescribing practice in pediatric patients and thus to identify drug utilization irrationalities in local hospitals. Prescribing drugs in children is an important skill, which needs continuous assessment for rationality of pharmacotherapy

Material & Method: The present study was conducted in the month of March 2000. Children aged between 6 months to 15 years of both sex attending pediatric OPD of S .N. Medical College, Agra & other local Hospitals included in the study. 250 prescriptions were randomly collected and analyzed. The total number of drugs prescribed in these 1250 prescriptions were average number of drugs per prescription was 5. The percentage of commonly used drugs were-Multi vitamins/ Liver tonics/ Digestive enzymes/ Proteins–53%, Antimicrobials- 48%, Antituberculars 18%,Antipyretic/ analgesics-25,ORS/ Anti diarrheal- 11%,,Corticosteroids-22%,Topical application- 7%,Cough expectorant/ syrup & bronchodilators 7%, Antiemetic-6%,Antispasmodic-5%, Alkalizer – 2%,Muscle Relaxant-2%,Anticonvulsants-2%.

Observations: The study reveals that overall drug utilization in children is too high. Average child takes about 3to 7 drugs. Some children are taking higher doses than recommended especially of anti- microbials and vitamins/tonic/ liver tonic/digestive enzymes/protein preparations. Use of nutrients are encouraged by prescribers however use of antiepileptics remained stable.

Analysis also revealed that polypharmacy was commonly practiced. Attempts to make necessary changes in the prescribing habits seems to be indicated. Future prescription audits in different specialties will allow a more comprehensive study and promote rational prescribing practice.

POV7

PHARMACOVIGILANCE IN CONTROLLING THE MENACE OF SPURIOUS DRUGS IN THE INDIAN SCENARIO

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Drugs are essential components in the healthcare of public, so, the quality of drugs is of paramount

as there are consumed mostly by the ailing patients. The circulation of spurious drugs is of great concern to everybody i.e., the drug industry, regulators, medical profession and the general public. The spurious drug company is becoming well established in India. According to W.H.O. 2001 statistics, 35% of the world's spurious drugs are produced in India. Even when spurious drugs do not endanger life, they can leave the patient seriously ill and those with inadequate potency do bigger harm to the society in general. Drug resistance develops when patients consume drugs with inadequate potency forcing them to look for costlier new generation drugs. Unlike other cases where the consumer knows his intent, the spurious drug industry thrives on consumr's ignorance, lack of stiff penalty for indulging in such activity and finally on lax regulatory system. Packaging is so nearly perfect that distinguishing a spurious drug from a genuine one is almost impossible. In the meanwhile the consumers can become more proactive by possible factors contributing to proliferation of spurious drugs are lack of enforcement of existing laws, weak penal action, very remunerative trade, availability of improved printing technology that helps counterfeiting, lack of coordination between various agencies, lack of control by importing and exporting countries. The suggestions to solve the above said problems is by creation of adequate infrastructure, creation of intelligent cum legal wing in state and zonal office, Monitoring of drugs through supply chain management, Proper control on the sllirf dupply industries and transporters, Exemplary punishments, at par with punishments under Narcotic and Psychotropic Substances, training manpower in investigational skills and foremost is to bring in an awareness and Pharmacovigilance at the pharmacist's level.

POV8

PHARMACOVIGILACE STUDY ON BRAND NAMES OF DRUGS.

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There are plenty of lacunae in the chain process of drug sale. Illiteracy rate, chemist shop being managed by matriculate boys who fill in for the mandatory pharmacists, illegible writing of most doctors, chemist known to substitute drugs under various pretexts, absence of crosscheck with doctors. Fierce competition among pharma companies making the choice of brand names appear like a big game on this comfort zone of drug sale chain process. The manufacturer to launch the drug first usually walks away with the name closes to pharmacological generic name. Some pick up words from dictionaries and twist a little to get catchy name, manufacturers as well as government agencies seems to get carried away by the names "creativity", that the needs of the patient for whom the drug is forgotten. About 8000 brands are available in the market which are similar looking are similar sounding. (TIBITOL/ TOBITIL)-(PRONIL/PRONIN)-(ELTOCIN/ ELTROXIN). These pairs of drugs are for diametrically different illnesses – Anti TB drug/ pain killer. Pharmacompanies launch one antibiotic with much fanfare and once it becomes popular, they launch a chemically different drug with same name, with the addition of just an alphabet, syllable, suffix or prefix. (TAXIM/TAXIM-O)- ANTIBIOTICS. We do frame rules and regulations copying from western countries, but unfortunately the implementation always seems unheard off. National network opines, all painkillers similar to VIOXX are under scrutiny. After making

public, the ban, we still find sale of drugs such as CELECOXIB, PARECOXIB, VALDECOXIB by appropriate labeling changes. There is valid reason for major concern among the prescribing physician, dispensing pharmacist, since the ultimate consumer – the patient, ends up bearing the loss. Hence there is a definite need to insist by the Drug Controller on the manufacturers to register afresh the confusing brand names of Drugs.

POV9

ADVERSE REACTION TO VACCINE IN PEDIATRIC IMMUNIZATION

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Objective: To detect the apeearance of adverse events following immunization.

Material & methods: It was descriptive study in which 200 baby, who attended immunization in the department of pediatrtics OPD, K.I.M.S. and who fulfilled inclusive and exclusive criteria, were studied for adverse reaction following immunization. The data was sourced from Childs case note, immunization record book, Childs parent or guardians interview etc. Pediatrician and clinical pharmacist identified the type of adverse reaction based on their diagnosis and judgement.

Result: Out of 200 subjects 37.5% of children experience adverse events. 60% of adverse events were pyrexia and 20% were inflammation. Most of the adverse reaction (56%) were seen only for a day. DPT vaccine showed more number of adverse reactions then any other vaccine. Most of the pyrexia and inflammation subsided by Paracetamol treatment. Adverse events in only 2.5% of children lead to hospitalization.

Conclusion: The adverse reaction though mino may create a negative opinion in the mind of the parent. But the risk of non-vaccination is very high, hence clinical pharmacist should play an important role in education and counseling the mothers, which may improve the rate of immunization.

THE CONCEPT AND PRINCIPLES OF THE PHARMACOVIGILANCE IN RATIONAL DRUG THERAPY OF UNANI MEDICINE

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Unani Medicine, which is an ancient system of medicine and more commonly practiced in Indian subcontinent, has an age-old concept and principles of rational drug management. They are cheap and used by majority of population. Some of Unani Medicine as a holistic approach. Study of Unani Medicine in relation with drug safety and quality assurance is thus imperative. The concept of 'Temperament' (Mizaj) and 'PulseExamination' (Moain-e Nabdh) in diagnosis and therapy, selection of drugs according to their 'Ptency' amongst 4 degrees (Darjat-e Advia), Use of 'Correctives' (Tadbir) & other traditional 'Procedures' to minimize toxicity on the basis of 'Temperament of Drugs' and its impact in minimizing side-effects and Use of 'Substitutes' (Abdal al Advia) for better efficacy and cost-effectiveness are the main concern for rational drug management in Unani Medicine. Various rules and procedures must be taken into account to avoid any obnoxious effects before the start of treatment by Unani Drugs.

Despite the above precautionary measures. Some cases of ADRs are still being reported due to some reasons or the other like mis-identification (pharmacognostic reasons), substandard quality, spurious and counterfeit drugs availability. The increase in reports reflects a rising awarencess that these natural products may also cause harm. ADR reporting systems for traditional medicines particularly from developing countries must be generated. The paper will discuss about the concept and principles of ADR monitoring and procedure to avoid ADRs.

Low Molecular Weight Heparin (LMWH)

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Introduction:

Low molecular weight heparin (LMWH) has emerged as an effective agent for prophylaxis of deep vein thrombosis, the harbinger of pulmonary – with relatively lesser risk of bleeding and independent of laboratory control. These are fragments of unfactionated heparin (UFH), obtained by chemical or enzymatic depolymerisation of the polysaccharide chains. These are hetergenous in size and their mean molecular weight is about 1/3rd of the heparin, ranging from 2000-15000 (4500-6500 doltorns) The pentsaccharide sequence in LMWH binds anti thrombin III and possess few longer 16-saccharide for binding to thrombin. Hence their thrombin inactivating capacity is lesser than their selective catalising capability to inhibit factor Xa by ant thrombin III. Activity of LMWH is expressed, therefore, as units of anti Xa activity, that varies in different commercial preparations in the range of anti Xa to anti IIa ratio from 4 to 2:1 unlike UFH where ratio is only 1:1. This is responsible for a decreased risk of bleeding for equivalent with Xa activity. This is important to note that anti Xa action is required for anti thrombotic activity and anti IIA . Activity is associated with bleeding. LMWH being as effective as standard activated partial thromboplastin time (APTT) monitored heparin, when given intravenously. It is becoming popular for convenience and simplicity in administration, but for price factor. (1-6)

Pharmacokinetics:

LMWH differs from standard heparin (UFH) both in pharmacokinetics and mechanism of action. Because of lower affinity to bind to plasma proteins and to endothelial cells, it results in more predictable plasma levels. Hence LMWH has an advantage of better bioavailability and pharmacokinetics to lower dosage, ranging from 90-100% as compared to UFH which is 15-20%given subcutaneously.

Factor Xa bound to the platelet membrane in the prothrombinase complex is resistant to inactivation by UFH but not resistant to LMWH. LMWH has features like higher bio-availability, reduced plasma clearance longer half life and lesser variability in anti coagulant response from person to person. (7-8) LMWH has lower affinity for von wile brand factor, (9) increase vascular permeability and has weaker effect on platelet function. This results in higher bioavailability of the anticoagulant response. Long half life permits once a day subcutaneous administration. Thrombocytopenia is less common as compared to UFH. (10, 11)

Although LMWH is obtained from standard heparin by gel filtration, chromatography or differential precipitation of ethanol, it demonstrates greater antithrombotic effect as compared to UFH possibly due to greater anti factor Xa effect. LMWH administered for maintenance dosage significantly improved objective measures of venous heamodynamics as well as subjective assessment of symptoms. Certain antithrombotic activities in plasma (anti Xa, anti IIA)can be easily measured, while archeological effect modulating fibrinolytic system and interaction with cellular components (platelets, leucocytes) are only partially measurable. (12) Comparison with UFH are shown in the table I.

Table I A

Property		LMWH	UFH
a)	Mean Molecular weight	5000	15000
b)	Mean saccharide units	15	45
c)	Anti coagulant property (ratio of antifactor IIa activity)	2-4	1
d)	Binding property		
	1) Plasma proteins and vascular wall matrix proteins	Minimal	Marked
	2) Macrophages and Endothelial cells	Minimal	Moderate
	3) Binding to platelets	Minimal	Moderate

Table I B

Comparison of features LMWH and UFH

Feature	LMWH	UFH
S/c absorption	+ + + +	+ +
Bioavailability	➢ 90%	35%
Half life	100-360	30-60 (Dose dependent)
Clearance	Renal	Renal after a saturation phase by endothelial binding
Co-factor	Anti thrombin III	Anti thrombin III
Binding to endothelium	Weak	+ + +
Plasma protein		
Platelet inhibition	+	+ + +
Inhibition by plasma factors	+	+ + +
Inhibition of bound factor Xa	+	+ +
Bleeding complications	+	+
Antigen city	Increased	Minimal
Vascular permeability	Can occur	Common
Transient increase in liver enzymes	Lesser incidence	2-4%
Thrombocytopenia		

Various preparations are available and almost 1-1/2 dozen of preparations are trying hard to come in the market. Being Biochemically and pharmacologically different their clinical drug responses too, are different in different individuals. Few preparation and their advantages and disadvantages are listed in Table II-IV.

Table- II (27)

Comparison of various LMWHs

LMWH	Mean Molecular weight	Anti activity (IU/mg)	Xa Anti Iia activity (IU/mg)	Ratio anti Xa/IIa
Dalteprin	5000	1222	60	2.0
Enoxaprin	4800	104	32	3.3
Nadroparin	4500	94	31	3.0
Tinzaparin	4500	90	50	1.8
Clivarine	3900	130	40	3.3

Table-III

Advantages of LMWH

1. Easy therapeutic dose adjustment
2. Laboratory control not required, and predictable response.
3. Lesser indene of throinbocytopenia.
4. Minimal osteoporosis in case of prolonged administration.
5. Potential for OPD treatment of proximal vein thrombosis.
6. Improved bio availability of anti coagulant response and prolonged half life reduces number of injections because of
   a) Inactivate factor X, bound to platelet membrane.
   b) Potent anti thrombotic effect due to greater anti factor Xa effect.
   c) Less binding to platelet factor 4, other plasma proteins and endothelial cells.
7. Lesser incidence of bleeding complications because of lower affinity for von will brand factor, weaker effect on platelet function and increase in vascular permeability.

Table-IV

Disadvantages of LMWH

1. Cost
2. Inability to reverse quickly
3. In high risk patients with unstable angina less effective due to no endothelium binding and no effect on platelets.
4. Multiple compounds.
5. Thrombotic rebound on discontinuation (because of inability to inhibit clot-bound thrombin)
6. Rarely spinal hecatomb (during spinal or epidural anesthesia). (28)

Indications of LMWH:

(1) Venous thromboembolism:

(A) Prophylaxis: Patients at risk especially post surgical, are given LMWH for prevention of deep vein thrombosis (DVT) and pulmonary embolism (PE), since post operative thromboembolic complications are known to occur in 10-70% of cases. Significance of use of LMWH as prophylaxis has been realized in immobilized medical patients and pre and post operatively to prevent DVT, LMWH and UFH can prevent deep venous thrombosis in legs in general and orthopedic surgery in 26% & 57% pulmonary emboli in an effective ratio of 10% to 6% respectively, without any difference in bleeding complications. (13-16) Prophylaxis is initiated usually 2 hours prior to surgery a practice consistent with the peak anti Xa activity

that is attained 2-4 hours after administration. In low risk patients of (developing DVT), a single LMWH 3200 IU is given 2 hours before surgery, followed by repeat injection every 24 hourly for seven days. In high risk cases (major orthopedic surgery), LMWH is given once or twice daily for 10 days. A however, no convincing evidence has been found by starting preoperative LMWH therapy in lowering the incidence of venous thromboembolism. Even perioperative regimens, if found to lower the risk to post operative thrombosis, the risk of increasing post operative major bleeding also increased simultaneously. (17. 18) In chronic phlebopathic syndromes, a single dose is given for 6-8 months.

(B) LMWH in the management of venous thromboembolism:

Both LMWH and UFH are effective in the treatment of deep vein thrombosis. LMWH has been found to reduce recurrent thromboembolism in 44% of cases and reduce lung embolism in 48% of cases in a meta analysis, thus reducing mortality in these cases. Initial dose of 1 mg/kg 12 hourly in acute venous thrombosis, can be reduced to 0.8 mg/kg/24 hourly for long term management. In case of pulmonary embolism. 0.5 mg/kg/intravenous initial dose is followed by 2-3 mg/kg/day continuous infusion for 10 days is suggested. Current recommendations include LMWH in a dose of 175 anti Xa-U/kg/24 hrs once daily. Even out Patients treatment with LMWH over preference to UFH or proximal venous thrombosis is being evaluated, since complications like bleeding, thrombocytopenia etc. are quite less with LMWH. (19)

(2) Phlebo pathies & other related syndromes

LMWH such as parnparin has been effective in chronic venous insufficiency (20)

(3) LMWH in CAD & arterial thrombosis:

Significance is being attached to LMWH in these areas of therapeutics. In stable (AI), exercise capacity has been found to be enhanced with LMWH, possibly because of enhanced functions. (21-22) Ischemia also decreases by 30% and exercise tolerance improves by 62%. In unstable angina & non Q infarction, LMWH has been tried in FRIC (Fragmin in ischemic coronary syndrome) with FRISC (Fragmin and risk of ML & death). In Acute myocardial infarction, incidence of mural thrombi has been found to reduce, without significant reduction in infarction rate. (23, 24) Use of LMWH is being evaluated in all patients of arterial occlusion. It has to be started as early as possible, along with other modalities such as angioplasty, stenting or surgical revascularization. (25, 26) Intravenous bolus followed by continuous infusion is preferred over intermittent bolus injections. Higher doses are however, complicated with bleeding. Rate of rest enosis after PTCA may be 50% lesser as compared to those on aspirin.

Haemodialysis & shunts:

Thrombosis in haemodialysis and extra corporeal shunts can be prevented by LMWH, as it helps in maintaining the patency of prosthetic conduits used during arterial repair. LMWH is preferred over UFH as the latter can aggravate hyperlipidemic in patients on haemodialusis

(4) Acute ischemic stroke:

Thrombosis in haemodialysis and extra corporeal shunts can be prevented by LMWH, as it helps in maintaining the patency of prosthetic conduits used during arterial repair. LMWH is preferred over UFH as the latter can aggravate hyperlipidemia in patients on haemodialysis.

(5) Acute ischemic stroke:

LMWH is safer and more effective than UFH as it allows these patients to achieve better functional outcome & with lesser Neurological deficient.

(6) DIC:

In a dose of 75 U/kg/day, Fragmin has been

successfully used in patients of
DIC associated with thrombosis.

(7) Anti phospholipids Syndrome:

LMWH is useful in preventing recurrence in APL syndrome when used
Intermittently by subcutaneous route.

(8) In pregnant patients, with metallic prosthetic valves, LMWH can be used safety By subcutaneous route in 1 st trimester.

(9) Inhalation therapy with LMWH is being explored in cardiopulmonary areas. Improvement in lung functions in patients of allergic asthma when LMWH is inhaled is being explored.

Long term management of atherosclerotic lesions does foresee the role of LMWH. LMWH inhalation has been able to inhibit coronary and peripheral atherosclerosis and can become part of long term management of these disorders. Drug interaction, indications and contraindications are given in tables V and VIA, B.

Table V

Drug interactions and adverse effects of LMWH

1. LMWH is similar to UF Heparin but has a very low incidence of adverse reactions.
2. Complications like major bleeding are significantly low.
3. Heparin induced thrombocytopenia is less (but can occur due to cross-reactivity).
4. Diagnosis of myocardial infarction pulmonary embolism or liver disease may be hindered as interpretation of I. FT may be affected due to (reversible) induction of transaminasers by LMWH.
5. (Reversible) ccsinophilia may occur.
6. Metabolic acidosis and hypoaldosteronism can occur.
7. Uncommon adverse effect includes lipolysis and osteoporosis.
8. Hyperkalemia may be precipitated.
9. Concomitant use of nitroglycerin infusion may decrease the effect of LMWH, possibly through alteration in AT III molecule.
10. Bleeding risk is increased when LMWH is co administered with drugs like aspirin, NSAIDS, coumarin derivatives and dertrax.

Table VI A

LMWH: Contraindications

1. Haemorrhagic diathesis
2. Hypersensitivity
3. Renal and hepatic failure
4. Peptic ulcer
5. Cardiovascular accident

Table VI A

LMWH: Indications

1. Deep vein thrombosis and pulmonary embolism.
2. Acute myocardial infarction, unstable coronary syndrome, chronic stable angina and coronary angioplasty and stenting.
3. Femoropopliteal bypass grafting
4. **Ischemic stroke.**

Conclusion:

LMWH has emerged as prophylactic therapeutic tool in medical and post surgical thrombotic disorders. It has become the preferred choice over UFH for convenience of dosage and independence of laboratory testing. It is being evaluated in treating the established cases of thrombosis and in preventing the post angioplasty occlusion and reclusion. It offers an opportunity in managing proximal vein thrombosis in OPD cases. Prophylactic once a day dose and twice a day dosage for therapeutic actions with minimal adverse reactions and not requiring regular laboratory controls have brought LMWH on forefront. Recently few Indians reports have appeared. Nevertheless, high cost is a major disadvantage at present; especially for the patient's population of countries like India. At the same time, it must be kept in mind that properties of a particular LMWH should not be applied in general to all LMWHs since all LMWHs are not same.

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Books and other Monographs:

Personal author(s): Ringsven MK, Bond D. Gerontology and leadership skills for nurses. 2nd ed. Albany (NY): Delmar Publishers; 1996

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