Topic: Study of Pharmacovigilance related drug

Propogol

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ABSTRACT

Pharmacovigilance, defined by the World Health Organisation as 'the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem' plays a key role in ensuring that patients receive safe drugs. Our knowledge of a drug's adverse reactions can be increased by various means, including spontaneous reporting, intensive monitoring and database studies

KEY WORD :- Drug regulation . Drug safety. Intensive monitoring . Pharmacovigilance . Spontaneous reporting . Transparency

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- ❖ **CLINICAL RESEARCH**
- ● **DEFINE AND PHASE OF CLINICAL TRIALS:**
- ➢ **DEFINITION**:

Clinical trials are prospective biomedical or behavioural research studies on human participants designed to answer specific questions about biomedical or behavioural interventions, including new treatments and known interventions that warrant further study and comparison.

- ➢ **PRECLINICAL TRIALS**
- ● **INTRODUCTION**

Details of non-clinical/per-clinical studies are discussed under ICH m3 guidance.

The Non-clinical study recommendations for the marketing approval of a pharmaceutical product include: safety pharmacology studies repeated dose toxicity Studies toxicokinetics and non-clinical pharmacokinetic studies reproduction toxicity studies and genotoxicity studies.

A Typically both In vitro and In Vivo tests will be performed Studies of drug Toxicity includes which organs are targeted by that drug, as well if there are any long term Carcinogenic effects or toxic effects causing illness.

- ● **PHASES OF PRECLINICAL TRIALS**

1) **SAFETY PHARMACOLOGY** :-
The core safety Pharmacology study includes the assessment of affect cardiovascular, central nervous, respiratory the consideration is given to an any in vivo valuation as addition to general toxicity. Care should be taken to reduce number of animal used

2) TOXICOKINETIC & PHARMACOKINETIC STUDIES:-
In vitro metabolic data for animals and humans & expose data in animals to prior initiating human clinical trials. Further absorption, distribution, metabolism and excretion in animals should be available for treading long duration.

3) :- ACUTE TOXICITY STUDIES:-

This information has been obtained From single dose toxicity studies in two mammation species using both the clinical and parenteral route of administration.

4) RESPECTED DOSE TOXICITY:

In principle the duration of animal toxicity studies conducted in two mammals species.

5) LOCAL TOLERANCE STUDIES:-

To evaluate local tolerance by the intended therapeutic bouts as a part of the general toxicity studied. To support limited human adm by non-therapeutic rough.

6) GENOTOXICITY STUDIES:-

An assay for gene mutation is generally considered sufficient to support all single dose clinical development trials.

7) CARCINOGENICITY STUDIES:-

It should be conducted for the marketing application.

For pharmaceutical development treat certain serious diseases for adults paediatrics patients carcinogenicity testing.

8) REPRODUCTIVE TOXICITY:-

It is Should be conducted as appropriate as the population that is to be exposed. There are four categories: women not of child bearing, women of child bearing in pregnant women.

9) OTHER TOXICITY:-Non-clinical study eg. Identify potential biomarkers

➢ **CLINICAL TRIALS**

- **INTRODUCTION**

The clinical trials are the Research studies performed in the people that are aimed at evaluating medical, surgical or behavioural intervention that is called clinical trials.

The evolution of the modern clinical trial dates back at least to the eighteenth century. Lind, in his classical study on board the Salisbury, evaluated six treatments for scurvy in 12 patients.

One of the two who was given oranges and lemons recovered quickly and was fit for duty after 6 days. The second was the best recovered of the others and was assigned the role of nurse to the remaining ten patients. Several other comparative studies were also conducted in the eighteenth and nineteenth centuries. The comparison groups comprised literature controls, other historical controls, and concurrent controls.

PHASES OF CLINICAL TRIALS

1 .PHASE 0:-

The Phase-0 trials are the exploratory trials that also exist as small clinical trials that involve dosing at a sub-therapeutic level.

Therapy area-any indication

Dosage -sub therapeutic dosing

Trial length -usually Less than one week

It involves 10 to 15 patients

2.PHASE 1:-

Phase 1 trials are the first studies of an investigational new drug in humans.

Phase 1 trials may be conducted in individuals who have the disease the drug is intended to treat.

The Phase-1 has a duration of 1 month to 12 months.

Phase 1 generally involves between 20 to 30 patients.

3.PHASE 2:-

Phase 2 clinical trials tense detector more about how safe the treatment is and now will it work Doctor also test whether a new treatment works for a specific cancer.

It is approximately 33% of drugs.

The duration is 12 to 24 months.

It involved no more than several 100 patients.

4.PHASE 3:-

The main objective of phase 3 is to verify the therapeutic action of a new substance in a large number of patients to determine the risk /benefit reaction.

The duration is 1 to 4 years.

It has 300 to 3000 volunteers involved.

5.PHASE 4:-

A type of clinical trials that studies the side effects caused over time by a new treatment after it has been approved and is a market this trious 100k side effects that were not seen in earlier trials that may study how well a new treatment works over a long period.

Its duration is a minimum of two years.

It involves several thousand volunteers who have the disease.

- **FUNCTION OF DRUG CONTROLLER GENERAL OF INDIA (DCGI)**

DCGI lays down the standard and quality of manufacturing, selling, import and distribution of drugs in India.

- Preparation and maintenance of national reference standards.
- To bring about uniformity in the enforcement of the Drugs and Cosmetics Act.
- Training of Drug Analysts deputed by State Drug Control Laboratories and other Institutions.
- Analysis of Cosmetics received as survey samples from CDSCO (central drug standard control organisation)
- **With the notification of Medical Device Rules 2017 by the Government of India, DCGI** will also act as Central Licensing Authority (CLA) for the medical devices which fall under the purview of these rules. Out of four Classes of medical devices from Class A to Class D, DCGI will be the direct licensing authority for Class C and Class D devices, whereas it will coordinate licensing for Class A and B devices through State drug controllers, who will act as State Licensing Authority or SLA.

- **FUNCTION OF CENTRAL DRUG STANDARD CONTROL ORGANIZATION (CDSCO)**

Under the Drug and Cosmetics Act, the regulation of manufacture, sale and distribution of Drugs is primarily the concern of the State authorities while the Central Authorities are responsible for approval of

New Drugs, Clinical Trials in the country, laying down the standards for Drugs, control over the quality of imported Drugs, coordination of the activities of State Drug Control Organisations and providing expert advice with a view of bring about the uniformity in the enforcement of the Drugs and Cosmetics Act.

➢ **TYPES OF REGULATORY APPLICATION:**

- **INVESTIGATIONAL NEW DRUG (IND)**

A drug that has not been approved for general use by the food and drug administration but is under investigation in clinical trials regarding its safety and effectiveness first by clinical investigators and then by practising physicians using patients who have given informed consent to participate.

- **DURATION**

30 days an IND application may 90 into effect 30 days after FDA receives the application unless FDA notifies the sponsor that the investigations described in the application are subjected to a clinical hold or on career notification by FDA that the clinical investigations in the IND may begin.

- **NEW DRUG APPLICATION (NDA)**

The identify and contact information of the sponsor and the phase of the trials. A commitment that an IRB will be responsible for initial and continuing review of The trials. The name of the drug is a list of its active ingredient and its dosage and route of Administration. The objective and planned duration of the proposed clinical trials. Identities and qualifications of all investigators

- **DURATION**

Submission of an NDA is the form step asking the FDA to consider a drug for marketing approval. The FDA has 60 days to decide whether to file it so it can be reviewed.

- **ABBREVIATED NEW DRUG APPLICATION (ANDA)**

AN abbreviated new drug application ANDA contains data which is submitted to FDA for the review and potentially approval of a generic drug product. Once approved an applicant may manufacture and market the generic drug product to provide a safe,effective,lower cost alternative to the brand name drug it references.

- **DURATION**

This act also premises brand name companies to apply for exclusive patient right to cover their new drug for up to 5 years.

❖ ***GOOD CLINICAL PRACTICE***

- **ICH-GOOD CLINICAL PRACTICE**

➢ **QUALITY DATA+ETHICS=GCP (GOOD CLINICAL PRACTICE)**

GOOD CLINICAL PRACTICE COVER THE STEP

1) **DESIGN**
2) **PERFORMANCE**
3) **MONITORING**
4) **AUDITING**
5) **ANALYSIS**
6) **REPORTING**

➢ **OBJECTIVE**

Facilitate the mutual acceptance of clinical data across ICH GCP region. Avoid trial duplication of clinical data across ICH GCP region. Protect the patient. To Provide a uniform standard for the European Union (EU) Japan Unite. States to facilitate mural acceptance of clinical data by the authorities in jurisdiction.

Avoid duplication (saving time, money , resources). Facilitate global submission through acceptance of data. Technical requirements for medical products containing new.

➢ **SCOPE OF GCP**

- Good Clinical laboratory should be used in all laboratories where tests are done on biological specimen diagnosis patients care for disease cannol.
- Microbiology and serology
- Haematology and blood banking
- Molecular biology and molecular pathology
- Clinical pathology
- Histopathology

➢ **KEY CHANGES IN 2019,NEW DRUG AND CLINICAL TRIALS RULES**

- In new rules 2019,such research has been defined to include studies on basic applied and operational research or clinical research designed primarily to increase scientific knowledge about disease and conditions, their detection cause and evolving strategies for health promotion, prevention or amelioration of disease and rehabilitation but does not include CT.
- The study type include:-
- In vitro diagnostics performance testing for research.
- New surgical intervention.
- Assisted reproductive technology (ART)
- Public health survey
- Epidemiological health survey
- Observational and non-interventional study of old drug

➢ **ACADEMIC CLINICAL TRIALS**

- New rules 2019 described academic clinical trials as clinical trials of a drug already approved for a certain claim and initiated by any investigators, academic or research institutions for a new indication or new dose or new dosage forms.
- Some important points for academic clinical trials include.
- Only for approval Drug
- CT initiated by investigators at an academic or research institute can be conducted for new indication, new route, new dose or dosage forms result only for academic or research.
- EC can seek clarity from century licensing authorities and CLA must respond in 30 days medical management.

➢ **ETHICS COMMITTEES (ECS)**

- As delineated in the 2019 CT rules and additional resource India has a neutralised process for the ethical review or clinical trials application and requires ethics committee FC approval for each trial site.
- Because there is no National EC in the country ECS are based at institution/organisation or function independently and must meet the requirements set forth in the 2019 CT rules and the ICME guidelines.
- Ethics committee topic authorising body subtopic for registration requirements is for BCS that over clinical trials is ECS that monitor biomedical and health research studies are also required to comply with the 2019 CT rules and the FCMR guidelines.

➢ **EC COMPOSITION**

- The 2019 CT rules and the ICMR guidelines state that an EC should appoint from among member hair people and a member secretary.
- The other members should represent a balance of affiliated and non affiliated Medical/non medical and scientific/non scientific peoples including the lay public.
- As per the 2019 CT rules and the ICMR guidelines preferably 50% of the members should also be non affiliated or from outside the institution.

➢ **AS PER THE 2019 CT RULES AND THE ICMR GUIDELINES THE COMPOSITION SHOULD INCLUDE THE FOLLOWING:**

- CHAIRPERSON from outside the institute
- One to two clinicians from various institutions

- Legal experts or retired sudge
- One philosopher / ethicist / theologian
- One lay person from the community
- Member secretary
- One member whose primary area of interest is non scientific
- Represent the scientific patients group as much as possible based on the research area requirements.

➢ **POST MARKETING SURVEILLANCE STUDIES**

Such studies are conducted with a new drug under approved conditions of its use and with scientific objectives approved by CLA.

➢ **ADVISED TO CHECK WITH CDSCO IF TRULY OLD DRUG:**

There is an expectation that the number of phase 4 studies being conducted in India will increase. This expectation is based on the assumption that with local clinical trials waiver a phase 4 study might need to be conducted except in special situations.

➢ **ORPHAN DRUG REGISTRATION**

2019 rules defined orphan drug as a drug intended to treat a condition which defects not more than five lakh people in India.

Provision for fast track approval process and special status for orphan drugs including a complete fee waiver for CT feeling.

Provision for expeditious review process.

Provision for waiver of local clinical study of phase 4 on satisfaction of CLA.

➢ **POST TRIAL ACCESS**

New rules 2019 defined post trial access as marking a new drug or investigational new drug available to a trial subject after completion of clinical trials through which the said drug has been found beneficial to a trial subject clinical trials for such period as considered necessary by the investigator and the ethics committee. These drugs should be free of charge upon approval of the ethics committee.

How long post trial access of medicine should be provided to patients?

How are safety signals monitored for this period? Should the sponsor/ethics committee have responsibilities to record and report safety issues after study competition?

➢ **OTHER SIGNIFICANT UPDATES**

Conditions for gene ratings stability data have been revised for drug substances and formulations intended to be stored under general condition for long term from zone IV (A) to zone IV (B) stability data conditions have been revised as per zone IV(B) for long term from 30°C ± 2° / 65% RH ± 5% RH to 30°± 2° / 75° RH ± 5% RH. Me

New clinical trials approval time lines also have been included for the clinical trials of drugs developed outside of India; there is a 90 working day limit of the CLA to responses

❖ **CONCEPT OF PHARMACOVIGILANACE.**

- **DEFINITION, OBJECTIVE, TYPES AND COMPONENTS OF PHARMACOVIGILANCE**

➢ **DEFINITION**

Pharmacovigilance is the science and activities relating to the detection assessment, understanding and prevention of adverse effects or any other medicine vaccine related problems for patients safety.

➢ **OBJECTIVE**

Improvement of patients Career Safety in relation to the use of medicines with medical and paramedical interventions remains to be an important Parameter.

The main objective of Pharmacovigilance involves exhibiting the efficacy of drugs by monitoring their adverse effect profile for many years from the lab to the pharmacy! Improving tracking and drasting effect of drug Improving public health and Safety in

Relation to the use of medicines uncovering the safe rational and cost effective use of drugs.

Promoting understanding edvatio and clinical training in pharmacovigilance and effective communication to the generic public.

In addition providing information to the effective use of drugs along designing programs and procedures for collecting and analysing reports from patients and clinical conclusions to the objective of pharmacovigilance.

➢ **TYPES**

- There are four important types in pharmacovigilance:

1) Passive surveillance
2) Active surveillance
3) Cohort event monitoring.
4) Targeted clinical investigation

1.PASSIVE SURVEILLANCE

- Passive surveillance methods involve the usage of spontaneous adverse event reports voluntarily sent by healthcare professionals or patients to the marketing authorization holder or regulatory authority. Here, data related to the adverse reactions are collected in a central or regional database. The identity of the reporter remains anonymous, but patient-related details like country, age, gender, and pre-existing comorbidities can be recovered from the reporting forms.
- Examples of spontaneous reporting systems include the –
- FAERS (FDA Adverse Event Reporting System) database run by FDA
  LVigiBase, the WHO Global Individual Case Safety Report (ICSR) database
  For Europe:EudraVigilance maintained by the European Medicines Agency.

2.ACTIVE SURVEILLANCE

- This method aims to monitor certain specific drug-related adverse events and seeks to ascertain the number of adverse drug reactions entirely through a pre-planned process. It is commonly known as toxicity monitoring or safety monitoring.

3.COHORT EVENT MONITORING

- THIS method, the surveillance study is planned prior to beginning the treatment with the medication. A group of people are exposed to a drug for a defined period and actively followed up during treatment.
- Adverse events of the target drug or the events associated with one or more medicines taken with that drug are monitored.

4.TARGETED CLINICAL INVESTIGATION

- These kinds of investigations are performed to identify and characterise the adverse reactions related to a drug among special populations like people with some genetic disorders, pregnant women, and older people.

➢ **COMPONENTS**

1.ADVERSE EVENT CASE MANAGEMENT INCLUDING EXPEDITED REPORT

Fact:- EU pharmacovigilance laws mean that ALL spontaneous reports regarding serious adverse reactions must be expedited within 15 days. In addition, as of 22nd November 2017 all non-serious adverse reactions, with an origin within the EU, require expediting EMA within 90 days.

These laws will mean that ALL suspected reactions provoked by a medicinal product must be expedited – regardless of seriousness.

EXPEDITED REPORTS

Remaining compliant throughout all the changes to EU legislation can be a challenging endeavour for any company. This is particularly the case with Expedited Reporting – one of the pillars of all EU pharmacovigilance work.

- **WHAT IS EXPEDITED REPORTING?**

In the EU post-marketing environment, an Individual Case Safety Report (ICSR) may involve a serious or non-serious adverse reaction – regardless of expectedness. Such cases must be submitted to the regulatory authorities within 15 days or 90 days respectively. As a Marketing Authorisation Holder, you need to be fully versed in each change to the drug safety laws in concerned territories around expedited reporting as and when it happens. With regards to these updates, you as the Marketing Authorisation Holder need to implement them to remain fully compliant. With the right support, you can rapidly respond to the challenges in line with your Standard Operating Procedures.

- **POST-MARKETING PHASES**

Any clinical trials including post-authorization studies during the post-marketing phase of a product will need to be correctly processed and expedited according to regulatory requirements

2.AGGREGATE REPORTING

- Aggregate reporting is the process that reviews the cumulative safety information from a wide range of sources, on a periodic basis and submits the findings to regulators worldwide.
- The aggregate safety reports are presented to regulators as soon as the medicine is marketed anywhere in the world and enables understanding of the risk and benefit profile of the product over a period of time.
- These reports focus not so much on individual cases, but rather on overview, assessment of the safety profile and benefit-risk-evaluation of Adverse Drug Reaction (ADR) and the Serious Adverse Event (SAE) and pregnancy reports.

- **WHY IS AGGREGATE REPORTING IMPORTANT?**

- Though the Individual case safety reports were submitted on expedited basis to regulatory authorities, detailed analysis and evaluation of the benefit/risk ratio of a drug is not possible at this level. Therefore periodically reviewing safety reports received cumulatively worldwide, becomes highly significant to analyse the benefit/risk balance of the product.

➢ **TYPES OF AGGREGATE REPORTS:**

- **PRE-MARKETING REPORT:**

IND annual reports • Clinical study reports (CSR)

Development Safety Update Report (DSUR)

Annual safety reports (ASRS) in Europe

- **POST-MARKETING REPORT:**

Periodic Benefit Risk Evaluation Report (PBRER)/Periodic Safety Update Report (PSUR)

Periodic Adverse Drug Experience Report (PADER).

NDA and ANDA annual reports

Addendum to clinical overviews (ACO).

3.SINGLE INTELLIGENCE

Signal detection in Pharmacovigilance involves looking at the adverse reaction data for patterns that suggest new safety information. This page provides a brief introduction to the definition and purpose of signals and some of the key methodologies employed to generate them.

- **WHAT IS A SIGNAL?**

The term is most commonly associated with drugs during the post-marketing phase, although it may also be used during pre-marketing clinical trials. The definition of a signal as provided by the CIOMS Working Group 8 is:

Information that arises from one or multiple sources (including observations and experiments), which suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify verificatory action".

- **WHAT IS SIGNAL MANAGEMENT IN PHARMACOVIGILANCE?**

The process of signal management in pharmacovigilance is a set of activities which aim to determine:

Whether there are new risks associated with a particular drug, or

Whether risks associated with a particular drug have changed

Sources for the detection of signals can come from:

Spontaneous reporting

Active monitoring systems

Interventional studies (clinical trials)

Non-interventional studies (pharmacoepidemiology studies)

Non-clinical studies (e.g. animal toxicology studies)

Systematic reviews (i.e. thorough review of the published literature)

Meta-analyses (i.e. mathematical pooling of all the clinical trial data)

Other relevant sources.

4.RISK MANAGEMENT

Risk management in pharmacovigilance is undertaken to promote safe use of medicines and safeguard health of patients. It is a set of activities performed for identification of risk, risk assessment, and risk minimization and prevention. Risk management has the following stages: identification and characterization of the safety profile of the medicinal product; planning of pharmacovigilance activities to characterise risks and identify new risks; planning and implementation of risk minimization and mitigation and assessment of the effectiveness of these activities; and document postapproval obligations that have been imposed as a condition of the marketing authorization.

All these activities together constitute the risk management plan, which is required to be submitted during the authorization of the drug. The overall aim of risk management is to ensure that the benefits of the medicinal product outweigh the risks by a wide margin for the treatment of a particular indication both at individual level and for the target population as a whole.2) Constitutional objective of pharmacovigilance of india :-

The purpose of the Pharmacovigilance Program of India is to collect, collate and analyse data to arrive at an inference to recommend regulatory interventions, besides communicating risks to healthcare professionals and the public.

- **PHARMACOVIGILANCE PROGRAMME OF INDIA (PVPI):-**

The Central Drugs Standard Control Organization (CDSCO), Directorate General of Health Services under the aegis of Ministry of Health & Family Welfare, Government of India in collaboration with Department of Pharmacology, All India Institute of Medical Sciences (AIIMS), New Delhi has launched the nation-wide Pharmacovigilance

programme for protecting the health of the patients by ensuring drug safety. The programme is coordinated by the Department of Pharmacology at AIIMS as a National Coordinating Centre (NCC).

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- **OBJECTIVE**:-

To monitor Adverse Drug Reactions (ADRs) in the Indian population.

To create awareness amongst health care professionals about the importance of ADR reporting in India.

To monitor benefit-risk profile of medicines

Generate independent, evidence based recommendations on the safety of medicines

Support the CDSCO for formulating safety related regulatory decisions for medicines

Communicate findings with all key stakeholders

Create a national centre of excellence at par with global drug safety monitoring standards

List of national adverse drug monitoring centres(AMCS) and their functions:

National Coordinating Centre (NCC):-

Address :-Department of Pharmacology, All India Institute of Medical Sciences, New Delhi.

Coordinators :- Dr. Y.K. Gupta National Coordinator

- **Function of AMC**
- To monitor the ADR.
- To optimize safe and effective use of medicines in over set up.
- To create awareness amongst healthcare professionals about the importance of ADR Reporting.
- To monitor benefits risk profile of medicines.
- Generate independent, evidence based recommendations on the safety of medicines.
- Support the CDSCO for formulating safety related regulatory decisions for medicines.
- Communicate finding with all key stakeholders.
- Create a national centre of excellence as per with global drug safety monitoring standards.

PHASES OF CLINICAL TRIALS

HISTORY OF PROPOFOL

PROPOFOL drug was discovered in 1973 by JOHN B GALEN he is a veterinarian and researcher at the chemical industry he spent 30 year for developing a propofol drug and effort which leads to the awarding to him of the Oscar award 2018 for the clinical researcher

The clinical trials of propofol are followed in 1977 but due to some anaphylactic reaction on the drug was removed from the market and subsequently reformulated as an emulsion of soya oil and propofol mixture water

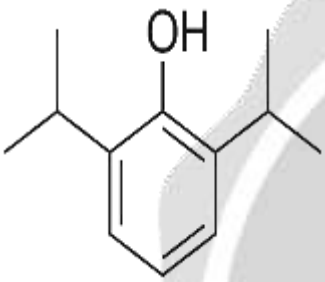
Development

a product has been developed and tested with the positive result .fospropofol is rapidly broken down by the enzyme alkaline phosphate to form of propofol this formulation may not be produced pain and injection at the site

brand name

- celofol
- citrifol
- diprivan
- fresofol
- neorof
- propovan

structure



Clinical formula- C12H18O

- SYNONYMS
- 2,6-Diisopropylphenol
- Disoprofol

PROPOFOL INJECTION

PHARMACOKINETICS

propofol is a γ-aminobutyric acid (GABA) receptor agonist. It has a favourable pharmacokinetic which has resulted in it becoming the most commonly used intravenous anaesthetic for the past three decade

Absorption

Is only suitable for intravenous use it is not suitable for external or other route of administration due to its bitter taste and low polar availability caused by high first pass effect

Distribution

After the administration intravenously propofol is extensively bound to the plasma protein and electrocytes take action at the site

METABOLISM

Propofol undergoes rapid and extensive metabolism to water-soluble inactive metabolites. The liver is the major metabolic site, but extrahepatic clearance of propofol has also been suggested since systemic propofol clearance exceeds hepatic blood flow

ELIMINATION

Propofol is mainly eliminated (73% of the dose in 24 h and 88% in 120 h) by glomerular filtration (renal clearance of 120 ml/min) as water-soluble metabolites and/or bile less than 1% of propofol is excreted unchanged in urine, and clearance is reduced in renal failure; only 2% is excreted in feces up to 48 h after dose . In humans, the major metabolite in urine is the glucuronic acid conjugate of propofol, which accounts for 53–73% of the total metabolites,

Toxicology- Overdosage may increase pharmacologic and adverse effects or cause death.propofol levels in blood and tissue were within or below the therapeutic range. Thus, victims did not die from propofol toxicity, per se. Instead, examiners concluded that propofol induced **respiratory depression, apnea, and hypoxia** as a mechanism of death.

Safety pharmacology-

Propofol is a versatile and short acting drug. It is initially marketed as an anaesthetic and now also widelly used for the sedation of patient in the intensive care unit at the room tempreture propofol is an oil and is insoluble in water

EFFICACY OF PROPOFOL

Propofol has a fast beginning of the action and its therapeutic effect is almost intanneous after injection it normally induces hypnosis within 20 to 40 sec of injection.

MECHANISM OF ACTION

Propofol is related to its intermediate with (GABA) which is inhibitory neurotransmitter in CNS

Prpofol work by increasing GABA mediated inhibitory tone in the cns

Decrease the rate of dissociation of the GABA from the receptor

DRUG DRUG INTERACTION

1 . BENZODIAZEPINE

The risk or severity of adverse effect can be increased when prpofol is combined 1,2 benzodiazepine

2**. ADENINE**

The metabolism of propofol can be decrease when combine with adenine

3. **ADENOSINE**

The risk or severity of OTC prolongation can be increased when propofol is combined with adenosine

4. **ALBENDAZOLE**

The metabolism of albendazole can be decrease when combined with propofol

5. **ATROPINE**

Propofol may increase the central nervous system depressant activity of atropine

DRUG FOOD REACTION

Alcohol can increase the nervous system side effects of propofol such as dizziness, drowsiness, and difficulty concentrating. Some people may also experience impairment in thinking and judgment. You should avoid or limit the use of alcohol while being treated with propofol.

Selection of drugs class for pharmacovigilance study using different criteria.

(eg) Commercial availability , selling of drug

AVAILABILITY OF PROPOFOL

Propofol have negligible bio availability in human it may be possible to administer systematic propofol with an oral transmucosal delivery system that bypasses hepatic first pass metabolism.

METHOD:-

With approval from the institutional research and ethics committee and after obtaining written information enrolled six healthy male volunteers in the open label unblended pilot study the first three male volunteers received 20 min of oral propofol 1% where enrolled collected at 2,4,6,8,16,30&60 min after oral injection of Propofol emulsion.

Propofol is not orally bioavailable in animal is admi has only grally intravenously Practice been route Such 93 anesthesia it Suggested that alter Could be utilized nebulized inhalation. trans mucosal rectal upper gastrointestinal The hepatic extraction ratio Gf Propofol is in range Priori 0.8 to og Thus th expectation is that the oral bio avalibility of propof greater than 20 in the the no

Selling of propofal The drug was sold in Sealed Condition and stored per recommendation and role is 2000 a day's 26 Brand of Propofol as 144 over selling Celofol market made by- Themis Pharmaceutical.

IDENTIFICATION OF MOST WIDELY PRESCRIBED DRUG FROM A SELECTED CLASS BY APPROACHING PHARMACY STORING COMPANY REPRESENTATIVE AND PHRAMACOMPANIES WEB PORTAL

Consumption of propofol is given by injection. the maximum effect occur Vein and - a about 7w0 minute to typically lasts Propofol is take and five to ten minute also known used for medical assistance in dying in Canada The medication for this Use during appears Pregnancy. to be Sap but has been well Studied for use case not before you given Propofol you must Sandoz + G not be given Propofol if you have an allergimedicine Containing propofol any of the other ingredient listed at the end of this leafleting .

Symptom of allergic reaction may include Shortness of breath wheezing or difficulty breathing swelling of the other rash inching face lips tongue A parts of hives body the skin the Before epilepsy heart are given it C Fit's Convulsions).Things

IDENTIFICATION OF ADVERSE EFFECT OF SELECTED DRUG

you should not receive proof of call if you are allergic to eat if you have allergies to eggs eggs products soybean or soy product to make sure medicine is safe for you…. Doctor if you have epilepsy or other or disorder

warning for dosage and administration and handling procedure

administration of propofol should we initiate as a continuous infusion and the changes in rate of administration made slowly in order minimize hypotension and avoid acute overdose

patient should be monitored for early sign of significant hypotension and cardiovascular depression

side effects of propofol

- blurry vision
- dizziness
- fitness
- pounding in ear
- problem with movement

❖ **ADVERSE DRUG REACTION (ADR) MONITORING FORM** :-

● PREPARATION OF ADR MONITORING FORM AS PER GUIDELINES GIVEN BY AMCS (E.G. INDIAN PHARMACOPOEIA COMMISSION)

● **ADVERSE DRUG REACTIONS MONITORING FORM:**

Sr no	Indian pharmacopoeia commission	For AMC/NCC Use only
	Report type clinical follow up -	AMC report no

Sr no		World wide unique no -
1	Patient information	12-Relevant test/laboratory date with date
2	Patient initial	13-Relevant medical history e.g- pregnancy allergy
3	Age at time event	
4	M-. F-. Other -	
5	Weigh. Kg/s	

B	Suspect adverse reactions	14- serious relations
6	Date of started	Congited death
7	Date of recovery	Life threatening
8	D described reaction problem	Disability

➢ **SUSPECTED MEDICATION:-**

Sr.no	Name Brand generic	Manufacturers	Batch no	Exp date	Dose used	Frequency	Route use
1							
2							
3							

2:- CONCENTRATION COMITANT MEDICAL PRODUCTS INCLUDING MEDICATION AND HERBAL REMEDIES WITH DATE (EXCLUDE THOSE AND TREATMENT)

Additional information :-	D. Reporter details 16- name and professional adrss- Pin-. E-mail - Help no- (with STD code)- Occupation -. Sign-. 17- date this report -

HOSPITAL VISIT

Common side effect

- Blurred vision.
- dizziness,
- faintness,
- lightheadedness when getting up suddenly from a lying or sitting position.
- fast, slow, irregular, or pounding heartbeat or pulse.
- pounding in the ears.
- problems with movement.
- Hypotension

SERIOUS SIDE EFFECT

- can cause a decrease in blood pressure
- it can depress or even stop breathing
- and it can cause pain on injection effect
- Severe headache

Serious allergic reaction

rash, itching, hoarseness, trouble breathing, trouble swallowing, or any swelling of your hands, face, mouth, or throat

patient interview

hospital name: Saideep hospital Ahmednagar

patient name: Sandip tukaram Kapse

age: 27

gender: male

disease:

1. drug: Propofol

- drug ADR : Transient local pain at the injection site is the most common adverse reaction. This may be decreased by administering IV lidocaine before propofol bolus.
- Hypotension
- Myoclonus
- Occasionally has been seen to cause EKG changes (QT interval prolongation). This is rarely clinically significant.
- Discolored urine (a green tint); this adverse event is exceedingly rare

Reference

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● https://clincalc.com/DrugStats/Drugs/Lidocaine

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