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Review Article

IMPORTANT ASPECTS OF CLINICAL RESEARCH

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ABSTRACT

Clinical Research is a study involving human subjects which is performed as per the clinical trial protocol in accordance with the ethical guidelines laid down by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). This consists of a series of clinical studies in which human subjects are administered test and reference products under the fed or fasting conditions as per the requirements of the study. The clinical studies involve five phase viz., phase zero, phase I, phase II, phase III, and phase IV. The human subjects are monitored under the supervision of study investigators as well as clinical research associates or co-ordinators. Clinical research plays a vital role in the drug discovery process and it consumes a lot of investment as well as time. It ensures the safety as well as afficacy of a drug prior to the marketing authorization of a new drug. In the present article, the all about the clinical research, its important aspects, various processes, and their purposes have been briefly described.

Keywords: *Clinical Research, clinical trial, human studies, drug discover*

INTRODUCTION

A clinical trial is a research study to investigate the new drugs involving human volunteer that adds to medical knowledge. It is involved in learning about the potential treatment and its effect on human [1]. Clinical trial gives an evidence which is helping in determining the which treatment is best and which is harmful. A clinical trial is the important role and it gives invaluable information about the benefit and safety of existing therapy. Clinical trail also has a research team where may include medical practitioners, social workers, etc. [2]. The clinical trial can take place many locations like hospitals, university, doctor's office and community clinic.

Various phases [3] involved in clinical trial are:

Phase1: It is usually conducted on a small number of healthy volunteers to monitoring the safety effectiveness. And to determining the action of drugs in the human body.

Phase 2: It is conducted in a small number of patients with the illness and to search the therapeutic efficacy of the drug.

Phase 3: It is conducted large number of population and to confirm the therapeutic efficacy of the drug and also collect more information about the safety drug.

Phase 4: It is conducted to gather additional information about the drug safety and also known about the post-marketing studies.

ROLE OF ICH GUIDELINE

ICH stands for "International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use". These are technical norms which are helpful for pharmaceutical product registration [4].

A clinical trial is an international ethical and scientific standard to understand about the design, monitoring, recording, analysis and reporting of the drug by using ICH guideline. It is very important to know about the ICH guideline and today it has the important role in the clinical trial for protecting and preserving the human rights [5].

- A clinical trial is performed according to the ICH guideline which is in the declaration of Helsinki.
- Before the trial is starting, the risks and inconvenience should be weighed against the anticipated benefit for the individual trial.
- The trail should be conducted by the prior institutional review board (IRB) /independent ethics committee (IEC) approval/favorable opinion.
- Before the clinical trial, for each participate should be obtained informed consent.
- All clinical trial information should be stored.
- Ease the implementation of guidelines of ICH in ICH's own regions.
- Guideline mainly contains the format and contents the clinical and statistical section of the New drug investigation [6, 7].

BLINDING

Blinding is associated with one or more individual groups involved in the clinical trial. The History of blinding is very rich over the entire period of centuries. The term blinding includes trial Participant, Investigator (health care provider), Assessors (person who conducts the outcome data). Blinding reduces the variation or different types of changes into the outcomes (information bias). Confidentiality of the process is maintained to improve the safety, efficacy and validity.

Blinding is the process which is used under the study of epidemiology and clinical trials. It is also known as masking. The subjects/participants, investigator, also the Organiser sometimes do not know about the final report of the trial. All of them kept under the blinded environment [8].

TYPES OF BLINDING

Three types of blinding are single blinding, double blinding and triple blinding.

Single blinding is the process in which only the subjects/participants are unsuspecting what treatment he/she receives. Double blinding is the process in which investigator and the subjects/participants, both are unsuspecting what treatment he/she receives. Triple blinding is the process in which the originator is unsuspecting what treatment he/she receives [9].

PURPOSE OF BLINDING

To remove the Investigator inclination and biasness, patient biasness, evaluation inclination and, outcome biasness [10]

UNBLINDING

For secure the life of Subjects/participants during the severe and critical condition in the trials, the process of unblinding can be done [11].

RANDOMISATION

Randomisation is the experimental design which is essential for the clinical trials. In 1920 R. A. Fisher was a statistician and geneticist who introduced about the randomisation as an assignment which includes the statistical theory of the various trials. In the session of 1947-1948, streptomycin in tuberculosis - The British Medical journal by the British Medical Research Council published the first randomized controlled trial (RCT) in 1948. Randomisation is the methods of clinical trials which assign participants/subjects to treatment groups. It provides equal chances for each participant/subjects to become the part of the trials. Participants/subjects can assign to any of the groups. The process of the randomisation can become successful if there is no prediction of the groups in advance. Randomized controlled trial is the type of statistical process, where the participants/subjects being studied are randomly allocated process one or other of the different treatments under study [12, 13]. Randomisation is the GOLD standard for the research design.

Types of randomization

i. Simple randomisation
ii. Random permuted blocks
iii. Stratified randomisation
iv. Biased coin

Simple randomisation- This method can be achieved through conscious decision or random. In simple randomisation there is the absence of alternating assignment. E.g., tossing a coin. H- Intervention/cohort, T-control.

Random permuted blocks: The method of blocking is to maintain and equalize the participants/subjects into the treatment group. This method is used to ensure the identical number of participants/subjects.It enhances the validity of the treatment. E.g., with blocks

of A, B, C, D. There is equal no. designed for each treatment group.

Block A	Block B	Block C	Block D
2112	1212	1221	2121

Stratified randomization: Important risk factor can be used to avoid the imbalance. E.g., age, center, disease condition or stage.

Block randomisation can be used within each strata to create strata with equal risk factors.

Stratification by smaller numbers of risk factors can be possible.

Ex - age group (5 level), disease stage (6 level), centre (12different)

5 x 6 x 12 = 360 strata. Many empty strata and incomplete blocks.

Biased coin: It is a type of the adaptive technique. There is the variation between the treatment groups due to the change in their probability. Variation/ Imbalance between the groups with respect to the presence of two or more covariates [14, 15].

RANDOMISATION IS NECESSARY FOR FOLLOWING REASONS

- Enhances the validity of the statistical trials.
- To remove the biasness from the trials.
- Preventing deciphering.
- It provides the ethical aspects
- The groups are treated under the similar environment and Circumstances.

NON - RANDOMISATION STUDY

- Non randomisation is also known as Quasi-randomisation.
- This study includes theoretical, empirical research, statistical Discussion among the members of non randomized study methods group (NRSMG) for the estimation of new challenges in the trials.
- It is a type of quantitative study which helps to observe the effectiveness of a cohort/intervention (harm/benefit).

Randomisation process is not involved in quasi process to allocate units to comparison groups [16, 17].

CONCLUSION

- Clinical trials help to prove the safety and efficacy of the new drug entity.
- Clinical trials are the experiments with human beings including studies of the specimen collected from specific patients.
- Lots of changes took place in modern medication and the different types of various approaches for the advancement in the

research and development are due to the clinical trials.

- A clinical study is conducted at the different types of site with the variety of specific species.

- Random assignment is the GOLD standard of the research design. The best method for producing comparable group is a random design.

- Blinding is the type of a confidential process to maintain the safety and efficacy. It removes the biasness.

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