ISSN 2581-6217

World Journal of Pharmaceutical Science & Technology

Journal homepage: www.wjpst.com

Review Article

ADVANCING NOVEL TECHNOLOGY BASED TECHNIQUES TO DIGITALIZE CLINICAL TRIALS

Vaishali Mundhe[1], Archana Gawade[2]

1. Department of Quality Assurance techniques, MET's Institute of Pharmacy, Savitribai Phule Pune University, Nashik, India. and Advance Diploma in Pharmacovigilance and clinical research Scholar from Elite institute of Pharma Skills Pune.
2. Managing Director, Elite Institute Of Pharma Skills, Pune

Address for correspondence:

Vaishali Mundhe, Department of Quality Assurance techniques, MET's Institute of Pharmacy, Savitribai Ph Pune University, Nashik, India. and Advance Diploma in Pharmacovigilance and clinical research Scholar fr Elite institute of Pharma Skills Pune.
E-mail- mundhevaishali0721@gmail.com

Received: 15-1-2022, Revised: 29-1-2022, Accepted: 31-1-2022

ABSTRACT

Novel medicines are tested in human volunteers in clinical trials to see if they should be licenced for general use. In recent years, India has emerged as a global leader in clinical trials. Human volunteers are studied in phase I pharmacokinetics, safety, and gross effects by clinical pharmacologists. Clinical trials are dynamic and complicated systems that include biological, pharmacologic, and trial-related aspects. Clinical trial design, assessment, and participant involvement can all benefit from new tools and approaches. Wearable devices, remote monitoring, and virtual clinical visits are some of the emerging technologies that could be beneficial.

KEYWORDS: Clinical Trials, Novel, Artificial Intelligence, Disease Modelling and Simulation, Wearable Devices.

INTRODUCTION:

Clinical trials are required in today's worldwide scientific era to bring newer and better medications to market. Clinical trials evaluate novel treatments in human volunteers to determine whether they should be approved for general use. Due to a variety of causes, India has been a global powerhouse for clinical trials in recent

years. Clinical trials have an impact not only on the individual patient by expanding the number of effective therapies available, but also on society as a whole by increasing the value of health care given.

A clinical trial is defined as "any research study that prospectively assigns human individuals or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes," according to the World Health Organization. [1]

Clinical trials are a type of biological experiment that is used to determine the efficacy of a treatment. Clinical pharmacologists study human volunteers in phase I pharmacokinetics, safety, and gross effects. If the drug passes the test, it moves on to phase II testing, where clinical pharmacologists examine pharmacokinetics, safety, and therapeutic efficacy in a small group of patients. If the drug passes phase II, clinical investigators examine hundreds of patients in phase III, primarily for safety and therapeutic efficacy. If this is approved, the medicine will be available for sale. Physicians from various hospitals and clinics continue to give their feedback on the medicine, including ADR and efficacy in phase IV. [2]

Monitoring Clinical Trials:

The goal of clinical trial monitoring is to ensure that:

1) Human subjects' rights and well-being are safeguarded.
2) The results of the trials that have been reported are treated with confidentiality.
3) The trial is being conducted in accordance with the existing approved protocol/amendments, GCP, and applicable regulatory requirements. [3]

All industries, including health care and drug research, are being disrupted by new technologies. Although they have yet to have a significant influence on clinical trials, technology advancements have the potential to increase efficiency and productivity through the use of novel outcomes, more patient participation, reduced patient burden, and better trial administration. Health care is rapidly changing as a result of new technologies. However, their impact on medication development has been limited to date. Increased use of innovative tools and methodologies in clinical trials in the future can improve design, assessment, and participant engagement in the evaluation of novel medicines for clinical trials. Clinical trials are complex and dynamic systems with biological, pharmacologic, and trial-related elements.[4]

In order to take use of new technology in clinical trial design, the drug development community will need to incorporate lessons acquired from other industries, such as a greater focus on the consumer. The majority of study participants today have extensive expertise and familiarity using technology in their daily lives, and consumer technology businesses have been developed entirely around the concept of improving the user experience. [5]

Even before receiving any input on the study's viability, the traditional research paradigm involves a significant upfront investment of money and time to design a study, buy the technologies, identify clinical sites, and recruit patients. Through the use of novel outcomes, enhanced patient engagement, and reduced patient burden, technological advances may improve the efficiency and productivity of neuroscience clinical

trials, but they also create regulatory and operational problems. Wearable devices, remote monitoring, and virtual clinical visits are examples of new technologies that could help achieve the goal of making clinical trials more patient-centered. [6]

Now a day, the following technologies have been employed in clinical trials:

A. Wearable Devices
B. Remote Monitoring
C. Disease Modelling and Simulation
D. Artificial Intelligence

A. Wearable Devices

The benefits that can be obtained by both the sponsor and the patient are driving up interest in clinical trials. Wearable gadgets are electronic components and software-controlled goods that can be incorporated into clothing or worn on the body as accessories. They can detect relapse early and show if a person's health has deteriorated following a time of recovery. Wearable devices can also enable physiological monitoring and early detection of harmful effects during clinical trials, such as in the case of novel drug development. [7]

Wearable devices have been demonstrated to boost effectiveness in the majority of these trials by reducing clinical site time and manpower requirements. While data is available before a patient arrives at the clinical site, professionals can make faster choices and send faster alerts regarding non-compliance when the patient is Patients may not need to keep manual data records with wearable medical devices because data can be collected digitally and automatically. They may also feel less compelled to recall this information at a later time not present. Patients may not need to keep manual data records with wearable medical devices because data can be collected digitally and automatically. They may also feel less compelled to recall this information at a later time. [8]

Wearable healthcare devices are already providing a valuable tool to use in conjunction with more traditional methods of research by offering results in an improved context. For example, they may allow researchers to analyse and personalise treatment for specific patient groups. In addition, the use of wearable medical devices in clinical trials can also offer patients a more consistent and convenient experience and encourage patient enrolment and participation in future trials. [9] Actigraph, Fitbit, Garmin, Apple, and Empatica are among the most commonly utilised wearable devices in the 1,400 clinical trials that are currently ongoing or completed. Activity tracking, heart rate, heart rate variability, sleep, glucose monitoring, haptics, sweat analysis, electro-stimulation, UV tracking, and pressure sensors are among the features of these devices and the types of data fed into the database to be evaluated in these clinical trials. While the bulk of the research used activity tracking to track things like energy expenditure and steps, other biometric data is starting to appear in these studies more frequently. [10]

The most common therapeutic category for which wearable devices were employed in these researches

was cardiovascular.

- Neuroscience
- Respiratory
- Sleep
- Stress
- Metabolic problems, such as diabetes and obesity
- Rheumatology
- Pain

These are some of the others.

Smartphone apps, chest straps, sports watches, patches, and other monitoring sensors that may be worn on the body, such as pulse oximeters, are examples of consumer healthcare wearables. [7]

B. Remote Monitoring

In clinical studies, remote monitoring means that monitors do not visit the site to transfer and review data. Rather, data monitoring is carried out virtually. CROs and research sponsors/stakeholders can access data from wherever they are thanks to digital technologies.

Remote risk-based monitoring was able to discover important data and process mistakes as well as on-site monitoring with 100% source data verification, saving time and money on travel and monitoring. Remote risk-based monitoring is a viable alternative to standard on-site clinical trial monitoring. [11] Remote access to patient eMRs for SDV is possible and could be a way to better utilise resources. [12] Physical activity monitors, such as the FitBit fitness tracker, the Vivoactive smartwatch, and the Apple Watch, use accelerometer, gyroscope, and heart rate sensors to collect data passively while the device is worn. Steps taken, distance walked or ran, flights climbed, number of workout minutes, cycling distance, heart rate, sedentary minutes, mild activity minutes, and strenuous activity minutes are all examples of data recorded. Some of these data are taken on a continuous basis, whereas others are collected just when the individual specifies that a certain activity, such as cycling, is being performed. Depending on the user's request and amount of activity, heart rate monitoring may occur at various time intervals. [13]

It is expected to enhance patient outcomes, minimise healthcare utilisation, lower costs, give ample data for research, and boost physician satisfaction. [14] Non-invasive biosensors that allow for RPM provide real-time data to patients and doctors, which have the potential to enhance care timeliness, treatment adherence, and health outcomes. [15]

C. Disease Modelling and Simulation

In the drug development process, modelling and simulation (M&S) is an industry-proven scientific approach that is used to inform important drug development decisions like dosing, drug-drug interaction (DDI), and other vital safety and effectiveness problems. [16]

Over the last two decades, computer simulation of clinical trials has progressed from a basic educational

game to "full" simulation models that produce pharmacologically sound, realistic trial outcomes. Over the last decade, the use of simulation of clinical trials in pharmaceutical product development has expanded significantly due to the need to make drug development more efficient and informative, as well as the recognition that many sectors utilise simulation extensively in product development.

The clinical trial procedure is abstracted in clinical trial simulation. It's used to look into assumptions and affect trial design in order to get as much useful information about the medicine as possible throughout the procedure. Many aspects of the clinical trial process can be simulated. [17]

The primary motivation for clinical trial simulation in pharmaceutical product development is to improve development efficiency, such as reducing cost and time while maximising the usefulness of trial data. Before resources are invested in executing the actual clinical study, clinical trial simulation tries to incorporate important information and enable critical review of assumptions. [18]

Simulation has been employed as an instructive tool for analysing complex clinical trial designs as a natural evolution from the rising usage of mathematical models in clinical pharmacology. The randomised concentration-controlled trial is one such design (RCCT). In the face of substantial between-subject pharmacokinetic variability, simulation was utilised to study trial designs that efficiently produce accurate and precise estimates of pharmacokinetic parameters describing the dose-concentration-effect relationship. [19]

Simulation of a new drug's PK characteristics, mostly acquired from phase I normal volunteer research, is occasionally used to determine dosing regimens for phase II trials.

Another important next step in improving the quality, utility, and confidence in this unique technology is to evaluate, improve, and implement the draft simulation good practices guidance. [20]

Clinical trial simulation entails a number of processes, each of which can be carried out with the help of a separate software programme.

1) Model of Input/Output
2) Model of Covariate Distribution
3) Model of Trial Execution [21]

D. Artificial Intelligence

Traditional analytics and clinical decision-making tools provide a lot of advantages that AI does not. As humans engage with training data, learning algorithms can become more exact and accurate, allowing humans to obtain unparalleled insights into diagnoses, care processes, treatment variability, and patient outcomes.

Artificial intelligence (AI) is a hot topic, with tremendous incentives to get innovative interventions published, implemented, and on the market as quickly as possible. While AI systems have been studied for a long time, new advancements in deep learning and neural networks have sparked interest due to their potential in health-related applications. AI systems for screening and triage, diagnosis, prognostication

decision-support, and therapy suggestion are only a few examples of such applications. [22]

Artificial intelligence techniques have matured to the point that they can be used in real-life situations to help human decision-makers.

AI has the ability to revolutionise crucial stages of clinical trial design, such as study preparation and execution, in order to improve trial success rates and reduce pharma R&D costs. [23] Using generative and prediction-based AI, ML, and reasoning tools, preclinical compound discovery, compound-target testing and defining lead compounds for clinical trials can all be aided. [24] A larger and more efficient search for correlations between indications and biomarkers has been reported, for example, than traditional discovery strategies. This could enable for the selection of lead candidates with a better possibility of success in clinical trials, as well as the rejection of those who are more likely to fail before entering the clinical phase. [25]

Recent advances in AI hardware and software show that AI and wearable sensors can be integrated to create an automated, real-time patient monitoring and analytics system.

CONCLUSION:

Future clinical trials could benefit from increased use of new tools and methodologies to improve design, assessment, and participation in the evaluation of innovative therapeutics for neurologic illnesses. With the establishment of value-based health care, health care is transitioning from these old measurements. The adoption of a value-based strategy in clinical trials, on the other hand, has been slow. The use of digital and wearable technologies can assist in this quest since it can ensure that disease burden is measured objectively, more regularly, at home, and on an individual level.

REFERENCES:

1. Clinical trial Wikipedia, the free encyclopedia. Available from: URL http://en.wikipedia.org/ wiki/clinical_trial.
2. S.B. Thorat, S.K. Banarjee, D.D. Gaikwad, S.L. Jadhav, R.M. Thorat, ‘Clinical Trial: A Review’, International journal of pharmaceutical sciences review and research, 2020; 1(2):101-106.
3. Kulkarni S. K., ‘Hand Book of Experimental Pharmacology’, 3rd ed, Vallabh Prakashan New Delhi, 2004; 21.
4. E. Ray Dorsey, Charles Venuto, Vinayak Venkataraman, et al, ‘Novel methods and technologies for 21st- century clinical trials’, JAMA neurology, 2015; 72(5): 582-588.
5. Daniel I. Sessler, Paul S. Myles, ‘Novel clinical trial designs to improve the efficiency of research’, Anaesthesiology, 2020; 132(1): 69-81
6. Sheena M. Posey Norris, Lisa Bain, Clare Stroud, ‘Transforming clinical trials with technologies’, Rapporteurs, 2016; 37-42.
7. Elena S. Izmailova, John A. Wagner, Eric D. Perakslis, ‘Wearable devices in clinical trials: hype and hypothesis’, Clinical Pharmacology and Therapeutics, 2018; 104(1): 42-52.
8. Niklas Morton, David Blackman, ‘The growing availability of wearable devices: a perspective on current applications in clinical trials’, Applied clinical trials, 2016.
9. Joshua M. Pevnick, Kade Birkeland RPH, Raymond Zimmer, Yaron Elad, Ilan Kedan, ‘Wearable technology for cardiology: An update and framework for the future’, Trends in cardiovascular medicine, 2018; 28(2):144-150.
10. Ryan craudel , ‘Wearables in clinical trials: opportunities and challenges’, Valencell, 2019

11. Osamu Yamada, et al, 'Clinical trial monitoring effectiveness: Remote risk based monitoring versus on-site monitoring with 100% source data verification', SAGE journals, 2020; 18(2):158-167.
12. Shannon C. Uren, Mitchell B. Kirkman, Brad S. Dalton, John R. Zalcberg, 'Reducing clinical trial monitoring resource allocation and costs through remote access to electronic medical records', JCO Oncology Practice, 2012; 9(1): e13-e16.
13. Yue Liao, Carrie Thompson, Susan Peterson, John Mandrola, Muhammad Shaalan Beg, 'The future of wearable technologies and remote monitoring in healthcare' Care Delivery and Practice Management, 2019; 115-121.
14. Sima Ajami, Footoheh Teimouri, 'Features and applications of wearable biosensors in medical care', Journal of research in medical sciences, 2015; 20(12): 1208-1215.
15. Joshua M. Pevnick, Garth Fuller, Ray Duncan, Brennan M.R. Spiegel, ' A large-scale initiative inviting patients to share personal fitness tracker data with their providers: intial results', Plos One, 2016; 11(11): e0165908.
16. Michael Eckstut, 'The role of modelling and simulation in clinical trials', Clinical leader, 2017.
17. Holford NHG, 'The target concentration approach to clinical drug development', Clin. Pharmacokinet, 1995; 29(5): 287–91.
18. Sanathanan LP, Peck C, Temple R, Lieberman R, Pledger G., 'Randomization, PK-controlled dosing, and titration: an integrated approach for designing clinical trials', Drug Inf. J., 1991; 25: 425–31.
19. Endrenyi L, Zha J., 'Comparative efficiencies of randomized concentration and dose controlled clinical trials', Clin. Pharmacol. Ther., 1994; 56: 331-38
20. Holford NHG, Hale M, Ko HC, Steimer J-L, Sheiner LB, et al., 'Simulation in Drug Development: Good Practices,1999; 1-22
21. Gieschke r, Reigner BG, Steimer J-L, 'Exploring clinical study design by computer simulation based on pharmacokinetic / pharmacodynamic modelling, J. Clin. Pharmacol. Ther., 1997; 35(10): 469-74.
22. He J, Baxter SL, Xu J, Zhou X, Zhang K, 'The practical implementation of artificial intelligence technologies in medicine', Nat Med, 2019; 25: 30-6.
23. N. Bakkar, et al., 'Artificial intelligence in neurodegenerative research: Use of IBM Watson to identify additional RNA-binding proteins altered in amyotrophic lateral sclerosis', Acta neuropathol, 2018; 135: 227-247.
24. S. Spangler*, et al., '*Automated hypothesis generation based on mining scientific literature', Proceedings of the 20th ACM SIGKDD International Conference on Knowledge Discovery and Data Mining, ACM , 2014; 1877-1886
25. Y. Chen, et al, IBM Watson: how cognitive computing can be applied to big data challenges in life sciences research, Clin. Ther., 2016; 38: 688-701