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Review Article

Pharmacology Section

Novel Methods and Regulation on Electronic Data Collection in Clinical Trials

SYED MUJTABA HUSSAIN NAQVI[1], SUYOG C MEHTA[2], AKHILESH D SHARMA[3]

ABSTRACT

The data collection is a pivotal part of clinical studies and impacts how the data is managed and analysed and the outcome of the clinical research besides contributing to the cost and duration of the clinical studies. Paper based method is a common method for clinical research data collection, because of certain advantages of paper over computer based approaches. The use of multicenter trials with centers across the globe strongly benefits from electronic data systems for the effective management in the collection and transfer of data. Online data collection utilises internet to enter data from the clinical study site to a central database. Novel convenient handheld devices are used in clinical research to record and process data especially in field studies and self reporting data collection processes. Personal Digital Assistants (PDA) and tablet personal computers (Tablet PC) allow real time data collection at the point of care in clinical studies. There are technical issues which need to be considered in Electronic Data Capture (EDC). The Indian Good Clinical Practice (GCP) gives guidelines on electronic data collection and Food and Drug Administration (FDA) describes the regulation in 21 Code of Federal Regulations (CFR) regarding electronic data collection.

Keywords: Electronic data systems, Online data collection, Paper based methods

INTRODUCTION

India is a potential site for clinical research due to its competent manpower, presence of large patient pool suffering from various diseases, cost efficiency, availability of advanced diagnostic and technical expertise. The availability of investigators with clear understanding of GCP guidelines for conduct of clinical research add a significant value for the sponsors to conduct clinical studies in India. One of the patient related advantage for clinical research in India is availability of treatment naïve patients, patients with rare and orphan diseases and patients with other comorbid conditions, hence treatment effect can be assessed in naïve patients and in those with associated comorbidities and rare diseases [1]. The data collection is a pivotal part of clinical studies and impacts how the data is managed and analysed and the outcome of the clinical research besides contributing to the cost and duration of the clinical studies. Various types of data collection method used in clinical studies from paper data collection forms to portable electronic devices is discussed in this review to understand the advantages and challenges associated with these method.

Paper Based Methods

It is a common practice for clinical research data collection, because of certain 'Perceptile' so called advantages of paper over computer based approaches. Paper method is at times deemed as simple, low cost, and requires minimal expertise, equipment, and training. The paper based method is limited by lack of online verification and online monitoring and duplication of documentation and tardiness of manual handling of loads of data in paper form, and in addition it lack audit trails which may at times may not support arguments on data integrity. The confidentiality of patient information may likely get affected if the information is not properly handled. Comparison of controlled trials involving handheld computers with paper methods showed improvement in storage, management and collection of data and preference by users [2].

Electronic Data Capture (EDC)

The EDC is used in all the phases of clinical trials for collecting, managing, and reporting clinical and laboratory data. The type of electronic system used in clinical trial depends on the complexity of data to be captured in the study. The basic stand alone database is sufficient for a single center trial but the multicenter global clinical trials require more sophisticated systems with remote data entry over web, online data validation, real time status of overall and status of each center, status of each subject, and options for online randomisation [3].

Electronic Health Records (EHRs) contains data collected in electronic form, so they can be merged with other electronic data sources. The multicenter trials with centers across the globe strongly benefit from electronic data systems for the effective management in the collection and transfer of data. Novel computer based data collection methods like tablet PCs provides ease of data collection compared to paper based methods, but they also introduce issues around data security and connectivity with cloud based storage where the collected data are stored and managed by an external company, and outside the direct control of the researchers, if the firewall settings are not mantained by internal information technology team of the company and strong passwords or access controls are not created. The ethics committees and the regulatory bodies ensure that the sponsor takes necessary measures to maintain confidentiality of patient information when such storage methods are used in clinical studies. To address connectivity issues a local application is created on the device rather than using tablet computer as browser for web based forms. This carries the risk of losing information from device similarly to losing paper data, but can be secured with a password and function to automatically delete data if device is missing or stolen.

The tablets used in clinical studies have functions for entering data, record and take pictures for assessment of various clinical parameters [4]. The choice of data collection method should match the study design; investigator should know the benefit and limitations of various data collection methods to select the appropriate technology.

Online Data Collection

This method of data collection utilises internet to enter data from the clinical study site to a central database. The data entry is decentralised with individual applications or clients connected through internet with the central database server. This is useful in connecting clinical trial centers which are geographically separated by large distance in a multicenter trial. The three tier online system contains browser requests which submit data, web application server which in turn submits or request data from and to the database server [5].

The electronic data can also be validated online using internet where a wrong entry can send message to operator for checking the wrong data entered in the system. For example if diastolic blood pressure is entered as 900 mmHg instead of 90 mmHg, the system automatically send's wrong entry signal to the operator. This reduces the data entry errors and tends to reduce time for data verification required in paper based method. The online statistical software like Statistical Analysis System (SAS), Strata and Statistical Package for the Social Sciences (SPSS) enables the data analysis for the data entered during the study.

Since the confidentiality is one of the important principle for ethical conduct of the clinical trial, the investigator and sponsor need to ensure security of data when internet is used for exchanging the patient's sensitive information. The appropriate measure should be taken to protect database servers from being used by unauthorised person and clients connected to local area network. Measures need to be taken to monitor network traffic and to prevent unauthorised access to the clinical data. The technical issues related to training, network speed and selection bias if internet and electronic data collection becomes criteria for enrollment of sites are some of the disadvantages associated with electronic data collection.

Handheld Computing Devices

As number of clinical studies using electronic data collection methods is increasing, novel convenient handhelds devices are used in clinical research to record and process data especially in field studies and self-reporting data collection processes [6]. In a population based, cross sectional study conducted by Gupta PC et al., in Mumbai, data input from house to house survey with face to face interview was directly entered into a programmed, handheld computer (electronic diary). The handheld computers were particularly useful to perform a survey on more than 99,598 tobacco users in Mumbai, India [7]. A study conducted by Lal SO et al., showed that the handheld computers are 23% faster and 58% more accurate than paper and pencil recording. The use of user friendly touch screen technologies makes them particularly attractive compared to paper based diaries or questionnaires for patients self reporting use, particularly in children and young adults [8]. These devices can be used to conduct quality of life studies in patients in the controlled clinical trials.

Personal Digital Assistants (PDA)

The PDA are increasingly used for electronic point of care data collection. The PDA system increases speed and storage capacity of data collected in clinical studies that require collection of limited amounts of data. The text size should match the small screen size, easier to answer options like pick lists and numbers with care on the number of selections available are preferred. Most PDA screens support approximately 12 lines in a screen; it is easier if the selection involves picking up from the single drop down list, rather than from a list which requires scrolling down the screen [9]. "In a study conducted by Shirima K et al., data were collected from 21,600 households (83,346 individuals) with 13 survey teams over a seven week period. The data was backed up after completion of each module onto storage card in the PDA and at the end of the day in the laptop computers and on Compact Disc (CD) at the end of day for each team. There was no PDA related problems or data loss encountered in this study" [10].

Tablet PCs

These are the light weight computers that allow user to enter data on a touch screen with a sufficiently sized hard drives [10]. The issues with the use of these devices in data collection for clinical research is related to data security as the tablet applications store the data on the servers owned by the software developers, hence the research sponsor should have agreement in place with the software developers for the confidentiality of the information [11].

Technical Issues

The hardware that is used for data collection should be convenient for the responders, security should be ensured with the web and database server, software utilised, network protection, access control, replacement and backup of data.

General Principles for using Computerised Systems in Clinical Trials [12]

FDA has described general principles for using computerised systems in clinical trials. The clinical study protocol should define the use of computerised systems used for collecting, modifying, maintaining, archiving, retrieving or transmitting data. The software and hardware used in clinical trial should be defined as a part of documentation of study records. Source documents should be retained for reconstruction and evaluation of the trials. Electronic document is used as a source document when original observation is directly entered into the computer. The computerised system should be according to regulatory requirements for record keeping and record retention is maintained in clinical trials. Any changes made to a data during the study should not obscure the original information and permit an audit trail, as to who made the changes to the documentation, when, and why they were made. Regulators may inspect all records submitted to the agency. Data on each individual subject participating in study should be retrieved from the computer. Data should be entered in the electronic forms according to the protocol requirement. The security of the system should be in place to prevent unauthorised access to the data. The Standard Operating Procedures (SOPs) should be created for system installation, data collection and handling, system maintenance, data backup, recovery and contingency plans and security. The SOPs should define the measures taken to prevent data loss with backup and recovery procedures. The data collected during the study should be backed up regularly to prevent catastrophic loss and all the backup records should be stored at a secure location mentioned in the SOPs typically at the offsite. The nature and scope of data loss can be assessed through backup and recovery logs.

Indian Regulation on Electronic Data Collection in Clinical Trials [13]

The Indian regulations also mention similar guidelines for use of electronic data collection in clinical studies. To prevent the unauthorised access to the clinical trial data only authorised person should have access to the entering or modifying data with the recorded trial of changes and deletions made. A security system with electronic signatures should be used to prevent unauthorised access to the data. A log of authorised persons accessing data should be maintained. The data should be regularly backed up to prevent data loss. The computerised systems including both hardware as well as software should be validated. The electronic data processing system should conform for completeness, accuracy, reliability and consistent validated performance. The SOPs for using these systems must be maintained with the adequate measures to ensure that no data is overlooked. The confidentiality of the participants should be maintained through blinding and using subject identification code that provides data reported for each subject.

CONCLUSION

The novel electronic data collection methods are widely used in clinical trials. The applicability of these methods should be assessed before using them for data collection. Measures should be taken to maintain confidentiality and security of data.

REFERENCES

[1] Dan S, Karmakar S, Ghosh B, Pal TK. Digitization of clinical trials in India: a new step by CDSCO towards ensuring the data credibility and patient safety. Pharmaceut Reg Affairs. 2015;4:149.

[2] Lane SJ, Heddle NM, Arnold E, Walker I. A review of randomized controlled trials comparing the effectiveness of hand held computers with paper methods for data collection. BMC Med Inform Decis Mak. 2006;6:23.

[3] Khaled El Emam, Jonker E, Sampson M, Krleza-Jerić K, Neisa A. The use of electronic data capture tool in clinical trials. Web survey of 259 Canadian clinical trials. J Med Internet Res. 2009;11(1):e8.

[4] Wilcox AB, Gallagher KD, Boden-Albala B, Bakken SR. Research data collection methods: From paper to tablet computers. Med Care. 2012;50 Suppl:S68-73.

[5] Paul J, Seib R, Prescott T. The internet and clinical trials: background, online resources, examples and issues. J Med Internet Res. 2005;7(1):e5.

[6] Haller G, Haller DM, Courvoisier DS, Lovis C. Handheld vs. laptop computers for electronic data collection in clinical research: A crossover randomized trial. J Am Med Inform Assoc. 2009;16(5):651-59.

[7] Gupta PC. Survey of sociodemographic characteristics of tobacco use among 99,598 individuals in Bombay, India using handheld computers. Tob Control. 1996;5(2):114-20.

[8] Lal SO, Smith FW, Davis JP, Castro HY, Smith DW, Chinkes DL, Barrow RE. Palm computer demonstrates a fast and accurate means of burn data collection. J Burn Care Rehabil. 2000;21(6):559-61.

[9] Pace WD, Staton EW. Electronic data collection options for practice-based research networks. Ann Fam Med. 2005;3(Suppl 1):S21-29.

[10] Shirima K, Mukasa O, Schellenberg JA, Manzi F, John D, Mushi A, et al. The use of personal digital assistants for data entry at the point of collection in a large household survey in southern Tanzania. Emerg Themes in Epidemiol. 2007;04:05.

[11] Wilcox AB, Gallagher K, Bakken S. Security approaches in using tablet computers for primary data collection in clinical research. EGEMS (Wash DC). 2013;1(1):1008.

[12] Guidance for Industry Computerized Systems Used in Clinical Investigations. https://www.fda.gov/ohrms/dockets/98fr/04d-0440-gdl0002.pdf. Accessed on 20th July 2017.

[13] Good clinical practice, Indian guidelines. http://www.cdsco.nic.in/html/GCP1.html. Accessed on 20th July 2017.

PARTICULARS OF CONTRIBUTORS:

1. Senior Manager, Department of Medical Affairs, Dr Reddys Laboratory, Hyderabad, Telangana, India.
2. Senior Director, Department of Medical Affairs, Dr Reddys Laboratory, Hyderabad, Telangana, India.
3. Senior Vice President, Department of Medical Affairs, Dr Reddys Laboratory, Hyderabad, Telangana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Syed Mujtaba Hussain Naqvi,
Global Generics India, Ameerpet, Hyderabad, Telangana, India.
E-mail: mujtabanaqvi@drreddys.com

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