CLINICAL RESEARCH NURSE AND HER ROLES

Abstract

The paper is a contribution to the knowledge about the role and responsibilities of the study nurse within the clinical trial, in practice. It presents the basic theoretical and practical sources of clinical research and basic principles of Good Clinical Practice. It analyses the specific roles of the clinical research nurse in practice, her responsibilities in each of the clinical trial stage and her value.

Key words: Clinical trial. Nurse’s role. Clinical research nurse. Study nurse. Good Clinical Practice.

Introduction

Clinical research is part of the complex procedure to demonstrate the effectiveness and safety of drugs and other products of the pharmaceutical industry. None of medications can get on the market without clinical research. Every drug must be clinically tested before the licence is obtained from health authority, and the efficacy and safety must predominate the risks and side effects. It is neccessary to have the qualified clinical research team besides the volunteers as the subjects of the research for the successful clinical trial conduct. Besides the investigators, co-investigators and the other clinical personnel, clinical research nurses are also an unsubstitued part of the team. The topic of the clinical research nurse importance, her roles, tasks and responsibilities is not sufficiently compiled in available literature in Slovakia – it should require more attention as it is highly specialized and prestigious activity in terms of nursing.

Clinical research of medications is inevitable step in procedure of development of new therapeutical possibilities and also in improvement of the care about the patient. Despite the large progress in medicine during the last century, there is a lack of effective treatments for more serious illnesses. There is a higher need for the new or better medication in some therapeutical areas, e.g. in oncology or neurology for dementia treatment. Clinical research
conducted by the commercial or non-commercial organizations, continues in finding the new treatments of different diseases. As an example - in 2008 there were more than 60,000 clinical trials conducted worldwide. There is a summary of total number of new medications in research and development during the last 10 years in Appendix no. 1.

The new drug development can take up to 15 years and the price of research can reach billion of dollars. However, only one from three new substances that reach to be marketed will achieve the level of sale in such a level that the research expenses are covered. A chance to success and registration of licence depend on application quality and so on quality of clinical trial, as the final results are reported to regulatory authority.

The development of new drugs consists of many stages of the research. Pre-clinical studies are undertaken on a new compound to determine the toxicity, teratology and basic pharmacokinetics and pharmacodynamics. On the basis of initial tests, compounds are selected for further study in man, clinical trial.

The basic rules of clinical trial conducting

Each clinical trial must be conducted according the plan based on the well-designed study protocol. The study protocol contains at least the following topics:

- clinical trial objectives and purpose
- clinical trial design
- background information
- selection and withdrawal of subjects
- treatment of subjects
- assessment of efficacy
- assessment of safety
- statistics
- direct access to source data
- quality control and quality assurance
- ethics
- data handling and record keeping
- financing and insurance
- publication policy
Study protocol is a „recipe“, a main working tool for clinical study conduct. The possible changes in the procedures during the study are described in Protocol Amendment.

The other important document is Case Report Forms (CRF), where the relevant data about the subjects are completed. The mostly preferred CRF is electronic version today which saves both: time and paper. The data are sent directly on-line to Data management centre and statistical analysis is quicklier.

The essential key to the successful conducting and finishing of clinical trial is the site selection with the competent investigators team where the clinical trial will be performed. It does not matter if it is a clinic or an out-patient department – the most important task is on the personnel qualification: investigator, nurse or other staff. The potential number of suitable patients that might be enrolled into the study is also an important factor.

A Clinical Research Associate (CRA) visit the potential sites after the final site selection and prepares the basic documentation for the application to Ethics committee and Health authority. Each clinical trial must be approved by the authorities in written form before start of the study. There are independent Ethics committees at each hospital and also regional Ethics committees in case of the private practice. If a clinical trial is multicentric, the approval from Multicentric Ethics committee must be obtained.

Ethics committees and Health authority are independent authorities that review the relevant submitted clinical trial documentation according to Good Clinical Practice guidelines. They make a decision in case of the premature end of trial and they follow the ongoing of the clinical trial during the whole period by interim reports.

The sponsor is responsible for conducting of clinical trial, its proper monitoring and the final report preparation which is neccessary for the successful registration of the study medication by the health authority.

The investigator is responsible for the correct patients enrollment according the inclusion and exclusion criteria described in the study protocol. Written informed consent has to be obtained from every subject who enters a clinical trial, before any study related procedures are undertaken. Every subject must be informed also verbally about all the details of the clinical trial and the conditions in case of his participation. The Patient Informed Consent form must be signed and dated by the patient himself. The investigator sign and date
the form by the same way. A copy of the signed document is given to the subject and the original is archived in the patient’s medical documentation. Any amendments of the protocol are documented in the updated version of Patient Information sheet and Patient Informed Consent form and it must be signed and dated by the same manner as at the beginning of the study.

Patient Informed Consent form in some cases, for example at children or mental disorder’s patients, can be signed by the legal representative of the subject.

Patient Informed Consent form and Patient Information sheet should be written in uncomplicated language, avoiding jargon and medical terminology. It should also be in the native language of the patient, who must have a sufficient time for making decision about his participation in the clinical trial. He must not be forced to make the quick decision and he must sign it free before any procedure related to the clinical trial is performed, for example blood taking procedure or any other study related examination. It is not sufficient that the document is signed just before using the study medication.

The investigator can delegate the consent process to an appropriately qualified person, for example a study nurse.

The subject keep the terms of the scheduled visits and all the instructions obtained from the investigator and study personnel, including the using of study medication. In some cases he must complete the questionnaires or patient diaries. The study personnel must have the sufficient time for the communication with a patient at the time of his visit, so adverse reactions or events can be found. The relationship between the patient and the study personnel should be based on the responsible approach and bilateral confidence. A study nurse has a great role in the communication with the patient as she is often the first contact person for them.

Study medication must be kept in the safe storage at the room temperature or in the refrigerator by the temperature which is exactly determined by the study protocol. The actual temperature is monitored and documented at Temperature Log on daily basis (in the morning and in the afternoon). The expiration date and dispensation of study medication must be accurately documented. Drug compliance is checked by counting the amount of returned drugs and documented.
The sponsor should ensure that the clinical trial is adequately monitored. This is responsibility of a Clinical Research Associate (CRA) or a Clinical Monitor. Their role is the protection of the rights and well-being of the subjects and checking that the reported data are accurate, complete and verifiable from source documents. The other purpose is that the clinical trial conducting is in compliance with the approved protocol, GCP and regulatory requirements.

Besides monitoring, the study can be audited or inspected by the independent auditors or inspectors that evaluate trial conduct and compliance with the protocol, GCP and regulatory requirements. This is a quality control activity. Inspectors are usually from local health authorities, from the European Union (European Medicines Agency) or from FDA (Food and Drug Administration). The primary aim of the clinical trial audit is to be sure that the rights of the subjects are respected based on the Declaration of Helsinki and that the integrity of reported data are reliable.

It is expected that the sponsors of clinical trials will provide the systematic performing of all procedures according to the Standard operating procedures (SOP). That affects the quality standard in all aspects of clinical research. SOPs are one of topics for quality control when an audit or inspection is performed.

Clinical trials have a different duration depending on the enrollment of the required number of subjects by the protocol. During the clinical trial the enrolled subjects´ data are collected by the Clinical Research Associate in written or electronic form and they are sent to Data Management. The statisticians must ensure the integrity of the data during their processing and, in addition, that an account is made of missing, unused or spurious data during the statistical analysis. The results of the statistical analyses are presented in a statistical report which is usually integrated in the final report.

From the legislative point of view the clinical trials are conducted according the guidelines 2001/20/EC and 2005/28/EC within the European Union. In USA there are basic legislative requirements in document 21 CFR 50, 54, 56 and 312. During the last years each country has implemented its own legislative rules, so in Slovakia in 2011.

**Good Clinical Practice**
Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.

In 1990 relevant regulatory agencies and associations of pharmaceutical industry from USA, Europe and Japan have initiated International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) so the unified standard of drugs development will be achieved. ICH has approved ICH GCP Guideline in 1996. The guideline was developed with consideration of the current good clinical practices of the European Union, Japan, and the United States, as well as those of Australia, Canada, the Nordic countries and the World Health Organization (WHO).

The objective of this ICH GCP Guideline is to provide a unified standard for the European Union, Japan and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions.

This guideline should be followed when generating clinical trial data that are intended to be submitted to regulatory authorities. The principles established in this guideline may also be applied to other clinical investigations that may have an impact on the safety and well-being of human subjects.

ICH GCP Guidelines describe in details the rules, responsibilities of ethics committee, investigator and sponsor of clinical trial. The other topics are: study protocol requirements, Investigator’s brochure and essential documents for the conduct of a clinical trial. All the clinical trials should be conducted according GCP rules and ethics committees and health authorities should follow it, too.

ICH GCP Guidelines highlights that the protection, safety and well-being of the clinical trial subjects is a priority and any of the study participants must not be harmed. This is also a reason why every member of clinical trial staff must attend GCP training every two years either as a classroom course or e-learning course which must be documented. The sponsor can refuse the investigator’s participation in a clinical trial if he does not fulfill this requirement.
GCP training is recommended also for the other clinical trial staff especially for study nurses that directly participate in clinical trial. The experience is much different in Slovakia – study nurses do not attend the GCP training very often, in majority they do not attend it at all. The reason is lack of time, overworking, no interest or no information about the training possibility, or demotivation as some of them participate in clinical trial because they must. GCP trainings are usually a part of the Investigator’s meetings organized by pharmaceutical companies in different foreign countries and the majority of nurses have the language problem if they want to participate. English knowledge is essential for this kind of training.

Slovak Medical University organizes a certified course of GCP that consists of two parts with the final examination. Clinical research nurses are not informed about this possibility in most cases so they attend it very rarely.

**Clinical research nurse and her roles**

Clinical research nurse fulfills the important roles within the whole clinical trial site team. A nurse can participate on clinical research in various ways. She is destined by her unique qualification so she can associate her communication, clinical and administrative abilities that are necessary for successful clinical trial conducting.

Nurse closely cooperates with the investigator in clinical trials procedures while she carries out the complex, divergent and interesting work.

The basic background for work as a clinical research nurse is: sufficient and appropriate practice, master of basic theoretical clinical research knowledge, understanding of terminology used in clinical research and minimal basic knowledge of English as the most of documentation is written in this language. There is a problem if a nurse performs routinely the activities without proper understanding for example a Central Laboratory Manual with the procedures described, details of blood sample taking procedures, its treating and distribution etc. There might be also problems in communication with central laboratory, in case of lost shipping box, unclear test results and other acute issues as the central laboratories are located outside Slovakia and English is the common used language within communication.

Some of the study documents are translated into Slovak, e.g. Protocol Synopsis, Patient Information Sheet and Patient Informed Consent, Patient Diary, questionnaires,
Patient Card. Though sometimes it might happen that study nurse need to review the other part of documentation in English and so the new problem araised.

It might happen that the investigator’s site must contact the central IVRS (Interactive Voice Response System), a site for patient randomization and the acute problems need to be discussed, the investigator or the co-investigator is not available and the nurse might help but she cannot make herself understood. This short overview of English knowledge application reffers to the importance of foreign language skills of study nurse, especially English that is often underestimated in practice.

According the theoretical principles of nursing roles we demonstrate on the individual role samples that they can be applied also for a clinical research nurse not only globally but also in Slovakia.

1) Nurse - Provider of the care

Clinical research nurse performs: blood taking procedures, measurement and monitoring of vital functions, patient height and weight, investigator’s orders and assessments according to the protocol (ECG, Holter monitoring, spirometry, densitometry etc.), study medication and other drugs administration, and in case of hospitalized patients she performs the complex nursing care.

2) Nurse – Educator

Clinical research nurse explains to patient the relevant information if the patient need some information obtained for the investigator to be reviewed, though the investigator must delegate this responsibility to the nurse by written form in Delegation Log.

A nurse often educates the patient how to complete the questionnaires of quality of life, Patient diary or how to proceed in case of adverse events reporting.

3) Nurse – Advisor

Nurse as an advisor fulfills this role not only for patients but also for other members of research team, e.g. nurses and other staff that do not understand completely the problems and who are in direct contact with patients.
4) Nurse – Representative of change

Clinical research nurse should support the initiatives for the change in her competency within clinical trials or within the following education. She can initiate a rise of an organization or a group of clinical research nursing team.

5) Nurse – Advocate

Nurse as the patient’s advocate fulfills one of the most important roles in clinical research as the protection of subjects is the priority. She helps to patients to understand the Patient Information and Patient Informed Consent form and also to follow the adverse events and report them if there are any.

6) Nurse - Manager

Clinical research nurse coordinates and manages the daily clinical study activities though the final responsibility are a matter of Principal Investigator. This role anticipates perfect managerial, organizational and communication skills and also flexible and assertive approach.

7) Nurse – Leader

Study nurse in this role fullfils the similar tasks as the coordinator but the main aim is the correct communication with patients, colleagues or other team members.

8) Nurse – Coordinator

Clinical research nurse coordinates the patients’ visits according the Study Protocol schedule as well as monitor’s visits and distribution of the samples to the central laboratory.

9) Nurse – Researcher

Study nurse in this role cooperates with Clinical Research Associate who monitor the study according the study schedule. She can assist in case of an audit or inspection. She writes the articles to the specialized nursing journals, she works on her own additional education and actively participates in nursing research.

10) Nurse – Mentor

Study nurse with the longer experience in clinical research helps to trainees that need to be trained properly and often need a help and the professional advice, and she can also help to the new co-investigators with no practice in clinical research.
The foreign results of research and survey describe the basic requirements that every clinical research nurse should meet, e.g. managerial and organizational skills, ability to make independent decisions as they often work individually etc.

Experiences in abroad show that study nurses must be excellent specialists in their area of medicine but they must have a wide scale knowledge about research process, about relevant legislative procedures and a wide scale of computer skills. There are responsibilities for study nurse such as preparation of the protocol and other documentation, preparation for application for approvals, coordination of start-up, conducting and finishing of the study. Study nurse helps with screening of patients, mostly at the out-patient departments and at working team meetings. She cooperates in Patient Informed Consent obtaining procedures and she can ensure that the patient understood the Patient Information sheet´s contents – this requires perfect communication and interpersonal skills. Study nurse can be responsible for the randomization, data collection and completion after patient enrollment. All the data must be reliable, precious and accurate when completed into the relevant documentation – this requests a high sense for details and high level of integrity. Study nurse can play a very important role at adverse event reporting procedures as she is often the first contact person for the patient. Finally, study nurse can act as a teacher, mentor or advisor for the other healthcare personnel, or she can have lectures at the professional conferences or similar events.

Some authors of foreign literature mention the requirement of GCP training every two years which is a must not only for investigators but also for study nurses. They can participate in activities of the professional organizations - Royal College of Nursing (RCN), Association of Clinical Research Professionals (ACRP) and others where groups of clinical research professionals exchange their experiences on their meetings and so widespread their knowledge.

During the last 20 years the number of clinical research nurses has increased because the number of clinical trials has been increased, too. Nurses can influence the quality of clinical trials, but the general extent and portion of their role on the clinical trial is not known. Some of surveys with study nurses in multicentric clinical trials have proved the lack of job satisfaction, conflict of roles nurse and researcher, self-motivation problems and problems related with the cooperation with nursing staff when following the study protocol. Study nurses also identified fields of the insufficient treatment, management and care caused by the
organizational and clinical aspects of nursing care. They expressed their expectations and observation. Study nurses participated in clinical trials without sufficient training and appropriate management – they were just „data collectors“ and unformal „observers“. The results of these studies were used by investigators for finding the best optimalization of clinical research nurses` skills and competencies.

The nurses` roles in clinical research include more activities, such as screening of potential patients, discussion about clinical trial with the participants, informed consent obtaining, registration and randomization, assessment plan, adverse events reporting and data collection. Study nurses with longer experience and specialization can take patient history, they can perform physical examinations, documentation of laboratory reports and order the study medication according the protocol. Study nurses with more longer experience and higher education can work as project managers or programme managers as coordinators of the whole team within the large project. There are also study nurse positions in academic centres, in communities and in the pharmaceutical industry. Education and trainings are organized by academic centres and professional research organizations. Certification of clinical research professionals can be available at ACRP – Association of Clinical Research Professionals (www.acrpnet.org) or Society of Clinical Research Associates (www.socra.org).

We can find more differences in clinical research nurse job when comparing situation in Slovakia and other countries. According to available literature, the study nurses in other countries have more competencies than in Slovakia. They perform more specialized activities such as Patient Informed Consent obtaining, different administrative tasks, data collection etc. Nurses in USA or UK have no language problem as English is their native language. The level of nursing education is nearly the same but the level of clinical research and GCP knowledge as well as continuing education possibilities are better in foreign countries. The prestige of study nurse job is higher in abroad than in Slovakia, where the majority of nurses have no idea about the importance of their work performed besides their common daily duties and very often without the appropriate appraisal.

The availability of participation in professional organizations that care about the needs of their members and care about their professional growth is more common in other countries than in Slovakia. It is possible for nurses in Slovakia they can become members of ACRP but membership fee is rather high for them, they have no advantage if they cannot speak English as they are not able to participate in education, events, lectures and any trainings or
reading the available literature (The Monitor). There are certified courses available at ACRP for different levels of professionals in clinical research: Certified Clinical Research Associate – CCRA, Certified Clinical Research Coordinator – CCRC, Certified Principal Investigator - CPI. The certificate can be renewed every two years by the exam or by valid amount of credits obtained by continuing education. Certified experts are very haunted in abroad. Clinical research nurse can pass the CCRC exam (Certified Clinical Research Coordinator).

In 2012 an author of this article has performed a survey with the aim to find out the level of basic knowledge about clinical research of study nurses in Slovakia, also the level of their English knowledge and the level of their training experience within clinical research projects. Another aim was to find out the interest of study nurse’s sample in systematic training before each new project and their interest in other continuing education and obtaining specialization degree in clinical research if possible.

A survey results have proven that clinical research nurses in Slovakia do not have sufficient basic knowledge about clinical research, what is quite surprising considering their practice and experience. On the other hand, there is a fact that study nurses are interested in further education and improvement in this area – this is very positive fact and this information might be used as the motivation for study nurses in future. The similar condition is in their willingness to study English or improve their English. Contemporary prospects for the improvement of clinical research nurses education are relatively limited but the situation is solvable.

References


Appendix No. 1
Total amount of drugs in research and development world wide

Total Number of Drugs in Research and Development World Wide

Source: Pharmaprojects (www.ciscrp.org)

Contact details of the author:
PhDr. Mária Gáliková, CCRA, MSW, Department of Nursing, The University of Healthcare and Social Work of St. Elisabeth, Bratislava.

Address: Bezekova 24, 841 02 Bratislava, Slovakia.

Tel. no. 00421 903 227 594

Email: maria.galikova@magamed.sk

**POSTER „THE TASKS AND RESPONSIBILITIES OF CLINICAL RESEARCH NURSE“**