

MULTICENTER COLLABORATIVE CLINICAL TRIALS IN DEVELOPING COUNTRIES: A DOUBLE EDGE SWORD

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Global population is growing rapidly with recent figures of 7.3 billion people living across the world. As expected, more than 6 billion people are living in less developed countries.¹ This huge population is threatened by diseases, disabilities, injuries and death. According to Global Burden of Disease Study 2013, only 4.3% of the global population was without any disease or injury sequelae, while 2.3 billion people were having more than five illnesses.² Global disease burden is shared more by the less developed countries as compared to developed countries. However, research to prevent and treat these health related problems is mainly conducted in developed countries. Research output in general and conducting clinical trials in particular, is lacking in developing countries.³ From 2005 to 2012, out of 189,213 trials registered with 15 World Health Organization-approved clinical trial registries, only 13% of the clinical trials were contributed by lower-middle income countries and low-income countries.⁴ The possible reasons for limited number of good quality clinical trials in developing countries are lack of funding, inadequate trained researchers, limited research resources/infrastructure, poor access to the published literature and non-existence of research and ethical regulatory bodies.^{3,5}

One solution to these problems is conducting collaborative clinical trials.⁶ A collaborative clinical trial can be

conducted by multiple investigators, at more than one site, following same study protocol. Multicentre collaborative trials are helpful in efficient evaluation of new drugs or procedures by recruiting large number of subjects within a short period of time. This is specifically useful in investigating rare diseases. Multicentre collaborative trials in resource-limited countries are usually cost effective and help in improving the external validity of the treatment by subsequent generalisation of its findings. However, it needs to ensure that standardization of the procedures and implementation of the protocol is comparable at all centres.⁷⁻⁹

There are many successful examples of large scale, multicentre, multinational collaborative clinical trials on important issues. Involvement of researchers from different background and settings resulted in enthusiasm, energy and dedication for “doing the undoable” research.^{10,11} Participation with large collaborative groups provides opportunity to researchers of resource-poor countries to gain experience of conducting a good quality clinical trial. Some collaborative trial’s management offer good clinical practice (GCP) to the trial collaborators. GCP is a globally applicable quality standard, set by International Council on Harmonisation (ICH) for designing, conducting, recording, and reporting trials, conducted on human subjects.¹²

Reduced cost, faster recruitment rate and commercial interest of pharmaceu-

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tical industry is leading to shift of clinical research to low- and middle-income Asian countries. This recent trend of global migration of clinical trials to developing countries has important clinical, economic, socio-cultural, regulatory, and ethical implications.^{3-5,9} The most critical issue is the selection of centres other than sponsoring country by trial management or sponsor, based on the loose control of regulatory and ethical bodies or economic benefits only. In past, serious ethical issues have been raised on clinical trials conducted in developing countries by researchers from developed countries where the trial could not be conducted due to ethical restrictions of the sponsoring developed country.¹³⁻¹⁵ Issues of informed consent, adherence to study protocol and protection of rights of the participants are particularly vulnerable to violation in these trials. Credibility and integrity of research ethical committees for review and monitoring of research in developing countries has been questioned in past on these pages.¹⁶

Looking at the risks and benefits of multicentre collaborative trials, it is felt that multicenter collaborative clinical trials should be encouraged provided that recommendations of the U.S. National Bioethics Advisory Commission Bethesda¹⁵ are respected. Efforts should be taken to protect the rights and welfare of trial participants by addressing issues related to both substantive and procedural ethics in collaborative research. Research questions related to health needs of developing countries should be preferred. Training like GCP and capacity building of local collaborators for planning, conducting, monitoring and reporting of clinical trials may be ensured. Management of multinational collaborative trials should select national coordinator for each country and princi-

pal investigator for each site which can train and supervise other collaborators. Frequent meetings of collaborators at national level will be helpful in training and facilitation of collaborators, resolving practical problems and ensuring uniformity in conducting trial procedures. A very important issue is to provide training and capacity building of autonomous national regulatory bodies and research ethics review committees for review and monitoring of clinical trials in developing countries.

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CONFLICT OF INTEREST

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