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RESEARCH ARTICLE

ROLE OF INSTITUTIONAL REVIEW BOARDS IN THE REGULATION OF ETHICAL GUIDELINES FOR CLINICAL RESEARCH IN INDIA

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ABSTRACT

Recently, the increasing area of attention is the Research funding in the developing countries. The Global Forum for Health Research has pointed out that less than 10% of the world's research resources are earmarked for 90% of the health problems. Over the last decade, Indian clinical research environment has witnessed two forces pulling in opposite directions. The regulatory changes – Indian Good Clinical Practice(GCP) guidelines, Amended Schedule Y, Indian Council of Clinical Research's Ethical Guidelines for Biomedical Research on Human Participants, Clinical Trial Registry of India – all, together with focus on education and training of clinical research professionals in academia and industry, promoted the growth of clinical research and clinical trials. In parallel, frequent media stories of commercialization of clinical research and exploitation of subjects have impeded the growth of clinical research. The Independent Ethics Committee (IEC) also referred to as Institutional Review Board (IRB) in many countries, serves as an independent representative and competent body to review, evaluate and decide on the scientific and ethical merits of research proposals. As per the Bulletin report of the World Health Organization (WHO) there are less than 40 ECs/IRBs in India, which are properly constituted and functioning. This brief review and summary seeks to highlight important arguments and make suggestions to institutional review boards (IRBs) in India to contribute to the future evolution of ethics in clinical research as we advance forward.

INTRODUCTION

Clinical research has expanded tremendously in the past few decades and consequently there has been growing interest in the ethical guidelines that are being followed for the protection of human subjects. Recently, the increasing area of attention is the Research funding in the developing countries. The Global Forum for Health Research has pointed out that less than 10% of the world's research resources are earmarked for 90% of the health problems.[1] Important steps in redressing this imbalance are to promote equity in health research globally and to strengthen the capacity within developing countries to undertake research that is relevant to them.[2] The fundamental principles of human dignity and ethics guides the planning and execution of such research.

Adherence to the principles of good clinical practices (GCPs), including adequate human subject protection (HSP) is universally recognized as a critical requirement to the conduct of research involving human subjects.[3]WHO and UNESCO jointly established Council for International Organizations of Medical Sciences (CIOMS),an international, non-government, not-for-profit organization to serve the scientific interests of the general international biomedical community, and has been active in dispersing guidelines for the ethical conduct of research.[4]

The Independent Ethics Committee (IEC) also referred to as Institutional Review Board (IRB) in many countries, serves as an independent representative and competent body to review, evaluate and decide on the scientific and ethical merits of research proposals. The primary purpose of this committee is to protect the rights, safety and well-being of human subjects who participate in a research project.[5]

Into day's scenario with India being portrayed as hub for global clinical research has lead to the mushrooming of several non-institutional ethics committee's (NEC) all over the

country. Both the IRB and NEC form the foundation stone for initiation and conduct of Ethical human research. The groups of diverse individuals forming the members of the IRB/NEC are entrusted with the valuable task of protecting human subjects and promoting ethically sound research.[6]

At present, there are a large number of (Ethics Committees) ECs operating in India, as 565 IRBs have been registered by Central Drug Standards and Control Organization (CDSCO).The three amendments (GSR 53 (E) of 30.01.2013,GSR 63 (E) of 01.02.2013 and GSR 72 (E) of 08.02.2013)have detailed rules for compensation of injuries, IRB review and IRB registration, respectively.[7]Not much information is available on the detailed functioning of these IRBs.

LITERATURE SEARCH

Literature search for the present article was done both electronically and manually. Electronic search was conducted using databases like Pub Med, Medline, and so on extracting relevant articles published in peer reviewed journals. Various web based search engines like Google Scholar were also used for finding relevant articles. Full text of the articles which were not available electronically was manually retrieved from Sudha Rustagi College of dental sciences and research, Faridabad. Various key words and their combinations were used for literature search like institutional review boards, ethical committees, medical profession, dental profession, etc.

Indian Perspective

The first step in regulating the medical research in India was by the Indian Council of Medical Research (ICMR), in 1980, with the release of a 'Policy Statement on Ethical Considerations involving Research on Human Subjects'. This was the first policy statement giving official guidelines for establishment of ethics committees (ECs) in all medical colleges and research centres. These guidelines were not followed strictly and were neglected by many researchers.[8]
This led to the development and finalization of the 'Ethical Guidelines for Biomedical Research on Human Subjects' in the year 2000. These guidelines were put into force through Schedule Y and considered mandatory for everybody conducting the biomedical research involving the human subjects in India.[8]Later on, the guidelines were revised in the year 2006 to co-inside with the changing scenario.[9]Later on, further changes were brought about by CDSCO in the amendment to Schedule Y, 2013 which addressed the registration of ECs.[10]

Responsibilities of IRB

The purpose of IRB review is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in the research. To accomplish this purpose, IRBs use a group process to review research protocols and related materials (e.g., informed consent documents and investigator brochures) to ensure protection of the rights and welfare of human subjects of research.[11]

IRBs are also responsible for ensuring that informed consent is obtained from study participants. The regulations specify a wide range of information that must be provided to study participants, including a statement that the study involves research, and a description of the procedures, expected duration, and reasonably foreseeable risks to the subject. An IRB may approve an abbreviated consent procedure or waive consent entirely under limited circumstances.[12]

Composition of IRBs

Institutional Review Boards (IRBs) stand as a bridge between the researcher and the ethical guidelines of the country.[8]The IRBs are set up by the institution involved in clinical research; the institute is likely to choose members who are known to the institute with some selection bias in the IRB. During selection of members, institute heads need to be clear about the qualifications of members required to constitute a compliant IRB.[7]

The chosen IRB members should be trained in regards to the ethical codes (both international and local) for the bio-medical research and their roles and responsibilities as members. There should not be differences in training among the IRBs members across the country or even locally.[13]IRB training must include local regulations and some countries have developed their own modules for ethics education.[14]

The requirements for IRB in India are that it should be composed of at least seven members; with a minimum of five persons are required.[5]The composition of the IRB in India is as follows:[5] one Chairperson, 1-2 basic medical scientists, 1-2 clinicians from various Institutes, One legal expert or retired judge, One social scientist/ representative of non-governmental voluntary agency, One philosopher/ethicist/theologian, One lay person from the community and Member Secretary.

The independence of the committee can be maintained by selection of the Chairperson of the Ethics Committee from outside the institute. The Member Secretary in most of the cases is from the institution where the research will be carried out. Others members should be a mix of medical/non-medical, scientific and non-scientific persons including lay public.[5]

The committee must include one member who is independent of the institution/trial site and one member whose primary area of interest/ specializiation is non-scientific. There is also requirement for adequate gender representation of the Committee. The subject experts concerning particular subjects of interest may be invited if required. Specific patient groups may also be represented in the committee, for example HIV/AIDS, genetic disorders etc, if required. Members should be aware of local, social and cultural norms.[5]

The role of the lay person on the IRB is to view the research from a nonscientific point of view and opine whether the informed consent form is in a language that is comprehensible to a lay person. It may therefore be essential to have a person with nonscientific bent of mind, though he or she could be an expert in a different field.[15]

Challenges faced by the IRBs

However, a lot of questions have been rising about the competence of IRBs in India. These questions center on the various issues related to the composition of the IRBs, the competence and training of their members, their independence to take decisions, and their overall approach towards protection of human subjects.[6]IRBs face numerous challenges, in establishment, composition, and their working. Some of these challenges are due to conflict of guidelines, some inherent to guidelines, and some may be due to other reasons which are difficult to comhrehend.[6]

In spite of the roles and responsibilities of IRBs, the fact is that many are overloaded, understaffed and faced with a variety of skeptical criticism. Many IRBs are lacking the resources and staff to carry out the hefty task of reviewingresearch.[16]There are differences in training among the various IRBs, which might lead to wide disparities, and this might affect their efficiency and quality of work.[13]

The most basic and neglected activity of an IRB is the Continuous review and monitoring of its ongoing activities. The efforts should be made to make this activity consume the maximum amount of meeting time of the IRB, and in the era of multicentric trials, would not have much effect on increasing the subject safety.[17]Medical or surgical management of injuries during clinical research and compensation to subjects are the issues of concern and guidelines have to be developed regarding the same.[17]

IRBs members comprise of highly educated and experienced representatives from non-scientific communities, but most of them are silent observers during meeting proceedings and do not participate in scientific or ethical deliberations in the review procedures.[18]Some of the members also might have lack of formal training in bioethics, which might lead to limited knowledge of complex ethical issues such as reduced autonomy, distributive justice, subject vulnerability, and subject compensation. Most of the times, IRB members feel that their responsibilities are limited to only providing approval to research proposals submitted for review and many a times, there are not sure of what risks and complications might be involved and there might be a need for continuous review. Very rarely do IRBs undertake detailed monitoring of studies and scrutinize the informed consentprocess.[18]

DISCUSSION

As per the Bulletin report of the World Health Organization (WHO), there are less than 40 ECs/IRBs in our country, which are properly constituted and functioning.[19]This report also raises concerns about the independence of ECs/IRBs citing that there is no legal requirement for members declaring Conflict of Interest (COI). This is an important issue given the increasing number of privately owned hospitals participating in clinical research. The presence of members with conflicting interests is likely to limit the ability of an impartial review by the EC/ IRB.

The ICMR guidelines are not legislated, hence, the IRBs cannot act against those who violate the prescribed guidelines. The role of the IRB is merely restricted to being an advisory or to facilitate research. The DCGI has given IRBs the power to reject trials not conforming to the recommended ethical standards and clearance is given to those trials that have been reviewed and approved by the concerned IRB. Thus, apart from governing the ethical aspects of research, the IRB also plays a significant role of an ethical regulator for the DCGI. However, the lack of a national ethics body, with a strong regulatory control, has further hampered the establishment of a legal ethics policy.[20]

One of the particularly concerning issues before the IRBs is the Medical or surgical management of the injuries that might occur to the participants during experimental research work and compensation for the same. A lot of discussion has already been around about these rules.[21,22,23]The Drug Technical Advisory Board has already made recommendations tothe government to revisit the compensation rules due to the issues raised by the industry members and others.[24]

Indian policy on biomedical clinical trials originating outside the country, although not necessarily effective in practice,[25]is fairly welled fined, and in theory comparable with the systems in developed nations. Although suggested guidelines exist,[26] there is a limited formal ethical review infrastructure in place for non-invasive research on human subjects. Participation is completely voluntary, with no incentives or compensation provided to the subjects involved in this type of research.
Meetings of existing IRBs are sporadic, and most are unwilling to review independent international research proposals; some indicated that they would be unable to convene unless financial support was provided, which would have resulted in a major conflict of interest. Moreover, from an international perspective, information on the options for ethical review in India are acutely scarce. Obtaining an effective approval from the local IRB in this case seemedimprobable.[27]

Also, the area of concern is that the task of evaluating the risks can be cumbersome for an EC member. The risks related to the research may be presented by the researcher/sponsor in the form of Investigator brochure (IB), a voluminous or Informed consent form. The medical EC and non-medical EC members have to review the IB vigilantly and ensure that findings of the IB are reflected in the risks section of the informed consent document (ICD). The incidence of the risks/adverse events must be mentioned in the ICD. The extensive review of the IB and formal calculation of the risk benefit ratio may pose difficulties to the EC member especially from the non-medical background. Is EC member (though medical members are entrusted the task of evaluating risk-benefit ratio) trained to this calculation effectively or there will be high element of subjectivity among different EC members will be a debatable issue.[6]

CONCLUSION

The Indian Society of Clinical Research (ISCR) represents organizations and people who have the largest stake in clinical research in India. A core committee needs to be developed by ICSR by working out with as many Indian IRBs as possible. There is a need for uniform guidelines for regulation and training of IRBs to be developed.[7]

The future of IRB committees in India depends upon the several challenges and the following recommendations are suggested:

- There is strong need for ECs in our country to focus on capacity building.
- Obtaining resources for administration and training to be incorporated as a budget priority.
- Gaining official support for researchers to abide by IRB decisions.
- Selection of members and operating procedures appropriately by establishing the uniform guidelines.
- Members of ECs should be trained in the principles of bioethics, local regulatory guidelines, and Gaining official support for researchers to abide by IRB decisions.
- Government agencies like the ICMR along with the Forum for Ethics Committee Review in India (FERCI) need to take forefront initiatives in organizing training programs for EC members.[28]

- Training programs should be conducted keeping in mind both International ethical guidelines; and social and cultural scenario in perspective and aim at community welfare and protection.[29]
- Establishment of a Central Registration System for ECs in India at par with the Central trial registry of India (CTRI). This should be an important step towards introducing regulatory control in the proceedings of the ECs.[28]

The IRBs are one of the most important mechanisms for protecting subjects. All efforts must be made to ensure that IRBs across the country are competent. There is urgent need for oversight of IRB functions and the regulators needs to have a division which will have oversight over IRB functions, monitoring them regularly, auditing them sometimes, and help to protect human subjects.

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