Review Article

Endnote: Vision of research ethics

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The word ethics derives from the Greak word ethos, which means customs or character and determines what is the right and wrong thing to do. In past 60-70 years several International and National guidelines for ethics in research have been developed.

However practicalities of implementing the guidelines, keeping updated on rules, regulation and guidelines, developing new guidelines as science advances, dealing with different views and expectations of society, media, senior practitioner, young researcher and industry have been our challenges.

Our vision of ethics in clinical research has to be in the context of these challenges, current health education, practice of healthcare and research scenario in the country. It needs to consider the pharmaceutical industry, socio economic and political situation and the effect of mass communication media.

CURRENT SCENARIO

Healthcare

Allopathic systems, Alternative systems, dental, nursing and pharmacy education is regulated by various Councils and implemented through Colleges and Universities. Practice of healthcare is regulated by State Councils. Compared to global average, in India, the Healthcare providers to population ratio and its geographical distribution is inadequate. Our country is lagging behind in key healthcare indices. Even the projected improvements, over next 10 years, in the millennium development goals of reducing maternal mortality and below five years of age mortality, are not good if we continue with business as usual.[1] Providing health service is therefore primary goal. There is little time for research. Salaries and promotions are largely not linked to research. So there is no much pressure to write grants and carry out research. What researchers do is out of urge to excel. Practioners conduct clinical trials to gain experience, interact with peers and for financial gains.

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Research training

The Medical Council of India and Health Universities have made a certificate course in basic research methodology mandatory, for post graduate students and teachers. The State Medical Council requires for reregistration mandatory credit points from attending seminars and conferences (although attending research methodology session is not mandatory).

Clinical research

At present publication on clinical research and clinical trials in India form only 1.2% of 0.76 million global publications (in pubmed) on the subject. There is also considerable regional disparity. Although there are over 50 training institutes and over 100 programs devoted to clinical research, many of these have several deficiencies such as shortage of well trained faculty and lack of hands on experience.[2]

Regulation for ethics in research

Indian Council of Medical Research has published Ethical Guidelines for biomedical research on human participants, for stem cell research and for good clinical practice. Schedule Y of Drugs and Cosmetic Act and Rules state the regulatory requirements for clinical trials.

In practice, Ethics Committees, which are established as per these guidelines and regulations, carry out ethics review and also scientific review. Institutional administrative rules are usually dealt with separately.

Industry and market

Until 1991, Nehru's socialistic ideology with strong focus on self reliance, local production and high degree of protection for small scale producers, partly a legacy of Mahatma Gandhi governed us. This boosted the local industry.

In 1991 India made a 180 degree turn and started the process of globalization with jump in growth rate, spurt in national income, cuts in taxes and import duties. India signed TRIPS agreement in 1994. With liberalization multinationals forayed and changed the market in India. However Indian market also required a new way of thinking for the multinationals.[3]

From being treated with suspicion and mistrust, Indian business has come a long way in past 20-25 years. Indian business leaders have been celebrated and feted and held up as role models. However there is declining credibility and lack of confidence. Industry's response to this has been so far incoherent.[4]

Society

India wants continuity with the past while looking forward to future. For e.g., Society's faith in astrology has not decreased with rising level of scientific education. Society simply moved to computerised horoscope.[3]

Indians still believe that Lakshmi and Saraswati cannot live together. We believe in mythological stories. In one story Kuber the treasurer God offered to feed Ganesha God of knowledge. He emptied his whole treasure but could not appease God Ganesha. This story emphasized that knowledge is infinite while wealth in finite.[5]

Clinical trial participants

Meta analysis of published articles[6] identified factors that favour or hamper decision by patients or healthy volunteers to participate in clinical trials [Table 1].

Study by Burt *et al.*,[7] found that most (90%) participants believed that clinical research is an essential step in developing new treatment and it benefits society. They (80%) trusted information provided by academic institutions, but only 50% trusted information provided by pharmaceutical companies.

Media

Mass communication media report mishaps. Editors of journals National dailies and TV network carry a special responsibility and should be scrutinizing relevant documents when reporting.[8] Detailed enquiry takes long time to be published and is often not provided in lay press. This causes further mistrust.

Vulnerability of population like tribals, villagers and students, compensation for death injury or serious after effects, availability and access to drug after clinical trials, weak laws controlling clinical trials in India are other important issues highlighted by media. Parliamentary Committee report has also recently highlighted deaths in clinical trials.[9]

SOME SUGGESTIONS

Mahatma Gandhi has said "it is not our patient who is dependent on us but we are dependent on him" we should forever be mindful of this obligation to our patients.

My high school going exceptionally bright, 15 year old grandniece who is studying in England remarked that the most important issues for ethics in research are providing and communicating transparently information on risks and benefits including financial and taking care of health of participants.

She was recently faced with question of whether to take HPV vaccine and is thus well aware of the issues involved.

Table 1: Factors favouring and hampering participation-percentage contributing to each of the factors favouring and hampering participation in clinical trial

	Percentage of response
Factors favouring	
Personal health benefits	47
Altruism	43
Source of extra income	31
Trust in physicians,	8
Detailed knowledge about	21
Methods used for motivating participants	34
Factors hampering	
Mistrust on trial organization	26
Concern about efficacy and safety	21
Psychological reason	6
Burden	11
Loss of confidentiality	17
Dependency issue	19
Language	1

Physicians and academicians

Physicians and Academic Institutions often have the faith of people and should hold constructive debates with stakeholders frequently and help develop new guidelines as sciences advances.

Media

Media have done a commendable job in bringing to light some issues in clinical trials and will continue to do so. Media usually highlight enthusiastly discoveries and innovations specially if International and specially on issues of great human interest.

Media could play an important role in communicating to people what information the patients should seek while participating in clinical research.

Clinical trials related issues are media highlights as breaking news. These broken pieces need to be put together to bring out the reasons for mishaps and how to avoid these mishaps and how to protect public interest.

Pharmaceutical industry

Patients put themselves to risk to benefit self and others and sometime sacrifice individual privacy to safeguard public health [Table 2].

Pharmaceutical industry should disclose information and provide access to medicines as part of ethical and moral obligation to protect research participants and serve humanity. In a recent analysis on rosiglitazone, Mello *et al.*, have commented how data from premarketing studies was not made public until a court order. Out of 42 clinical trials only seven were published causing considerable delay in the meta analysis that provided evidence of the risk.[10]

It is claimed that there needs to be balance between transparency and disclosure of information and proprietary interest. Manufacturer should really articulate a persuasive reason how disclosure of information gives such competitive harm as to outweigh public health benefit.[10]

Disclosures are not just about ethics but about earning trust of society. Industry should not wait for information to be asked under Right to Information (RTI) Act or through court order. The pharmaceutical companies can introspect on how to build trust of society and how to build the capacity for good ethical clinical research and societal participation specially in trial sites across the country. Pharmaceutical companies and CROs could give public information statements on global happenings about their drugs undergoing clinical trials as well as marketed drugs and take affirmative action.

Table 2: Ethical dilemmas

Transparency and disclosure of information	Vs	Proprietary interest
Access to medicines	Vs	Patent protection
Safeguarding public health,	Vs	Protecting individual privacy
Benefits to self, others	Vs	Volunteer risk to self

Ethics committees

Opinions of Ethics Committees on even observational studies vary.[11] Ethical review reflects diversity of thinking, searching and arguing for general consensus. Sponsors should provide information in simple language so that all members can understand and contribute to the process.

A dialogue amongst ethics committees of multicentric studies would also strengthen and expedite the process. Ethics Committees could help investigators to give announcements about clinical trials, that are informative, understandable and devoid of unsuitable inaccurate phrasing.

Monitoring

Frequent dialogue between investigators and ethics committees can improve conduct and review process. There should be interaction with participants of clinical trials to understand their concerns, fears and to inform and reassure them.

Education

Ethics, informed consent, truthfulness are vital for conducting clinical research, for gaining acceptance and support from society and generating valid, relevant information and knowledge. Talks by respected role models and experts to guide young minds into developing appropriate attitudes towards patients and research would be a good long term investment. Ethics should be part of programs for management students and all those who regulate, finance, implement, monitor, review and opine on clinical research.[2]

END NOTE

Conducting clinical research, reviewing it or participating in it should be a delight, not a burden. A patient should look forward to reading like a novel the information on the new product which he will be consenting to take, with trust, whether to benefit him or the society. An ethics committee member should be eager to gain knowledge and contribute to it when he/she reviews the protocol which should be like an interesting well written article.

In the midst of heavy burden of work, an investigator and team should look forward to the pleasure of interacting with colleagues and experts and the challenge to formulate hypotheses, design the study and conduct it, confident

that it will benefit participants, gain knowledge and find solutions to problems.

Financial gains and intellectual fame should not muddle our thoughts. We have today the greatest opportunity of translational research and clinical research.

John Kotter[12] says to deal with change you should build effective team based on trust and common goal. Benefitting patient and society is our common goal. Stakeholders should work as effective team with common goal.

Noble Laureate poet Ravindranath Tagore wrote

Where the mind is without fear and the head is held high;
Where knowledge is free;
Where the world has not been broken up into fragments by narrow domestic walls;
Where words come out from the depth of truth;
Where tireless striving stretches its arms towards perfection;
Where the clear stream of reason has not lost its way into the dreary desert sand of dead habit;
Where the mind is led forward by thee into ever-widening thought and action
Into that heaven of freedom, my Father, let my country awake.

To this poem by Ravindranath Tagore, one could add "Into that heaven of freedom my Father let clinical research serve the society".

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