

ETHICS IN CLINICAL RESEARCH

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"Biomedical Research has acquired dimensions which are at once exciting and awesome. It raises some delicate and difficult issues of ethics which need to be dealt with sensitivity to human values and with great circumspection. While research which promises to mankind the great blessings of Science should not be stifled by too restrictive an approach, however, great care should be taken to ensure that something does not go out of hand. Therefore, any system of ethical guidelines on research needs to be cognizant of, and informed by, a sensitive balance of the risks and benefits."

Justice M. N. Venkatachaliah¹

Ethical principles

The health care team involved in research is ethically bound to respect human life and peoples' autonomy. Good research practice demands that researchers must respect the rights of their subjects, listen to and share information with them, and treat them courteously and caringly.

Ethics refers to moral principles governing human character and conduct. The principles of medical ethics, introduced by Beauchamp and Childress² in 1979, are as much relevant to the medical research as they are to healthcare.

The principle of **autonomy** requires us to treat subjects as autonomous individuals whose welfare and rights need to be respected.

The principles of **beneficence** (do good) and **non-maleficence** (do not harm) requires investigators to minimize the harm and enhance benefits to the study population.

The principle of **justice** requires priority to be given to the interests of worst off even if the total welfare in society is thereby diminished.

Guidelines for research on human subjects

In 1964, the World Medical Association Declaration of Helsinki underscored 12 basic principles for the conduct of human biomedical research. The guidelines underwent revisions recently.³ The issue of research in developing countries was taken up by the Council for International Organization of Medical Sciences (CIOMS) which in collaboration with World Health Organization, proposed guidelines for international research. The guidelines were further amended in 1993 as the *International ethical guidelines for biomedical research involving human*

subjects.⁴ The Indian Council of Medical Research¹ has also set out the standards expected of all healthcare providers conducting research. These guidelines stress that clinical investigators must be aware of -and apply- ethical principles in practice and research. By doing so, they safeguard the health, rights, privacy, and dignity of their subjects. As Calman⁵ aptly describes, "To begin the journey or lay the foundations, requires definition of a series of characteristics which might include truth, openness and sharing; respect for the views of others and tolerance; the rights of others to make decisions and autonomy; doing your best for others, not doing harm; keeping promises; sharing difficult times together."

More recently, Emanuel and others⁶ have proposed requirements that explain a framework for assessing the ethics of clinical research studies. Here, I discuss how addressing ethical aspects may improve attention to ethical issues in planning and conduct of research.

Ask an answerable research question

Research has been defined as "an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge".⁷ An unclear research question destroys the validity of research and breeds an unethical study. Hulley and Cummings⁸ argue that a good research question must be feasible, interesting, novel, ethical and relevant. It should also clearly define subjects, intervention and outcome of the study. Compare the following two research questions, and decide which one is focused and answerable: (a) "In paediatric patients, is intranasal route of fentanyl better than intravenous route for providing faster post-operative pain relief?" (b) "What is the role of fentanyl in post-operative analgesia?"

We live in an era of 'publish or perish'. Young researchers often succumb to the pressure for academic success and promotion and the institutional demands to secure research grants.⁹ An ethical researcher must rise above these selfish motives. A research study should

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advance scientific knowledge, lead to improvements in health and should have social, scientific and clinical value. A researcher should always be conscious of ethical principles during conception, design and execution of a research study. Research integrity spans study design, collection and collation of results, data analysis and presentation.⁹

Pay attention to study design

For research to be ethical, the study design must be scientifically sound. It should have sufficient power to test the hypothesis. A poorly designed and underpowered study would fail to provide an accurate and reliable answer to the research question, even though the question has been well framed. It is unethical to conduct a study with major flaws in its design.

Choose your subjects without bias

The principles of benevolence and justice require that we must choose our subjects without any bias. We must safeguard the rights of poor, illiterate, disadvantaged and vulnerable patients: the population that houses general wards of a public hospital. Fearful of the fact that rich and powerful can be 'problem subjects' researchers selectively exclude them in their study. For a study to be ethical, the inclusion and the exclusion criteria need to be described properly. When the subjects in a study are well chosen, its results can be applied to the population that will receive the interventions.

Enhance benefits, minimize risks

We are often confronted with difficult decisions that go well beyond the choice of drugs, devices and interventions. Because we want to contain cost and increase operation room efficiency, we often take short cuts in practice. We do not tell subjects that during study some tests or procedures may harm them; that they might have to take more tests, pay more and stay longer in the hospital because study design demands so. We should not callously disregard their welfare for the sake of research goals. According to the principles of non-maleficence and beneficence, we should minimize risks by using procedures which are consistent with sound research design. We must ensure that benefits from the research outweigh the risks. It is unethical to ask a group to bear the burden of trial while the benefits are passed on to the advantageous group.

Have your protocol reviewed

Before a study begins, it must be approved by a research ethics committee (institutional review board). This ensures that the people who enroll in trials are informed what the study is about, their welfare and rights

are protected and they are not harmed. We often want to finish- and publish- our study quickly. This desire can cloud the value judgment of even well-meaning investigators regarding the design, conduct and analysis of research and may lead them to use unscientific and unethical methods.

Respect your subject's rights

The first principle of medical ethics (autonomy) requires us to respect people and their rights. Informed consent ensures that individuals can decide to participate only when the research is consistent with their values, interests and preferences. Though written consent forms are used to document the consent, the process of informed consent is more important than a subject's signature on the form. The General Medical Council, UK¹⁰ provides following simple guidelines for obtaining informed consent in medical research:

"Research involving clinical trials of drugs or treatments, and research into the causes of, or possible treatment for, a particular condition, is important in increasing doctors' ability to provide effective care for present and future patients. The benefits of the research may, however, be uncertain and may not be experienced by the person participating in the research. In addition, the risk involved for research participants may be difficult to identify or to assess in advance. If you carry out or participate in research involving patients or volunteers, it is particularly important that you ensure: (a) as far as you are able, that the research is not contrary to the individual's interests; (b) that participants understand that it is research and that the results are not predictable.

You must take particular care to be sure that anyone you ask to consider taking part in research is given the fullest possible information, presented in terms and a form that they can understand. This must include any information about possible benefits and risks; evidence that a research ethics committee has given approval; and advice that they can withdraw at any time. You should ensure that participants have the opportunity to read and consider the research information leaflet. You must allow them sufficient time to reflect on the implications of participating in the study. You must not put pressure on anyone to take part in research. You must obtain the person's consent in writing.

Unfortunately, for most clinical investigators in India, informed consent is a dispensable formality and few of them explain to patients what the trial is all about. The consent forms are lengthy, complicated and difficult to understand. Obtaining consent from a patient is often

delegated, in public hospitals, to the junior most nurses or a resident. Also, the patients are poor and even if they do not want to enter the trial they do not refuse. They believe that this would displease their treating clinicians who may deliberately ignore them during their hospital stay. On the other hand, doctors in the private sector are worried that on hearing the very term 'trial' patients might choose to get treated elsewhere. Investigators often shorten the consent form or deliberately omit some 'offensive' parts that might deter patients from agreeing to participate.¹¹

Ethics, evidence, elegance- research so graced is a great achievement. Medical researchers have an opportunity to work together to achieve and maintain ethical standards in research. We need to show that we are committed to achieve this objective.

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ANNOUNCEMENTS

- u The Indian Journal of Anaesthesia has been indexed with **INDEX MEDICUS FOR WHO SOUTH-EAST ASIA REGION (IMSEAR)**.
- u For adequate publicity and dissemination of Indian Biomedical Research Indian Medlars Centre of National Informatics Centre (NIC) has indexed **Indian Journal of Anaesthesia in IndMED**.
- u Readers will be delighted to note that Indian Journal of Anaesthesia is being disseminated through Internet by NIC. This great leap forward heralds a new era for Indian Journal of Anaesthesia even before we welcome the millennium. Access to our journal of internet will be at the website. <http://indmed.delhi.nic.in>.

- Editor

MEDICO LEGAL QUERY?

Dear Members,

Of late, cases under CPA, against anaesthesiologists, are increasing throughout the country. Though most of the cases are dismissed, ultimately by the court of law, they are causing lot of tension and worry for the doctors and their families. One of the G.C.Members of ISA, **Dr. S. C. Parakh MD (Anaesth), LL.M**, is well versed in medico-legal aspects and he has kindly volunteered to answer any of the medico legal queries related to our profession from any of the ISA members. Please contact him at 4-2, Daffodil Apt., DD Colony, Hyderabad 500 007.

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President, ISA