CLINICAL TRIALS IN INDIA: SHOULD YOU OR SHOULD YOU NOT PARTICIPATE?

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The last 10 years have been witness to an increasing number of clinical trials conducted in India. Indian pharmaceutical companies are investing higher amounts in R & D as they nurture global ambitions. Significantly, many multinational pharmaceutical companies are eyeing the opportunities available in India to augment their R & D productivity. The result has been an exponential growth in the number of clinical trials conducted in India. This growth is mirrored in large measure by the increase in the debate on the ethics of such trials in India. A number of commentators, in India and abroad have alluded to the participation of Indians in clinical trials as the "guinea pig syndrome". Though the debate has been good to bring clinical trials into limelight, it is also responsible for shaping the attitudes of most Indians towards clinical trials. Any ambiguity about the role of such clinical trials in our society reflects the confidence (or lack thereof) we repose in the process for development of new drugs. Imagine a patient who goes to his doctor looking for a cure. What is he to make of a clinical trial his doctor offers to enroll him in? What is the trial? Is it really needed? Why is my doctor offering this? What's in it for him? Do I have any options? Will he bear a grudge against me for saying no to participation? Am I really safe if I enroll in this trial? These are some thoughts that are likely to cross the mind of any patient. It is important to examine the reservations that shape these questions and the perception of clinical trials in the country.

What is a clinical trial?

A clinical trial, simply put is an experiment conducted to study if a new medication is safe and effective in the treatment of a particular medical condition. Because not much is known about the new medication at the time of a clinical trial, doctors are required to follow a rigorous schedule to oversee patient safety. Patients may be required to follow-up with the doctor more often than in routine practice and the doctor's team is expected to spend much more time with the patient than in routine practice. This usually works to provide much more stringent oversight for patients in a clinical trial than they might have access to otherwise.

Why does a clinical trial need to be conducted? Why can't we just use the current medicines available?

The premise of any clinical trial is the "principle of essentiality" elucidated by the Indian Council of Medical Research. A clinical trial is done, simply because, it needs to be done. If other methods were available to evaluate new medicines, scientists and governments would be more than happy to use those for evaluation of new agents. However, even though a number of initiatives are being explored to reduce the number of patients exposed to new clinical trials, the fact remains that the clinical trial remains the most robust way to evaluate new agents today. It's also important to appreciate that modern medicine, though highly evolved, is yet an imperfect science. To quote a recent Businessweek story "From heart surgery to prostate care, the health industry knows little about which common treatments really work". Most medicines used today offer significant alleviation of suffering in relative terms, but in absolution, modern drugs suffer from safety and efficacy issues. Scientists and doctors over the world continue the search to understand which treatments are safer and better for their patients. So when a doctor offers to enroll a patient into a clinical trial, he's really requesting the patient's collaboration in an experiment to further the understanding of medicine. The objective is to allow patients access to better medicines in the future to come.

Do patients really understand clinical trials?

They must! All doctors are obliged by the law and by international guidelines for ethical research to seek informed consent from patients. Informed consent means that doctors must explain the trial to patients, make sure they understand their rights and obligations and have the chance to make a fully informed decision, to participate or not to participate. The exact nature of the discussion is privileged between the doctor and the

patient, but broadly a well taken informed consent requires the patient to understand that he has the option to not participate in the trial, that the trial represents an experiment, that the patient has certain responsibilities should he choose to participate and that there are both potential benefits and risks of participation in the trial.

How does the patient know if the doctor can be trusted? Who makes sure the patient is protected?
The best person to protect the patient is the patient himself! Patients are becoming more a part of the medical management process today, an effort in which they collaborate with their physicians. An empowered patient should take on the responsibility of understanding all aspects of the trial. It's also important to note that all trials of experimental drugs (not approved for a particular indication) are required to be approved by the Indian regulators – the Drugs Controller General of India. All trials are also reviewed and approved by an Ethics Committee. The Ethics Committee is composed of individuals that represent a cross section of society, doctors, scientists and non-scientists. The members of the ethics committee approve the conduct of a trial after careful consideration and after establishing that the trial is ethically and scientifically justified. On an ongoing basis, ethics committees are required to monitor the conduct of trials to ensure that they are being conducted in an ethical and law-abiding manner. Patients should know that at any given time, they have the right to approach their doctor and/ or a designated member of the ethics committee with questions about the trial. This provision is to allow free and frank exchange between patients, their doctors and the ethics committees. Needless to say, the better informed a patient is, the better informed he will be to make a decision on participation in a trial. Most doctors on an average take an hour to two of discussions with their patients (usually over 1-2 meetings) and the patient's family/ spouse before seeking the informed consent. Discussions must be held in the language the patients are most comfortable in. Patients must retain a copy of the signed informed consent form. In many cases, patients refuse to provide consent and choose simply to be placed on one of the other treatment choices. In many other cases, patients choose to participate and may opt out of the trial later for various reasons. Either way, it is imperative to know that the choice of participation or of continued participation is the patient's to exercise.

How safe is a patient in a clinical trial?
The honest answer – nobody is sure! The better question to ask is – how safe is a patient every time he takes a medicine? Patients tend to think of marketed medicines as safe and experimental medicines as unsafe products. The fact is that most marketed medicines come with a long list of side effects that have been observed with them. It is true that in relative terms, much more knowledge might exist about most marketed medicines than there is about experimental medicines.
However, it is also true that if the existing medicines were really safe and effective, there would not be a need to test new experimental medicines. A recent study in the US showed that 70% of physicians surveyed had safety concerns about the drugs they prescribed to their patients. Further, given that most patients will be better monitored in clinical trials than they will be in routine practice, from an oversight perspective, many would argue that patients are not unsafe in a trial. The key thing for patients to remember is that they are integral to a clinical trial and must continue to discuss options with their doctors on an ongoing basis. It's also pertinent for patients to bear in mind that they have certain responsibilities when they participate in clinical trials. The need to comply with the trial visit requirements, the use of medication and the need to reach out to the trial physician in case of any adverse health occurrence are necessary to ensure that patients can be extended the care and oversight that they are entitled to. The purpose of this article is not to scare patients about the lack of effective therapies for them. The rapid strides in modern medicine are borne out by the significant alleviation of disease over the last 50 years. In the face of many uncertainties, it is gratifying to appreciate the skilled and balanced approach modern physicians take in striking the balance between risks and benefits of various options available.

Are Indians being used as guinea pigs in clinical trials?
This is the most common criticism leveled at clinical trials in India and has various components to it. Lets examine the various components –
Informed consent is not possible in India: There is a commonly held myth that patients in India are not

capable of understanding choices available to them. To understand these choices, one does not need to be a doctor. Many doctors would not necessarily understand all aspects of all new medicines. Neither will most scientists. But to suggest that an Indian patient cannot understand that he is being asked to enroll in an experiment, that he has options available to him and that there are potential risks and benefits of all options is being elitist. Most patients will understand these options very well.

How can illiterate patients provide consent –Clinical trials in India include a large proportion of literate and illiterate patients, reflecting the reality of our society. It is a bit frivolous to confuse illiteracy with incompetence. A large portion of the Indian population is illiterate, however this does not call into question the credibility of the political vote they exercise every 5 years. Repeated business technology initiatives in the recent past have demonstrated the native intelligence of the rural Indian as well as the illiterate Indian. The e choupal initiative by the Indian business conglomerate ITC has taught rural Indians to use the power of the internet to analyze market trends and make smart business decisions that impact their livelihood. The "Computer in the Wall" initiative by NIIT (an IT training company) showed how illiterate Indian children can learn to use the power of the internet without any training whatsoever. There is ample evidence that even the average rural and illiterate Indian (two distinct classes that do not necessarily converge) is capable of understanding and making choices. There's no evidence to suggest that if explained a trial properly, Indian patients will be less competent to exercise their choices in a clinical trial An illiterate patient may not understand all the safety aspects of a new drug (for that matter, neither would most literates!), but will very well understand the options available to him. The moot point is to ensure that the trial is explained appropriately to the patients. A good informed consent takes time, patience and effective articulation on the part of the consenting physician. But once this is done, Indian patients are as capable (and free to) exercise choices as citizens in any other country. It is important to appreciate that informed consent can be taken ethically, and if it is not, then that is an aberration that can and must be addressed.

Why should Indian patients be used for clinical trials? Western pharmaceutical companies are using poor Indian patients to test their expensive drugs.

It is true that in the last 5 years, more and more multinational pharmaceutical companies are placing parts of their clinical trials in India. It is important to note that the trials done in India are simply part of trials done in other parts of the world. Indian patients are not treated differently than patients in Australia or Europe or North America. Further, despite all the recent buzz of increasing clinical trials in India, the number of Indian patients participating in clinical trials remains a tiny fraction of those in other countries. Estimates would place this number at less than 5% of clinical trial patients globally. And finally, what is wrong with the participation of Indian doctors, hospitals and patients in clinical trials? For the last 50 years, Indian patients have benefited immensely from trials of new drugs conducted on patients in the US and Western Europe. To be a part of mainstream global clinical research is an opportunity that we must be happy to participate in and contribute to.

Admittedly, concerns about improperly conducted clinical trials are not to be dismissed. There have been instances in the past, in India as much as in other countries, when guidelines for the conduct of ethical research may have been flouted. The informed consent may not have been exercised appropriately in some instances. It is also important to beware of research misconduct, mala fide or otherwise on the part of the doctor investigators. The research community is aware of and always on guard against the possibility of such conduct. These are all instances that can and will impair public faith in the clinical trial process. However, these instances are not unique to the Indian milieu and represent the aberration rather than the norm in the clinical trial world. Mechanisms are available in India, as they are in other countries to guard against such instances. Further, it is useful to remember that in an environment where the incentive (or lack of disincentive to) to misconduct research is the same in India as in any other part of the world, a major systemic deterrent is the unique nature of the Indian society. The democratic institutions, the freedom of the press and the availability of open platforms for people to challenge each other serve as the perfect deterrents to any stakeholder that may wish to digress from ethical norms of clinical

research. This constitutes as much of a deterrent as any that may exist in other societies. And this systemic transparency in our social system makes India an attractive country to conduct credible and scrupulous clinical research.

Over the last 50 years, pharmaceutical research has added much to the body of knowledge in the healthcare community. India, a passive participant in most of this new drug development, will inevitably contribute much more to this research over the next 50 years. As a society, it is important for doctors, regulators, ethics committees and most importantly, patients to work together to ensure conduct of ethical research. There might surface instances that question our ability to conduct good clinical research. However, to throw the baby out with the bathwater is not the answer. We have fantastic doctors and researchers in India that are interested as much in the knowledge accrued from new research as they are in the ethical process of gaining that knowledge. It's time for India to take center stage in collaborative global pharmaceutical research. Talking openly about the clinical trial process and measures to strengthen those can only serve to further strengthen the foundations of our research infrastructure and mindset.