Clinical trials: some ethical issues

Research often promotes commercial interests while exploiting vulnerable participants

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All research designs have their strengths and limitations. A comparison of lung cancer in the US and India with average tobacco intake in the two countries could say something about whether cigarette smoke causes cancer. So could following two groups, of smokers and of non-smokers, over ten years, to see how many get sick, and how many die, and of what. A look at a death register, tallying causes of death to the dead people's occupations could yield information on occupational risks. Comparing schoolchildren's exam score with their blood lead levels indicate the the effect of lead. Giving one group of AIDS patients AZT and the other a sugar pill, and then measuring the blood levels of the virus in the two groups will give information on whether the drug works.

The 'gold standard'

Clinical trials to introduce a new drug or other therapy, are based on the concept of the randomised, placebo-controlled clinical trial, sometimes called the 'gold standard' of research studies (1). A study sample representative of the population is divided, at random, into two groups, equal in every way. One (the experimental group) is given one drug and the other (the control group) either a placebo (a sugar pill) or perhaps another, older treatment. Researchers then measure for some predefined outcome, such as getting better faster, or evidence of a lower viral load. If people taking the drug get better faster than those taking the sugar pill, the drug works. Ideally, neither participant nor researcher should know which group a particular participant belongs to. All this is in order to reduce various biases on the final outcome.

The clinical trial is thus considered to be a potentially powerful research tool, and a source of very accurate knowledge. It is also a rich source of discussion on ethics.

Informed consent

Informed consent is a concept central to research. All the various scandals about clinical trials currently in the news involved the questions: did the participants know they were part of a trial? Did they give their informed consent to participate after being told of the possible risks, and the limited benefits? Too often, they did not.

Informed consent was not received from the 1,000 Indian women with early, pre-cancerous changes in the cervix, were recruited by an ICMR-approved research group and 'monitored' to record the progression to cervical cancer (2). It seems that the women were unaware of their health status, and the consequences of participating in such a trial. The notion of informed consent was incorporated into ICMR protocols much later.

Was informed consent obtained from the over-50,000 women in India and south-east Asia who were sterilised with the mutagenic anti-malarial drug quinacrine, adminstered with an IUD inserter, to cause inflammation and blockage of their fallopian tubes? Not likely, going by the comments of the doctor campaigning for such mass sterilisations of poor women. While noting the WHO's opposition to this technique in the absence of certain toxicological tests, this doctor suggests that his colleagures obtain signed informed consent -- but only from women in developed countries, because they might just decide to sue.

"Faced with the dilemma that the quinacrine pellet is the method of choice for some women even though quinacrine is not approved by governments or international bodies for this use, an increasing number of physicians in some countries have decided to offer it to some of their patients... Women should, of course, be informed of these risks and benefits. ***In industrialised countries where malpractice litigation is prevalent, it is recommended that written informed consent be signed by the patient." (3)*** **(emphasis added)**

Informed but not voluntary

Are potential participants always capable of giving informed consent? Clinical trials of drugs given to HIV-positive pregnant mothers, in Africa and Asia, to prevent maternal-foetal transmission of the virus, were attacked (4) because they were testing an experimental drug (lower doses of a standard treatment now being given to women in the West) without providing the control group the standard treatment -- something that wouldn't be permitted in developed countries. One of the investigators' arguments was that the women concerned had given their informed consent.

What kind of informed consent can be obtained in such circumstances? A woman knows she could pass on a fatal virus to her child, and is given the opportunity to participate in a trial which just **may** give her access to a **possibly** effective drug, a drug she cannot afford on her own. (This is a virus acquired because of her own vulnerability.) How voluntary can her consent be?

With the benefits of science

For some time, pharmaceutical companies wanting to market new drugs have been required to do siv[illegible]rials showing them

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to be both safe and efficacious on human beings, though there is plenty of scope for debate on these requirements.

If drugs undergo some measure of rigorous testing, new diagnostic methods and techniques have been introduced without such cautions. And procedures are being done in the name of trials, or justified by earlier 'trials', independent of regulation by any ethics committee.

Quinacrine sterilisation is being done in parts of India on the basis of unofficial trials: more than 50,000 women have been sterilised in this manner) despite the WHO's refusal to endorse it, and despite public interest litigation in the Supreme Court against the practice.

In fact, a 'demonstration video' of the procedure was screened at a recent "international conference on fallopian tubes", where doctors actually called for compulsory sterilisation of women after two children. And even as private doctors practice their own 'population control' campaigns, the Karnataka state government will reportedly include the procedure in its 'cafeteria' of contraceptive choices.

Incomplete information

Many new techniques are being promoted for use without the backing of clinical trials. Some techniques — tested or untested — mean money to the instrument manufacturer. Other techniques, involving profit to surgeon and manufacturer, may have specific, limited use, but are being promoted to the medical profession and the public as the latest, superceding earlier methods. For example, endoscopy is promoted through 'workshops' where doctors learn the technique, to the public through public relations companies, without discussing the risks and benefits compared to open surgery.

Evidence suggesting that endoscopic surgery is in many situations of no greater benefit than open surgery is not publicised.

Paying to be experimented on?

Another form of deception, profitable to doctor and instrumentation industry, at the cost of the patient, is the practice of using an experimental technique to gather information on safety and efficacy. Recently, the US FDA started requiring that manufacturers of new surgical devices prove their safety and efficacy in clinical trials before selling them commercially.

Manufacturers must then be forced to make their profits in developing countries, where scarce resources for health care are squandered on expensive techniques of doubtful efficacy.

It was recently pointed out that American patients would have access to a particular experimental procedure only through a randomised clinical trial in which they would hope to be assigned the treatment arm.

In India, however, patients with no other option of treatment are being offered this experimental procedure. Hospitals offering this procedure, which has been publicised through the press, don't have to spend a ruppee. The company maintains the machine free of charge, charging only for the special catheters — for which the patient pays. When a given number of catheters is used, the machine becomes the hospital's property. In other words, patients in India are paying for an experimental procedure — though they are not likely to know it.

How will the results of the Indian operations be used? Will Indian people be providing data -- of uncertain value -- to the company, in support of the procedure?

Suggestions have been made to ensure that research is conducted under committees that back both scientifically valid and ethical research.(5) Some examples follow:

Have the researchers gone through the literature and ensured they're not repeating old studies? Are the results of research being made publicly available?

The authors note [illegible]cy publicise research showing positive results and downplay those showing that a particular treatment doesn't make much of a difference, or even does some harm.

They point out:

"When research is conducted in this manner, the losers are patients who must: "accept the harmful side effects of ineffective forms of care; accept advice about the effects of health care which is based on evidence that is less complete than it should be; participate in research which has been conceptualised and designed on the basis of unnecessary incomplete information; and contribute to research (both as indirect funders and as patients) which may not be published if the results come as a disappointment or as an embarrassment to the investigators or sponsors."

In the final analysis, the people concerned are those who pay for such research, whether through government-funded trials, by participating in them, or by paying for the treatments which follow.

References

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