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Treating genetic disorders: challenges and recommendations

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The unravelling of the entire genetic sequence of humans and, more recently, of important pathogens such as the causative agents of tuberculosis and malaria are landmark events in science. This is just a beginning in improving our understanding of biology and disease. The tools and techniques for genomic research are costly and the full benefits are not easy to quantify, nor is it easy to predict possible misuse of this new information. Although Genomics as a science goes beyond genetic disorders, genetic diseases are an important component. India can learn a lot from its experience with genetic diseases, both in terms of our attempts towards research in this area and efforts to care for patients with genetic disorders. This may help guide our approach in the 'post-genomic era'. I will outline some of the challenges that physicians in India may face, taking the example of beta-thalassaemia, a relatively common genetic disorder.

Medical college curricula offer little formal and structured training in medical genetics, and there is inadequate exposure to modern molecular biology. Molecular biology tools are essential for the management of genetic disorders and research in this area. A good understanding of modern genetics and molecular biology is essential for patient care providers to take the benefits of newer advances to their patients. Trained genetic counsellors are few and, for patients, access to educational material and genetic counselling is limited. There are some excellent genetic laboratories in; however, with the exception of a few in superspecialty hospitals, these are not attached to medical centres. Access to patient material is difficult for laboratories not attached to treatment centres. Having treatment and research facilities under the same roof is of advantage to any researcher. Of the 180 or so medical schools attached to some of the biggest hospitals in the country, there are barely three or four departments of medical genetics within medical colleges. (AIIMS in Delhi and St John's Medical College Hospital in Bangalore are two such hospitals.) The reasons for such few genetics/molecular biology departments are many, including the shortage of medical and paramedical staff in the face of an incredible patient load. Overworked physicians barely have time for research, and poor resources and lack of political will have both compounded this inadequacy.

There is a need to have more centres capable of genetic diagnosis for better prevention and treatment of beta-thalassaemia and other genetic diseases. The Institute of Immunohaematology in Mumbai is one such centre that has done important work in defining the type of mutations in population groups, but more regional centres are required in areas with higher prevalence of particular genetic diseases.

Informed consent

Patient confidence is a major factor that limits many research studies. A patient is more likely to volunteer to donate a specimen or to participate in a clinical trial on the direct advice of their caregiver than that of an independent researcher. This is especially true if the patient is confident that the researcher is concerned about his well-being and the care provider has an inherent advantage in gaining such confidence. The patient's informed consent is mandatory for participation in any research study. For an informed consent to be truly informed, researchers seeking to enroll a patient in a study must be knowledgeable of the research tools and implications of the study. Physician who have been involved in modern clinical research during their training period are likely to be motivated in involving patients from their practice in such studies.

Let us consider beta-thalassaemia, which is the most common monogenic disorder in India. Of the population, 5% are carriers, carrying a mutation in a single beta globin allele. An estimated 10,000 children are born with the defect each year. There are an estimated 100,000 patients with mutations in both alleles which results in beta-thalassaemia. While in terms of sheer numbers this disease pales in comparison with infectious disease such as tuberculosis and the more recent scourge of AIDS, the economic impact is serious. Optimum treatment of an individual with beta-thalassaemia with repeated blood-transfusions and chelation therapy costs about Rs 100,000/year. Unlike many genetic disorders, there is a curative option for beta-thalassaemia—allogeneic bone marrow transplantation. However, only about 25%–30%

can find a suitable donor. Of such patients only a small fraction can afford the procedure, which costs Rs 6–12 lakh.

Management

What about management of the disease once it has been identified? Once a gene mutation for a genetic disorder such as beta-thalaessemia is diagnosed in an individual, the disease may be prevented in future generations by identifying carriers in that individual's family, by genetic counselling and by measures such as prenatal genetic testing. As mentioned above, cure by bone marrow transplantation is not possible for most individuals. However, even individuals fortunate enough to have families with both a suitable donor and the money for the procedure have to contend with long waiting lists or forego the procedure, there being only a few centres such as the Christian Medical College in Vellore with the required facilities and expertise and success rates that match the best hospitals in the West. Several other hospitals have acquired the capability for bone marrow transplantation. However, it is estimated that no more than 100 allogeneic bone marrow transplant procedures are carried out per year in the country. Bone marrow transplantation is not the answer for all genetic disorders, but is an example of a procedure for which capability exists within the country. It highlights the fact that technology-intensive procedures are expensive, but costs can be brought down and the success rate increased if done in sufficient numbers.

Research and development

Research and development (R&D) in such diseases is critical for us to find better treatment options. However, this needs to be done with the full realisation that such expensive research will need adequate funds. Despite the high level of investment required, it is all the more critical for us to now develop indigenous R&D capability because emerging intellectual property laws may make it more expensive for us to use the information and technology generated overseas. If we do not invest in research today, we may end up spending a lot more in the future. The argument against developing advanced technology for the diagnosis, therapy and research of genetic diseases is that these costlyexercises divert scarce resources and that there is not enough trained manpower to use such technology. Further, it is questioned whether it is ethical to use expensive technology when more prevalent diseases can be prevented by a fraction of the cost of prenatal testing or even one marrow transplantation. There is also the fear of unethical use of new technology, as has happened with prenatal sex determination in some northern states.

The argument in favour of advanced technology is that only by introducing it can we develop the capacity to understand and exploit it. One can adapt such technology to local needs and develop, test and absorb newer advances with efficiency. If resources do not allow the implementation of high technology in government-run hospitals, the private sector should be encouraged to develop and offer such facilities. Often, a great deal of effort is required to develop a technology-intensive operation that is economically viable in the private sector. In the long run, this effort can pay off. Such efforts should continue to be actively supported and encouraged, not only by the government but also by informed citizens. The benefits of new technology often spill over beyond what was originally envisaged as it evolves. Consider a procedure such as bone marrow transplantation; the indications for the procedure are many and it can benefit conditions such as cancers and other genetic diseases. One may well ask, 'Is it ethical not to exploit the benefits of advanced technology in healthcare and to make it as widely available as possible?'

Conclusion and recommendations

To fully exploit the advantages of the post-genomic era, we need to develop new technology while optimally utilising existing technology. I recommend that there be designated departments of genetics and/or molecular biology in at least one medical college in each state/geographical region; this should be a government priority. Greater efforts towards patient education and public information will no doubt help to bring technology closer to the people and help them make full and appropriate use of such developments. Patient support and advocacy groups are such as the Spastics and Thalassaemia societies play an invaluable role in such efforts. Lastly, agencies such as the Department of Biotechnology and the Indian Council of Medical Research that are best qualified to evaluate the scientific merit and determine societal priorities and ethical appropriateness of projects, should be empowered to fund them. Not only is there a need for these agencies to be better funded, the funding for approved projects should match the goals of the project and the funding process should be streamlined. Fortunately, in the past few years, both the Department of Biotechnology as well as the Indian Council of Medical Research have had a more active role. However, the resources that we make available remain a small fraction of what western countries spend on medical research. Indeed, compared to China, our expenditure in this area is miniscule. Hopefully, the momentum will not let up and continued efforts will be commensurate with the challenges we face.

Reference

1. Collaborative study on Thalassaemia. ICMR Task Force study. New Delhi: Indian Council of Medical Research, 1993.