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Ethical & Legal Issues In Medical Genetics: A review article

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ABSTRACT

Background: Ethical issues in human genetics poses more challenges because genetic identity impinges not only on the individual but also on the extended family and society in general. The fundamental ethical principles of autonomy (self determination), beneficence (to do good), non maleficence (not to harm) and justice (fairness for patient) are not absolute and limitations arise due to conflicts amongst the principles. Hence an acceptable ethical framework needs to be worked out that would balance the principles against each other.

Practical approach to ethics in medical genetics: Ethical issues need to be considered if the benefits are maximised and the harms minimised from the increasing ability to use genetic testing to analyse an individual's genetic information. The ethical issues generally arise from:

The shared nature and ownership of genetic information. The doctor's ethical responsibilities include balancing the privacy and confidentiality of the individual and prevention of harm to others. In patients of balanced translocations and X-linked recessive disorders confidentiality cannot be limited to the patient (the right to complete confidentiality has to be partially breached) and necessary disclosure has to be made to close family relatives who must understand carrier status (that they could be also carriers) & therefore the risk of having affected baby.

Limitations of genetic testing. The genetic tests are diagnostic (prenatal and newborn screening) and predictive (for late onset dominant autosomal disorders). The prenatal and screening tests should aim to provide maximum information to the patient so that they can make an "informed choice" of having a baby. Treatment options are limited for genetic disorders and moreover these diagnostic tests cannot predict the severity and the age of onset of the disease. To inform a child about adult onset dominant autosomal disorders will be unethical as it leads to social discrimination and should ideally be postponed till the child reaches the age of consent.

Ethical issues experienced in the application of human genetics technologies. The possibility of misuse of gene therapy for the purpose of eugenics, commercial exploitation of the donor mother in cases of "three parent babies" and conceiving "savior babies" through pre-implantation genetics tests are future ethical challenges.

Patenting of genes. A gene patent is a patent on a specific isolated gene sequence, its chemical composition, the processes for obtaining or using it. It is a constant ethical issue as to who owns the tissue (genes) – the patient or the laboratory. Patents act under Section 3C of Indian law states a gene is "patentable" only if it is "recombinant".

Conclusion: There are no easy or correct solutions for difficult ethical problems in medical genetics. With new discoveries new ethical dilemmas will emerge. Medical genetics community has to ensure that interests of their patients & families take precedence.

KEYWORDS : Ethical issues, Informed choice, Human genetics technologies, Patenting of genes

Introduction

When the news of the completion of the Human Genome Project was announced in 2003 the scientific world predicted that this scientific analysis will bring an end to inherited disorders, screen people for their vulnerability to diseases, customize treatment based on individual's genetic makeup, create thousands of drugs based on pharmacogenomics and extend human life span.[1,2] Today almost after a decade we have a range of genetic tests that have changed the methodologies and strategies in health care. Though the advances in Genetic research has provided enough scope to practice predictive and preventive medicine it has shown limited success in developing curative medicine. [3] In the absence of effective treatment, the potential for psychological harm and social discrimination is a matter of concern which requires to be addressed with sincerity. Patients must evaluate whether the benefit of testing is worth the information gained.[4] When integrating these new technologies with our health care system in an environment of limited potential to provide cure for most genetic disorders it is important to provide responsible framework of medical ethics in order to preserve the trust and confidence of the clients. The complexity of providing information on inherited disorders are mainly due to the controversial nature of clinical options available ranging from suggesting abortion to opting for donor sperm/ovum for healthy baby .In addition there is often the dilemma of sharing the so attained information with close relatives specially in case of carriers posing an enormous ethical and legal challenge.[5] Most genetic information is by nature are highly personal yet familial, thereby raising ethical issues on confidentiality. The possibility of insurance discrimination and biased victimisation in career choices has made the confidentiality of genetic information even more relevant in today's time.[6]

When genetic testing is for research purpose, the exact scope of the study including commercial outcomes should be made clear to the patient (participant) and uncertainties that might arise as a result of testing discussed.[7] Patients have the right to acquire and control the genetic information so obtained during the research.[8]

Ethical issues in human genetics pose more challenges because genetic identity impinges not only on the individual but also on the extended family and society in general. The fundamental ethical principles of autonomy (self determination), beneficence (to do good), non maleficence (do no harm) and justice (fairness to patient) are not absolute and limitations arise due to conflicts amongst the principles. Hence an acceptable ethical framework needs to be worked out that can balance the principles one against another.[9]

Ethical issues in clinical practice

A patient physician relationship is unique which involves imparting scientific knowledge and medical care within a framework of ethics and trust. In recent times this relationship has come under lot of scrutiny in view of the emerging technologies that has made plenty of genetic tests available yet not affordable. The complexity has been compounded by poor prospect of treatment and cure involving these disorders. Once diagnosed there are issues of confidentiality, sharing of information with close relatives, insurance discrimination, social stigmatisation, bias against career choices and most importantly the violation of the rights of the unborn. Ethical issues need to be considered if the benefits are maximised and the harms minimised from the increasing ability to use genetic testing to analyse an individual's genetic information.

The medical world acknowledges that in any decision making the interests of the individual patient is foremost and all interventions are

based on the principle "not to harm".

Right to know: The patient has the right to have full information on the result of the genetic test done and the interpretation of the result. Full disclosure is necessary for upholding the trust that marks the relationship between physician and layperson. If the individual or family later discovers non-disclosure, confidence in health care providers could well be damaged. In situations where the nature of the information to be conveyed like disclosing the sex of a child born with ambiguous genitalia or where there is mismatch between the genetic sex and socially acceptable sex and these information are of grave psychological consequence to the individual or family, the delayed disclosure is allowable till phenotypic expressions are complete. Situations justifying delayed disclosure include immaturity and lack of education of the patient. The therapeutic privilege presumes full disclosure, but postpones it until the person is psychologically and cognitively ready.[10]

Autonomy: This is one of the four basic principles of medical ethics. This empowers the individual for self determination. The extent to which this is possible is a function of the quality of information given. In clinical genetics many patients undergoing the genetic tests are children or patients with intellectual disability thereby raising concern on their ability to give consent. It is strongly suggested that predictive tests which are of no immediate benefit should be postponed till the child reaches an age of consent.[11,12]

The autosomal dominant disorders like Huntington's disease that run in a family pose us with ethical dilemma of suggesting the test in an individual who has not yet developed the disease. Since a positive test will have to be endorsed in the health record it will invariably lead to issues of stigmatisation at school, discrimination for insurance and biased victimisation at career selection in addition to psychological distress associated with the uncertainty. The individual may take critical life altering decision based on the positive genetic test which may be more detrimental to life than his present state. Hence all such predictive testing should be undertaken after calculating the burden/benefit ratio keeping the interest of the patient foremost. Wherever disclosure of the genetic result is required to be made to the immediate and extended family members the good of society may supersede the good of the individual. However the family members will always have the right "not to know" which is supported by the principle of non maleficence.

In short the patient is entitled to full information about all available options so that he can make an "informed choice" including "not to choose" any medical intervention. It is important for the health official to be non directive in the process of counselling so that the patient can take an autonomous decision.

Confidentiality and privacy: A patient has right to complete confidentiality. However since the nature of genetic disorders are such that inspite of being personal they are familial in nature. The carrier status of the wife must be disclosed to the husband. Similarly carrier status screening has to be advised to the extended family and the community at risk. Hence consensus opinion is being built upon the concept that the human genome belongs to the entire mankind and all genetic information should be shared with the intension to benefit many.[13]

Ethical issues in screening tests

Diagnostic versus screening tests: Many lives could be saved by screening individuals at risk and targeting preventive behaviour to them but there will always be risk of making healthy people 'sick' through detecting presence of predisposing genes and potential for stigmatization and discrimination by society, insurance companies & employers.[14] Whereas screening applies to populations with unknown risks to individuals, diagnostic testing is offered to individuals and families at higher risk because of family history of a genetic disorder, history of environmental exposure, advanced maternal age, or positive results of a prior screening procedure, or clinical signs in the persons to be tested.

Voluntary versus mandatory tests: All screening tests should be voluntary after an informed consent. Population screening programmes offering carrier detection is only possible through voluntary participation of the target population. Only exception where mandatory screening tests are sometimes permissible is for newborn screening. Newborns deserve the special protection afforded by mandatory screening for disorders where early diagnosis and treatment favourably affect outcome. The benefits of having a diagnosis in the absence of treatment are not sufficient to justify mandatory screening. For example, screening for fragile X syndrome is not warranted because there is no evidence of medical benefit to the newborn. To justify mandatory screening, benefits must accrue to the newborn.

The primary purpose of mandatory newborn screening is to benefit the newborn through early treatment or abort pregnancy by first/second trimester if severity of the disease is high.

Prenatal diagnosis and newborn screening: The most difficult problem in prenatal diagnosis is those involving autonomy and individual choice. This relates particularly to disease severity where accurate quantification is not always possible and with whom rests the decision that termination is justified. There is a dual obligation for the clinician, one to the pregnant woman and other to the growing foetus. The dilemma arises when parents with inherited condition wish to continue with pregnancy. Thus selective abortion should be made available to the client however the final decision on it should rest with the parents.[15]

The issue on individual choice may also arise when the foetus is likely to be born with a mild abnormality like cleft lip/palate where surgical correction is possible and life expectancy is normal but the parents decide not to continue the pregnancy. These situations create ethical dilemma for the clinician however autonomy of the patients will always take precedence.

Presently the British society of Human Genetics has expressed support for application of genetic prenatal tests for serious disorders and strong reservations on its application for genetic enhancement (eugenics). [16]

Employment screening: Screening in the workplace is with the purpose of making the workplace safer. All screening, whether before or after hiring, should be voluntary, and workers should be informed of their own test results and the meaning of these results. Any individual who is rejected on basis of positive genetic screening result has a right to understand his disease and the justification for such rejection. For example those with strong history of Huntington's chorea may be screened before hiring them for jobs involving public safety like driving a bus.

Genetic screening in workplace is often criticized as a violation of an individual's right to privacy but others defend genetic screening on the grounds that all individuals have a basic right not to be harmed, and employers thus have a duty to provide a safe workplace.[17]

Screening for carrier status: This involves screening people with certain genetic tests so as to determine whether they are a carrier of certain defective genes. One of the genes that is important in this instance is the gene that codes for Cystic Fibrosis. In a couple where both are carriers will have 25% risk of having a baby with cystic fibrosis. They will have to weigh the risk themselves and take a decision on having own baby. The two common arguments against the screening for carrier status are first likely chances of discrimination against individuals who possess the inferior genes and secondly the reproductive decisions which will always be inclined towards selection of a better child. Population screening for carrier status for diseases like cystic fibrosis should be carried out only with voluntary participation of the target population.[18] Similarly pre-marital screening for specific inherited conditions may be opted to, with cooperation of the community and the mutual understanding between the partners however it should be by choice and preceded by full education on the subject.

Genetic Screening for breast cancer: BRCA 1 and BRCA 2 are breast cancer susceptibility genes mutation in which may be responsible for 70% chance of developing breast cancer. Such mutations have the ability to be passed from generation to generation, producing an inherited susceptibility to cancer. This major recent scientific discovery, enable us to identify women at very high risk yet it carries medical, psychological, ethical and social implications. On one hand it gives enough scope to prevent breast cancer in the susceptible group

through extensive screening by self examination/mammogram and prophylactic mastectomy but on the other hand it has deep psychological impact leading to stress and depression. Thus some women who test positive but never develop the disease will go through this needless psychological stress and few others who test negative may live with false sense of security when they may end up developing the disease.[19] Since these tests are very expensive and not readily available in India the risk benefit analysis must be done before advising the test.[20]

Ethical issues in genetic research

Researchers have a responsibility to make sure that the public is adequately informed about the purpose and potential benefit of the project without raising false hopes or expectations. The researcher should inform about potential benefits, direct and indirect, medical and commercial to allow the subject to weigh carefully before arriving at a decision. They must apprise the subject of all possible dangers however trivial it may be. With regards to genetic research there should be clarity on the ownership of the DNA material. The gene patents broadly cover 3 types of inventions based on (a) diagnostics – disease gene patents. For example invention of gene loci mutations for BRCA1 and BRCA2 genes that can be used for diagnosis and prognosis for breast cancer (b) chemical composition – isolation of a gene sequence and all its derivative products (recombinant proteins) and (c) functional use of gene. For example patent for 'selective inhibition of Cox 2 gene' for prevention of pain and inflammation. While on one hand the biotechnology companies want to patent their findings and derive sufficient return on their investments the more idealistic world emphasize use and spread of the invention in larger interest of mankind. The participant of the research project should be aware about the possible commercial benefit and whether any clause exists that make them party to the share of commercial gains. For the researchers a blanket informed consent that allows use of a sample in future projects is the most efficient approach. The research team must ensure that the confidentiality of the data is ensured; all conflict of interest should be disclosed. There should be clarity on secondary use of sample, patent and benefit sharing if any. Potentially valuable specimens that could be useful to concerned families in the future should be saved and should be available.[21,22]

Ethical issues in gene therapy

There are two prominent ethical issues in gene therapy. One is to get a fair informed consent from participants of gene therapy research projects without giving them false hope of curability as most participants will be patients of genetic disorders which have no cure. Second is the abuse potential of gene therapy to be used for eugenic purposes. Hence we require a robust monitoring body that will ensure that human gene manipulation is not abused.

The law

In India the ethical issues and genomics are governed by statement of 'Specific Principles for Human Genetics Research', ICMR Ethical Guidelines for Biomedical Research on Human Subjects of year 2000.[23] Much of it is based on WHO's International Guidelines on Ethical Issues in Medical Genetics.

Present policies in India are now guided by directions laid down under Ethical Policies on Human Genome, Genetic Research and Services. Department of Biotechnology, GOI, January 2002. [24]

On the controversy surrounding the patent of naturally occurring human DNA sequences the Patents act of India under Section 3C states discovery of any living thing or non living substance occurring in nature is not patentable - Implying a gene is "patentable" only if it is "recombinant". Further elaboration and clarity is still pending.

Future Concerns

With the advent of gene therapy and its possible usage for the purpose of "Eugenics" there is need and scope of many more deliberations within and outside the scientific world. Protocols for experimental human gene therapy should receive national review, with attention to the potential benefits or risks arising from various approaches to therapy.

Post 1996 cloning and stem cell research has posed new and challenging ethical issues. Though therapeutic cloning using stem cells have huge prospects to cure several human diseases the misuse potential of this technology can be devastating. Hence strict and clear laws must be put in place to prevent manmade disaster.

Pre-implantation genetic tests, saviour babies and three parent baby (mitochondrial DNA from donor egg) are areas of future concern where new ethical guidelines are required to be incorporated.

Conclusion

Ethical issues in medical genetics are of major concern in the rapidly developing world. With each new discovery new dilemmas cross our path and poses entirely new challenges which require to be immediately addressed. There are no easy or correct solutions for difficult ethical problems in medical genetics. The medical genetics community will have to ensure that the interests of the patients come first, today and always.

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