Genetic testing in clinical practice: An ethical perspective

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ABSTRACT

The complexity of interpreting the results of genome-scale testing and the interplay of ethical principles present a challenge to the medical establishment regarding genomic information disclosure. This article focuses on the most problematic ethical issues regarding the disclosure of genetic information to biological relatives who might benefit from such vital information for their health or future well-being. The justification for concealing an individual's genetic information and the rationale behind disclosing these valuable data are elucidated. Furthermore, this article analyses various societal factors and the different ways in which individuals understand concepts of family and self that might hinder disclosure and how not discussing these topics and understanding the social and cultural differences at the very beginning of genetic counselling complicates the decision. As the partial overlap of ethical principles might conceal significant moral nuances, genetics professionals need to make decisions on a case-by-case basis and use their judgement by weighing up the benefits against potential risks to make a rational yet realistic decision. Detailed genetic counselling to encourage the patients to communicate with their at-risk family members before the genetic testing and striking a balance between the potential advantages and the possible risks for each case are essential.

Keywords: Genome-scale testing, ethical principles, genetic counselling

INTRODUCTION

Throughout the decision-making processes of disclosure, clinical geneticists were confronted with conflicting responsibilities towards different members within the same family and often need to deal with diverse issues in the context of the patients' best interests and the nature of genetic testing. The familial nature and sensitivity of genetic data adds yet another layer of complexity to the situation and raises a plethora of ethical and legal dilemmas that have yet to be satisfactorily addressed.

This is compounded by the variations in the societal, cultural and ethnic backgrounds of different communities. Thus, medical law is struggling to achieve a clear consensus to harmonize moral principles into a wider code of bioethics (Andorno, 2004; Foster et al., 2015; Patuzzo and Pulice, 2015).

ETHICAL ISSUES

The right not to know is a confirmed and respected right in medical practice, thus, replacing the old paternalistic model as patients can autonomously choose not to be informed about their genetic characteristics. Nevertheless, provided that there is informed consent (Human Genetics Commission, 2002), this right needs to be considered in the context of the interests of other at-risk family members when the patients' autonomous decision conceals vital information (Andorno, 2004).

In such cases, the duty of beneficence should be prioritized over the obligation to respect the patient's autonomy (Shkedi-Rafid et al., 2014). Individuals are completely free to make choices affecting
them as long as they are not acting adversely with respect to others. For example, genetic testing might identify that an individual has a highly penetrant cancer risk mutation for which, in breast cancer for example, intensive surveillance or bilateral mastectomy for relatives makes a huge difference and justifies the disclosure (Chivers, 2013; Gallo et al., 2009; Laberge and Burke, 2009). However, this disclosure without consent should be handled in such a way as not to cause any significant psychological harm to the patient, as health professionals are obliged to respect patients' autonomy by "more than non-interfering in their personal affairs" but helping them build their capacity to choose autonomously (Hallowell, 2006). In the event that the identified variants are uninterpretable incidental findings of uncertain significance (Shkedi-Rafid et al., 2014; Lawrence et al., 2014) and the situation would become more challenging as with some predictive tests in which informing the patient could inflict psychological pain due to the difficulty and perplexity of translating these non-actionable findings into effective or preventative measures.

Although confidentiality is a presumed right and broadly congruent with daily clinical practice, it needs to be considered in the context of public interest (Knoppers et al., 1998; Knoppers, 2002). In contrast, "the relational joint account model" that considers disclosure as the default position is in accordance with the essence of clinical genetics practice (Dheensa et al., 2015). Geneticists are engaged with families and have a duty of care and moral commitment towards them as genetic services are mainly found to treat and prevent genetic disorders (Parker and Lucassen, 2004). For instance, if a patient refuses to share his/her genetic test results with at-risk biological relatives, clinical geneticists must emphasize the implications of the results for at-risk relatives and write a letter to persuade the patients to share it with their family members (Chan-Smutko et al., 2008). Eventually, clinicians might feel ethically obliged to warn at-risk relatives provided that this data was of proven clinical importance (Wouters et al., 2016; Parker, 2015). Nevertheless, any deviation from medical confidentiality needs to be strongly justified (Human Genetics Commission, 2002; Dheensa et al., 2015) and genetics professionals should attempt to obtain the patient's consent (Knoppers et al., 1998) and not refer to the patient's name. Moreover, the patient should be notified about how their genetic data would be disclosed, if this is possible (Dheensa et al., 2015; Dupras and Ravitsky, 2013).

The International Declaration on Human Genetic Data (2003) and the UNESCO Declaration on the Human Genome and Human Rights (1997) adopted a solidarity-based approach and emphasized on the familial aspect of genetic information and that the duty of health care providers is to care for the patient and family members (UNESCO, 1997; 2003). In contrast, General Medical Council in the UK (GMC) guidance (2009) states that doctors should persuade the patients to discuss their genetic disorders with relatives. If the patient resist disclosing to at-risk relatives, the GMC permits doctors to divulge relevant information to protect relatives from "serious" threat to life. However, clinicians still need to be protected from "statutory liability" in case they have made the disclosure (Otlowski, 2007). Insurance in the case of legal action is a possible system that might be used for such protection.

On the other hand, such disclosure might weaken the trust between the patient and medical professionals thereby leading to the impairment of the treatment the patient needs. Also, this could cause a more extensive and far-reaching lack of confidence in other health workers as patients might feel reluctant to seek medical advice when needed. However, affected family members who are not warned about their genetic risks could lose faith in their doctors, thus, inducing a crisis of trust in the field of medical genetics.

In various situations in genetics, a comprehensive family history is required to evaluate and estimate the benefits of genetic testing, seldom with those relatives' consent (Rose et al., 1999). Hence, the outcome should be recognized as familial and be accessible to all extended at-risk relatives unless there are strong grounds to act differently. If the mutation was de novo, only then, genetic data could be fundamentally personal.

Beneficence obligates health professionals to help patients get better. Even so, clinicians need to use their judgment in disclosing information that could be vital to family members' health. Egalitarian views of justice stress that people have equal values and should have the same rights of access to benefits. Nevertheless, it is important to maintain the distinction between the clinician's duty of beneficence to the patient and the non-obligatory responsibility towards family members.

Non-maleficence is defined as the principle of not doing harm to the patient. Divulging patients' genetic information could be regarded as harming them if their choice has been to keep the information private. However, "communitarian interest" in preventing damage to others should be considered (Otlowski, 2007) and the duty of beneficence could be prioritized over non-maleficence (Beauchamp, 2001). When non-disclosure harms other family members by depriving them of crucial informed reproductive choice of evading serious diseases (Ormond et al., 2003; Petersen, 2006), such concealment is inevitably challenged.

The decision to abort a pregnancy could depend on what those concerned consider unethical (Henneman et al., 2002) based on how they individually or socially perceive specific terms such as serious injury or disability. Peoples' perceptions of abortion vary; for some, abortion has eugenic overtones and they could view it as discrimination against those with disabilities. Also, it could be argued that any decision about the foetus/embryo life is a breach of his/her personhood. The conflict here is mainly between the perception of the patient who is asked to disclose their genetic information and the differing view of the parents of...
the future baby. This issue is compounded by the various prenatal genetic tests that are offered for even findings of uncertain significance that cause perplexity to both the family and health professionals with concerns about false positives; also, these findings might be considered serious now but in the future might prove to be harmless or vice versa.

In the personalized medicine era, disclosing actionable information could have huge pharmacogenetic benefits for other family members (Shkedi et al., 2014). Nonetheless, the mutations could be de novo or the diseases non-hereditary and caused by prenatal environmental exposures that might mimic genetic disorders; in such cases, there could not be any substantial pharmacogenetic benefits even in the future.

SOCIETAL ISSUE

The advent of the inexpensive multiplexing OMICS and NGS techniques has given rise to 'geneticising' the way we look at diseases and transfigured our 'relationships, commitments and values’ (Lippman, 1992), medicalized our comprehension of biological connectedness (Parker, 2012) and sometimes transformed families into 'risky relations' (Hallowell, 2006).

Clinical geneticists usually encounter the patient’s two families instead of one: the biological and social family with the intricate disjunctions and interdependencies between them in different contexts (Atkinson et al., 2013). Moreover, each of these families could radiate to more extended ones as individuals are connected to one another in various biological, social and cultural manners (Parker, 2012).

Although the very wide definition of “genetic relative” (Ołowski, 2007) and lack of closeness within families (Lalberge and Burke, 2009; Ormond et al., 2003; Petersen, 2006; Henneman et al., 2002; Tercyak et al., 2013) are morally troubling for clinical geneticists; the biological and social families are interrelated and clinical geneticists might need to work with both. The divergence between the blood ties as drawn up by clinical geneticists in families pedigrees across three or four generations and the complex cultural circumstances between individuals and families seem to become very intense when the information to be shared is viewed by some as private or very personal. Nevertheless, even if our genome is considered us or ours, we need to recognise that it could be valuable and beneficial to relatives and we might still need to use it this way.

One of the aspects to bear in mind in the field of family genetics is that the relationship between family members does not necessarily constitute cordial or convivial relations. This has serious consequences on how to use the genetic results and for genetics professionals to know the cultural and societal background of the family and understand specific concepts such as “serious” that defy precise definition when taken out of a specific context.

Cultural and societal background of the family and understand specific concepts such as “serious” that defy precise definition when taken out of a specific context. Whether family members have already discussed the different facets of the genetic testing and the potential outcome is also an important issue to pre-empt any further ethical quandaries unless this discussion risks loss of significant information or deter the patients.

This also brings us to societal coercion when families, peers and the media around us are subtly and indirectly pressurizing us to make decisions based on how they view different issues such as discrimination, stigma or harm, for instance, non-disclosure in order to protect relatives from worrying information (Tercyak et al., 2013).

When the socially-disjoined family applies pressure to obtain the consent of biologically related children against the guidelines (Parker, 2010; Lucassen, 2010; Lucassen and Fenwick, 2012) or vulnerable individuals with intellectual disabilities (O’Neill, 2003) who are exclusively able to provide significant genetic data such as in Duchenne Muscular Dystrophy, a plethora of bioethical complexities might arise. Although, it could be argued that there might be no pharmacogenetic benefits of disclosing the DMD patient’s genetic status, this information could at least offer a targeted prenatal testing to avoid having other affected children in the family.

If the genetic testing revealed non-paternity or adoption and there are high chances of having another affected baby, it is important to reveal the result to avoid possible disability (Wertz et al., 1990). In some situations, to eschew years of unnecessary invasive procedures or to achieve a bone-marrow transplant for a life-threatening illness, reviving the link between the biological and societal families could be inevitably non-avoidant. However, disclosing such information might adversely affect the future reproducibility and marriageability of extended social and biological family members (Shaw, 2000).

CONCLUSIONS

Although the human genome collectively could be viewed as the shared heritage of humanity (Knoppers, 2002), a patient’s genetic status is currently considered private as medical confidentiality overrides any other obligations. However, useful genetic information should be available for the management and treatment for all at-risk relatives which is at present not the norm. Mutuality in sharing genetic information in families and optimistically adopting humanity-based approach among populations at risk could possibly avoid consecutive pregnancies of affected foetuses with intractable diseases which outweighs the comparatively lesser damage could arise from violating the patient’s privacy or the consequent damage of trust in the medical milieu. There is an increasing recognition that even if we as individual patients are worried about our genetic
data to be shared, we are very likely to clinically benefit from having that data placed in a large database.

Although it will be necessary in the future to have a consensus regarding what is "serious" to the patient or family to substantiate the disclosure/non-disclosure, defining that "serious" should be determined on ad hoc grounds and read in the context of the very specific nature of the genetic testing performed (Lucassen and Parker, 2004).

Finally, it is crucial to establish guidelines that enable actionable information related to patients to be generated and fed back to and to have a clearer and more consistent policy such as notifying patients carrying out genetic testing in advance of testing about who is at risk, what type of information to be disclosed, when and how to inform a third party, the possibility that genetic testing might reveal non-paternity and/or adoption, the purpose and the manner in which genetic testing results could be utilized.

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