The Ethics of Germline Gene Editing and Nursing Ethics

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Abstract This paper explores the current ethical issues in the potential use of germline gene therapy. This paper will also discuss the ethical principles of beneficence and non-maleficence in the context of germline therapy. The balance between potential benefits and potential harm in its use will be appraised. Moreover, the principle of autonomy will be further studied. More specifically the issue of consent and the potential dilemma when the modified individual's will and those who chose the modifications do not align will be examined. Furthermore, the ethicality in the potential non-medical use of germline gene therapy will be investigated. Also, the consequences for the non-medical use in the therapy such as potential human rights violations and a breach in the ethical principle of justice will be speculated. Moreover, this paper highlights the use of the Canadian Nurses Association (CNA) Code of Ethics to help guide nurses through the complex ethical problems that they may face in germline gene therapy.

INTRODUCTION

Advances in the health sciences have created the potential to eliminate many genetic diseases that have negatively impacted people and their families. The development of technologies such as CRISPR-Cas 9 and adeno-associated viral vectors have propelled genetic research by making faster, more efficient, and cheaper ways to modify genes with broad applications in medicine and other sectors (Mahmoudian-sani et al., 2018; Wu et al., 2020; Zhu et al., 2020). Gene therapies currently exist in healthcare but are limited, highly regulated, and only affect somatic cells. Somatic gene therapy targets somatic cells; thus, it cannot pass on the genetic changes to future generations. In contrast, germline gene therapy results in changes that are passed on to subsequent generations (Ormond et al., 2017). This difference is one of the main reasons it requires more ethical and moral considerations. Some ethical issues that germline gene editing must consider are the principles of beneficence, non-maleficence, autonomy, and justice (Ayanoğlu et al., 2020; Gyngell et al., 2017). Also, the advancements in biotechnological capabilities to modify genes have created an unintentional possibility to create "Designer Babies". The term "Designer Baby" refers to a child whose genes have been manipulated with technology to impact non-medical traits (Pang & Ho, 2016). This raises additional moral issues such as the potential for use in a eugenics like movement and for creating a society that is less accepting of differences (Friedmann, 2019). The concept of germline gene therapy is an ethically and morally complex subject. Nurses must use the Canadian Nurses Association (CNA) Code of Ethics to help guide their research, education, and clinical practice during ethical problems they may encounter (Canadian Nurses Association [CNA], 2017). This paper will examine the major ethical principles of autonomy, beneficence, non-maleficence, and justice when it comes to germline gene editing. Furthermore, this paper will explore the concerns in the ethicality of non-medical germline gene therapy and will address nursing concerns in the context of the CNA Code of Ethics.

LITERATURE REVIEW

Beneficence and Non-maleficence in Germline Gene Therapy

The intention of altering the germline to fix genetic issues in generations of people is a life-changing and worthy cause. Thus, it is vital to consider this argument of potentially ameliorating the lives of multiple generations when discussing this therapy. However, one of the ethical dilemmas of this therapy is juxtaposing the benefits, such as repairing cancer-causing genes, against the risks such as causing unintended mutation that could result in harm (Katz & Pitts, 2017). It is important to note that potentially changing the germline is not a novel outcome in medicine. For example, current therapies such as radiation have the

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potential to cause unintentional changes in the germline. However, considering what is useful and potentially helpful outweigh the possible consequences of these treatments. Therefore, the risk to benefit ratio favors the use of such biotechnology (Smith, 2003).

When considering the potential risk to benefit ratio in germline therapy through an ethical and safety perspective, many issues go against the principles of beneficence and non-maleficence. Contrary to germline gene therapy's purpose in potentially eliminating diseases in the subsequent offspring, there are considerable risks associated with creating changes in the germline. There are currently high chances of passing down harmful genetic mutations with unknown effects that can have impacts on generations of children (Ormond et al., 2017; Pang & Ho, 2016). Although much progress has been made to reduce unintentional or off-target effects, CRISPR-Cas 9 is still not precise enough to completely prevent such mistakes (Zhang et al., 2015). Off-target effects occur when untargeted areas of genome are changed by accident. These changes can be detrimental to otherwise healthy genes and thus could result in more harm than good. Many researchers have identified the frequency of these off-target effects that can potentially cause deleterious effects as one of the major limiting factors in the use of CRISPR-Cas 9 in humans (Herai, 2019; Liang et al., 2015; Zhang et al., 2015). Because of the lack of research on germline editing in humans, the magnitude of these consequences are also unknown. Thus, germline gene therapy's current usage goes against the ethical principle of beneficence, which is defined as being responsible for doing what is beneficial for the patient (Stephany, 2020). By ignoring and not considering the possible negative impacts on future generations, one cannot fulfill the principle of beneficence nor of non-maleficence.

Moreover, there are unknown risks about the safety and adverse effects such as creating oncogenes that cause cancers in patients and creating unknown off-target effects (Ormond et al., 2017; Pang & Ho, 2016; Singh, 2021). Research by Ayanoğlu et al. (2020) suggests that germline editing is more challenging because of the risks associated with mutation and undesirable side effects are transmitted into the progeny. Furthermore, these side-effects and consequences may not appear until several years later. Non-maleficence is "the duty to prevent harm, whether intentional or unintentional" (Stephany, 2020, p. 46). It is evident that the current use of germline gene editing does not abide by the ethical principle of non-maleficence. This is because the therapy could cause serious harm to future offspring with unknown consequences. Furthermore, ethical concerns on non-maleficence arise in the context of the modified person and family. There is potential for the genetically modified individual's parents to be less accepting of future imperfections and differences in their children due to a sense of perfectionism, which can be psychologically detrimental to the child (Ormond et al., 2017). This therapy is different from other existing therapies as these therapies do not drastically impact the lives of individuals who are not receiving treatment. Germline gene therapies also have the ability to alter societal norms. As a society, we should move towards embracing differences within individuals and identify strengths within those differences. Not doing so could lead to severe consequences. After all, variation is the raw material of evolution and without it, society could become much more susceptible to disease or natural disaster. When examining this in the context of the Ethic of Care that places the person at the center of importance (Stephany, 2020), yielding the principles of non-maleficence and beneficence are not justifiable. Therefore, more research into how to ensure that beneficence and non-maleficence are respected is a prerequisite before further investigating its use.

Autonomy in Germline Gene Therapy

Another issue that people must consider in germline gene therapy is the ethical principle of autonomy. Patient autonomy continues to be essential in guiding research and practice. Autonomy is one of the four major bioethical principles based on the theory of deontology in a form called principlism (Stephany, 2020). Bioethical issues in genome editing may arise in the context of consent. The question of who will give consent and how have to be considered. Consent in the context of somatic cell gene therapy is clear because it only affects the individual. However, there is a sense of obscurity in consent when changes can affect future generations. How they will obtain consent from unborn generations and relay pertinent information, such as risks, is an ethical question that remains unanswered (Knoppers & Kleiderman, 2019; Singh, 2021). One possible avenue of interest is the use of recent biotechnological advancements, such as CRISPRoff (Nuñez et al., 2021). This biotechnology allows researchers to make gene edits reversible. This technology still requires further research; but, if it is proven to be safe and effective in humans, it can potentially help address such issues.

The ethical issue of autonomy also becomes complicated in the context of people's wills and choices. An ethical dilemma exists when the modified individual's will and those who chose the modifications do not align (Macpherson et al., 2019). For example, there can be a disconnect in what the modifier decides what is best and if the modified person agrees with that choice. Choosing what is best for somebody else is called the principle of paternalism. It does not respect the autonomy of the affected person (Stephany, 2020). One can also argue that this violates the human right of being born free and equal (United Nations, 1948). If a decision is made on the behalf of someone without their consent, and it predisposes them to an alternate lifestyle, that contradicts the right to being born equal. An argument can also be made that it should be up to the individuals who are getting modified to decide since it is occurring to their cells. It is important for healthcare professionals to respect the autonomy and decision making of the individual they are treating. Thus, in a debate of germline therapy autonomy, it becomes a question of whose autonomy precedes the other. Therefore, more research into the unborn persons autonomy and rights will need to be addressed.

Ethicality in Non-Medical Germline Gene Therapy

Currently, germline gene therapy is not an acceptable practice within the medical community, nor is it supported by legislation. One of the significant issues that it encounters is the question of treatment versus enhancement. Ethical problems arise when the intent of use is for enhancement instead of for treatment. People may begin to blur the lines between what is necessary and beneficial and what is preferential and unnecessary (Cwik, 2019). For example, there may be germline gene therapy options that treat muscular disorders. However, some people may choose to utilize this therapy for performance or aesthetics even if there are no muscular issues. This creates a problem of people deciding what traits or features are good and bad. Thus, it determines the worth and value of people who have those traits (Singh, 2021).

Historically, when society has acted upon characteristics deemed desirable, it has led to severe consequences such as the eugenics movement. An example would be Nazi Germany that almost successfully eliminated what they thought were undesirable traits in people. Not only is this morally wrong, but it also violates ethical principles and infringes upon human rights. It is important to note that the aforementioned is highly speculative. However, one must consider all the potential possibilities that could create unrealized ethical issues before its use.

Furthermore, the potential use of germline gene therapy for enhancement is concerning because of the ethical principle of justice. According to Stephany (2020), the principle of justice is defined as the idea of fairness and equal treatment. Germline gene editing might increase the problematic inequities already existing in our society. There is the potential for unequal accessibility, creating further division and widening society's injustices (Ayanoğlu, 2020; Singh, 2021). Moreover, medical conditions may become an identifier to a class or culture, resulting in stigmatization and further discrimination (Ormond et al., 2017). A change in what people accept as normal would further emphasize prejudice and intolerance against others that do not have access. This would go against the ethic of care and the ethic of justice (Stephany, 2020). Therefore, nurses must be advocates for the disenfranchised to prevent further division in society. This can be done by being aware of factors such as determinants of health that impact people and supporting policies that are equitable.

Germline Gene Editing and The CNA Code of Ethics

The CNA Code of Ethics is an important document that is "designed to inform everyone about the ethical values and subsequent responsibilities and endeavors of nurses" (CNA, 2017, p. 2). Therefore, nurses must use the CNA Code of Ethics to help guide their research, education, and clinical practice during ethical problems they may encounter. The first value that nurses must consider in the context of germline gene editing is "Providing Safe, Compassionate, Competent and Ethical Care" (CNA, 2017, p. 8). According to the CNA (2017), the ethical responsibility of a nurse under this value is that:

> "Nurses support, use and engage in research and other activities that promote safe, competent, compassionate and ethical care, and they use guidelines for ethical research that are in keeping with nursing values. Nurses involved in research respect the well-being of persons receiving care above all other objectives, including the search for knowledge. They pay attention to the safety of persons receiving care and to informed consent, the risk-benefit balance, the privacy and confidentiality of data and the monitoring of research." (p. 9)

Consequently, the current research in germline gene therapy does not abide by the CNA Code of Ethics in which we have to conduct ourselves. An example of this comes from research done in China. In late 2018, a biophysicist by the name He Jiankui edited the genome of two twin babies prior to their birth to make them less susceptible to HIV despite them not being at high risk of contracting the disease. He neglected protocol and safety procedures and attempted this experiment despite no evidence of potential success. He was severely condemned by the scientific community and was eventually sentenced to three years in prison with a lifetime ban from reproductive technology. The twins were eventually born and have yet to develop any adverse conditions. However, their future health is unknown, and they require continuous monitoring, including genetic testing to detect potentially fatal mutations (Alonso & Savulescu, 2021; Caplan, 2019). It is crucial that nurses not be involved in unethical research and be accountable in reporting instances that violate the law and ethical principles in practice. It is important to note that nursing ethics and social ethics very similar as both emphasize concern for society and for societal change (Fowler, 2016). Therefore, regardless of which lens one decides to approach the issue above, it would have been unethical.

Furthermore, if this therapy were to become a reality, the nurse's ethical obligation would be to ensure that patients receive consent and an explanation of the risk-benefit ratio. This would abide by the ethical conduct of "Promoting and Respecting Informed Decision-Making" (CNA, 2017, p. 11). According to the CNA (2017), it is the responsibility of a nurse to "recognize, respect and promote a person's right to be informed and make decisions" (p. 11). Moreover, nurses must be impartial when providing information to prevent any bias in people's decision-making. Nurses may disagree with the use of germline gene therapy. However, it is essential to understand that the nurse's role is to provide the best evidence to allow their clients to make an informed decision and respect that decision. That is part of not only the CNA Code of Ethics but is also one of the professional standards that nurses abide by in their practice (British Columbia College of Nurses and Midwives, 2021; CNA, 2017). As science makes advances and CRISPR's potential in humans become more concrete, it will become ever more important to practice evidence-based medicine (British Columbia College of Nurses and Midwives, 2021; CNA, 2017).

CONCLUSIONS

The ethicality of germline gene editing will continue to be a highly debated topic in the future. Whether in the context of research or about its use, researchers and ethicists will require considerable introspection, contemplation, and discussion. As more information is uncovered about the human genome and as biotechnology advances, germline gene editing may become a realistic possibility in the future. Germline gene therapy has the potential to alter human genetics in generations of people saving and bettering their lives. However, there are still unknown variables such as the morality, ethicality, and consequences of its use that researchers must address beforehand. Therefore, to contribute, nurses must understand the ethical principles of non-maleficence, beneficence, autonomy, and justice in addition to the ethicality of non-intended uses of germline gene therapy. This ensures that nurses do not inflict further harm and infringe upon the rights of people. Furthermore, nurses must be aware of these factors to best abide by the ethical principles set in the CNA Code of Ethics to advocate for practices that best represent the meaning of being a nurse. Lastly, nurses must use the CNA Code of Ethics to help guide their practice when encountering difficult situations to ensure that their actions abide by nursing values and professional standards.

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Conflicts of Interest

The author declares no conflicts of interest.

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