



Application of Stem Cell Technology for Treatment of Diabetes Mellitus: Ethical Considerations

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Abstract

The clinical potentials of stem cells in cell-based therapies have raised great hopes in diabetes mellitus as well. However, there are complex ethical, legal, and socio-cultural issues surrounding the subject. In this paper, we intend to review in brief the main ethical issues for endocrinologists and other clinicians who are interested and work in the field of cell therapy and research.

Keywords: Cell therapy, Diabetes mellitus, Stem cell, Ethics

Introduction

Cell therapy is one of the most promising technologies in the new millennium. It can help repair damaged cells in various diseases including hormonal dysfunction (e.g. Diabetes type I), neurodegenerative diseases (e.g. Alzheimer), cardiovascular lesions (e.g. myocardial infarction), and lesions in other organs and tissues such as cornea, skin and joints (1). Stem cells (SCs) have the potential of differentiation into insulin producing cells; so, they are now considered as a therapeutic strategy for diabetes mellitus type I. In addition, SCs have had promising results in treatment of diabetic foot ulcers (2). Despite the great hope and advantages, medical practitioners and researchers have to take into account disadvantages and related ethical concerns arisen in this field. Some problems, which influence on ethical analysis of the issue, are consisted of:

- Cancer and tumors: the potential of introducing cancer into patients because of rapid growth of embryonic stem cells (ESCs)
- Tissue rejection
- Genetic abnormalities
- High failure rate (hundreds of thousands to millions of stem cell lines would be required to treat the majority of patients)
- Extremely high cost

There are moral arguments for and against stem cell research and therapy, which concentrate on issues such as the types of cells, the sources and techniques of production, and utilization (3).

Finding ethical sources for stem cells is a challenge (4). Available studies showed that different types of SCs including ESCs, mesenchymal cells, bone marrow stem cells, placenta-derived stem cells, and Human induced pluripotent stem (iPS) cells may be used for treatment of diabetes melli-

tus and its complications. The use of ESCs is accompanied with the most challenges, since decimation of embryos during the process of ESCs harvesting is necessary.

Considering the ever-increasing interests in stem cell research and therapy (5), we aim to look on the main ethical challenges in this regard.

Ethical considerations

Concerns about the safety

Safety issues play an important role in ethical decision making in experimental treatments. In stem cell research and therapy, also, safety is a main component, which has a strong link with the ethical principles of “beneficence” and “non-maleficence”.

Actually, scientific data on safety of stem cell therapies in various diseases is limited and there are concerns for tumorigenicity, infection, and immune response (6). There are uncertainties and knowledge gaps about the efficacy of such treatments as well (7). Full evaluations of safety and efficacy of transplants are still in progress. Approaching the scientific integrity and evidence-based medicine in stem cell research is so essential. Moreover, safety awareness is important to obtain a valid informed consent. A cross-sectional survey has shown that knowledge regarding the risks and benefits of stem cells is insufficient to attain informed consent (8).

Personhood

A fact that makes the use of hES cells challenging is that these cells cannot be obtained without destruction of human embryos (9). For this reason, there are many arguments about permissibility of stem cell research and therapy (10), particularly in religious contexts. It is widely accepted that human person has ethical value; however, there are debates on when the personhood begins. The broad diversity of views about the moral status of human embryo may confuse researchers. Conception (11-14), implementation (15, 16), formation of the primitive streak about day 14 (17, 18), brain activity (19), quickening (20), ensoulment (21-23), viability (24), birth (25) and having sentience (26)

are different stages at which personhood is believed to begin.

The certain milestones in embryonic development influence on decision making on permissibility of stem cell research and therapy. For instance, if we believe that human personhood begins at conception, the destruction of embryos for research cannot be justified. In case of ensoulment, however, destruction of embryos can be justified before the milestone to provide a treatment for patients (27). As mentioned, religious context have an influential effect on the issue of personhood. For example: given the Islamic teachings, while “ensoulment” is the milestone, the embryo, even in the first days of its existence, has the right to live and no one has the right to kill it; but the punishment of fetus eradication in the pre-ensoulment stages will be much less than abortion after ensoulment. Due to majority of Muslim scholars, human being is ensouled at 120 days after conception (23). In Christianity, however, despite a wide range of views, the current dominant belief is that singularity occurs now of conception (28).

Confidentiality

The source of stem cells may be an inquiry for patients who receive cell therapy. The policy on confidentiality should be clarified for people who want to utilize it. Safeguards of the rights of donors and patients are required; so, appropriate standards should be defined by cell and tissue banks (4).

Stem Cell Tourism

SC tourism is common in recent years around the world. Increasingly, more people are traveling abroad to acquire cell therapies. Issue of safety is a main concern. Since the regulatory standards are not established in some countries, unregulated clinics may use experimental approaches without necessary transparency. They may exaggerate the benefits and understate the harms. Insufficient protection of patients put them to harm. Likewise, such patients are vulnerable to financial exploitation (8).

Patenting of cell lines and Intellectual property

Patentability of ESCs has been a challenge in many countries, especially in the Europe in recent decades (29, 30). Some insist on non-patentability of stem cell related inventions in order to prevent commercialization of human embryos. However, it is obvious that conflicts between interests of industry, researchers, and patients should be managed in an ethical way. Indeed, a fair balance should be between the interests of rewarding the inventor, protecting the industry, and making inventions available to those who need them (7).

Stem cell Banking

There are various ethical doubts with banking of stem cells including issue of ownership, donor rights, withdrawal of consent, confidentiality, concern of safety, the cost, duration of storage, the use for research, commercialization, etc.

Commercialization

As Burningham et al. say: “*The field of stem cell research in particular has been subject to significant commercialization pressure.*” (31). Making profit of human tissues has pros and cons (4). Undoubtedly, commercialization could increase the speed of progresses in the field of stem cell research through raising financial investment. As other positive effect, commercialization results in a faster knowledge translation of research into clinical products. However, commercialization may be associated with some negative consequences. It may compel researchers to focus more on products with strongest marketable potential. In addition, scientists may be tempted to conceal some negative results. Conflicts of interests, also, influence research. All these factors could negatively affect on public trust (31).

The Issue of Subsidiarity

Stem cell research and therapeutic cloning can only be morally acceptable if there are no good alternatives (32). There is doubt that whether there are resources to supersede ESCs. Some proposed other sources such as hiPS cells (6, 33). However, there are arguments about their similarities

and differences (6). As Hug and Hermeren concluded in their illustrative paper, considering uncertainties and some concerns including safety and efficacy, it is too early to decide that hiPS cells can be a substitute for hES cells (6).

Social Justice and Resource Allocation

Priority setting in health budgets is necessary in order to achieve distributive justice and meet needs fairly. Cell therapy and related research are very expensive, so allocation of public resources is highly debatable in many societies.

In the United States, federal funding for stem cell research has been a challenging issue in recent decade (34, 35).

Experimental Stem cell Therapy

Stem cell clinical trials in human may be ethically justifiable in specific situations; for example, in cases of the severity of diseases and when there is no any alternative treatment and the risks of “cell therapy” and “doing nothing” are the same.

There should be sufficient safety data before the experimental use of stem cells. Informed and voluntary consent is a fundamental ethical requirement. Harms and benefits should be described transparently without giving unrealistic hope and “therapeutic misconception” should be avoided (36). Institutional review boards (IRBs) must ensure that these ethical requirements are met.

The experimental use of cell therapy outside of clinical trials is allowed in exceptional circumstances (37, 38). International Society for Stem Cell Research (ISSCR), which is an independent nonprofit organization, founded in 2002 (<http://www.isscr.org/home/about-us>), in the 7th part of “Guidelines for the Clinical Translation of Stem Cells” (2008) “...acknowledges that in some very limited cases, clinicians may be justified in attempting medically innovative stem-cell based interventions in a small number of their seriously ill patients.” (39). Scientific rationale and justification, elucidate the necessity despite alternative approaches, peer review by specialized committee, voluntary informed consent, and financial coverage of any complication are some sub-articles of this part of ISSCR guideline. Actually, in this way, seriously ill

patients with hopeless life-threatening diseases could have access to investigational drugs.

Conclusion

The use of pluripotent stem cells is a promising therapeutic approach for diabetes mellitus (33). However, stem cell research and therapy involves serious ethical issues concerning the status of human embryo, safety of procedure, and other above-mentioned issues. These may be some barriers to translating stem cell biology into clinical management of diabetic patients, which should be addressed.

Exaggerated hopes about the benefits of stem cells have risen by media, which should be clarified for patients who nominate for treatment. At the same time, equipped clinics should be established to obtain voluntary informed consent and to monitor probable complications. Volunteers should be clearly informed about the safety issues, harms and benefits in comparison to standard treatments.

To manage issues, compiling appropriate ethical guidelines and strengthening regional and international cooperation is necessary.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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