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Physicians' Preference towards Stem Cells as Regenerative Medicine-Lacks Clarity

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Abstract

Stem Cells and Regenerative Medicine has been focused to be the major counterparts in the current research perspectives. Clinical trials have shown its efficacy as well as its instability. Reproducibility is found to be lacking nevertheless has enabled promise to certain subjects. Physician's interests have also been unstable since several physicians show differences in their understanding and opinion. Though Stem cells has been projected to be an experimental therapy for those incurable diseases which otherwise do not have any options, this review focuses on ideas and experiences along with the dilemma existing among physicians to undertake stem cells as routine clinical practice.

Keywords: Stem cells; Cell therapy; Regenerative medicine; Mesenchymal stem cells; Induced pluripotent stem cells (iPS); Clinical trials

Introduction

Clinical evidences on stem cell remain theoretical, where patients are adopting to pursue unproven stem cell therapies in jurisdictions all over the world [1]. Physicians are considered to be in a critical position deciding their involvement [2]. Though the interest with stem cells and the cells derived from them are debated about their therapeutic value, to directly focus on human diseases, many hurdles with respect to biological, technological and regulatory concerns are required to overcome before it is made available in commercial scenario [3,4]. However, with the existing controversy to undertake research on any form of stem cells, there are concerns raised in social perspectives [4,5].

As per a commentary released by Dr. Wong, immense possibilities in Regenerative Medicine and future practice of medicine has been highlighted mentioning about its great potential and promise of human stem cells to protect public health. Clear and strict governmental laws and regulations must be in place for license and medical/business operation requirements [6]. Literatures published have also questioned the ethical issues associated with the practice of stem cells in medicine. Physicians make great attempts to help millions of patients but there are ethical considerations that cripple them to use the newer methods and technologies because of economic and political influences. It is also mentioned about the stormy evolution of human culture with respect to diseases. Thus recommendations for theoretical-methodological interdisciplinary research, especially in theoretical and experimental biology and theoretical and clinical medicine, as well as philosophy is highly invaluable to find solutions to some problems connected with cell therapy [7].

Nature journal has published about the use of as-yet-unapproved therapies allowed on emergency basis for dying individuals who have no other options and the service has to be provided for free. However, enormous debates have been made about that to be ambiguous, alchemy and not legitimate [8]. Stem Cells have been commented to be of initial enthusiasm that is associated with several burdens observed in clinical practice. The hallmark properties of stem cells such as self-renewal and plasticity are also characterized to cancer cells that are hypothesized to lose control on transplanted stem cells to enable tumor development [9]. With the high degree of media attending to the stem cells, public are not much aware of unscrupulous opportunists who prey on patients by overstressing the potential applications of stem cells to enhance their marketing potential [6].

Medical Specialists and Experts Views on Stem Cell Research

With an intention to arrive at knowledge of stem cell research principle among medical students, a questionnaire when circulated stated that 46% males and 39% females were in favor of stem cell research but only 31% males and 28% females supported the embryonic stem cell research. The concerns were commonly with respect to ethical considerations [10]. Doctors believe that there are certain areas of biomedical research such as stem cell research that holds potential but has not shown any incredible proofs towards treatment with respect to safety or efficacy. Moreover, consists of enormous money involvement that inevitably denotes these clinics to exploit individuals by providing insufficient information on the efficacy part [11].

Experts are concerned that doctors in developing countries are treating patients with adult stem cells without waiting for clinical trials to authenticate the risks involved related to the health issues. Certainty has been arrived at some proven trials that involve blood disorders, bone marrow transplantation, and rare immune deficiency. Nevertheless, the attempts that are commonly used are to inject the adult stem cells into the blood, the lumbar region, or damaged tissue. At the present scenario, clinical trials pertaining to heart diseases have become more common. It is unconvincing when some doctors questioned about the

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use of stem cells for a patient in Russia malformed to the growth of brain tumors. PLoS Medicine has also reported about Sheba Medical Center's first case of human brain tumor related to neural stem cell therapy, where the patient who suffered a rare degenerative brain disease, ataxia telangiectasia, received several injections of fetal neural stem cells in 2001. Nonetheless, a cardiologist Henry has quoted that adult stem cell research has been very challenging with all the misinformation and confusion about embryonic stem cells [12].

Experts feel that with the presently existing hype surrounding stem cell research, majority of clinics around the world offer "stem cell therapies" for a variety of medical conditions. Considerable population travel to receive these unproven therapies [13]. With these strategies around the patients follow, there are worthy publications mentioning the use of stem cells as a cure for diabetes [14-16] which again cohort people to get overwhelmed with these unconvincing instincts. Experts have also been questioning whether stand-alone embryonic stem cell research organizations are still required [17] but there has been arguments existing in this context mentioning about too many inconsistencies between ES research organizations that worry about filling in the expertise gap would disappear [17]. Concerns have already been raised when a court decision by US government suspended funding for human embryonic stem-cell research [18]. Surprisingly, a poll conducted among Americans, have revealed that about 62% believe that medical research that involves the usage of embryonic stem cells is morally acceptable and they have also accepted the tests to be carried out using those stem cells [19].

Public Opinion and Views on Stem Cell Research

People feel that stem cell science relies on the advancement of technology, societal concepts of ethical behavior and the role of government. There had been series of discussions related to some specified topics with respect to ethics and efficacy [20]. Public has invariably shown higher interests on University scientists rather than the privately funded scientists as it is believed that public funded scientists are perceived to be motivated generously, and are more productive that would be accessible by public. Contrastingly, the private scientists are more self-interested than public scientists [21]. Astonishingly, there are diversity among the public views towards stem cell sources and policies [22]. Democratic campaign strategists have observed stem cell research as politically favorable to win votes from moderate and weak-identified Republicans [23].

Notably, the combination of stem cell and genome technologies is a dynamic idea to understand human development and disease which will be an effective way of improving treatments [24]. Interestingly, when the debates on stem cell applications still increasingly exist, the media coverage and economic expectations of therapies using stored umbilical cord blood cells is enormously projected though the therapeutic use of stem cells derived from the blood is not yet clear [25]. In this scenario, public interest towards stem cell science and technology is already documented publicly in United Kingdom with interests seen to be favorable for stem cells to be approved (73%) and research using embryos (76%) [26]. From the public point of view, patients are believed to win political support and with due commitment. It is felt that public investment will be able to speed up the research and bring accountability to stem cell technology [27].

Gray areas with public opinion include religious reluctance in understanding the actuals of stem cells. Mostly, conflicts of interests and poor debating capabilities have been prominently existing [28-34]. With these insights surrounding religious responses, it is suggested to contribute adverse health outcomes in transplant patients, and would impact the importance of negative or strained religious responses [35].

Market and Marketing Potential of Stem Cells

Injection of cells into a patient has gained attention recently. Approved products for clinical use are vastly under investigation worldwide and the market for cells and its products is expected to grow enormously in future [36-38]. Market potential towards cell therapy is expected to grow up to 6.6 billion dollars by 2016 from 3.5 billion in 2012. Developed country such as United States is found to share biggest market share amounting to 1.3 billion dollars and European market for 872 million dollars [37]. It is well known with the current market of ever increasing demands on stem cell therapies. However, there is a failure in capturing the actual requirement with respect to innovation that are considered to be quality standards which imposes a threat on the illicit supply of stem cell therapy for the poorly reviewed or negligible data outcomes [39].

Scientists have been claiming cell therapy to be a different platform technology which may be a disruptive technology but still, cell therapy has progressed considerably which developed it to be a fourth and final therapeutic pillar for healthcare in accordance with pharmaceuticals, bio-pharmaceuticals and medical devices [40].

Discussion

Statements pertaining to medical advancement for the inclusion of cell therapy as fourth and final therapeutic pillar for healthcare etc., has rather created reservations and to knowingly neglect or not consider such unproven advancements. It is known that cell therapies are quite different when considering pharmaceuticals with respect to batch consistency, stability, safety and efficacy [41]. There are areas which cell therapies has never been attempted or not required in preclinical scenario [42,43] or claims of irrelevance [44,45]. Establishing cell therapy with proof of concept to Indian scenario is highly challenging because of socio-political, cultural and ethical issues [46].

In order to make a scientific driven community, Indian cell biologists and scientists lack motivation and encouragement to precede performing quality research. Even though the current Indian scenario holds hope for stem cell research as the government has set up various centers promoting stem cell research, the Indian government with the Ministry of Health welfare organizations like Indian Council of Medical Research (ICMR) and Department of Biotechnology (DBT) has laid down the guidelines for stem cell research conducting in India [47]. India lacks improved quality of researches related to cell therapy with discussions on ethical and policy issues that enables barriers to settle. It is because of the inexistence of strong governance or legal backing that the researchers are free to consult their own integrities and make critical decisions by themselves [46].

The controversy exists because of the mixed results with minor or short-lived confining to extracellular factors [48]. Embryonic stem cells consists of ethical issues concerning to the use of embryos for research nevertheless, adult stem cells are harvested from living donors of bone marrow and other tissues which exerts a controversy over the morality of conducting research and therapy [49]. Moreover, there are known and unknowns with respect to the dose, route of injection and/or efficacy confining to the subjects along with the expected physiological changes happenings after the administration [50].

Though scientific community is advancing with improved developmental modalities to tackle current persistence of burdens

on the society with ineffective treatment modalities, the progress that has been made with the use of patient specific, patient-derived induced Pluripotent Stem Cells (iPSCs) [51-53] has to become reachable routinely with safe, viral-free human iPS cells in near future [54]. Moreover, the attention that requires moving ahead with the iPS technology is to address the immunogenicity, the variability of differentiation potential and inevitably the tumor formation of the iPS derivative cells [55]. Wide array of coverage with the application of iPSCs has already been documented for neurological disorders, hematologic diseases, cardiac diseases, liver diseases etc. with the generation of disease-free autologous cells from patient-specific iPSCs [56] but they haven't been exposed publicly.

Extensively studied and well documented evidences published for Mesenchymal Stem Cells (MSCs) is noteworthy. It paved way to understand their ability to differentiate into tissues including bone, cartilage and adipose in addition to neurons [57-59]. But they have their own trophic, paracrine and immunomodulatory functions which have produced devastating impact *in vivo* [60]. Advantages pertaining to MSCs oversee the therapeutic potentials that these cells possess and in combination with genetic engineering, the other areas such as low survival, engraftment, and homing to affected region along with the efficiencies into fully functional tissues is strongly believed to circumvent with these considerations [61-64].

Conclusion

Stability with respect to the administration of cell therapy has not still provided a complete understanding in favor. Certain unnoticed areas are dark sides though admirable results have been generated with the so far conducted trials. Interestingly, physicians have not opened up widely to justify cell therapy and also there is no underestimation of the new addition of healthcare modality. Upon clear predictable outcomes, and contemplated results, physicians joining together with cell biologists may frame studies that will provide encouraging breakthroughs considering all ethics and safety concerns.

Stem cell based regenerative and cellular medicine has now become a fascination for all. There are a number of physicians acknowledging it under the title stem cell therapy or regenerative medicine. This swiftly growing technology has attracted many to opt for this fascinating technology. However, the physicians lack clarity in vibrant practice of this technique. The current lack of training for physicians in this area combined with the sharply increasing practice of regenerative and cellular medicine is a recipe for serious trouble manifesting in a number of ways, which are detrimental to patients and largely avoidable, castigatory conflicts between FDA and physicians.

Whatsoever the type of stem cells is to be attempted, it requires proper validation and clear justification of the results to follow upon administration. The ethics if framed accordingly to avoid unauthorized usage, can precede the fascinating area of research using stem cells to medically important and sustainable form of cure for various diseases which otherwise does not have any option with routine therapeutic modules.

The potentials created by adult and embryonic stem cells in the treatment of various diseases have generated waves of excitement globally. The medical application of stem cells and its result is not transparent yet. Hence their potential uses need to be established by evidence prior to accepting them as safe and effective in treatment. Since stem cell based therapies are in its early stage of clinical trials and developments it is feasible to afford. But later it might turn out to be expensive and will be affordable to wealthy few and developed countries. The challenge is to ensure that it is available to all patients who require them.

The science of medicine is always evolving and developing and any new scientific invention or discovery is associated with ethical and legal issues in its pioneer stage. The usage of appropriate and liberal ethical and legal principle will help resolve these issues and bring these wonderful inventions in reality for the benefit of the future generations.

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