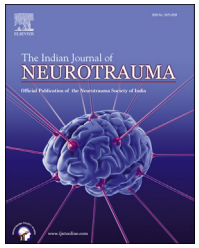
Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/ijnt



Editorial

Flimsy roots do not make a strong stem

Eliza Barclay wrote in The Lancet, Vol. 373, March 14, 2009: Stem-cell experts are worried that some doctors in developing countries are treating patients with adult stem cells without waiting for clinical trials to validate the safety of using them for health problems. Now, the developed world has gone a step further. The Italian Senate on 22nd May 2013 gave its final green light in favor of a new bill, already approved by the Chamber of Deputies on 16th May, which sets aside €3 million for a clinical trial of the treatment, devised by the Stamina Foundation in Turin. The law offers no specifics on the study's setup, or the disease it should target; it however, contains the provision for the creation of a Scientific Board to design the trial. This will probably be the first time that a parliament will order a clinical trial, under the existing Italian law, wherein unproven stem cell therapies can be administered on a case-by-case basis to patients with untreatable, severe illnesses, who have no other options. It provided that the treatment could be administered to thousands of patients without any prior clinical trials and apparently outside the European Union's regulation for so-called advanced therapies. The Italian Parliament legalized unproven 'stem cell therapies' as a *bona fide* treatment, without having been tested in rigorous clinical trials, and based on highly debatable preclinical evidence.

The future of medicine is Regenerative Medicine wherein stem cell therapy is going to play a major role. However there is still a lack of clarity on stem cell therapy. To date, there are very few examples of proven stem cell therapies. These therapies include BMT with populations that contain hematopoietic stem cells, corneal resurfacing with populations that contain limbal stem cells and skin regeneration with populations that contain epidermal stem cells. The best current example of a stem cell therapy is bone marrow transplantation (BMT), an accepted medical practice that saves thousands of lives a year. But even though there is a very sound scientific rationale for this therapy and it went on to become the standard of care for many hematological conditions yet the first clinical trial of a BMT among unrelated patients led to the deaths of all patients in the trial. Nobel Laureate Donnell Thomas went back to the laboratory and spent 14 years learning why donors had to be matched to recipients during transplants.

There is no therapy without adverse effects which are brought to light by proper clinical experimentation. Cell therapies are no exception. Importance of regulatory oversight at many stages in the development of new stem cell therapies and the testing of these therapies in controlled clinical trials to generate knowledge is the only way forward. The unscrupulous use can discredit this promising field of cell therapy.

The global stem cell market was projected to be around $1.2 billion by 2012 and is expected to reach around $16 billion in 2017. Stem cell market in India is still underdeveloped. In the next few years, the field of stem cell biology and regenerative medicine is likely to move toward translational research and eventually to clinical practice in India. According to the Global business intelligence research report, the stem cell market in India is estimated to touch $600 million by 2017. The Indian Council of Medical Research (ICMR), the apex body for the regulation of medical research in India and the Department of Biotechnology (DBT) have until now only approved indications for stem cell therapies in bone marrow transplantation, labeling all other procedures as experimental and it needs to be conducted only in the form of clinical trials. The government has drafted guidelines for stem cell R&D, but a definitive law is yet to be formulated. The Indian Council of Medical Research (ICMR)—Department of Biotechnology (DBT) '*Guidelines for Stem Cell Research (Draft) 2012*' is a 45 page document which is supposed to be an improvisation of '*Guidelines for Stem Cell Research and Therapy 2007*' by Department of Biotechnology and The Indian Council of Medical Research. The science behind cell therapy is advancing rapidly more so in the last 10 years. ICMR—DBT Guidelines 2012 and 2007 have practically remained the same. They are quite vague on issues which require clear answers. As a result, regulatory gaps and delays are frustrating and these hurdles hit the growth of this nascent field of stem cell. Any application for clinical trial especially cell therapy is tossed between Drug Controller General of India (DCGI) and ICMR. As a result, you will hardly find any cell based therapy trials on clinical trial registry of the Indian Council of Medical Research. This has led to expensive procedural delays of 12–18 months. India represents a growing market for regenerative medicines and stem cell therapies. This further highlights the need to take immediate steps to develop strong regulatory policies so that the country does not miss out on this opportunity to provide cheap and innovative healthcare solutions. India has the potential to become a leading global player for cell based

therapies. It is for the government to take a call and come up with a clear policy for cell therapy.

The ICMR guideline clearly says that "all institutions and investigators carrying out research on human stem cells should be registered with a national apex committee through an institutional committee". Also, it is stipulated that all new human cell lines shall be created with prior approval of either of the two committees and registered with both of them. To conduct clinical trials (trials in humans) with any stem cells, the investigator requires to have prior approval of the institutional committee and, in case of a marketable product, the prior approval of DCGI is also required, besides having to register with the National Committee. Sadly, the apparent exactitude of the ICMR guideline is not translated into reality and largely exists only on paper. The National Committee that is supposed to exercise centralized control on human embryonic stem cell research is yet to be in place! And if this is not enough, ICMR is yet to even publish the annexure to its guideline in which it was expected to specify the cGMP standards for embryonic stem cell lines. Actually the Health Ministry should give the required legal backing to the guidelines and the stem cell policy but doesn't seem to be in any hurry to do this, even as an increasing number of institutions are doing stem research in the country and testing its usefulness as a therapeutic tool. But the actual prevalence of stem cell-related activities is much larger than what these institutions represent.

However, given the multi-tiered system of registration and approvals recommended in the ICMR's guidelines, coupled with quality and ethical issues, has been a deterrent to the growth of stem cell therapy sector in India. Regulation should not stifle research and investigation. Clearly, these agencies are not playing a pro-active role in ensuring that stem cell research (which comprises creation of cell lines from multiple sources, including human embryo, adult cells and umbilical cord blood) or therapy is undertaken in the country only with their knowledge and permission and also under their supervision. In fact, there is not even proper co-ordination among these agencies and they appear to be on their separate trips. Perhaps, the fault is not squarely theirs as they lack the infrastructure and the legal sanction to be effective regulators. There should be clear-cut regulatory directions for stem cell research and therapy even while this frontier area of medical research is given policy impetus.

Acknowledgment

The authors are thankful to MS. Aanchal Sarah Bahadur, Departmental Secretary, Department of Neurosciences, MIND, for providing the necessary secretarial help for the preparation of the editorial.

Yashbir Dewan*
Senior Consultant, Max Institute of Neuroscience Dehradun – MIND, Max Superspeciality Hospital, Mussoorie Diversion, Malsi, Dehradun 248001, India

Sanjeev Dua
Additional Director, Max Institute of Neuroscience Dehradun – MIND, Max Superspeciality Hospital, Mussoorie Diversion, Malsi, Dehradun 248001, India

*Corresponding author.
E-mail address: ydewan@yahoo.com

Available online 15 June 2013

0973-0508/$ – see front matter

http://dx.doi.org/10.1016/j.ijnt.2013.06.001