A Professional Standard for Informed Consent for Stem Cell Therapies

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In November 2018, the US Food & Drug Administration (FDA) issued a press release that stated: “The potential health benefits of regenerative medicine have spurred major progress in stem-cell biology over the past several decades. But we continue to see bad actors exploit the scientific promise of this field to mislead vulnerable patients into believing they’re being given safe, effective treatments; when instead these stem cell producers are leveraging the field’s hype to push unapproved, unproven, illegal, and potentially unsafe products."[1]

Over the last decade, there has been an increase in the number of "clinics" (570 in the United States alone according to a recent estimate) offering what is portrayed as "stem cell therapy" for conditions ranging from orthopedic injuries to Alzheimer disease.[2] The unproven nature of these interventions suggests that patients who received them were, at a minimum, misled. At worst, they were severely injured, as in the case of at least three women who were left legally blind after intravitreal injections of platelet-rich plasma derived from tissue obtained through liposuction.[3]

The situation may soon improve, given the FDA's increased focus on enforcement of its human cellular and tissue products regulations (which has led to an injunction shutting down at least one of the companies running these clinics)[4] and interest by plaintiff attorneys, which has resulted in the successful filing for class action certification in California. This means that a “lawsuit alleging fraud in marketing …will proceed and may have 100s of patients involved.”[5] Class action certification may offer significant advantages to plaintiffs by reducing the need for duplication of efforts on behalf of each individual and consolidating the research necessary to pursue a case. If successful, patients who have received unproven stem cell-based interventions (SCBIs) may be positioned to recover the cost of their procedures and (for some) compensation for their injuries. The effect is a deterrent that is designed to encourage a change in industry practices.

Despite these efforts, however, hundreds of clinics remain active and continue to advertise unproven products. Because SCBIs are being delivered to patients in both research and clinical settings, and some SCBIs have been shown to be safe and effective (e.g., bone marrow transplantation for certain malignancies), it can be difficult for patients to distinguish between receiving a SCBI as standard of care, vs in a proper clinical trial vs in clinical practice for unproven indications, which are potentially associated with harm. Well-intended efforts to alert patients to the potential hazards of seeking unproven SCBIs, such as providing general information on reputable websites[6], have not so far proven effective in curtailing the use of unproven SCBIs. To supplement these approaches, the International Society of Stem Cell Research (ISSCR), a nonprofit professional organization, created a task force to develop a professional standard for consent for SCBIs offered outside of a clinical trial. Such a standard could help to ensure patients get the relevant information they need regarding a proposed intervention.

Expectations for Consent

Ethically, obtaining consent is a means of respecting patients’ autonomous wishes. Legally, informed consent protects patients’ liberty interests, specifically the right not to be touched or treated without their informed and voluntary permission. As a practical matter, informed consent provides an opportunity for patients to obtain the information they need about risks, benefits, and alternatives before they decide whether to proceed with an intervention.

In the research setting, in the US, regulations and Institutional Review Boards provide guidance about the information that should be included in the process of obtaining consent and how it should be communicated. By contrast, outside the research setting clinicians generally develop and deliver the necessary information on their own, with the help of an array of professional guidelines but with little definitive guidance or oversight. Given this general lack of specificity, there have been debates regarding the content of what must be disclosed during the informed consent process. In some jurisdictions (e.g., states in the US), the standard rests on what a reasonable patient would want to know. In others, it rests on what other clinicians tend to offer. Ideally, these two standards would converge, but especially in a rapidly evolving field that includes marketing of interventions that have yet to be fully studied, there can be little credible guidance from other individual practitioners, nor can patients be expected to know the questions they need to ask. Developing a model for the content that should be conveyed to patients should benefit both patients and practitioners.

A Professional Standard for SCBIs

The ISSCR developed a professional standard for consent by assembling a task force of experts in stem cells, clinical practice, ethics and the law. The task force created a draft standard, which was then reviewed by 30 individuals from 9 countries and revised based upon their comments. The standard articulates the information that needs to be provided to patients (or their legally valid surrogates) to help them make an informed decision if offered a SCBI outside of a clinical trial. Any clinic or practitioner offering such an intervention in this setting should include this information, along with anything else required by applicable laws, policies, practices, and regulations during the informed consent process. The full standard is available on the ISSCR website[7]. However, the basic elements are listed in the Table.

Complete, unbiased information is particularly important in situations that present both serious risks and ambiguous evidence. Thus, having a professional standard for consent is important if patients are to be given a chance to make an informed and considered decision about receiving a SCBI, many of which have not been proven to be either safe or effective. This is the primary reason for having a standard to help ensure all patients receive this information.

The unproven nature of many SCBIs also makes it difficult for patients to complain of medical malpractice in the event of injury as there is no accepted standard of practice against which to judge clinics and their practitioners. However, a failure to meet an applicable standard for informed consent would provide an independent basis for liability. In other words, clinicians who do not meet the appropriate standard for disclosure can be sued for not obtaining proper consent. Having a respected organization identify the essential elements of consent gives patients another avenue for complaint and courts a clear standard against which to judge the adequacy of consent. While malpractice litigation is a problematic and time-consuming means of deterring substandard care, in this rapidly developing, rapidly commercializing field it may be an important adjunct to educational and regulatory efforts.

Conclusion

By developing a standard for consent, the ISSCR does not endorse the administration of unproven SCBIs, which should rather be subject to properly designed and conducted clinical trials. However, until such time as regulatory efforts catch up with this burgeoning field, unproven SCBIs will continue to be offered outside of research trials. Patients deserve every means to protect themselves.

Table

Consent Elements

1. Rationale for treatment
2. Nature of the intervention
3. Oversight
4. Benefits
5. Risks
6. Immunosuppression
7. Adverse events
8. Manufacturing method and related risks
9. Costs
10. Rights
11. Organization
12. Alternatives
13. Data

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