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Extended Abstract
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# Stem Cell Research 2018-Autologous Stromal Vascular Fraction Containing Stem Cells Combined with Low Intensity Shock Wave for the Treatment of Human Erectile Dysfunction- Elliot B Lander- Cell Surgical Network

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Low-Intensity Shock Wave Therapy (LIST) has recently gained wide attention in the urologic community for its potential effects in improving ED. Shock waves appear to stimulate vascular flow and erectile function and one possible mechanism of action are through an endogenous stem cell-mediated regenerative effect. Assuming that endogenous progenitor cells are implicated in vascular repair and proliferation there might exist an opportunity for synergizing LIST with augmented numbers of autologous stem cells deployed into the corporal target tissues to amplify the regenerative effect. Stem cell therapy alone for ED is starting to gain attention but the marketing appears to have outpaced the science. There have been numerous animal studies in the literature since 2004 dealing with the use of various progenitor cells deployed in different ways to improve erectile tissue histology or function, with the vast majority demonstrating positive results. The number of human publications on the effects of cellular therapy on ED is extremely low considering that ED is prevalent in more than 30 million men in the United States alone. We report on 52 patients with ED who received a concurrent combination of shock wave therapy and intracavernosal injection of autologous SVF (rich in MSCs and HSCs) from human lipoaspirate. SVF is a heterogeneous population of cells obtained from the enzymatic digestion of lipoaspirate. SVF composition generally includes ADSCs, similar in morphology to adult MSCs, HSCs, endothelial progenitor cells, pericyte progenitor cells, macrophages, red blood cells, platelets, and T-regulatory cells, and various growth factors . There is extensive veterinary experience mostly for orthopedic purposes of positive outcomes in safely treating animals with SVF. Using recent technologic advances, we are currently able to isolate autologous SVF from adipose tissue in a sterile, rapid, surgically "closed" system in the operating room or clinic and deploy the product back into patients during the same surgical setting. Adult Stem Cells were serendipitously identified in lipoaspirate in 2001 [24] and were originally used by plastic surgeons in conjunction with fat as a way to fortify the graft material for improved uptake in reconstructive cosmetic procedures. Yoshimura, et al. [25] have been particularly significant in advancing this concept in Japan and in 2008 coined the term "Cell Assisted Lipo-Transfer." The Cell Surgical Network began using similar technology for procuring SVF in 2010 but focused on therapeutic purposes rather than cosmetic enhancement indications. Since that time, Cell Surgical Network clinical research teams have performed over 9000 procedures under IRB protocols collecting data in an online database for a variety of conditions including orthopedic, neurologic, pulmonary, urologic, cardiac and several other areas including chronic pain and auto-immune diseases. Flow cytometry was utilized to evaluate the cellular composition of SVF samples on 44 patients not included in this ED study but who underwent identical processing of their lipo-aspirate using the Time Machine protocol. Flow cytometric evaluation was performed using the FACScalibur (BD Biosciences Franklin Lakes, NJ). Cellular analysis showed that freshly isolated SVF was very heterogeneous (as expected with an autologous biologic) and harbored four major subsets of progenitor cells specific to adipose tissue; CD34high CD45- CD31- CD146- ADSCs, CD34 low CD45+ CD206+ CD31- CD146- HSC-progenitors, CD34high CD45- CD31+ CD146+ adipose tissueendothelial progenitor cells and CD45-CD34-CD31-CD146+ pericytes progenitor cells. The clinical correlations underscore the regenerative role of HSCs since the ratio of mesenchymal ADSC's to HSCs within SVF may impact clinical outcomes [26]. The majority of clinical information on HSCs has traditionally been based on cancer research supporting bone marrow ablation and replacement strategies with the regenerative contributions of HSCs now just coming to light. There is a plethora of evidence [27-33] based information to suggest that adult MSCs may have a significant

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beneficial use for a large variety of inflammatory, autoimmune and degenerative conditions. SVF has been used extensively for degenerative orthopedic conditions and arthritis. Michalek [34], from the Czech Republic, reported excellent safety data and very favorable outcomes using intra-articular SVF on 1128 patients evaluated for arthritic conditions. Cell Surgical Network published a safety paper in 2016 on 1524 patients for the safety of SVF deployment over a 5 year period. 97% of the patients treated also received systemic intravenous therapy in addition to their regional SVF deployment. As in most studies using SVF, safety was shown to be excellent with no severe adverse events related to SVF deployment into the soft tissue.

Materials and Methods:

Fifty-two patients with ED of various etiologies but mostly vascular origin received a short weekly series (1-6) of low-intensity acoustic shock waves This IRB approved (International Cell Surgical Society) pilot study evaluated men who met selection criteria for ED due to various etiologies including post-surgical iatrogenic trauma, microvascular disease, diabetes mellitus, and idiopathic. Contraindications to inclusion in the study included age less than 18, severe coagulopathy, significant concurrent infections, and uncontrolled cancer. Patient's age range was 27-80 (mean 59). Patients were told that they would be treated with intracavernosal SVF deployment with concurrent LIST and signed IRB approved informed consents emphasizing the investigational nature of their SVF deployments and the "off-label" use of shock wave therapy. All patients underwent history and physical exams prior to their procedures. Serum testosterone and nitric oxide levels were optimized when indicated.

Discussion:

There have been several reports describing the combination of adipose-derived MSCs with penile shock wave in a Racine model demonstrating positive effects on the cavernosal tissue [9,36,37]. In one such study, combination treated penile tissue showed significantly increased levels of cavernous nerve beta-III tubulin expression, smooth muscle actin, neural and endothelial NOS nitric oxide synthase, cGMP, and reduced cavernosal apoptotic index

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