OSTEOARTHRITIS

INTRODUCTION

Osteoarthritis (OA) is a common, chronic and incurable degenerative disorder of the joints. Pain, swelling and stiffness are the main presenting symptoms. Disability, difficulty with activities of daily living and self-care, and chronic pain arise as the disease progresses. Changes to bone, cartilage, synovium, and other joint tissues in early disease typically do not create consistent symptoms. Thus, patients do not usually know they have OA until the disease is widespread, irreversible, and shows up on x-rays. While cartilage damage and loss are important components to OA development and provide an explanation for the loss of joint space in x-rays, all joint tissues are affected. Many factors increase OA risk, but the specific pathways to OA for individual patients remain unknown and this substantially limits treatment options. Consequently, patients with severe pain and an inability to work, perform self care,or even walk may therefore explore cell therapies as alternatives to chronic pain, disability, or total joint replacement.

RATIONALE FOR USING CELL BASED THERAPIES FOR OA

Frequently cited goals of cell therapies for OA include pain relief, anti-inflammatory effect, and regeneration of joint tissues. The role of cell therapy in joint tissue regeneration and repair has primarily been explored in the treatment of small, focal or “pothole” like defects in the joint surface cartilage, and not for the more generalized cartilage loss and joint damage seen in OA. This is an important distinction. Currently used cell therapies for knee OA have not been shown to regenerate joint tissues. Inflammation plays a role in OA and many patients obtain short-term relief from anti-inflammatory therapies such as corticosteroid injections or oral nonsteroidal anti-inflammatory medications. New information suggests that dampening joint inflammation and modulating the inflammatory and degradatory processes from altered gene expression and metabolism of joint tissue cells may be appropriate therapeutic targets. Mesenchymal stromal cells (MSC) have been defined by the International Society for Cell Therapy (ISCT) as culture expanded cell populations that are plastic adherent, express certain cell markers but not others, and are able to differentiate into bone, cartilage, and fat forming cells (Dominici et al, 2006). Numerous studies have shown that cells meeting this definition of MSCs can be derived from the heterogeneous connective tissue progenitors present in native tissues such as bone marrow, fat, and synovium. Such culture expanded populations are reported to have immunomodulatory and anti-inflammatory properties, or to stimulate other cells to improve repair processes (Caplan, 2017). Less is known about the direct injection of mixed, uncultured and uncharacterized cells from patient’s blood, fat or bone marrow that have been marketed recently and incorrectly as “stem cell” or “MSC” therapies. The biological properties and therapeutic potential of both culture-expanded MSCs and uncultured directly injected cells remain controversial and in need of substantial additional scientific inquiry.(Sipp et al., Nature 2018).

WHERE ARE WE WITH CELL BASED THERAPIES FOR HUMAN OA?

Cell therapies to treat human OA are used worldwide without clear support from high quality studies. In the United States, cell therapies for OA primarily involve the use of cells obtained from autologous and minimally manipulated tissues such as concentrated bone marrow aspirate and adipose stromal vascular fraction. A recent review of the english language literature on cell therapies for knee OA revealed only 3 studies involving small numbers of patients with differing methodologies, low serious adverse events, and mixed clinical outcomes (Chahla et al, 2016). One study injecting marrow-derived cells into the knees of patients with OA showed no serious adverse events but outcomes similar to saline injection (Shapiro et al, 2017). Limited international studies on the use of allogenic culture-expanded MSC in knee OA showed improvement in joint pain and swelling in some studies but with

no to mild symptomatic improvement (Gupta et al, 2016 and Pers et al, 2016). Overall, high quality studies evaluating the effectiveness of cell therapies in the treatment of knee OA are lacking.

WHEN WILL TRIALS BEGIN?

Several clinical trials of cell therapies in the treatment of OA have been entered into clinicaltrials.gov. Entry into clinicaltrials.gov does not mean that the studies have been peer reviewed, vetted, or endorsed by the United States government, or any scientific, academic or regulatory body.

SUMMARY

The effects and effectiveness of cell therapies for the treatment of OA in humans remain unproven and as such cannot be recommended at the present time.

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Constance R. Chu, MD, Stanford University
Scott Rodeo MD, Hospital for Special Surgery
George Muschler MD, Cleveland Clinic

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