Stem cell treatments for shoulder and elbow injuries flourish, but so far there's little evidence they work

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The utilization of stem cell therapies for augmentation of tissue healing has far outpaced the supporting scientific and clinical data, largely due to aggressive marketing that has led to widespread and often inappropriate use of cell therapy approaches in the United States. Two critical reviews in the *Journal of Shoulder and Elbow Surgery* examine the current status of biologic approaches for common shoulder and elbow problems. The authors discuss areas where the current evidence base is weak or controversial and recommend where further studies are required.

There is significant interest in biologic treatment options to improve healing and reduce symptoms more rapidly in elbow and shoulder injuries, such as osteoarthritis (OA), tendinopathy, ligament injuries, and other inflammatory conditions. However, there is uncertainty among physicians and patients about what works and what does not since many of these treatments are still unproven. While the authors caution that the future outlook is positive, the clinical data for their use are currently limited.

Additionally, a large number of patient-specific factors affect the composition and biologic activity of products, including age, sex, medical comorbidities, concomitant medications, and genetic and epigenetic factors. These variables as well as unpredictability of the "biologic product" are then added to the variability of the underlying pathology being treated.

The authors review several biologic agents, including platelet-rich plasma (PRP), bone marrow aspirate concentrate (BMAC), and mesenchymal stromal cells (MSCs) derived from adipose tissues, in order to provide medical specialists and their patients with up-to-date clinical data and stimulate further research in this important and growing area of musculoskeletal medicine. They conclude that these treatments have great potential based on laboratory studies demonstrating a positive effect of these materials on the basic biology of tissue healing, however, the clinical data for their use in both shoulder and elbow pathologies are very limited. The authors point out a that serious limitation is the significant variability and heterogeneity among these biologic formulations.

In an insightful review of biologics for managing shoulder pathology, James B. Carr II, MD, HSS Sports Medicine Institute, Hospital for Special Surgery, New York, NY, USA, and Scott A. Rodeo, MD, HSS Sports Medicine Institute, Hospital for Special Surgery and Weill Medical College of Cornell University, New York, NY, USA, evaluate the basic science and clinical evidence for the most commonly used biologic agents for treating common shoulder pathologies such as rotator cuff tears, shoulder OA, and tendinopathy. Rotator cuff tears occur in more than 20 percent of the general adult population, with a progressively higher incidence as age increases, while shoulder OA has been estimated to affect up to 33 percent of individuals over 60.

The authors' goals are to help physicians better understand the appropriate terminology for the most commonly used biologic agents; critically review the current literature on the use of various biologic agents in the treatment of the most common shoulder pathologies; and highlight emerging therapies and potential future applications of biologic agents in the management of these shoulder pathologies.

"There is a critical need for strategies to improve rotator cuff tendon

healing following surgical repair and for methods to reverse the progressive muscle atrophy that occurs in patients with rotator cuff tears," explained Dr. Carr and Dr. Rodeo. "The shoulder is therefore an area in which biologic agents are especially appealing."

Although the outlook may be positive, the authors call for further laboratory and clinical research to define optimal formulations, dosing schedules, and approaches for various tissues and injuries. As the safety and efficacy of these approaches are further defined, changes in the regulatory environment at the FDA level may also aid progress.

Tennis elbow (lateral epicondylitis) affects one to three percent of adults each year. At the elbow, this is the most common indication for biologic therapy and it is often compared to steroid injections. A detailed review by Jason L. Dragoo, MD, Department of Orthopedic Surgery, University of Colorado, Denver, CO, USA, and Molly C. Meadows, MD, Stanford University, Redwood City, CA, USA, identified studies on the use of biologics to treat elbow pathology. They found significant research on the use of PRP for lateral epicondylitis, but few studies on golfer's elbow (medial epicondylitis), ulnar collateral ligament (UCL) injuries, and biceps tendinopathy. They also found studies using MSC-containing therapy in the treatment of lateral epicondylitis, but studies using MSCs in other areas of elbow pathology were generally lacking.

The authors conclude that despite fairly widespread use of biologic agents such as PRP in lateral epicondylitis, further research is needed to determine the optimal formulation and administration of PRP injections. Additional rigorous studies are necessary to provide definitive data. Current research on the use of cell therapy in other elbow injuries is limited and further research on biologic therapy for golfer's elbow, UCL injuries, and biceps tendinitis is needed.

"Basic science research suggests that the use of 'biologic therapies' such

as PRP and bone marrow cells have the potential to improve tissue healing in a number of conditions," Dr. Dragoo and Dr. Meadows emphasized. "Clinical studies demonstrate that PRP injections are more effective than steroid injections in the treatment of tennis elbow and can guide practitioners to recommend more effective treatment options for patients with this condition. Further research for treatment of other elbow pathologies is needed before making any formal recommendations for these conditions. We need to define the most effective formulations and dosing of platelet and cell-based therapy for each type of injury."

"Orthopedic surgeons must be well informed when discussing biologic agents with patients," added Dr. Rodeo. "It is paramount that orthopedic surgeons provide leadership in this area and work toward developing practice guidelines and policies for the use of biologic agents. A rigorous approach to the use of 'regenerative medicine' therapies and the maintenance of high clinical and research standards are required to move the field forward."

Laboratory studies in the US can be hampered because of government restrictions on clinical applications of cell therapy. Scientists and clinicians are not able to isolate and then culture a patient's cells in order to increase the population of "desired" cells in the laboratory environment. This has led many US patients to pursue "medical tourism," traveling overseas to countries such as Germany, the Republic of Korea, and Japan, as well as other European countries, seeking stem cell treatment where there may be a risk of infection or other complications in less regulated environments.

More information: James B. Carr et al, The role of biologic agents in the management of common shoulder pathologies: current state and future directions, *Journal of Shoulder and Elbow Surgery* (2019). DOI: 10.1016/j.jse.2019.07.025

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