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Editorial

ORTHOBIOLOGICS: FILLING THE GAPS IN CURRENT ORTHOPAEDIC SURGICAL TREATMENT

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Most orthopaedic intervention for trauma or pathological processes is unambiguous. However, when venturing into the realm of treatment for degenerative conditions or soft tissue injuries the indication for treatment has mostly been supported by level 3 evidence in the top orthopaedic surgery journals.[1] In the past few of decades it has been concerning to see a growing number of treatments designed for end-stage disease being applied to younger individuals. As life expectancy increases, the risks of multiple revision interventions are likely and from a public health standpoint, more expensive, and predictably unsustainable. Enter the possibility of minimally invasive interventions with lower morbidity and, if properly utilized, adding critical time prior to end-stage disease intervention.

The use of biological therapies to treat degenerative conditions such as osteoarthritis and tennis elbow has grown immensely over the past five decades. Additionally, the application of cellular based therapies have been recommended, and provided for a wide range of conditions. Unfortunately, orthobiologics has been oversold by some parties - some of these disorders clearly lack supporting evidence for both safety and efficacy. The orthobiologics "field" investigational output of supporting basic science as well as clinical studies is unrivaled. What is unique about the current movement are the researchers from the community that are making significant contributions to the body of knowledge. Combine this with institutional publication and there is a convincing story emerging that orthobiologics could indeed have a role in the treatment of osteoarthritis. A growing number of systematic reviews and meta-analyses demonstrate not only long-term safety, but efficacy of treatments in comparison to commonly administered therapies with effect sizes that are difficult to ignore.

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The purpose of this editorial is to acknowledge the effort of investigators around the world by bringing light to their significant contributions to the current body of evidence. This data will ultimately be used to improve the health and well-being of patients suffering from the debilitating and painful disease of osteoarthritis. These are relatively easy to administer orthobiologic therapies that will provide meaningful improvement in people's lives.

Orthopaedic Surgeons (AAOS), American Association of Hip and Knee Surgeons (AAHKS), Hip Society, and the Knee Society that have likened the treatment of orthobiologics to snake oil. This is seen in the AAOS Now article published December 2020, and limited evidence stance communicated by Browne et al. in the Journal of Arthroplasty, June 2019, position statement that asserts that the evidence available is limited to primarily patient testimonials and expert opinions.[2,3] Furthermore, they state that only a limited amount of scientific evidences are available that supports the adoption of the clinical use of orthobiologics. Additionally, that rigorous trials need to be conducted to establish safety, efficacy, and cost effectiveness.

Even without the rigorous review of published literature and evidence, it is clinically evident that arthroplasty helps many patients. However, when concerning orthobiologics, these organizations have overlooked the available evidence contrary to the position statements being made. The establishment of such a high clinical barrier of entry for orthobiologics, is a bit hypocritical, in consideration of the nature of the benign treatment. Orthobiologics as a whole are far less invasive with fewer adverse events when compared to joint arthroplasty. It is a rather surreptitious fact that the clinical use of arthroplasty was established, largely by trial and error over more than 100 years instead of being established from clinical trials.[4]

The evidence to support the use of total joint arthroplasty, even today, is inconclusive as well. From the standpoint of demonstrated superiority, safety, cost effectiveness as compared to non-operative therapy such as weight-loss and physical rehabilitation. Total joint replacement has demonstrated cost-effectiveness that limits surgery to the just the most severe of cases.[5-8] The evidences of efficacy of orthobiologics are also inconclusive and are certainly evolving. The compilations of studies, including randomized controlled trials, systematic reviews, and meta-analyses completed to date are nothing short of impressive as many of these investigations have come without institutional support, and have been carried out over a relatively short period of time. Very few would argue that an autologous platelet-rich plasma (PRP) injections was unsafe to patients. The same cannot be said of the advocated standard of care, insurance approved, antiquated recurrent corticosteroid injections recommended for arthritic knee joints as not harmful.[9]

The appeal to the fallacious argument that because insurance pays for a procedure, that it is actually safe, efficacious, regulatory approved, and cost effective. There are many examples in orthopaedic surgery where the established evidences conflicts with common practice, and insurance approval. Examples include: knee arthroscopy for degenerative meniscus tears/ osteoarthritis, arthroscopic subacromial decompression for rotator cuff tear repair, lumbar fusion for lumbar disc disease, and total knee replacement for early stage osteoarthritis after failing less than 6 weeks of standard non-operative therapy. Arguments have been made that the expense of orthobiologics treatment of knee osteoarthritis (e.g., PRP) is predatory, expensive, and has no evidence to support its use. We clearly know, that for knee OA, not only are PRP injections the

most effective injectable treatment, but also not harmful to the patient. PRP does have a greater cost as compared to hyaluronic acid, however, out to one year and comparatively, it is, cost effective.[10,11]

We know that the autologous use of mesenchymal stromal cells, mixed soft tissue progenitors administered both in the same day procedures, or when culture expanded are safe, with minimal adverse events as demonstrated in a multi-centric study of over 2,000 patients with average time of follow-up of more than 8 years.[12] Although the efficacy of the use of mesenchymal stromal cells are also not conclusive, the results of a recent meta-analysis of 35 studies in over 2,000 patients seems to suggest efficacy in improving pain, self-reported function, and cartilage quality. However, as outlined by the authors, better quality studies are warranted as heterogeneity and risk of bias were high.[13] As far as cost effectiveness is concerned, this is an area requiring significant development, especially concerning the use of mesenchymal stromal cells and mixed soft tissue progenitors, however investigators are quite aware of its importance.[14]

The focus of many investigators is to understand the area where these orthobiologic therapies complement existing non-operative treatments, augment current surgical intervention, or provide critical bridge to end-stage disease conditions resulting in arthroplasty. Typically, for 40-55 year-old individuals, but also to provide viable alternative therapies to elderly patients 60 - 70 year-olds that do not want to undergo arthroplasty.[15]

In the face of the desire and great efforts to integrate orthobiologics into readily accepted treatments, there remains considerable work to demonstrate further, their safety, efficacy, and cost effectiveness. In order to accomplish these goals toward an accepted viable therapy, every injection that is performed in a healthcare facility or clinic should be fully characterized for cellular components, cellular counts, viability, and sterility. The injectate should be created from a written, standardized protocol that is reproducible, transparent, and meets all medicinal labelling requirements. To date, this is rarely done. Additionally, the tracking of orthobiologics attendant complications and adverse events as well as outcomes have to be universally recorded and compiled to provide short-term, intermediate, and, most importantly, define long-term outcomes of treatment. In addition, close attention has to be given to observing and recording the patient factors that may have significant impact on outcome. This task is far more challenging, especially for the community-based practitioner, but despite the difficulty, the data is being collected. Finally, orthobiologics use has to demonstrate that it will lower the cost of disease management in specified time frames if it is to complement and or supplant existing treatment.

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