Wharton Jelly derived-Mesenchymal Stromal Cell (WJ-MSC) therapy: Translation into clinical practice in orthopedics degenerative conditions.

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ABSTRACT

Statement of the Problem.

Among some orthopedic conditions that have mostly been the target of research with ortho-biologics and regenerative medicine, it is known that the conventional treatment approach for degenerative conditions such as Knee Osteoarthritis (KOA) and Degenerative Disc Disease (DDD) focuses on alleviating symptoms through various measures, including physical therapy, weight reduction, and the use of medications to control pain and inflammation. Although current conventional therapies provide symptomatic relief, their impact on the cartilage or disc is limited. Additionally, surgical procedures such as discectomies and arthroplasties have limitations and risks.

The above highlights the need to continue researching new therapies for KOA and DDD. Specifically, regenerative therapy based on ortho-biologicals can complement traditional management and has been shown in clinical studies to relieve pain, improve functionality and contribute to quality of life. The administration of ortho-biologicals, specifically from mesenchymal stromal cells (MSCs), has been shown to have a favorable impact on the process of joint and disc degeneration, given their immunomodulatory effects, as well as their effects on tissue growth, formation of collagen and differentiation into chondrocytes. In particular, studies suggest that WJ-MSC therapies are safe and well tolerated, with the potential to relieve pain and improve knee and spine functionality. These cells act in various ways, such as migration towards damaged cartilage, adaptation to their hypoxic environment, promoting the survival and differentiation of endogenous MSCs, synthesis and protection of the cartilage extracellular matrix, and exhibiting anti-inflammatory and immunomodulatory properties.

It is intended to share the experience of a clinical and research center treatment with WJ-MSCs, which were delivered locally (into the knee joint and intervertebral disc) in patients with chronic degenerative orthopedic conditions.

Methodology.

Two retrospective cohorts were analyzed according to the effects following therapy based on WJ-MSC in KOA and DDD patients. Ethical approvals were obtained by an independent ethics committee (CEI-0435-11-2022 and CEI-0324-07-2022). Informed consent forms were signed by patients. Clinical outcomes were measured by the Short-Form12 questionnaire, Visual-Analog-Scale (VAS), and Western-Ontario-McMaster-Index (WOMAC) for KOA patients and Oswestry-Disability-Index (ODI) for DDD patients. KOA patients were treated with a single dose of $40x10^6$ WJ-MSC per target knee (MSC were delivered by intra-articular route), and DDD patients were treated with $10x10^6$ WJ-MSC per target intervertebral spine disc (MSC were delivered by intradiscally and facetally route). Previously, the allogeneic WJ-MSCs were expanded in a culture medium supplemented with 10% human platelet lysate (hPL) up to passage 7. Cell marker expression and in vitro differentiation to mesodermal lineage were verified, as well as microbiological tests.

Findings.

During 2022, 39 KOA patients started follow-up, of whom 26 (67%) answered the questionnaires at 6 months. There was an improvement according to pain assessment at 6 months post-therapy with an average 1.5-point reduction (↓32%) and according to pain, stiffness, and functionality assessment it was demonstrated an improvement in total WOMAC with an average reduction of 12.5 points (↓36%) in patients who had a baseline score of ≥10%. In the meanwhile, during the same period, 32 DDD patients were treated for thoracolumbar back pain and started follow-up, of whom 29 (91%) answered the questionnaires at 3 months, 30 (94%) answered at 6 months, and 22 (69%) at 12 months post-therapy. There was an

improvement according to pain assessment at 6 months with an average reduction of 2.3 points (↓37%), which was maintained up to 12 months post-therapy and according to disability assessment, it was demonstrated an improvement at 6 months post-therapy with an average ODI score reduction of 9.8 points (↓29%), which was maintained until 12 months post-therapy. No adverse events were noted neither in KOA nor DDD-treated patients.

Conclusion and significance.

Despite the evolving nature of the evidence, the study´s findings contribute to our understanding of the therapeutic benefits of WJ-MSC in KOA and DDD-diagnosed patients, who sought treatment for failure of conservative therapy and for pain and functional limitation. The improvements evidenced involve changes in the patient's quality of life. There were no serious adverse events reported, demonstrating that these therapies are safe.

BIOGRAPHY



Karolynn Halpert is a medical doctor and specialist in Emergency Medicine. She currently serves as the Chief Medical Officer and co-founder of BioXcellerator and BioXtech, where she leads scientific, medical, and research teams dedicated to translational research in regenerative medicine and advanced cellular therapy. Throughout her career, Dr. Halpert has earned a reputation for pioneering the establishment of multidisciplinary teams and strategic research platforms to advance the science of cell therapy, primarily through clinical studies using WJ-MSC to treat various conditions. Thanks to her leadership, BioXcellerator has become a global leader in cellular therapy. In fact, Dr. Halpert, and the medical and scientific teams she oversees have contributed to the company obtaining ISO certification and certification in good clinical practices. She and her team have published several articles on MSC in major scientific journals. She is also a co-founder of BioXscience, a research and innovation center focused on evidence-based knowledge development of advanced therapies. Dr. Halpert has been a recognized international speaker at many cell therapy conferences around the world.

ABOUT RESEARCH TOPIC

KOA is a global public health issue, affecting around 250 million people worldwide, with 27 million cases in the United States. This degenerative joint disorder causes pain, inflammation, and restricted mobility, significantly impacting patients' quality of life. KOA prevalence is substantial, with 16% of people aged 15 and older affected worldwide, and 22.9% among those aged 40 and older. This translates to approximately 654.1 million people aged 40 and above suffering from KOA worldwide. Furthermore, it is estimated that around 86.7 million new cases of KOA occurred in 2020.

On the other hand, spinal degeneration affects around 90% of the general population over 50, with the L4-L5 and C5-C6 discs being the most affected. This condition has implications for patients' quality of life and the global economy. While some patients can improve their symptoms with daily physical therapy and medical recommendations, up to 10% of patients may not respond to conservative treatment, leading to disabling lumbar pain and necessitating consideration of surgical or non-surgical alternatives. While disc degeneration may be part of the normal aging process, it can also be triggered by various factors. The pathogenesis of abnormal disc degeneration represents a biomechanical continuum, closely linked to clinical and sociodemographic factors.

ABOUT INSTITUTION

BioXcellerator is a US company based in the USA and Colombia, specializing in WJ-MSC and other regenerative medicine therapies. The company is dedicated to the research and development of advanced medical treatments based on WJ-MSC to address a variety of medical conditions, injuries, and chronic diseases. BioXcellerator has excelled in the field of regenerative medicine and has worked on the application of these therapies to treat conditions such as osteoarthritis, sports injuries, neurodegenerative diseases, autoimmune diseases and other health problems. The company has conducted research to evaluate the safety and efficacy of these treatments.

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