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Short Commentary

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Cervical facet joints injections of stem cells in treatment of neck pain after whiplash injury

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Commentary

Neck pain is a very common and often disabling conditions. Neck pain lifetime prevalence rates are 48.5% [1]. Pain originating from the complex of two bilateral Facet Joints (FJ) and one intervertebral disc often produces one of the most common conditions-mechanical neck pain [2]. The usual reasons for the pain are the degenerative process, inflammation and/or trauma. Pain from FJ is most frequently non-radiating but still can produce "pseudo-radicular" symptoms. Cervical FJ are a primary source of pain in 26-70% of the patients with chronic neck pain and 54-60% of the patients with neck pain after whiplash injury [3]. On examination patients experience increase in discomfort with extension, side flexion and rotation. Additionally, paraspinal palpation is most of the time increase the pain. A large prospective study showed proper examination has an 84% specificity for diagnosing cervical FJ pain [4]. Radiography, CT or MRI are often not very helpful in establishing the diagnosis of FJ pain (with exception of cases of FJ hypertrophy due to osteoarthritis) and serve mostly to rule out other potential sources of pain [3]. Mechanical injury (whiplash) is a very common initiating factor for cervical FJ pain [5]. In patients with cervical FJ pain due to whiplash injury MRI failed to show findings that were correlating with the presence or severity of pain [6,7]. Multiple modalities of treatment for this condition exist. However, there is no consensus on the selection of proper treatment or the order in which these options should be employed [2]. The general recommendation is to employ 6-week trial of conservative management (PT, chiropractor, NSAIDs, massage, etc.) prior to consideration of interventional treatment [3]. Current standard interventional treatment consists of either intra-articular injection of steroids (usually with local anesthetic) or diagnostic/prognostic medial branch block with local anesthetic followed by Radiofrequency Ablation (RFA) performed under fluoroscopy guidance [2,3]. Unfortunately, it seems that steroids are not improving or prolonging the effect of intra-articular local anesthetic injection [8]. In general, intra-articular injections or medial branch blocks are not a reliably long-lasting treatment of FJ pain [3-9]. RFA is not a very reliable way of reduction of cervical FJ pain despite producing clearly longer effect than simple injections. One prospective study [10] showed that 2 months after cervical RFA only 58% of patients reported 30% or better reduction of pain. Another study [11] revealed that 54% of the patients reported 50% or better pain relief after RFA. Not surprisingly, about a third of patients who have had RFA have to undergo repeat procedures [12]. Stem Cell (SC) based treatment is currently approved by the FDA only as a hematopoietic stem cell transplant for certain types of cancer. Despite this, SC

therapy has been used fairly often in the last decade for various conditions of the joints. It has been shown that Mesenchymal Stem Cells (MSC) promote FJ articular cartilage regeneration and attenuate FJ osteoarthritis [13,14]. Most of the published studies are dedicated to treatment of lumbar FJ pain [15,16]. Our search of cervical FJ pain treatment with MSC in the literature produced only one published article [17]. While most of the patients in this study were treated for lower back pain, ten patients were treated with cervical FJ injection of MSC. For reason not completely understood, all of this patients also received IV infusion of MSC as well as lumbar epidural injection of WSC. Authors reported significant improvement over a period of 12 months even though 50% of the patients were lost to follow-up. All of this prevents from assessing the real efficacy of FJ injection by itself. In our practice we perform a significant number of SC injections for different painful conditions of the spine with very promising results. The hUC-MSC (human Umbilical Cord tissue derived Mesenchymal Stem Cells) used in our clinic are generated from umbilical cord tissue, and are characterized to have standard MSC phenotype according to the International Society for Cellular Therapy criteria. Briefly, the umbilical cord tissue was obtained after full-term deliveries from healthy human donors and were tested negative for infectious agents to meet the eligibility for tissue donation in compliance with Title 21 of the Code of Federal Regulations (21 CFR) part 1271 in the USA. hUC-MSC were isolated and culture expanded from the eligible umbilical cord tissue in a cGMP compliant facility. hUC-MSC suspension was prepared at a concentration of 2 million cells/mL and has been subject to viability, identity, purity and safety testing (sterility, mycoplasma, endotoxin etc.) before release for use in our patients [18]. We have recently reported very promising results of treatment of spinal stenosis with MSC epidural injections [19]. In light of our positive experience, we performed a retrospective review of cases with cervical FJ pain after whiplash injury treated with MSC injections 6-12 months prior to data collection. During this period 19 patients (11 male and 8 female with age varying from 24 to 64) were treated with cervical FJ stem cell injections. Eleven patients received unilateral injections and eight patients had bilateral injections. All patients received fluoroscopy-controlled cervical FJ injections of hUC-MSC: twelve patients had two levels of FJ injected with 4 million MSC while seven had three levels of FJ injected with 6 million MSC. During follow-up in 6-12 months the average pain relief was 82%. Only one patient received less than 50% pain relief (he eventually received a MSC epidural injection with significant improvement). No complications or serious side-effects were observed. No patients required repeat FJ injection during the period of observation. Our report has the largest number of patients treated with cervical FJ injections of MSC in the literature. It is also the first one to assess the results of cervical FJ treatment with MSC as a solo modality of treatment. Nevertheless, it encompasses only a small group of subjects in relatively short period of time evaluated in a retrospective fashion. Based on a very positive results, we believe that a larger prospective study is needed to have a full assessment of treatment efficacy using cervical FJ injections with MSC.

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