Learn from the Past, Treat in the Present, and Keep an Eye on the Future

Commentary on: Injectable Orthobiologic Substances

I trained at Oswestry (UK) two decades ago, at a time when Professor Richardson pioneered autologous chondrocyte implantation (ACI). This demanding procedure required two operations: An arthroscopy to harvest chondrocytes and an open arthrotomy for transplantation. Harvested cells were cultured to expand chondrocytes fifty times, and then injected under a watertight drum of the periosteum or seeded in a collagen membrane.[1] At its infancy, ACI was not recommended for routine primary treatment of cartilage defects of the knee in the National Health Services but was only offered as part of clinical trials in participating centers (technology appraisal guidance number 16, the National Institute for clinical excellence – December 2000). With further randomized controlled trials (RCTs) becoming available, ACI is now a recommended treatment option for symptomatic articular cartilage defects over 2 cm^2 in size, involving the knee in patients with minimal osteoarthritic damage.[2] Once the knee started to develop osteoarthritis, this option is no longer effective. It is not difficult to perceive why progress in the case of ACI has been slow given that harvest and implantation both necessitate an operation and processing tissue cultures took a long time.

On the opposite side, Orthobiologics have gained wider popularity, given the simplicity of the procedure. The "biologics"[3] are much easier to harvest (might even be as simple as taking a blood sample), require minimal manipulation, and do not require surgery to deliver to the knee. It is not difficult to understand why patients with early (or even late) stages of knee osteoarthritis who failed other conservative measures and who are not yet candidates for (or wish to avoid) arthroplasty, seek this kind of therapy. However, the public perception that biologics might have a "regenerative potential," coupled with the financial benefits to the physicians and organizations have resulted in wide publicity of these therapies (which has even outpaced scientific evidence).[3,4] Orthobiologics have been portrayed in the media alike snake oil (a good for everything liniment sold in the USA and Canada in the 18th century as a remedy for pain and lameness). My meeting this year with Nicolás in Cairo helped confirm my impressions about this emerging field.

Nicolás Piuzzi is a talented orthopedic surgeon working at Cleveland Clinic, Ohio. In addition to authoring several publications and reviews,[3,5,6] he and his group looked at this subject from patient and social media perspectives.[7,8] In one study, they contacted US centers, which marketed stem cell therapies directly to customers with orthopedic conditions. They used a simulated 57-year-old male patient who claimed to have moderate knee pain, have failed nonoperative treatment, and was told he needed a knee replacement. The average positive patient satisfaction rate marketed to consumers in their study was 82.2% and the mean cost for each therapy was $5,156 (about 9.9% of the mean annual US household income). Patients were, therefore, exposed to much "hype (excitement)," which was unproven or insufficiently proven by scientific data. In the other study, Piuzzi and his colleagues analyzed social media posts on Instagram and Twitter, using 28 hashtags related to cell therapy and arthritis. They reported that overall, 94% of the posts had a positive tone and only 6% had a negative tone. The media perspective was most frequently (83%) from a business marketing Orthobiologics directly to consumers. Those posts portrayed an almost exclusively positive tone, without providing a "fair balance" on the risks, benefits, and limitations. Whereas 91% and 92% of social media posts related to the hip/knee replacement and anterior cruciate ligament reconstruction, respectively, were patient-generated; only 13% of posts related to cell therapy injections came from patients. Those were 60% positive and 40% negative (a different picture from that advertised by companies).

Overall, the development and implementation of orthobiologics with potential disease-modifying effects remain a challenge. Their effective clinical assessment and improvement will demand:

- Standardized nomenclature and quantitative methods for harvesting, processing, characterization, and delivery
- High-quality methodology in study design (blinded RCTs and prospective cohorts)
- High-quality patient registries.[3]

In this issue of the Journal Patel *et al*.[9] reviewed the current evidence and future applications for injectable Orthobiologic substances for the treatment of knee osteoarthritis. The reader is referred to this article for a balanced narrative of different types, indications, and evidence for the efficacy of those injections. A second article in the same issue by Sahoo *et al*.,[10] showed that platelet-rich plasma resulted in a better and more lasting pain relief and patient satisfaction than steroid injections in patients with plantar fasciitis, which might suggest a regenerative potential.

The quote that "A surgeon must be a physician first and last. Otherwise, he is little more than a meddler, an amateur

mechanic, and often an indifferent one at that"[1] is especially true in the situation where the treating physician is supposed to keep a balance between hype and evidence in recommending orthobiologic injections for a patient with knee osteoarthritis.

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Conflicts of interest

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Emad S. B. Saweeres

Department of Orthopaedic Surgery, El-Sahel Teaching and Good Shepherd Hospitals, Cairo, Egypt

Address for correspondence: Prof. Emad S. B. Saweeres, El-Sahel Teaching and Good Shepherd Hospitals, Cairo, Egypt.
E-mail: prof.saweeres.ortho@gothi.gov.eg

References

1. Richardson JB. Classical ACI for chondral and osteochondral defects. In: Shetty AA, Kim SJ, Nakamura N, Brittberg M, editors. Techniques in Cartilage Repair Surgery. Berlin, Heidelberg: Springer Berlin Heidelberg; 2014. p. 165-74.
2. NICE.org.uk. Autologous chondrocyte implantation for treating symptomatic articular cartilage defects of the knee. Technology appraisal guidance [TA477] London, UK: National Institute for Health and Care Excellence; 2017. Available from: https://www.nice.org.uk/guidance/ta477. [Last accessed on 2020 Jul 13].
3. Chu CR, Rodeo S, Bhutani N, Goodrich LR, Huard J, Irrgang J, *et al*. Optimizing clinical use of biologics in orthopaedic surgery: Consensus recommendations from the 2018 AAOS/NIH U-13 Conference. J Am Acad Orthop Surg 2019;27:e50-63.
4. Miller MD. OrthoBiologics: Science or snake Oil? Clin Sports Med 2019;38:xi-ii.
5. Piuzzi NS, Khlopas A, Newman JM, Ng M, Roche M, Husni ME, *et al*. Bone marrow cellular therapies: Novel therapy for knee osteoarthritis. J Knee Surg 2018;31:22-6.
6. Piuzzi NS, Dominici M, Long M, Pascual-Garrido C, Rodeo S, Huard J, *et al*. Proceedings of the signature series symposium "cellular therapies for orthopaedics and musculoskeletal disease proven and unproven therapies–promise, facts and fantasy," International society for cellular therapies, Montreal, Canada, May 2, 2018. Cytotherapy 2018;20:1381-400.
7. Piuzzi NS, Ng M, Chughtai M, Khlopas A, Ng K, Mont MA, *et al*. The Stem-cell market for the treatment of knee osteoarthritis: A patient perspective. J Knee Surg 2018;31:551-6.
8. Ramkumar PN, Navarro SM, Haeberle HS, Chughtai M, Demetriades C, Piuzzi NS, *et al*. Cellular therapy injections in today's orthopedic market: A social media analysis. Cytotherapy 2017;19:1392-9.
9. Patel S, Jindal K, Dhillon MS. The future of injectable orthobiologic substances for knee osteoarthritis: Options beyond platele-trich plasma. J Musculoskelet Surg Res 2020;4:173-81.
10. Sahoo PK, Ujade NA, Das SP. Effectiveness of single injection of platelet-rich plasma over corticosteroid in the treatment of plantar fasciitis – A randomized, comparative study. J Musculoskelet Surg Res 2020;4:187-93.

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