Systematic Review

The Clinical Evidence Behind Biologic Therapies Promoted at Annual Orthopaedic Meetings: A Systematic Review

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Purpose: The purpose of this study is to systematically evaluate the available clinical data for biologic therapies promoted for articular cartilage defects and osteoarthritis of the knee at the 2016 American Orthopaedic Society for Sports Medicine Meeting (AOSSM) and the 2017 Arthroscopy Association of North America meeting (AANA). **Methods:** Our sample included all exhibitors at the 2016 AOSSM meeting and 2017 AANA meeting. All biologic products marketed at each conference were identified by reviewing exhibition booths and company websites. A systematic review of the clinical data on each product was then completed using PubMed, EMBASE, and the product's own webpage. All clinical peer-reviewed studies with level I-IV evidence were included in the study. Basic science or preclinical studies were excluded. **Results:** There were 16 products promoted for biologic therapy for articular cartilage defects or osteoarthritis of the knee at the AOSSM meeting and 11 products promoted at the AANA meeting. A total of 280 articles detailed clinical findings for the articular cartilage products displayed at AOSSM and AANA. Of the 280, there were 36 level I evidence studies, 37 level II evidence studies, 18 level III evidence studies, and 189 level IV evidence studies. Of these articles, 91% were for 4 products. Of all biologic products promoted at the 2 meetings, 65% did not have any peer-reviewed clinical data supporting their use. **Conclusion:** Overall, many biologic therapies promoted at leading arthroscopy and sports medicine conferences did not have clinical evidence evaluating their use in the peer-reviewed literature. Although scientific advancement requires new technology, orthopaedic surgeons should be cautious about using biologic therapies in their practice with no proven efficacy. There are likely promising new interventions that, with additional scientific research, will be proven efficacious for our patients. **Clinical Relevance:** This article gives orthopaedic surgeons a detailed example of some of the biologic treatments being offered on the market for the treatment of knee articular cartilage disease. When patients request these treatments, physicians must be able to explain the data supporting their use.

Biologic therapies may very well be the future of sports medicine because basic science studies are discovering new signaling pathways and cell lineages that could result in tissue repair and regeneration.[1] In recent years, biologic therapies ("biologics") have increasingly garnered media attention.[1] As a result of greater exposure, many patients are asking physicians for stem cell or other biologic treatments.[1] Biologics such as mesenchymal stem cell therapy (MSC) could have the potential to modify and perhaps even inhibit the natural progression of osteoarthritis (OA).[2] Animal studies evaluating the use of cellular therapies, cytokines, and in vitro tissue–engineered implants have been promising, demonstrating safety.[1] In fact, animal studies have shown that MSCs can regenerate a full-thickness lesion with high histologic correlation scores to the neighboring cartilage.[3] However, preclinical studies may not correlate with human outcomes, prompting the need for high-level human clinical trials to demonstrate efficacy and disease modification.

Studies have shown companies spend billions of dollars on direct-to-physician advertisements (DTPA) and direct-to-consumer advertisements (DTCA).[4] However, these advertisement strategies may involve

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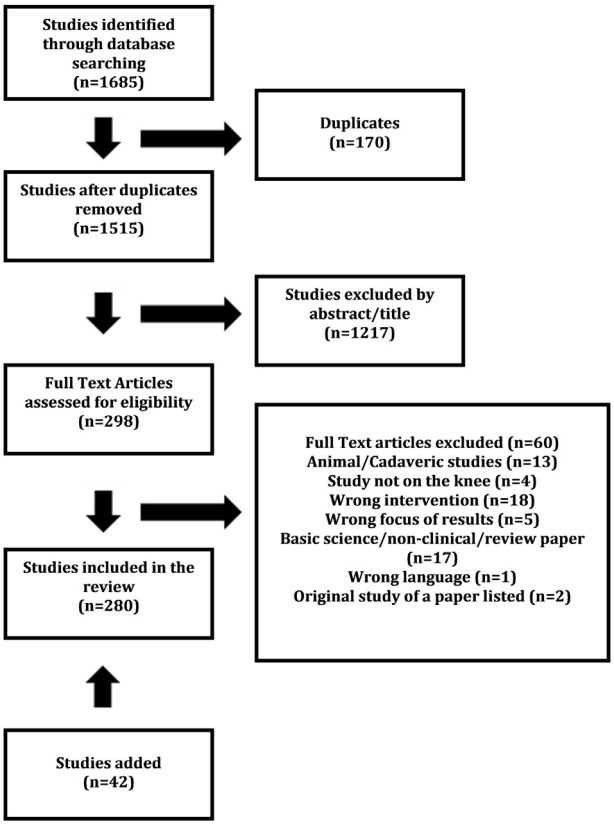

Fig 1. PRISMA (preferred reporting items for systematic reviews and meta-analyses) chart outlining the review of articles from the search.

exaggeration of claims along with admission of some adverse effects.[4] It was reported in multiple studies that during DTPA events, 15% to 65% of the promotional literature was contradictory to the scientific data in published literature at the time.[4] In addition, in a review of advertised products in peer-reviewed orthopaedic journals, it was found that only 12 of 50 products had high-quality evidence to back their claims.[5] Many of these potential treatments do not have clinical data. For physicians to practice evidence-based medicine, further supporting data for many of these therapies is necessary.

Although the Food and Drug Administration (FDA) typically ensures product efficacy and safety before reaching the market, there are certain loopholes that allow some biologics to be approved for the market without the rigors of the general FDA process. A device that manipulates a patient's own tissue, such as mini-centrifuges for the creation of platelet-rich plasma (PRP), can enter directly to the market, without approval from the FDA, on a 510 (k) exemption because the device is similar to previous devices that have obtained full FDA acceptance.[6] Similarly, biologic products can obtain a similar exemption through a 361 form.[7]

The American Orthopaedic Society for Sports Medicine (AOSSM) and the Arthroscopy Association of North America (AANA) Annual Meetings are some of the premier orthopaedic sports medicine conferences. At the 2016 AOSSM meeting, there were 1200 attendees, with 70% of them being orthopaedic surgeons. At the 2017 AANA meeting, there were 800 attendees, with 98% of them being orthopaedic surgeons. This offers the potential opportunity for marketing to a high volume of orthopaedic surgeons using new biologic treatments for their patients.

The purpose of this study is to systematically evaluate the available clinical data for biologic therapies promoted for articular cartilage defects and osteoarthritis of the knee at the 2016 American Orthopaedic Society for Sports Medicine Meeting (AOSSM) and the 2017 Arthroscopy Association of North America meeting (AANA). We hypothesize that many new products promoted on the market do not have the peer-reviewed clinical data to support their claims.

Material and Methods

Our sample included all exhibitors at the 2016 AOSSM meeting in Colorado Springs, CO, and the 2017 AANA meeting in Denver, CO. Biologics were defined as cellular products aimed to alter disease progression. Biologic products were identified at the conference, with 2 independent attending orthopaedic surgeons (J.P.S. and K.B.F.) reviewing all the exhibition booths and obtaining their promotion catalogs. Afterward, the meeting brochure was examined, and each exhibit was analyzed for possible biologic products through their website and their promotional material at the meeting.

The clinical evidence for injections for each product identified was evaluated through an evidence based systematic review of the literature. The last search was completed on August 15, 2017. The literature search was completed using PubMed (MEDLINE) and EMBASE. The search was completed using a complex search build targeting "osteoarthritis," "knee," "clinical studies," and "chondral." The search resulted in 1482 articles after duplicates were removed (Fig 1). The title and abstract were screened for inclusion criteria, followed by full text manuscript screening. The screening was completed by 2 independent reviewers (W.J.S. and C.J.H.). If there was an article detailing follow-up data on a previously published cohort, only the most recent article was included in the study. In addition, the individual product websites were also reviewed for any clinical data. All studies were assigned a level of evidence using the evidence grading tool developed by the Centre for Evidence-Based Medicine in Oxford, United Kingdom.[8] Furthermore, the reference section of each included study was reviewed for further inclusion.

Table 1. Biologic Products Marketed at 2016 AOSSM Annual Meeting

Product	Company	Type of Product	Description	In House Data
Chondrofix	Zimmer Biomet	Intraoperative treatment	Osteochondral allograft composed of donated human decellularized hyaline cartilage and cancellous bone[9]	0
DeNovo NT Natural Tissue Graft		Intraoperative treatment	Juvenile cartilage implant for repair of articular cartilage damage	1
GPS III Platelet Concentration System		Biologic device	Prepares PRP	
OATS instrumentation set	Arthrex	Biologic device	Used for OATS[10]	0
Cartiform		Intraoperative treatment	Osteochondral allograft composed of viable chondrocytes, chondrogenic growth factors, and extracellular matrix proteins[11]	0
ACP Double Syringe System		Biologic device	Prepares PRP[12]	0
ProChondrix	Allosource	Intraoperative treatment	Cartilage restoration matrix that contains growth factors and viable chondrocytes[13]	1
FloGraft (amniotic fluid allograft)	Applied Biologics	Injection	A cryopreserved, injectable, amniotic fluid −derived allograft[14]	0
LIPOGEMS	Lipogems	Biologic device	A single-use kit designed to obtain a micro-fractured nonexpanded adipose tissue intended for autologous use[15]	0 +3 Peer-reviewed basic science article
OrthoFlo	MiMedx Group	Injection	An amniotic fluid−derived allograft that helps to cushion, lubricate and protect the joint[16]	0 + 2 Peer-reviewed basic science article
Affinity	NuTech	Healing adjunct	A fresh amniotic membrane product that has regenerative and angiogenic properties[17]	1 + 1 Peer-reviewed basic science article
NuCel		Injection	Allograft derived from human amnion and amniotic fluid that promotes tissue growth, repair, and healing[18]	0
Carticel	Vericel	Intraoperative treatment	Autologous cultured chondrocytes that are multiplied and reimplanted into the knee cartilage in a procedure called ACI[19]	0
Matrix-induced Autologous Chondrocyte Implantation		Intraoperative treatment	An implant with autologous chondrocytes on bio-resorbable type I/III collagen membrane[20]	0
CartiONE	Orteq Sports Medicine	Intraoperative treatment	Freshly isolated chondrocytes enhanced with bone marrow cells in one surgery[21]	1
Fresh osteochondral allograft	JRF Ortho	Intraoperative treatment	Viable chondrocytes and subchondral bone together[22]	0

Inclusion/Exclusion Criteria

All articles included were for a treatment presented at AOSSM 2016 Annual Meeting or AANA 2017 Annual Meeting for osteochondral defects or OA for the knee. Only treatments specifically for knee OA or knee osteochondral lesions were included, and treatments for OA of other joints were excluded. All articles in English, including translated articles, were included. However, only clinical peer-reviewed studies from the database search were included, so any studies done on animals, cadavers, or basic science articles were excluded from this study. Only articles with a level of evidence of I to IV were included. Any articles from the product website were also tallied, but any unpublished data were noted. In-house research was labeled as such and recorded in a separate section. Preferred Reporting Items for Systematic Reviews and Meta-Analyses criteria were followed throughout the systematic review.

Results

At AOSSM, of 75 total exhibitors, there were 10 companies (10/75; 13%) with products that met the inclusion criteria (Table 1). A total of 16 products were identified. Of these available products, 8 of the treatments were intraoperative treatments, 3 were injections, 4 were biologic devices used to prepare a biologic treatment, and 1 was an adjunct to healing (Table 1). At AANA, of 54 total exhibitors, 7 companies (7/54; 13%) had products that met the inclusion criteria (Table 2). A total of 11 products, 4 intraoperative treatments, 2 injections, 2 biologic devices, and 3 were an adjunct to healing. Four advertised products overlapped between the 2 meetings.

There were a total of 280 articles that detailed clinical findings for the biologic products displayed. Of the 280 studies, there were 23 level I studies, 16 level II studies, 12 level III studies, 76 level IV studies, and 153 studies that did not specify their level of evidence. Based on our

Table 2. Biologic Products Marketed at 2017 AANA Annual Meeting

Product	Company	Type of Product	Description	In House Data
Novocart 3d	Aesculap USA	Intraoperative treatment	Biologic-device combination product for repair or articular cartilage of femoral condyle and trochlear groove.[23]	0
NeoCart	Histogenics	Intraoperative treatment	Cartilage tissue implant made from patient's own cells to treat certain knee cartilage injuries.[24]	0 + 3 Peer-reviewed basic science article
Lipogems	Lipogems	Biologic device	A single-use medical device for the processing of lipoaspirated adipose tissue.[15]	0 +3 Peer-reviewed basic science article
AmnioFix	MiMedx Group	Healing adjunct	Composite amniotic tissue membrane minimally manipulated to protect the collagen matrix and its natural properties.[25]	1 + 3 Peer reviewed basic science article
EpiFix		Healing adjunct	Dehydrated human amnion/ chorion membrane allograft that is composed of a single layer of epithelial cells, a basement membrane and an avascular connective tissue matrix.[26]	0 + 2 Peer-reviewed basic science article
OrthoFlo		Injection	An amniotic fluid derived allograft which helps to cushion, lubricate and protect the joint.[16]	1 + 2 Peer-reviewed basic science article
Affinity	NuTech	Healing adjunct	A fresh amniotic membrane product that has regenerative and angiogenic properties.[17]	1 + 1 Peer reviewed basic science article
NuShield		Intraoperative treatment	Biologic that preserves the native structure or the amnion and chorion membranes.[27]	0
ReNu		Injection	Multiple anti-inflammatory and other healing factors found in human amniotic tissues.[28]	1 + 2 Peer reviewed basic science article
Marrow Cellution Aspiration Device	Regenacell Therapy, Inc	Biologic device	Bone marrow system and stem cell harvesting system.[29]	1 + 3 Peer reviewed basic science article
Matrix-induced Autologous Chondrocyte Implantation	Vericel	Intraoperative treatment	An implant with autologous chondrocytes on bio-resorbable type I/III collagen membrane[20]	0

classification, the level of evidence did differ; because there were a total of 36 level I evidence studies, 37 level II evidence studies, 18 level III evidence studies, and 189 level IV evidence studies (Table 3). This difference is largely accounted for by classifying the 153 studies that did not define a level of evidence. Of the 280 studies, 90 studies disclosed a potential conflict of interest, 94 studies did not list a conflict of interest/ disclosure within their article, and 96 studies had no conflicts of interest declared by the authors (Table 4).

PRP had the most clinical articles on efficacy, with 19 level I articles. Autologous chondrocyte implantation (ACI) had 11 level I published articles, and matrix-induced autologous chondrocyte implantation (MACI) had 5 level I articles. Lastly, osteochondral autograft transfer system (OATS) had 1 level 1 article. No other treatment modalities had any level I evidence articles detailing clinical results. Fresh osteochondral allografts had 41 level IV evidence studies and 1 level III study. Stored osteochondral allografts had 2 level IV evidence studies.

Autologous chondrocyte implantation had the highest number of articles, with 99 total clinical studies. PRP had 48 total articles, and MACI had 44 total articles. The osteochondral autograft transfer system procedure had 20 total articles. Chondrofi Zimmer (Zimmer Biomet, Warsaw, IN) and DeNovo NT Graft (Zimmer Biomet) each had one level IV evidence article. Cartiform (Arthrex Inc., Naples, FL), ProChondrix (AlloSource, Centennial, CO), FloGraft (Applied Biologics, Scottsdale, AZ), Lipogems (Lipogems International, Milano, Italy) , OrthoFlo (MiMedx, Marietta, GA), Affinity (NuTech, Birmingham, AL), NuCel (NuTech) , CartiONE (Cartilage Repair Systems, New York, NY), Novocart 3D (Aesculap Biologics, Breinigsville, PA), AmnioFix (MiMedx), NeoCart (Histogenics, Waltham, MA), EpiFix (MiMedx), NuShield (NuTech), ReNu (NuTech), and the Marrow Cellution Aspiration Device (Ranfac Corp., Avon, MA) did not have any clinical articles. Juvenile cartilage implant allograft as prepared by DeNovo NT Graft had 1 level IV article that showed improvement in clinical symptoms, as well as filling of cartilage defects on MRI at 2 years' follow-up.[30]

ProChondrix and CartiONE had in-house data presented in their brochure.[13,21] In addition, Lipogems, OrthoFlo, and Affinity had peer-reviewed basic science articles cited on the product website but no human clinical trials.[15-17] ProChondrix had in-house data showing that ProChondrix stimulates new hyaline cartilage growth through cell migration and proliferation while providing the viable chondrocytes, growth factors, and extracellular matrix to support this growth.[13] Lipogems claims their new technique can simplify the process of extracting adipose-derived mesenchymal stem cells, and Lipogems has shown positive results in other fields of medicine.[31] Affinity

Table 3. Published Literature for Each Treatment Modality and Level of Evidence for Clinical Data

Treatment Modality	Level of Evidence				
	I	II	III	IV	Total
ACI	11	15	4	74	104
PRP	19	12	5	23	59
MACI	5	8	7	29	49
Fresh osteochondral allograft	0	0	1	41	42
Stored osteochondral allograft	0	0	0	2	2
OATS	1	2	1	18	22
DeNovo NT graft	0	0	0	1	1
Chondrofix	0	0	0	1	1
Cartiform	0	0	0	0	0
FloGraft	0	0	0	0	0
LIPOGEMS	0	0	0	0	0
OrthoFlo	0	0	0	0	0
Affinity	0	0	0	0	0
NuCel	0	0	0	0	0
ProChondrix	0	0	0	0	0
CartiONE	0	0	0	0	0
Novocart 3D	0	0	0	0	0
NeoCart	0	0	0	0	0
AmnioFix	0	0	0	0	0
EpiFix	0	0	0	0	0
NuShield	0	0	0	0	0
ReNu	0	0	0	0	0
MarrowCellution Aspiration Device	0	0	0	0	0
Total	36	37	18	189	280

has been shown by in-house data to retain native amniotic membrane's biophysical properties.[17] CartiONE states that their 1 procedure combination of bone marrow and cartilage taken from debridement and non-weight-bearing regions of the knee results in synergy that allows for the regeneration of cartilage.[21] AmnioFix has some basic science articles and claims to reduce scar tissue formation and enhance healing.[25] EpiFix is a dehydrated human amnion/chorion membrane allograft to help healing.[26]

Discussion

Our study confirmed the hypothesis that many new products promoted on the market do not have the peer-reviewed clinical data to support their claims, because 65% (15/23) of the biologic treatments promoted at the AOSSM 2016 and AANA 2017 meetings had no peer-reviewed publications directly supporting their use. Biologics have had a significant impact on the practice of orthopaedics, especially sports medicine. Biologic treatments have shown some application in a wide range of injuries from enhancing fracture healing to regenerating cartilage. Mesenchymal stem cells have been investigated for treatment of tendinopathy, ligament injury, rotator cuff tears, and articular cartilage defects.[32] In addition, growth factors are currently being used to modify how certain cells proliferate, migrate, and differentiate, in addition to promoting angiogenesis in certain regions of the body.[32] These growth factors, such as those found in PRP, are used to enhance musculoskeletal tissue healing. Lastly, both MSC and PRP are helpful in the treatment of tendinopathy because of their ability to inhibit inflammation.[32] With the wide use of biologics and the increased amount of new biologic treatments hitting the market, a thorough review of the evidence supporting their use is mandatory.

There were 6 intraoperative treatments (Cartiform, Novocart 3D , NeoCart, NuShield, ProChondrix, CartiONE), 4 injection treatments (FloGraft, OrthoFlo, ReNu, NuCel), 2 biologic devices (Marrow Cellution Aspiration Device, Lipogems), and 3 adjuncts to healing (EpiFix, AmnioFix, Affinity) that did not have any clinical articles supporting their efficacy. Although Cartiform is listed as an osteochondral allograft, it is not the same as fresh osteochondral allografts. These manufactured products have no clinical data to support that they have the same benefits and safety as fresh osteochondral allografts. In addition, Lipogems injects a solution of adipose tissue, citing evidence that adipose-derived stem cells help with OA, but their product is not the same concentrated stem cell dose as those being evaluated in the clinical trials. The same can be said for amniotic fluid products; although amniotic stem cells are in clinical trials for treatment of OA, amniotic fluid itself has no literature to support its use in the treatment of knee OA.

Biologics are regulated by the FDA as a part of the US Department of Health and Human Services, which was created to ensure public health through monitoring the safety and efficacy of drugs and devices.[33] Although the normal process through the FDA is lengthy and expensive, biologics are able to skip the process by using

Table 4. Summary of the Conflicts of Interest Disclosed in the Included Studies

Conflict of Interest	Number of Studies
Conflicts of interest not listed/disclosed	94
No conflicts of interest reported	97
Studies disclosing a potential conflict of interest (many studies reported more than one conflict)	89
Funding from a foundation/institution grant	31
Consulting fees/royalties from a private entity	23
Received support from/sponsored by Genzyme (now Sanofi Biosurgery)	17
Shareholder in a potential conflicting company	12
Funding from a private entity	11
Employee of potential conflicting company	10
Funding from National Institutes of Health	10
One or more of the authors received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article.	9
One or more authors received institutional support from a private entity	4
Advisory board membership	1

the 361 exemption or the 510(k) exemption for biologic devices.[6,7,34] Although these exemptions usually result in off-label use of the products, the FDA does allow off-label use as long as the clinician is well informed about the product, bases use on medical and scientific evidence, and maintains record of the product's use and effects.[34] In addition, for the 361 exemption, the product must be minimally manipulated, intended for homologous use, not combined with another agent, have no systemic or metabolic effect before autologous use, is for allogeneic use in first- or second- degree blood relative, or reproductive use.[7] Lastly, the 510(k) application is only for devices that are "substantially equivalent" to devices that were marketed before 1976 to bypass normal FDA approval.[6,34]

There have been many studies done on the expensive approval process of the FDA, and 5 studies have shown that the cost of 1 approved drug ranges from 868 million dollars to 1241 million dollars.[35] Given these extreme costs, it is difficult for many drug companies to raise the necessary funding to go through the formal FDA approval process.

Patients themselves are anxiously seeking out biologic alternatives for treatment of their disease. Although this usually is a benefit to the patient and physician in making an informed decision, there are certain instances where this can be detrimental. When new, novel treatments arise, it is often difficult for patients to get the necessary, thorough information. Such is the case with these new treatments for early articular disease, OA, or osteochondral defects. Although doctors have always been targeted by pharmaceutical and device manufacturers, there has been a recent shift toward DTCA.[36] Whereas proponents for DTCA state it increases patient education, critics claim it leads to increased health care costs due to patients demanding newer interventions that typically have higher profit margins without proven efficacy.[36]

To ensure public health, the FDA was created to monitor the safety and efficacy of drugs and devices.[33] Therefore, when patients hear a new product has FDA approval, it may seem like a stamp of approval meaning the product is safe and effective. However, of all the products listed in Table 1, Carticel (ACI) is the only one that has full FDA approval.[19] Furthermore, the FDA just recently accepted MACI's Biologics License Application after years in a Superiority of MACI Implant to Microfracture Treatment prospective, multicenter, randomized, clinical trial.[37] All the remaining products listed in Table 1 have FDA approval through the 501(k) or 361 applications.

Osteochondral allografts are also considered minimally manipulated, which means it satisfies FDA exemption.[38] Giannini et al.[39] showed full integration of the allograft at 48 months with good clinical outcomes.[40] Gracitelli et al.[41] stated that osteochondral allografts were a successful salvage treatment for failed cartilage repair procedures despite a high reoperation rate. There is little data available on stored osteochondral allografts, but Davidson et al.[42] demonstrated that grafts stored in cell culture medium at 4°C for 4 to 6 weeks still provides good clinical outcomes. It is hoped there will be more data on this treatment in the future.

ACI is the only product to have FDA approval through proof of concept. Because ACI is not considered minimal manipulation, it could not get FDA approval through the 361 exemption. The literature has many studies detailing the safety and efficacy of treatment with ACI.[42-48] Saris et al.[49] showed in a randomized controlled trial that ACI was significantly better than microfracture at 36 months. However, just because ACI has FDA approval, this does not mean the data unanimously support its use. Knutsen et al.[45] showed at long-term follow-up (14-15 years) that there were no statistically significant differences between ACI and microfracture, even though both groups improved overall. Dozin et al.[43] found in a multicenter randomized trial that ACI and mosaicplasty had the same clinical outcomes. However, the study had inadequate power to draw any conclusions.[43] Although it is important to note the literature is mixed on the benefit of ACI, there are a large number of well-designed studies for surgeons to review and form an opinion.

PRP is an example of a product that uses the 510 (k) loophole that still has a multitude of clinical trials to show it is both safe and effective. PRP has studies detailing everything from uses in preventing blood loss to uses in prevention of OA.[49,50] Cerza et al.[51] stated in their randomized controlled trial that PRP sustained significantly better clinical outcomes when compared with hyaluronic acid. As with ACI, there are mixed results in the literature. Filardo et al.[52] showed that PRP did not show significant improvement when compared with hyaluronic acid. However, again, the large amount of well-designed studies conducted to assess PRP's efficacy allows patients and medical professionals to make informed decisions on its use.

Although PRP did use the 510(k) exemption, FDA trials are being conducted to obtain full FDA approval.[52] Smith[53] published an FDA-sanctioned, randomized, double-blinded, placebo-controlled clinical trial for Arthrex that showed PRP is safe and showed quantifiable improvement over placebo after 1 year.

Additionally, prior literature has challenged the claims made in DTPA advertising.[4,5] These studies support our results that the majority of these advertisements lack high-quality evidence to back their claims.[4,5] It is important to note that our study focuses specifically on biologics and not DTPA in general. Furthermore, the growth in biologics in recent years makes it essential to investigate the specific claims within this industry.

Preclinical and basic science studies were excluded from our study. We understand the importance these studies provide; however, for our article we were focused on the clinical application and results from the use of these products. The translation of basic science research into general application for widespread clinical use can be a long leap, and we did not want to mix translational basic science research with the primary purpose of our article, which was the clinical evidence on the use of the products being promoted for widespread use. More broadly, we would like to recognize that oftentimes clinical innovation comes with experimentation, and attempting new therapies (that are safe for human application) before evidence-based clinical trials demonstrating proven success has been a pathway to success in the past and should not be altogether discouraged. Having a pioneer such as Austin Moore perform one of the first hip replacements in 1940 at Columbia University goes a long way to advancing our science and many times can serve as a springboard to future innovation and clinical trials. There is clearly a role for specialists and researchers in a particular field such as sports medicine using new products. This allows for a limited launch of these products in a controlled environment to allow time for safety and efficacy to be proven through research. Likewise, basic science studies are important substrates for the development of well-done clinical trials; however, we don't believe that basic science studies (even those that are well done) in and of themselves should serve as the basis for clinical practice. We are currently entering a "new age" of biologics; as a result, there will be a lag in information regarding these products. Therefore it is essential that physicians, as well as the industry as a whole, remain vigilant and cautious as new information regarding these products becomes available. It has long been the dictum of smart orthopedists that "one does not want to be the first or the last" to use new technology. We would encourage researchers in the field to be "first," rather than promotion of widespread clinical use for unproven products.

This study has several strengths. It evaluated the clinical data available to support products marketed directly to orthopaedic sports surgeons at the AOSSM Meeting in 2016 and at the AANA Meeting in 2017. In addition, there was a comprehensive review of all data sources, including evaluation of product fliers from the AOSSM meeting and the AANA meeting, clinical data through a systematic review, and each individual product website for in-house or preclinical data.

Limitations

This study is not without limitations. First, although the AOSSM and AANA meetings are premier sports medicine meetings, they may not be representative of all the biologic products available or marketed to sports medicine surgeons. Also, there may be ongoing clinical trials that are currently not accounted for in this analysis. For example, Novocart 3D is currently in a phase III clinical trial that does not yet have published results.[54] Furthermore, it is important to recognize that some of therapies discussed in this analysis may now have clinical data supporting their use because there is a gap between the time period studied and publication. As a result, the conclusion of our article is based strictly on the results from the 2 meetings and the time period discussed. The overarching theme of our thesis, however, is still valid despite the subsequent publication of data refuting or accepting biologic therapies for clinical practice, because our analysis is concerned with the evidence behind therapies at the time of promotion at our society meetings.

Conclusion

Overall, many biologic therapies promoted at leading arthroscopy and sports medicine conferences did not have clinical evidence evaluating their use in the peer-reviewed literature. Although scientific advancement requires new technology, orthopaedic surgeons should be cautious about using biologic therapies in their practice with no proven efficacy. There are likely promising new interventions that, with additional scientific research, will be proven efficacious for our patients.

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