Orthobiologics in Pediatric Sports Medicine

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KEYWORDS

• Orthobiologics • Pediatric sports medicine • Bone grafting • Platelet-rich protein (PRP)
• Anterior cruciate ligament (ACL) • Osteochondral defect (OCD)

KEY POINTS

- Orthobiologics are biological substances that allow injured muscles, tendons, ligaments and bone to heal more quickly.Orthobiologics stimulate healing with a variety of osteoconductive, osteoinductive, and/or osteogenic properties.
- There is a paucity of literature involving pediatric patients; however, studies are underway with potentially transferrable results indicating their use in children.
- Autograft is the primary graft choice in most pediatric cases, including ligament reconstructions and osteochondral defects.
- Plasma-rich protein has shown promise in treating tendonopathies in adults and is used as an adjunct in other sports procedures. No specific pediatric studies have been conducted.
- The future of orthobiologics in pediatric sports medicine is promising, but more investigation must be done before its routine use in pediatric sports medicine.

INTRODUCTION

Orthobiologics are biological substances that allow injured muscles, tendons, ligaments, and bones to heal more quickly. These substances occur naturally in the body and, at higher concentrations, can aid in the healing process.[1] Autograft bone, allograft bone, demineralized bone matrix, autologous bone marrow aspirate, bone morphogenic protein (BMP), platelet-rich plasma (PRP), and ceramic grafts are all types of orthobiologics.[2] Over the last 2 decades, both surgeon interest and industry development have substantially increased. A PubMed search on "orthobiologics" resulted in 66 articles dating back to 2004. In 2013, the global orthobiologics market was estimated to be $3.7 billion dollars. It is expected to increase to $5.8 billion dollars by 2018.[3] Much of the market interest is distributed throughout the subspecialties in orthopedic surgery, including trauma, foot and ankle, spine, sports medicine, and pediatrics. Their use in sports medicine has exploded in efforts to increase graft incorporation, stimulate healing, and get athletes with problems such as anterior cruciate ligament (ACL) ruptures, tendinopathies, and cartilage injuries back to sport. Because of the healing and regenerative potential in pediatric patients, there is a paucity of studies involving the use of orthobiologics in children with sports injuries. Much of their use in children has involved spinal surgery, tibial pseudarthrosis, and benign bone lesions.[2,4] The purpose of this article is to review orthobiologics and their applications in pediatric sports medicine.

Disclosure Statement: D.D. Spence, receives publishing royalties, financial or material from Elsevier.
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Orthop Clin N Am ■ (2017) ■–■
http://dx.doi.org/10.1016/j.ocl.2017.03.006

PROPERTIES OF ORTHOBIOLOGICS

Three fundamental principles frequently are cited in describing the biology of bone grafting. All options provide unique combinations of osteoconductive, osteoinductive, and osteogenic properties (Table 1).[2,5–8]

Osteoconduction is the passive process by which a scaffold or trellis is implanted, allowing ingrowth of host capillaries, perivascular tissue, and mesenchymal stem cells (MSCs) to support ingrowth of new bone.[7,8] These osteoconductive scaffolds have structures similar to cancellous bone.[7,9] Bone autograft and allograft, demineralized bone matrix, calcium sulfate, and calcium phosphate are primary examples of osteoconductive grafts.

Osteoinduction is the process by which substances within the graft recruit pluripotent MSCs, which differentiate into osteoblasts and chondroblasts to form new bone through endosteal ossification.[5,7,8] Growth factors such as BMP, platelet-derived growth factor, interleukins, fibroblast growth factor, and vascular endothelial growth factor play a role in mediating this process. Examples of orthobiologics with osteoinductive properties include bone autograft, BMP, bone marrow aspirate, and PRP.

Osteogenesis is the synthesis of new bone from graft containing viable donor osteoblasts or their precursors. This process then promotes primary bone formation in the proper environment using MSCs, osteoblasts, and osteocytes. Fresh autologous grafts and bone marrow aspirate are orthobiologics with osteogenic properties.[5,7,8]

AUTOGRAFTS

Autologous grafting is the process by which bone and tissue are harvested from 1 site on the host and transplanted to another site in the same patient. It confers osteoconductive, osteoinductive, and osteogenic properties and is completely histocompatible. For these reasons, it is considered the "gold standard" to which all other orthobiologics are compared.[7] Autologous grafts, however, do have limitations. Donor site pain, increased blood loss, increased operative time, and the potential for donor site infection are all drawbacks. Furthermore, there is a limited supply from the host, particularly in pediatric patients.[2,7] Autologous grafts can be cortical, cancellous, or osteochondral, and include soft tissue components. Each graft varies in their biologic properties and rates and methods of incorporation. This is the predominant graft choice for most pediatric patients undergoing sports related procedures (Fig. 1).

ALLOGRAFTS

Allograft is a graft that is harvested from human cadavers, sterilely processed, and transplanted to a recipient. It can be cortical, cancellous, osteochondral, or formed into a highly processed derivative, such as demineralized bone matrix.[7] It is primarily osteoconductive, but, depending on the processing, may retain some osteoinductive properties. To prepare allograft, the soft tissues and cells are removed with ethanol and the graft is gamma irradiated for sterilization. This sterilization process adversely effects the biologic properties of the graft and

Table 1
Types of orthobiologics and their unique combinations of osteoconductive, osteoinductive, and osteogenic properties

	Osteoconductive	Osteoinductive	Osteogenic
Cortical autograft	+	+	+
Cancellous autograft	+++	+++	+++
Cortical allograft	+	+/–	–
Cancellous allograft	+	+/–	–
Demineralized bone matrix	+	++	–
Bone marrow aspirate	–	++	+++
Bone morphogenic protein	–	+	+
Plasma rich protein	–	+++	+
Ceramics	+	–	–

+, activity; –, no activity; +/–, activity depends on the preparation process.