Viscosupplementation in knee osteoarthritis

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Summary

Osteoarthritis of the knee is a frequently disabling disease, the incidence and severity of which increase with age, knee injury with or without surgical repair, and repetitive occupational trauma, as well as in women who are overweight.

The pathological changes in Osteoarthritis cartilage appear to be mediated by complex interactions between mechanical and biological factors including excessive enzymatic degradation, decreased synthesis of cartilage matrix, increased levels of cytokines and other inflammatory molecules, and dysregulation of Osteoarthritis chondrocytes. The net result includes disorganization of the cartilage matrix and fibrillation. As the disease advances, disorganization gives way to fissures, erosion, ulceration, and eventually cartilage is irreversibly destroyed. As the cartilage degenerates, joint stresses are increasingly transmitted to the underlying bone, initiating the bony remodeling process, which results in marginal osteophytes, subchondral sclerosis, and cysts.

The classic treatments which have been utilized for many years include the non-pharmacological treatments, the classic NSAIDs, corticosteroids injections and also joint lavage.

The more modern treatments consist particularly of Glucosamine, the new selective cycloxegenase-II (COX-II) inhibitors and the viscosupplementation.

With increased understanding of the pathogenesis of osteoarthritis, new therapies are being developed, one of which is viscosupplementation with hyaluronic acid.

Viscosupplementation came into clinical use in Japan and Italy in 1987, in Canada in 1992, in Europe in 1995, and in the United States in 1997

Hyaluronic acid has both viscous and elastic properties, and the degree to which either predominates depends on the amount of shear force applied.

Hyaluronic acid preparations differ with respect to origin, method of production, treatment schedule, molecular weight, half-life within the synovium, pharmacodynamics, and cost.

To increase the molecular weight of the viscosupplement, a process of cross-linking hyaluronan

molecules by means of terminal hydroxyl groups has been developed. These polymers are referred to as Hylans.

Although the predominant mechanism of HA is unknown, in vivo, in vitro, and clinical studies demonstrate various physiological effects of exogenous HA.

Many effects of exogenous HA on the extracellular matrix, inflammatory mediators, and immune cells have been reported in *in vitro* studies. The influence of HA on these factors may contribute to cartilage protection in OA.

Hyaluronic acid possesses a number of protective physiochemical functions that may provide some additional chondroprotective effects *in vivo* and may explain its longer term effects on articular cartilage.

Hyaluronic acid can reduce nerve impulses and nerve sensitivity associated with pain. In experimental osteoarthritis, this glycosaminoglycan has protective effects on cartilage; exogenous hyaluronic acid is known to be incorporated into cartilage.

Several studies done for assessment of efficacy of Hyaluronic Acid products injection in Knee OA

Some authors found greater effect of different hyaluronic acid products over placebo in treatment of knee

OA. Others found no significant effect of hyaluronic acid products. However, almost all authors agreed that IAHA use for knee OA has no or minimal adverse effect.

Conclusion

The efficacy of intraarticular hyaluronic acid in the treatment of Osteoarthritis remains controversial.

Additional well designed randomized controlled trials with high methodological quality are needed to resolve the continued uncertainty about the therapeutic effects of different types of hyaluronic acid products on osteoarthritis of the knee in various clinical situations and patient populations.

According to RACGP There is some evidence to suggest hyaluronic acid is of some benefit for OA of the knee.

The AAOS cannot make a recommendation for or against the use of intraarticular hyaluronic acid for patients with mild to moderate symptomatic OA of the knee.

While according to (NICE) guidelines Intra-articular hyaluronan injections are **not** recommended for the treatment of osteoarthritis.

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List of abbreviations

1. AAOS: American Academy of Orthopaedic Surgeons.
2. ACR :American College of Rheumatology.
3. AHRQ:Agency for Healthcare Research and Quality .
4. ANA: Anti nucleic acid test.
5. AST: aspartate aminotransferase test.
6. ASU :Avocado soybean unsponifiables
7. COX-II:cycloxegenase-II
8. CS:Chondroitin sulphate
9. CV:cardiovascular
10. D:Dalton
11. ECM : extracellular matrix
12. ESR : Erythrocyte sedimentation rate .
13. FDA:Food and Drug Administration
14. GAG :glycosaminoglycan .
15. GI :Gastrointestinal .
16. GPs: General Practitioners
17. HA :hyaluronic acid .
18. HMW:High Molecular weight
19. IA:Intra-articular.
20. IAHA :Intra-articular hyaluronic acid.
21. IL:inter leukin
22. KD: Kilo-Dalton
23. LMW:Low Molecular weight
24. MMP: matrix metalloproteinases.
25. MW: Molecular weight.
26. NICE: National Institute of Health and Clinical Excellence.
27. NO :Nitric oxide

28. NSAID: Non steroidal anti –inflammatory drugs .
29. OA: Osteoarthritis.
30. OARSI :OA Research Society International.
31. PG: proteoglycan
32. PGE2:prostaglandin E2
33. PMN:polymorphonuclear
34. PPI :proton pump inhibitor .
35. PRO: Patient-Reported Outcome
36. RA:Rheumatoid arthritis
37. RACGP:The Royal Australian College of General Practitioners .
38. RF: Rheumatoid Factor .
39. SMEP:Self management education programs .
40. Stz: superficial tangential zone.
41. TIMP :tissue inhibitor of metalloproteinases
42. TNF-α : tumor necrosis factor alpha.
43. VAS :Visual analogue scale
44. WOMAC :The Western Ontario and McMaster

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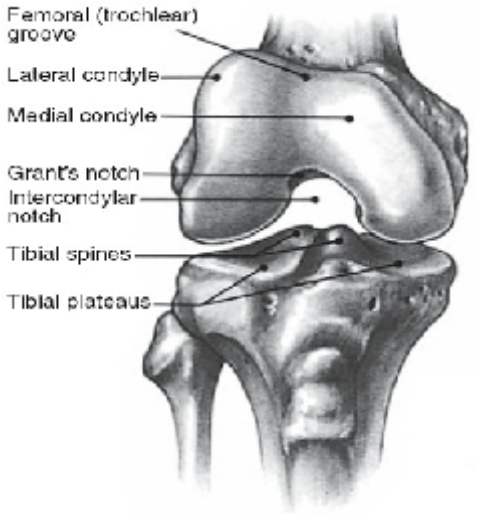
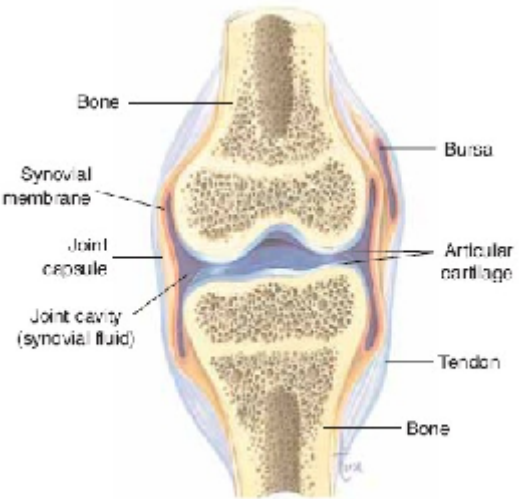
Articular surface of knee joint

The knee joint is a modified hinge of synovial joint, the largest in the body. [1] (Figure1, 2)



Figure(1) :Anatomy of knee joint[2]



Figure(2):Structure of synovial joint.[3]

The knee joint is a synovial joint so it shows the structure of typical synovial joint; on the joint surface of each bone is the articular cartilage, which provides a smooth surface. The joint capsule, made of fibrous connective tissue, encloses the joint in a strong sheath, like a sleeve. Lining the joint capsule is the synovial membrane, which secretes synovial fluid into the joint cavity. Synovial

fluid is thick and slippery and prevents friction as the bones move. [1] [3]

The Articular cartilage:

Articular cartilage, the resilient load-bearing tissue that forms the articulating surfaces of diarthrodial joints, provides these surfaces with the low friction, lubrication, and wear characteristics required for repetitive gliding motion. [4] It also absorbs mechanical shock and spreads the applied load onto subchondral bone. [5]

Structure of articular cartilage:

The type of articular cartilage that covers the ends of long bones is hyaline cartilage. [6]

Articular cartilage consists primarily of a large extracellular matrix (ECM) with a sparse population of highly specialized cells (chondrocytes) distributed throughout the tissue. The primary components of the ECM are water, proteoglycans, and collagens, with other proteins and glycoproteins present in lower amounts. These all combine to provide the tissue with its unique and complex structure and mechanical properties. [5]

Chondrocytes:

The formation and maintenance of articular cartilage depends on the chondrocytes. They are derived from mesenchymal cells, which differentiate during skeletal morphogenesis and development to form chondrocytes. During skeletal growth, these cells increase the volume of ECM, and in mature tissue, where they occupy less than 10% of the total tissue volume; they are responsible for the maintenance of the ECM. [5]

Matrix Composition[5] :

Because the chondrocytes of articular cartilage occupy only a small proportion of the total volume of the tissue, its composition is determined primarily by the matrix. (Figure 3)

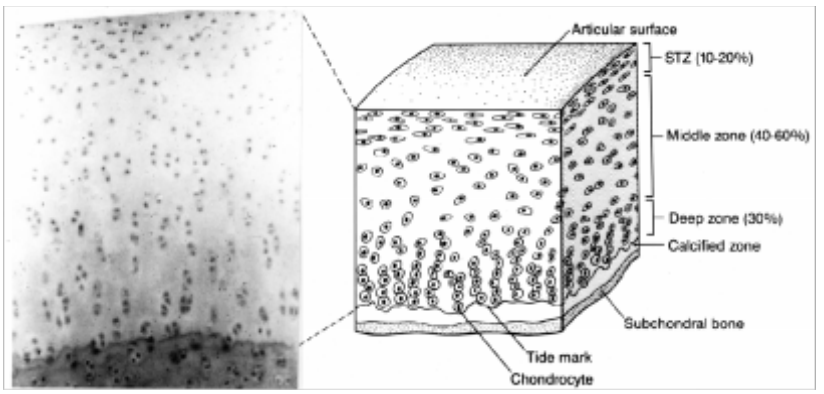


Figure 3 :Structure of normal adult articular cartilage:
Stz= superficial tangential zone [5]