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HYALURONAN GEL FOR POST TRAUMATIC OSTEOARTHRITIS

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ABSTRACT

Globally most common mucoskeletal disorder is osteoarthritis. osteoarthritis is caused by the cartilage around your joints wearing out over time around some years. It's the most common cause of arthritis also known as wear and tear arthritis. Post-traumatic osteoarthritis is a type of osteoarthritis that's caused by an injury like a bone fracture or dislocation. The damage from the injury creates arthritis quickly in the affected joint. It involves destroying of articular cartilage And reactive remodelling changes That lead to formation of osteophytes And subchondral bone cyst. The joint space is lost over time. Main Causes of post traumatic osteoarthritis include intra-articular fractures, ligamentous disruptions and dislocations, meniscal injuries, and chondral fractures. Post-traumatic arthritis, like other forms of arthritis, cannot be cured or reversed, but can be managed. The goal of treatment is to relieve symptoms and stop the condition from worsening. Viscosupplementation with intra-articular hyaluronic acid is a treatment option in knee OA that is included in the professional guidelines for treatment of this joint disease, but potentially should apply to all synovial joints in order to reduce pain and improve joint lubrication. Exogenous HA can enhance chondrocyte HA synthesis, prevent the degradation of cartilage and promote its regeneration. Moreover it can reduce the production of pro inflammatory mediators and matrix metalloproteinases involved in OA pathogenesis. it can be considered as long term therapy for post traumatic osteoarthritis.

KEYWORDS: Hyaluronic Acid, Subchondral Bone Cyst, Nanoparticles, Chondrocytes.

INTRODUCTION

Osteoarthritis is degenerative joint disease condition in which cartilage of bone which act as a cushion in the joint eventually break down over time that cause pain and stiffness in joints It's most likely to affect the Knees and Feet.

Causes

1] Age:- Osteoarthritis usually starts from the late 40s onwards. This may be due to bodily changes that come with ageing, such as weakening muscles, weight gain, and the body becoming less able to heal itself effectively.

2] Gender:- Gender is also most common factor. This disease is more severe in women than men

3] Obesity:- overweight is also cause of osteoarthritis, especially in weight bearing joints such knee and hip.

4] Joints Injury:- Joint injury can lead to osteoarthritis in future. Regular activity and exercise don't causes osteoarthritis.

5] Genetic factors:- The Gene inherited by parents have chances of getting osteoarthritis at Hand, Knee and Hip. In some case of osteoarthritis mutation can occur in single genes that affects protein called collagen. This may cause osteoarthritis in many joints.

6] Other types of Joint disease:- Two factors that can affect the symptoms of osteoarthritis such as Rheumatoid arthritis and Gout, but aren't the main cause of it.

Stages

1] Mild Osteoarthritis:- with mild knee osteoarthritis you will to have discomfort in the knee joint through the joint space appears normal the cartilage matrix has began to break down from combination of wear and Tear and increase production of degrading enzyme in addition bone spurs known as osteophytes may begin to develop on the edge of the joint. These small, smooth, dense growth of the bone are part of body's natural response to the loss of cartilage progression of diseases may be slowed at this stage by increase exercise and weight loss.

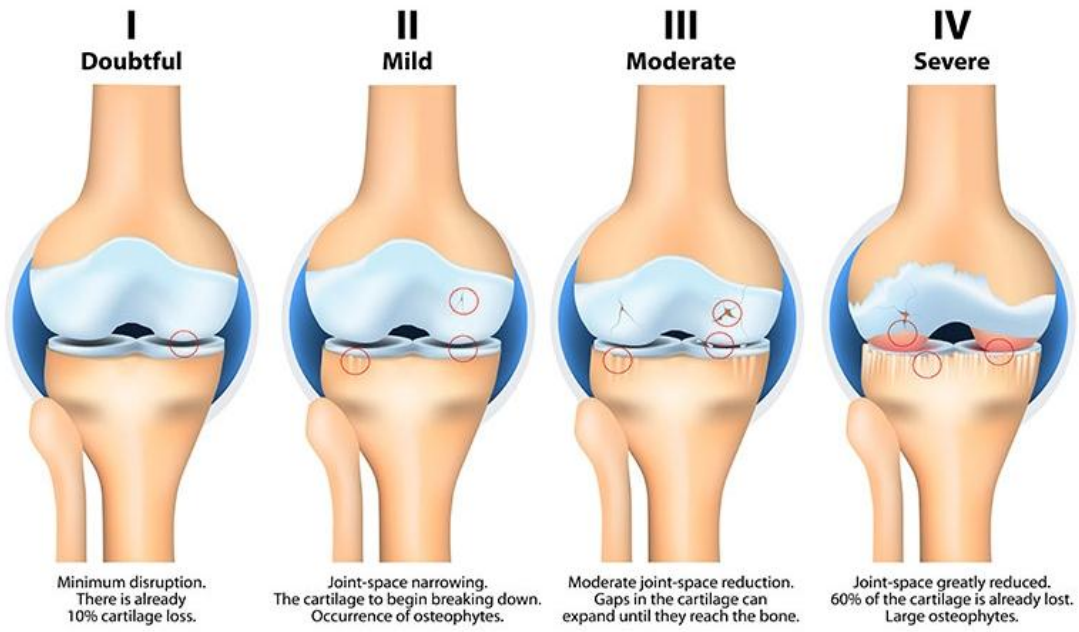


FIGURE: 1.1

2] Moderate Osteoarthritis:- With moderate Neo a changes in the joint are much more evident the cartilage surface between the bones has began to erode narrowing the gap between femur and the tibia. HA which helps synovial fluids lubricate the joint is now becoming less viscous elastic and concentrated.

a) Osteoarthritis often affects the subchondral bone located just underneath the cartilage.
b) Subchondral bone provides hydration and oxygen to the cartilage as subchondral bone flattens and tries to repair itself, Cytokines and protein are released into the synovial fluids. Osteophytes may increase in number and size making the bone rougher.

All these factors combine to make joint pain more severe and long-lasting both with movement and rest.

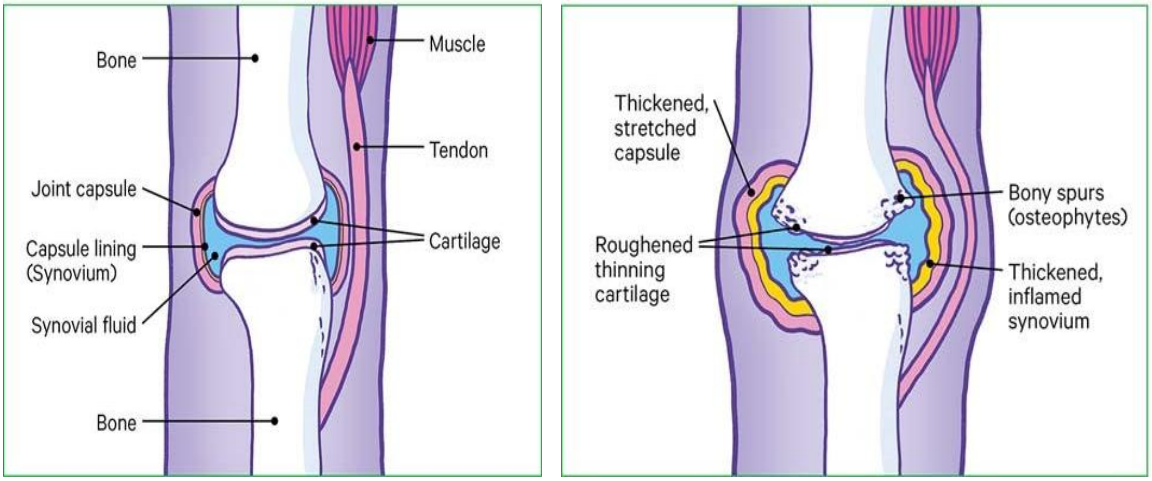
3] Severe Osteoarthritis:- With severe Osteoarthritis condition, worsened dramatically the joint space has become far narrower causing more rapid and severe destruction of the cartilage the knee becomes inflammed and sore.

Synovial fluid is increase and decrease friction and pain during movement within the synovial membrane destructive proteins are produced which further degrade cartilage and soft tissue arround the knee.

Osteophytes continued to develop bone moves against bone not cartilage, mobility, activities of the daily living and quality of life are impacted.

Pathogenesis: Pathogenesis of OA involves the Degradation of cartilage and remoulding of bone hence also called as Wear and Tear disease which occurs due to active response of chondrocytes in articular cartilage and Inflammatory cells in surrounding the tissue cells.

The release of enzymes from these cells break down collagen and proteoglycans, destroying the articular cartilage. The exposure of the underlying subchondral bone results in sclerosis, followed by reactive remodelling changes that lead to the formation of osteophytes and subchondral bone cysts. The joint space is progressively lost over time.



NORMAL BONE **OSTEOARTHRITIS**

FIGURE 1.2.

Hyaluronic Acid:- Osteoarthritis of the disease is chronic disease in characterized by loss of cartilage, inflammation, joint dysfunction, pain and disability.

Chronic study shows intra articular injection of Hyaluronic acid which is a primary components of the synovial fluids in the healthy joints can help reduce pain and increase joint function in patients with osteoarthritis.

Hyaluronic Acid is a large polymer composed of repeating disaccharide unit the average Hyaluronic Acid chain contain 10,000 disaccharide repeats and has molecular mass between 200,000 to 10,000,000 Dalton.

The network of Hyaluronic Acid that surrounds velas provides a molecular scaffold for many components of the extra cellular matrix.

Hyaluronic Acid has unique biomolecular properties it acts as both lubricants and a shock absorber within the joint in addition to its biomechanical properties, Hyaluronic acid has many biochemical activities including.

- Regulation of pain
- Tissue Homeostasis
- Inflammation

Binding of Hyaluronic acid to nerve cells reduces their sensitivity and ability to respond to pain stimuli.

Hyaluronic Acid helps to

- Maintain normal joints structure
- Promotes healing
- Regulates chondrocytes growth and viability
- Stimulates synthesis of articular cartilage components such as collagen proteoglycans.

The biochemical activities of Hyaluronic acid are regulated by the HA binding to the CD44 receptor which is expressed by many cell types including chondrocytes, synovial sites and Inflammatory cells.

Importantly, the cellular responses to hyaluronic acid binding varied depending on its molecular mass. in osteoarthritis affected joints the concentration and molecular weight of HA is reduced as results of decrease synthesis and increase activity of Matrix degradating enzymes which occurs in response to chronic inflammation. These low molecular HA fragments cannot maintain the mechanical integrity of the joint leading to increase in friction reduced function and pain.

In addition small HA fragments promote inflammation by stimulating production of Inflammatory Cytokines and matrix degradating enzymes. Research suggests that the differently sized HA molecules may affects receptor organization and the ability to activate specific signalling pathways by cell.

Longer HA fragments like those found in healthy tissue blocks receptor activation whereas shorter HA fragments allow receptor to cluster together and initiate a cellular response.

1. Hyaluronic Acid suppresses production of activity of matrix degradating enzymes that causes tissue damage.
2. Inhibits Inflammatory Cytokines that causes swelling and pain.
3. Blocks movement of Inflammatory cells that perpetuate the immune response.

The unique combination of biochemical and biomechanical properties makes hyaluronic acid important molecule for maintaining joint health.

Mechanism of Action

HA is a non-sulfated glycosaminoglycan consisting of alternately repeating D-glucuronic acid and N-acetylglucosamine units. HA exists naturally in various animal tissues, including rooster combs, shark skin, bovine eyeballs, bovine nasal cartilage, rabbit brain and heart and in various human tissues, including the umbilical cord, serum, vitreous body, dermis, epidermis, thoracic lymph, urine and synovial fluid (SF). HA reduces the action of joint nociceptors, which provides pain reduction within the joint. Sensitized nociceptive terminals within the joint tissue are affected by HA concentration, reducing the pain response exhibited by these terminals.

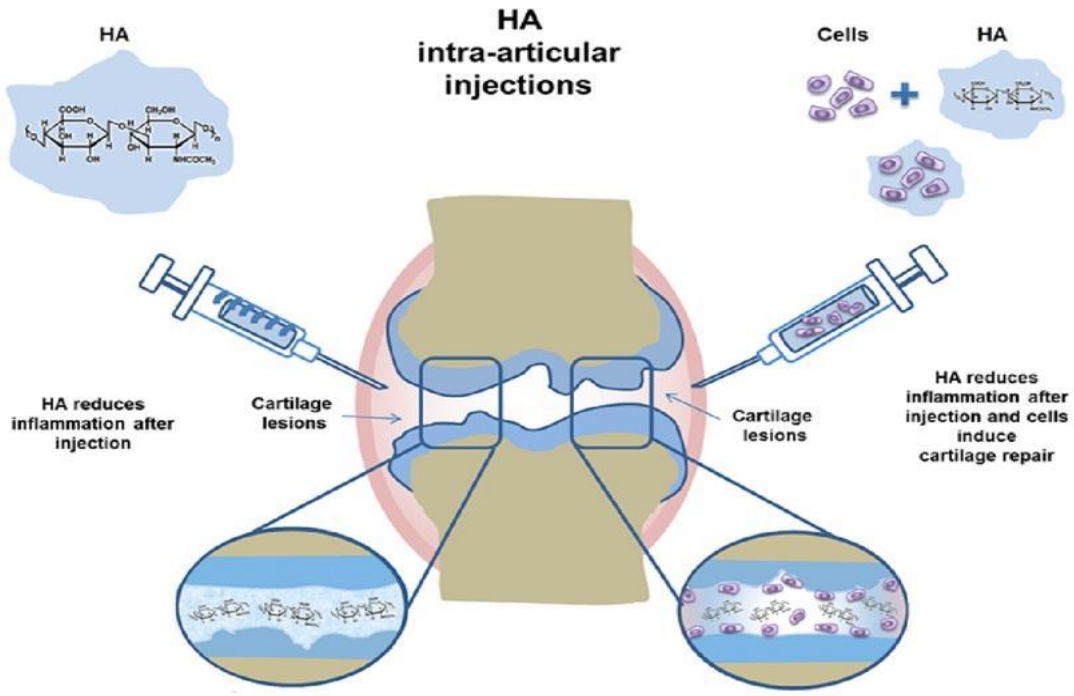


FIGURE 1.3:- Mechanism Action of Hyaluronic Acid.

2. Hyaluronic Acid With Nano Particles: First synthesised amphiphillic Hyaluronic acid conjugates by chemical conjugations of free LMW HA backbone (MW = 10 kDa) with hydrophobic 5β-cholanic acid (CA). Due to their amphiphilic nature, the conjugates self-assemble into NPs via hydrophobic interactions among CAs in aqueous conditions, in which CAs and Has compose the hydrophobic core for self-assembly and the hydrophilic.

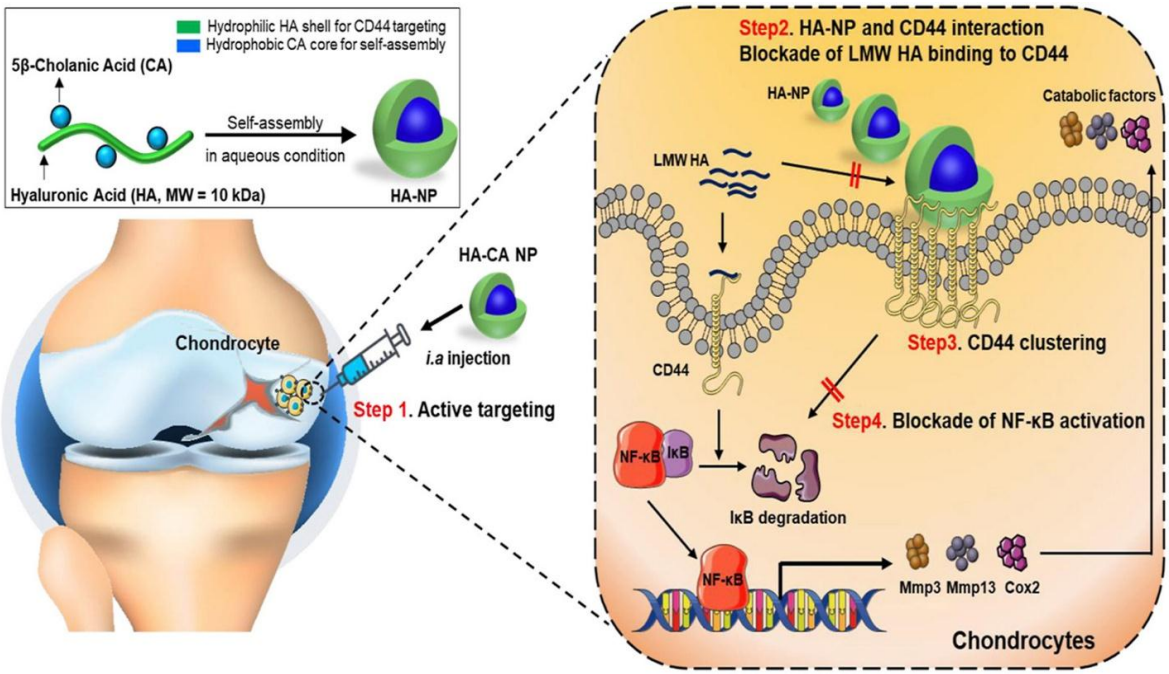


FIGURE 1.4:- Hyaluronic acid with nano particles.

Stage 1 :- Inject the injection into the targeted site.

Stage 2 :- Ideal OA therapy involves blocking pathogenic factors prior to the development of severe OA. Conventional drugs have been developed to target these pathways, including several classes of cytokine receptor antagonists and small anti-inflammatory molecules that neutralize inflammatory cytokines or block pathogenic receptors. Although such drugs relieve the symptoms and delay the advancement of deterioration, no current treatments can effectively restore the damaged cartilage. It has been also reported that interactions between the ECM and chondrocytes, mediated by matrix receptors, including integrin and CD44, respectively, are responsible for maintaining cartilage homeostasis. Altered ECM-chondrocyte interaction due to ECM decomposition under pathological conditions, including inflammation and tissue injury, plays a critical role in destruction and progressive loss of cartilage by triggering the expression of MMP3, MMP13, and COX2.[9],[10],[11] These catabolic factors promote cartilage destruction and release of fragmented ECM molecules, such as fragmented fibronectin, which further triggers catabolic gene expression in

chondrocytes.[9,11] Therefore, the inhibition of fragmented ECM molecule-chondrocyte interactions might be a potential therapeutic strategy for the treatment of OA.

1. CONCLUSION

Osteoarthritis of the disease is chronic disease in characterized by loss of cartilage, inflammation, joint dysfunction, pain and disability. The hyaluronic acid is the essential therapy in treating the Osteoarthritis in aged people, post traumatic osteoarthritis and Genetic factors etc. It is easy and effective method of treatment for relieving pain from OA. Among Mild, moderate and Severe Osteoarthritis, Severe Osteoarthritis can be treated by Injecting Hyaluronan. Hyaluronan is a non-sulfated glycosaminoglycan consisting of alternately repeating D-glucuronic acid and N-acetylglucosamine units. Hyaluronan production increases in proliferating cells, and the polymer may play a role in mitosis. It reduces the action of joint nociceptors, which provides pain reduction within the joint. Also, suppresses production of activity of matrix degrading enzymes that causes tissue damage. This mini review concluded that hyaluronic acid injectable is long term therapy for post traumatic osteoarthritis.

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