Comparison Between Low and High Molecular Weight Hyaluronan In The Treatment Of Osteoarthrosis Knee Joint

THESIS

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Abstract

Intra-articular treatment with HA and hylans has recently become more widely accepted in the armamentarium of therapies for OA pain Intra-articular HA treatment for osteoarthritis of the knee was approved by the US Food and Drug Administration in 1997

This study is the 1st study in Egypt that analyze the comparison between intra-articular injection of LMW and HMW hyaluronan in the treatment of osteoarthritis knee which was assessed using WOMAC index and visual analogue scale.

Key words:

Comparison between HMW and LMW hyaluronan in treatment of OA of the knee.

Table of Contents

List of Tables

List of Figures

List Of Abbreviations

IT	**iliotibial band**
MCL	**medial collateral ligament**
LCL	**lateral collateral ligament**
ACL	**anterior cruciate ligament**
PCL	**posteror cruciate ligament**
HA	**hyaluronic acid**
NSAID	**non-steroidal anti-inflammatory drugs**
OA	**osteoarthritis**
BMP	**bone morphogenetic protein**
BFGF	**basic fibroblastic growth factor**
IGF	**insulin like growth factor**
IL	**interleukin**
MMP	**matrix metalloproteinase**
PG	**proteoglycan**
TGF	**transforming growth factor**
TNF	**tumor necrosis factor**
WOMAC	**western Ontario and McMaster universities OA Index**
VAS	**Visual Analogue Scale**

PGE2	**prostagladin E2**
TIMP	**tissue inhibitor of metalloproteinases**
OMT	**osteopathic manipulative treatment**
OTC	**over the counter**
COX	**cyclooxygenase**
GI	**gastro-intestinal**
FDA	**food and drug association**
GAG	**Glycosaminogylcan**
NMR	**nuclear magnetic resonance**
MD	**molecular dynamic**
MW	**molecular weight**
NO	**nitric oxide**
PS	**post-surgery**
RA	**rheumatoid arthritis**
PMN	**polymorphonuclear**
IA	**intra-articular**

Introduction

Osteoarthritis, the most common form of arthritis, is a chronic disease characterized by the slow degradation of cartilage, pain, and increasing disability. The disease can have an impact on several aspects of a patient`s life, including functional and social activities, relationships, socioeconomic status, body image, and emotional well-being ***(carr., 1999).***

Intra-articular treatment with HA and hylans have recently become more widely accepted in the armamentarium of therapies for OA pain, HA is responsible for the vesicoelastic properties of synovial fluid. This fluid contains a lower concentration and molecular weight (MW) of HA in osteoarthretic joints than in healthy ones ***(Balaz, 1982).***

Thus the goal of intra-articular therapy with HA is to help replacement of synovial fluid that has lost its viscoelastic properties. The efficacy and tolerability of intra-articular HA for the treatment of pain associated with OA of the knee have been demonstrated in several clinical trials ***(Adams, et al., 1995).***

Three (hylane G-F 20) to five (sodium hyaluronate) injections can provide relief of knee pain from OA for up to 6 months ***(Altman., et al.,1998).***

Intraarticular hylan or HA is also generally well tolerated,with alow incidence of local adverse events (from 0% to 13% of patients) which was similar to that found with placebo ***(wobig,et al .,1999).***

Aim of the Work

This study aimed to analyze the comparison between intra-articular injection of low molecular weight and high molecular weight hyaluronan in the management of osteoarthritis knee, this difference is going to be assessed using Western Ontario and McMaster Universities osteoarthritis index (WOMAC) ***(Cocharne et al., 1991)*** and visual analogue scale VAS ***(Kjken et al., 1995)***.

Functional Anatomy of Knee Joint

The knee is a compound condylar joint with three articulations: the patellofemoral, the lateral and medial tibiofemoral condyles with their fibrocrtilagenous menisci ***(Press et al., 1996)***.

I. Soft-tissue Sleeve:

Protection and nutritional support of the knee are parovided by skin, fat, capsule, and synovium. Located in these soft tissues is a network of vessels (arteries, veins, lymphatics) and nerves. In general terms, the vessels and nerves pass from the hip to the ankle along the posterior aspect of the limb and send branches both medial and lateral around the knee to meet near the anterior midline ***(Bellemans et al., 2005)***.

Muscle-tendon units lie in the soft-tissue sleeve and are a significant component of the functional anatomy of the knee. The quadriceps (rectus femoris, vastus lateralis, vastus intermedius, vastus medialis) and articularis genu lie anterior to the femur. They arise from the pelvis (rectus femoris), the proximal femur (vastus lateralis, vastus intermedius, vastus medialis), and distal femur (articularis

genu), and attach by way of a conjoined tendon to the tibia to form the extensor mechanism of the knee. Invested in the conjoined tendon is the body's largest sesamoid bone, the patella. Retinaculum and synovium attaching to the patella and its tendon pass around the medial and lateral aspects of the knee to the distal femur and proximal tibia ***(Bellemans et al., 2005)***.

The muscle-tendon units lying posterior to the femur are referred to collectively as the hamstrings. The lateral hamstring (biceps femoris) and the medial hamstrings (sartorius, gracilis, semitendinosis, semimembrinosis) arise from the pelvis and attach to the fibular head and medial aspect of the tibia, respectively. These muscles function collectively in knee flexion. They also function in rotating the knee, with the lateral hamstrings rotating the tibia external relative to the femur and the medial hamstrings rotating the tibia internal relative to the femur ***(Eckhoff, 2005)***.

Also implicated in knee construction are the gastrocnemius muscles, the popliteal muscle, and the iliotibial band. The gastrocnemius originate just proximal and posterior to the femoral condyles and insert through the Achilles tendon on the calcaneus. The popliteal muscle arises from the posterior lateral femur and attaches to the posterior lateral tibia. The iliotibial (IT) band arises from

the lateral pelvis and attaches to the anterolateral tibia at Gerde's tubercle ***(Eckhoff, 2005)***.

Ligaments joining the femur and tibia are four in number, two cruciates and two collaterals. The medial collateral ligament (MCL) can be separated into two components, superficial and deep. The deep MCL originates from the area of the medial femoral epicondyle and inserts on the mid body of the medial meniscus and the proximal medial tibial plateau, forming a confluence with the coronary ligament attaching the meniscus to the tibia. The superficial MCL has an origin similar to that of the deep MCL but lacks any attachment to the meniscus and inserts more distally along the medial tibia. The MCL slopes from posterior proximally to anterior distally. The lateral collateral ligament originates from the area of the lateral epicondyle and inserts on the fibular head. It slopes opposite the MCL, passing from anterior proximally to posterior distally. The origins of the collaterals (MCL and LCL) lie on a line joining the femoral epicondyles, also known as the epicondylar line ***(Bellemans et al., 2005)***.

There are two cruciate ligaments. The anterior cruciate ligament (ACL) originates from the lateral wall of the femoral intercondylar notch and inserts on the mid tibia between the articular surfaces, passing from posterior proximally to anterior distally. Passing in the opposite

direction, from anterior proximally to posterior distally, is the posterior cruciate ligament (PCL), which arises from the medial wall of femoral intercondylar notch and inserts over an area approximately 2 cm in vertical length on the posterior aspect of the tibia. The origin of the cruciates (ACL and PCL) is not on the same line as the origins of the collaterals, i.e., the epicondylar line. The cruciate origins lie on a line passing through the center of the condyles, a line equidistant from points on the posterior articular surface of the condyles, but it is important to recognize for the purpose of balancing the soft tissues and restoring the kinematics of a knee that the origins of the cruciates and collaterals are not on the same line ***(Eckhoff, 2005)***.

II. Bony Architecture (Bone Morphology):

The distal femur has a unique three-dimensional shape marked by asymmetry. The two rounded asymmetrical prominences that articulate with the tibia, referred to as condyles, are separated by a space referred to as the intercondylar notch. The condyles are joined proximally by the femoral trochlear groove, the site of articulation between the patella and the femur. The trochlear groove is characterized as a trough with its