Review Article

Osteoarthritis of Knee Treated with Intra-articular Injections (Hyaluronic Acid, Platelet Rich Plasma, Corticosteroids) — A Systematic Review

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Abstract

Background : Osteoarthritis (OA) of the knee is a degenerative, progressive, long-term disease of the articular cartilage that causes pain and physical impairment in elderly people. Thirteen percent of senior citizens report having knee OA. The following categories could be used to group knee OA treatment options: surgical, pharmaceutical, procedural and conservative. Due to its higher risk of problems and joint revision, joint replacement is the gold standard and should only be used for severe grades of Osteoarthritis in the knee. The initial option for adults with knee OA and cartilage degradation is a nonsurgical strategy.Every year, about 10% of the individuals with Osteoarthritis (OA) in their knees receive intra-articular injections of various medications, particularly in the three months following OA diagnosis. Patients with knee OA can have their symptoms lessened by administering injections of corticosteroids, Hyaluronic Acid (HA) and Platelet-rich Plasma (PRP), among other substances. This review's objectives were to provide a summary of intra-articular injections used to treat OA and to list the traditional pharmaceuticals that were employed.

Key words : Knee Osteoarthritis, Intra-articular Injections, Corticosteroids, Hyaluronic Acid, Platelet Rich Plasma.

Degenerative Joint Disease, commonly referred to as Osteoarthritis (OA) of the knee, is usually caused by gradual loss of articular cartilage due to wear and stress. Seniors are most likely to experience it. Primary and secondary Osteoarthritis are the two categories of the condition. Articular degeneration in primary Osteoarthritis has no discernible underlying cause[1]. Either aberrant articular cartilage, as in Rheumatoid Arthritis (RA), or an aberrant concentration of force across the joint, as in post-traumatic reasons, can result in Secondary Osteoarthritis[2,3].

Because, radiographic results may not often match with symptoms, the diagnosis is primarily clinical. The primary symptoms, which frequently manifest as impairments in patients, include pain, soreness, restrictions in range of motion, joint effusion, and inflammation[4]. Three symptoms-decreased function, stiffness, and persistent knee pain-as well as three signs-limited movement, crepitus, and bony enlargement-are commonly used to diagnose knee OA. Activity and pain are typically associated; weight-bearing activities make the pain worse, while resting helps it get better. Joint failure is ultimately the final stage[5,6]. The "gold standard" for confirming a diagnosis and ruling out other conditions is frequently a radiograph. Anteroposterior and lateral knee x-rays reveal subchondral degenerative disease, osteophyte formation, and joint space narrowing.

Editor's Comment :

- Intra-articular injections are effective non-operative options for knee osteoarthritis, with PRP providing superior and longer-lasting pain relief and functional improvement, hyaluronic acid offering moderate, time-limited benefit, and corticosteroids giving rapid but short-term symptomatic relief; hence, treatment should be individualized based on disease severity, patient expectations, and cost-effectiveness.

The analgesics and anti-inflammatory drugs used in pharmacological therapy are given gradually. As per the guidelines, the first course of treatment for symptomatic OA should begin with acetaminophen (up to 4 g/day)[7]. This is because studies have shown that acetaminophen is as effective as Non-steroidal Anti-inflammatory Drugs (NSAIDs) but has fewer gastrointestinal side effects and a stronger correlation with warfarin maintenance[8]. In cases when acetaminophen is ineffective or symptoms are moderate to severe, NSAID medication (ibuprofen, naproxen, diclofenac) is advised.

The most widely used pharmacological compounds are NSAIDs, however their use is restricted due to a high frequency of gastrointestinal adverse effects, including peptic ulcer and gastrointestinal bleeding, as well as renal failure and elevated Blood Pressure[9]. Although Cyclooxygenase-2 inhibitors (COX-2) are known to lessen gastrointestinal side effects and enhance safety, they are also linked to increased costs and cardiovascular problems such Myocardial infarction and Stroke.

The main benefits of intra-articular injection are improvements in pain and function as well as temporary symptom alleviation. Hyaluronic Acid (HA), Platelet-rich Plasma (PRP) and corticosteroid injection are a few of

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the substances utilized to treat knee OA symptoms[10,11].

This review's objectives were to provide a summary of the traditional pharmaceuticals utilized and to give an overview of the intra-articular injections used to treat OA.

Intra Articular Injection of Knee :

When medication is no longer helpful, for patients who prefer to postpone or avoid surgery, or for those who do not tolerate pharmacological oral therapy, intra-articular injection of the knee may be a good option[12]. The shots ought to be as painless as feasible. Selecting the injection location correctly is essential; in fact, studies have shown that suprapatellar and medial infrapatellar injections hurt more than lateral infrapatellar injections[13,14]. The vastus medialis obliquus must be crossed in the medial subpatellar approach because the soft tissues are thinner there. With a mildly flexed joint, the patient lies supine during the lateral patellofemoral approach. When the needle reaches the middle of the patellar equator, it should be placed between the patella and the femoral condyle[15] (Table 1).

Technique :

The knee joint is the most often treated joint in the body because it has the biggest synovial space. It is the most accessible joint to enter and provide medication into because it frequently develops visible or palpable effusions[16]. Puncturing a balloon allows for easy access when there is a lot of fluid present.

The patient is typically supine during aspiration of the knee, with the knee supported and stretched to the greatest extent feasible. The typical site of entry is medial, roughly at the patella's midway, or just below the place where a line parallel to the medial border is crossed by a horizontal line tangential to the patella's superior pole[17,18]. A 1.5 to 2 inch long, 20-gauge needle is aimed either upward or downward and slides into the joint area below the patella's undersurface.

Firm pressure applied with the hand cephalad on the patella above the suprapatellar bursa site can aid in aspiration of the knee (Fig 1). The fluid is aspirated and the needle is retracted gently if any cartilage is contacted.

On the lateral side, a comparable method may be applied, particularly in cases when the peak fluid bulge is lateral[19]. When there is a significant amount of fluid in the suprapatellar bursa, the lateral approach is very useful. The entry site is superior to the patella and lateral.

Even though it is less frequently done, the infrapatellar approach can be helpful when there is little to no fluid present and the knee cannot be fully extended[20]. The needle is inserted cephalad to the infrapatellar fat pad and medially or laterally to the inferior patellar tendon while the knee is bent. Using this method to acquire fluid is challenging[21,22].

Table 1 — *Showing Some Cortico-steroid Suspensions for Intra-articular Injection*

Preparations	Concentration (mg/ML)	Usual Dose (mg)*
Hydrocortisone tabutate (Hydrocortone-TBA)	50	25-100
Betamathasone acetate and betamethasone sodium phosphate (celestone Soluspan)	6**	1.5-6
Methylprednisolone acetate (Depo-Medrol***)	20	4-40
Triamcinolone acetonide (Kenalog-40)	40	5-40
Triamcinolone diacetate (Aristocort Forte)	40	5-40
Triamcinolone hexacetonide (Aristospan)	20	5-40

*Amount injected varies depending on the size of the joint
**Available as 3 mg acetate and 3 mg phosphate
***Available in 20 mg/mL, 40 mg/mL, and 80 mg/mL preparations

Corticosteroids :

Joint discomfort can be effectively treated for short to medium periods of time by Intra-articular Steroid Injection (IASI) of the knee. Corticosteroids lessen the synovial inflammatory phase by downregulating aggrecans and collagenases, agents/modulators of proinflammatory mediators, and mononuclear cells. The intricate method

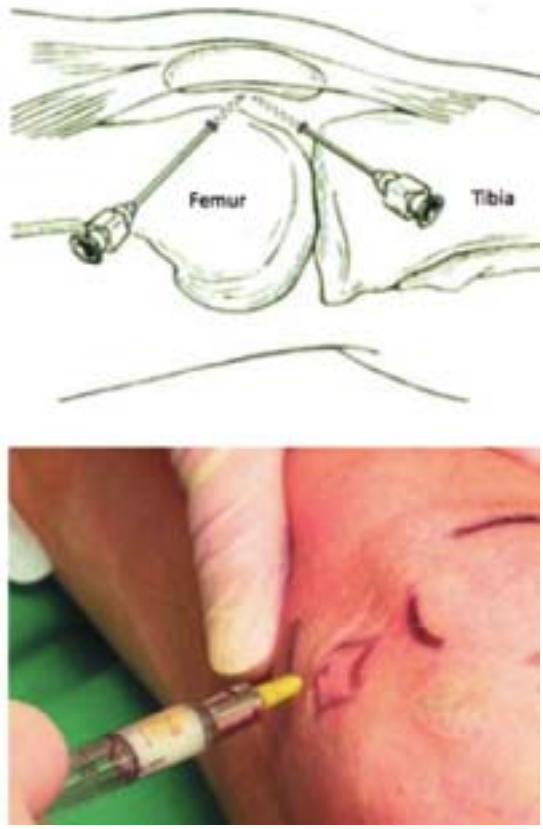

Fig 1 — Top, arthrocentesis of the knee joint via the usual medial entry. Bottom, actual injection of corticosteriod suspension into knee via medial approach.

of action results in a reduction of leukocyte counts and synovial blood flow, along with the release of inflammatory mediators[23-25]. Since the advancement of cartilage destruction in knee OA is linked to joint inflammation, IASI may slow the disease's progression.

Numerous corticosteroids are available for purchase, including betamethasone (Celestone), dexamethasone (Decadron) LA, triamcinolone acetonide (Kenalog), and methylprednisolone acetate (Depo-Medrol)[26]. Triamcinolone acetonide (Kenalog) and methyl-prednisolone acetate (Depo-Medrol) are the most commonly utilized. As indicated in Table, their usual dosage is 40 mg, with a minimum three-month gap between injections.

Hyaluronic Acid :

Synovial fluid and extracellular matrix naturally include high-molecular-weight glycosaminoglycan, or HA, which is made of chains of repeating disaccharide units. Its purpose is to increase the viscosity of synovial fluid by lubricating the joint and absorbing shocks during motions[27]. Moreover, HA helps to prevent nociceptors and the enzymatic breakdown of cartilage. Moreover, exogenous HA may function as a free-radical scavenger and promote the production of endogenous HA. Decreases in HA content and molecular weight can be attributed to aberrant generation of synoviocytes, molecular fragmentation, and dilution of synovial fluid due to effusion[28]. Experimental studies have indicated that the mechanical impact of exogenous HA cannot explain the sustained effects. Rather, the HA clearance is influenced within a few days by the Intra-articular Hyaluronic Acid (IAHA) preparation[29,30].

Three forms of HA are distinguished by their varying molecular weights and the range of possible varieties: There are three different kDa ranges: Low (500–730 kDa), Moderate (800–2000 kDa) and High (2000–6000 kDa), which includes crosslinked HA formulations (Table 2).

After receiving acetaminophen, NSAIDs, and symptomatic slow-acting medications continuously or intermittently, IAHA is recommended for patients who are not responding to treatment. For knee OA, IAHA has been acknowledged as a dependable and safe therapeutic method. According to earlier research, the side effects of IAHA, such pain or swelling, almost invariably happen at the injection site or inside the joint and are equally likely to happen in patients receiving a placebo as they are in those receiving active treatment. Rarely do serious adverse outcomes occur. Nothing about unanticipated adverse occurrences was reported after the product was launched, according to the Food and Drug Administration's premarket approval database.

Table 2 — *Showing Approved Hyaluronon Preparations*

	Sodium Hyaluronate (Hyalgan)	Sodium Hyaluronate (Supartz)	High-Molecular-Weight Hyaluronan (ORT Hovisc)	Hylin G-F 20 (synvisc)
Type of Product	Natural	Natural	Natural	Chemically cross-linked
Moleculat weight (X 106 deltons)	0.5-0.73	0.6-1.2	1.0-2.9	6.0
Concentration (mg/mL)	10	10	15	8
Dose volume (mL)	2	2.5	2	2
Dose interval	1 week	1 week	1 week	1 week
Number of doses	3 to 5	5	3 or 4	3

Platelet Rich Plasma :

Autologous plasma that has been enhanced with a concentration of platelets is what produces Platelet-rich plasma (PRP). PRP provides and releases growth factors, α-granules and cytokines, which can stimulate healing and facilitate tissue repair[31]. Fibrinogen, Tissue Growth Factors (TGFs), Platelet-derived Growth Factors (PDGFs), interleukin-1 receptor antagonist (IL-1RA) and Vascular Endothelial Growth Factors (VEGFs) can all be released in response to a PRP injection. These growth factors function both locally and systemically, promoting the inhibition of cytokines and catabolic enzymes, regulating inflammation and local angiogenesis, attracting local fibroblasts and stem cells to damaged areas and stimulating the production of more growth factors by healthy neighboring cells.

A wide range of PRP preparation methods, platelet counts, injection volumes, anticoagulant and activating agent usage, patient sex, physical attributes and OA severity have all been documented in the literature. Current research suggests that PRP injections can improve pain relief and functional improvement in patients with symptomatic knee OA for at least 12 months, though some authors have reported good score values up to 24 months after the start of treatment[32]. The duration of the beneficial effects of PRP injections is unknown. PRP therapy was found to be clinically superior to other injectable therapies (HA, IASI and Saline) in terms of lowering the symptomatology of pain related to Osteoarthritis (OA) and improving functional results with comparable or lower risks of adverse events[33].

The biggest barriers to therapy at the moment are the absence of standardization and the need for more investigation into how leukocytes, activation and platelet concentration affect therapeutic efficacy beyond PRP's cost-effectiveness.

Stem Cell Therapy :

Stem cell injections have been suggested as a new regenerative therapy for knee OA because of their ability for multilineage differentiation[34,35]. But according to a recent systematic review, there are very few RCTs in this

field, the studies that are available have a significant risk of bias, and there are no long-term findings[36]. We locate two studies comparing stem cell treatments for Osteoarthritis (OA) to PRP or HA[37].

Prolotherapy :

Small doses of an irritant solution, such as hyperosmolar dextrose (d-glucose), with concentrations ranging from 12.5 to 25%, are injected into painful joints during prolotherapy in an effort to promote the tensile strength of the ligaments, tendons, and joint capsules that stabilize the joint and restore joint stability[38,39]. Even though the current studies' results were statistically significant, the lack of a control group, short follow-up periods, limited sample sizes, and structural evaluations make it difficult to determine the therapeutic relevance or significance[40,41].

Conclusion :

IA corticosteroid has dubious long-term efficacy when compared head-to-head with alternative comparators such IA PRP, ketorolac, or normal saline, despite the fact that pain and function improve quickly. IA corticosteroid plus HA combination therapy may be more beneficial than IA corticosteroid therapy alone, however more research with a bigger sample size is required to prove this. While IA HA did not show any symptomatic improvement when compared to normal saline, small studies comparing HA with PRP or diclofenac showed a significant improvement in pain and function at least over 6 months when compared to HA therapy alone. These studies also need more investigation.

Using a range of comparators, including HA, ozone, and normal saline, conflicting outcomes were reported over IA PRP; some studies had follow-up periods of 36 or 60 months. Likewise, varying outcomes are documented in relation to stem cell treatments. Standardization of PRP and stem cell products is therefore desperately needed. Small studies have shown that prolotherapy can be useful in either a single or combo regimen. Not a single one of the IA treatments in the review showed evidence of septic arthritis or significant side effects.

With imaging guidance, joint injection accuracy and clinical results are improved. Future research should focus on topics including placebo effects, drug delivery technologies, cost-effectiveness of various IA therapies, potential negative effects of IA NSAIDs or local anesthetics on cartilage and product standardization.

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References

1 Martel-Pelletier J, Boileau C, Pelletier JP, Roughley PJ — Cartilage in normal and osteoarthritis conditions. *Best Pract Res Clin Rheumatol* 2008; **22:** 351-84. [PubMed] [Google Scholar]
2 National Collaborating Centre for Chronic Conditions (UK) Osteoarthritis: National clinical guideline for care and management in adults. London: Royal College of Physicians (UK); 2008. [PubMed] [Google Scholar]
3 Neogi T — The epidemiology and impact of pain in osteoarthritis. *Osteoarthritis Cartilage* 2013; **21:** 1145-53. [PMC free article] [PubMed] [Google Scholar]
4 Jevsevar DS, Brown GA, Jones DL, Matzkin EG, Manner PA, Mooar P, *et al* — The American Academy of Orthopaedic Surgeons evidence-based guideline on: treatment of osteoarthritis of the knee, 2nd edition. *J Bone Joint Surg Am* 2013; **95:** 1885-6. [PubMed] [Google Scholar]
5 Aigner T, McKenna L — Molecular pathology and pathobiology of osteoarthritic cartilage. *Cell Mol Life Sci* 2002; **59:** 5-18. [Google Scholar] [CrossRef]
6 Hinton R, Moody RL, David AW, Thomas SF — Osteoarthritis: Diagnosis and therapeutic considerations. *Am Fam Physician* 2002; **65:** 841-8. [Google Scholar]
7 Zhang W, Doherty M, Peat G, Bierma-Zeinstra MA, Arden NK, Bresnihan B, *et al* — EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. *Ann Rheum Dis* 2009; **69:** 483-9. [Google Scholar] [CrossRef] [PubMed] [Green Version]
8 Sinusas K — Osteoarthritis: Diagnosis and treatment. *Am Fam Phys* 2012; **85:** 49-56. [Google Scholar]
9 Jevsevar DS — Treatment of osteoarhritis of the knee: Evidence-based guideline, 2nd edition. *J Am Acad Orthop Surg* 2013; **21:** 571-6. [Google Scholar] [CrossRef] [PubMed]
10 Towheed TE, Maxwell L, Judd MG, Catton M, Hochberg MC, Wells G — Acetaminophen for osteoarthritis. *Cochrane Database Syst Rev* 2006; CD004257. [Google Scholar] [CrossRef] [PubMed]
11 Lazzaroni M, Bianchi Porro G — Gastrointestinal side-effects of traditional non-steroidal anti-inflammatory drugs and new formulations. *Aliment Pharmacol Ther* 2004; **20 (Suppl. 2):** 48-58. [Google Scholar] [CrossRef]
12 Garner SE, Fidan DD, Frankish RR, Judd MG, Towheed TE, Wells G, Tugwell P — Rofecoxib for rheumatoid arthritis. *Cochrane Database Syst Rev* 2005; CD00368. [Google Scholar] [CrossRef]
13 Hunter DJ, Lo GH — The management of osteoarthritis: An overview and call to appropriate conservative treatment. *Med Clin N Am* 2009; **93:** 127-43. [Google Scholar] [CrossRef]
14 Van Manen MD, Nace J, Mont MA — Management of primary knee osteoarthritis and indications for total knee arthroplasty for general practitioners. *J Am Osteopat Assoc* 2012, **112:** 709-15. [Google Scholar]
15 Rastogi AK, Davis KW, Ross A, Rosas HG — Fundamentals of Joint Injection. *Am J Roentgenol* 2016; **207:** 484-94. [Google Scholar] [CrossRef]
16 McAlindon TE — OARSI guidelines for the non-surgical management of knee osteoarthritis. *Osteoarthr. Cartil.* 22, 363–388. https://doi.org/10.1016/j.joca.2014.01.003 (2014). Article CAS PubMed Google Scholar
17 Hochberg MC — American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken)* 64: 465-74 (2012). Article CAS Google Scholar
18 Jordan KM — EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Ann Rheum Dis* 2003; **62:** 1145-55.
19 Hunter DJ — Osteoarthritis. *Lancet* 2019.
20 McAlindon TE — OARSI guidelines for the non-surgical manage-

ment of knee osteoarthritis. Osteoarthritis Cartilage (2014).
21 Bannuru RR — OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis Cartilage (2019).
22 Sellam S — Recommendations of the French Society of Rheumatology on pharmacological treatment of knee osteoarthritis. *Joint Bone Spine* (2020).
23 Jones AC — Intra-articular hyaluronic acid compared to intra-articular triamcinolone hexacetonide in inflammatory knee osteoarthritis. Osteoarthritis Cartilage (1995).
24 Leighton R, Fitzpatrick J, Smith H, Crandall D, Flannery CR, Conrozier T — Systematic clinical evidence review of NASHA (Durolane hyaluronic acid) for the treatment of knee osteoarthritis. *Open Access Rheumatol* 2018; **10:** 43-54. [Google Scholar] [CrossRef] [Green Version]
25 Cooper C, Rannou F, Richette P, Bruyère O, Al-Daghri N, Altman RD, *et al* — Use of intraarticular hyaluronic acid in the management of knee osteoarthritis in clinical practice. *Arthritis Care Res (Hoboken)* 2017; **69:** 1287-96. [Google Scholar] [CrossRef] [PubMed]
26 Newberry SJ, Fitzgerald JD, Maglione MA, O'Hanlon CE, Booth M, Motala A, *et al* — Systematic Review for Effectiveness of Hyaluronic Acid in the Treatment of Severe Degenerative Joint Disease (DJD) of the Knee; Agency for Healthcare Research and Quality (US): Rockville, MD, USA, 2015.
27 Malanga GA, Goldin M — PRP: Review of the current evidence for musculoskeletal conditions. *Curr Phys Med Rehabil Rep* 2014; **2:** 1-15. [Google Scholar] [CrossRef] [Green Version]
28 Peter I, Wu K, Diaz R, Borg-Stein J — Platelet-rich plasma. *Phys Med Rehabil Clin* 2016; **27:** 825-53. [Google Scholar] [CrossRef]
29 Asjid R, Faisal T, Qamar K, Khan SA, Khalil A, Zia MS — Platelet-rich Plasma-induced Inhibition of Chondrocyte Apoptosis Directly Affects Cartilage Thickness in Osteoarthritis. *Cureus* 2019; **11:** e6050. [Google Scholar] [CrossRef] [Green Version]
30 Dai WL, Zhou AG, Zhang H, Zhang J — Efficacy of platelet-rich plasma in the treatment of knee osteoarthritis: A meta-analysis of randomized controlled trials. *Arthrosc. J Arthrosc Relat Surg* 2017; **33:** 659-70. [Google Scholar] [CrossRef] [PubMed]
31 Cook CS, Smith PA — Clinical update: Why PRP should be your first choice for injection therapy in treating osteoarthritis of the knee. *Curr Rev Musculoskelet Med* 2018; **11:** 583-92. [Google Scholar] [CrossRef]
32 Shen L, Yuan T, Chen S, Xie X, Zhang C — The temporal effect of platelet-rich plasma on pain and physical function in the treatment of knee osteoarthritis: Systematic review and meta-analysis of randomized controlled trials. *J Orthop Surg Res* 2017; **12:** 16. [Google Scholar] [CrossRef] [PubMed] [Green Version]
33 Filardo G, Kon E, Buda R, Timoncini A, Di Martino A, Cenacchi A, *et al* — Platelet-rich plasma intra-articular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis. *Knee Surg. Sports Traumatol Arthrosc* 2011; **19:** 528-35. [Google Scholar] [CrossRef]
34 Filardo G, Previtali D, Napoli F, Candrian C, Zaffagnini S, Grassi A — PRP injections for the treatment of knee osteoarthritis: A meta-analysis of randomized controlled trials. *Cartilage* 2020, 1947603520931170. [Google Scholar] [CrossRef]
35 Bennell KL, Hunter DJ, Paterson KL — Platelet-rich plasma for the management of hip and knee osteoarthritis. *Curr Rheum Rep* 2017; **19:** 24. [Google Scholar] [CrossRef]
36 Chen X, Jones IA, Park C, Vangsness CT — The efficacy of platelet-rich plasma on tendon and ligament healing: A systematic review and meta-analysis with bias assessment. *Am J Sports Med* 2018; **46:** 2020-32. [Google Scholar] [CrossRef] [PubMed]
37 O'Connell B, Wragg NM, Wilson SL — The use of PRP injections in the management of knee osteoarthritis. *Cell Tissue Res* 2019; **376:** 143-52. [Google Scholar] [CrossRef] [PubMed] [Green Version]
38 Carstairs A, Genever P — Stem cell treatment for musculoskeletal disease. *Curr Opin Pharmacol* 2014; **16:** 1-6. [Google Scholar] [CrossRef] [PubMed]
39 Rodrigues MT, Lee SJ, Gomes ME, Reis RL, Atala A, Yoo JJ — Amniotic fluid-derived stem cells as a cell source for bone tissue engineering. *Tissue Eng Part A* 2012; **18:** 2518-27. [Google Scholar] [CrossRef]
40 Zhong YC, Wang SC, Han YH, Wen Y — Recent Advance in Source, Property, Differentiation, and Applications of Infrapatellar Fat Pad Adipose-Derived Stem Cells. *Stem Cells Int* 2020; **2020:** 2560174. [Google Scholar] [CrossRef]
41 Jayaram P, Ikpeama U, Rothenberg JB, Malanga GA — Bone Marrow-Derived and Adipose-Derived Mesenchymal Stem Cell Therapy in Primary Knee Osteoarthritis: A Narrative Review. *PMR* 2019; **11:** 177-91. [Google Scholar] [CrossRef]