OSTEOARTHRITIS: CAN IT BE REVERSED? A NEW BIOLOGICAL TREATMENT TECHNIQUE FOR TREATING PATIENTS WITH MODERATE TO ADVANCED GONARTHROSIS

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ABSTRACT

Osteoarthritis of the knee is leading cause of disability in the elderly, all times. Although there are pharmacological and nonpharmacological treatment methods, these are generally insufficient to alleviate pain and the disability in advanced cases Although total knee arthroplasty improves quality of life and provides a generally high level of patient satisfaction for treatment of advanced gonarthrosis, it is not always without complications. Herein we present a new technique consisting of patellofemoral joint irrigation, simple osteophytectomy if needed, lateral patellar retinaculum release, subchondral drilling of the proximal tibia, percutaneous medial collateral ligament release, intra-articular injection of proximal tibial bone marrow, and the results of this treatment applied under local anesthesia in 20 knees of 13 patients. The mean VAS (Visual Analogue Scale) was 8.20 ± 0.68 prior to treatment and 3.33 ± 0.72 after treatment; the values were 18.67 ± 3.34 and 4.10 ± 3.15 for leg measurements, 7.80 ± 0.77 and 1.07 ± 0.96 for pain, 5.07 ± 2.28 and 1.80 ± 1.42 for walking, and 5.80 ± 0.92 and 1.23 ± 0.92 for daily living activities, respectively. All decreases were statistically significant ($p = 0.001$ for $p < 0.01$ in all cases). Biological treatment solutions to gonarthrosis without using foreign materials could decrease the need for prosthetic surgery and its related complications, as well as the need for further attempts at revision. In this study we presented a new biologic treatment for gonarthrosis.

Keywords: *Gonarthrosis, Subchondral drilling, Bone Marrow injection, Osteophytectomy.*

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Introduction

Osteoarthritis (OA) is the most prevalent form of arthritis and is a leading cause of disability, a problem that becomes more pronounced with increasing age[(1)]. OA is found in almost 70% of the population over 60 years of age and is characterised by a breakdown of articular cartilage and proliferative changes to the surrounding bones[(1-4)].

Although various efforts are underway to identify different treatment modalities to prevent joint destruction and progression of the arthritis, an effective treatment protocol, particularly for advanced stages of gonartrosis, does not yet exist[(2, 5)]. The ideal treatment of OA should focus on prevention of articular cartilage dam¬age and many compounds are under investiga¬tion for this purpose.

Here, we present a new treatment approach and accompanying results for patients with moderate to advanced gonarthrosis. These patients had undergone a minimally invasive treatment protocol under local anaesthesia consisting of patellofemoral joint simple osteophytectomy with joint lavage, lateral patellar retinaculum release, subchondral retrograde drilling of the proximal tibia, percutaneous medial collateral ligament release, and whole bone marrow injection containing mesenchymal stem cells and supportive chondrogenic components.

Materials and methods

This was an institutional Review Board-approved retrospective review of patients diagnosed with Kellgren-Lawrence grades 2-4 knee osteoarthritis who had undergone patellofemoral joint simple osteophytectomy with joint irrigation, lateral patellar retinaculum release, subchondral retrograde drilling of the proximal tibia, percutaneous medial collateral ligament release, and intra-articular bone marrow injection at a single institution. Informed consent was obtained from all study participants and all procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and also with the 1964 Helsinki Declaration and its later amendments, or with comparable ethical standards.

The inclusion criteria were knee pain, gonarthrosis involving the medial compartment with or without lateral and patellar compartments of the knee, and unresponsiveness to conservative treatment.

The exclusion criteria were rheumatoid arthritis, blood diseases, known malignancy, immunodeficiency, hepatitis, infection or septicemia. The Visual Analogue Score (VAS) and Lequesne Score were evaluated at initial presentation and at postoperative months 3 and 12[6,7].

Technique

The technique was proposed by a senior surgeon who is an expert on cartilage repair surgery and one of the authors of this paper (B.K.). An appropriate local anaesthetic (bupivacaine plus prilocaine) injection to the patellofemoral joint and around the patella was performed 10 min before the start of technique through a 0,5 cm incision created at superolateral side of patella (Fig. 1a). In cases of decreased patellofemoral joint motion due to osteophytes, incision was expanded to 2 cm to reach the joint and perform simple patellofemoral joint osteophytectomy (Fig. 1b and 3). In cases of normal patellofemoral joint motion, only a lateral retinaculum release was performed through the same incision. Then the patients underwent joint irrigation using 1500 cc sterile isotonic solution with the aid of a sterile naso-gastric feeding tube(Fig. 1a).

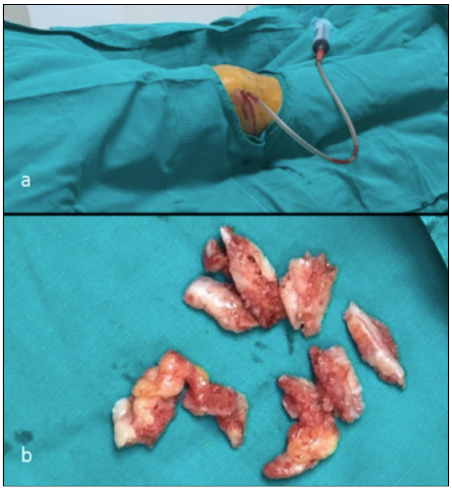


Figure 1: **a)** Picture showing first incision location and feeding tube used to deliver local injection and irrigation fluid. **b)** Osteophytes after patellofemoral joint osteophytectomy.

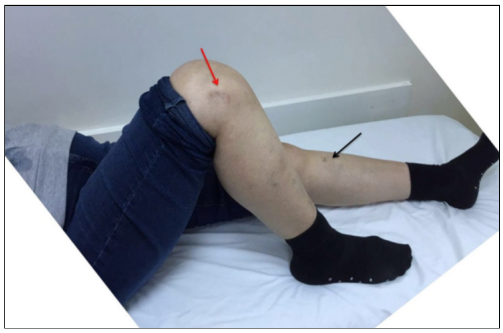


Figure 3: Image showing clinical appearance of the same patients as in Figure 2 at postoperative first month. Red arrow; 2 cm lateral incision used for simple osteophytectomi. Black arrow; entrance point for retrogarde drilling.

In the second step, local anaesthesia (bupivacaine plus prilocaine) was administered to the medial collateral ligament area and medial proximal tibia using injection syringes. Then a percutaneous pie-crusting technique was used to release the medial collateral ligament with an 18-gauge needle and the application of gentle valgus force.

After completion of the second stage, subchondral retrograde drilling with a 5 mm drill began. The entry point of the drill was 1 cm medial to the tuberositas tibia and 3-4 cm below the joint

line. Both medial and lateral plateaus of the tibia were drilled from this single hole and care was taken not to penetrate the articular cartilage (Fig 2a and 2b). Then, using an 18-gauge needle, 30 cc whole bone marrow was aspirated and the aspirate was injected into the knee joint. Range of motion exercises were started at postoperative first day and all patients were allowed to be weight-bearing as tolerated after the first day of procedure.

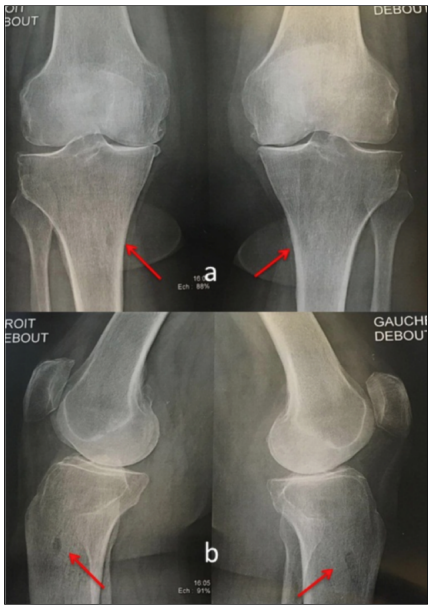


Figure 2: İnitial anterior-posterior **(a)** and lateral **(b)** x-rays of a 65 year-old a woman taken after procedure. Red arrows showing drilling holes.

Statistical analysis

The 2007 Number Cruncher Statistical System (NCSS; Kaysville, Utah, USA) statistical software was used for the statistical analysis. A Wilcoxon signed-rank test was used to assess the descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, and maximum), as well as measurements of variables without a normal distribution, before and after treatment. Significance was evaluated at a p-value < 0.01 or < 0.05

Results

The study included 20 knees of 13 individuals, including 4 males (30%) and 9 females (70%). The ages of the individuals ranged between 52 and 85 years and the mean age was 61.90 ± 9.62 years. Twenty different measurements for each knee were recorded.

Right-sided measurements were recorded for 60% of the individuals (n = 12) and left-sided measurements for 40% (n = 8). The body mass index (BMI) of the individuals ranged between 23.2 and 49.1 kg/m,2 and the mean BMI was 28.95 ± 7.68 kg/m2. Considering the osteoarthritis stages, 10 % of the individuals (n = 2) were classified as stage 2, 75 % of them (n = 15) as stage 3, and 15 % of them (n = 3) as stage 4 (Table 1 and 2).

		Min-Max	Mean ± SD
Age (year)		52-85	61.90 ± 9.62
BMI (kg/m²)		23.2-49.1	28.95 ± 7.68
		n	**%**
Gender	Male	4	30
	Female	9	70
Side	Right	12	60
	Left	8	40
Stage	2	2	10
	3	15	75
	4	3	15

Table 1: Distribution of descriptive characteristics.
SD: standard deviation; BMI: body mass index

n = 15		Before Treatment	After Treatment	p-value
VAS	Min-Max (Median)	7-9 (8)	2–4 (3)	***0.001*****
	Mean ± SD	8.20 ± 0.68	3.33 ± 0.72	
Leg	Min-Max (Median)	10.5-22.5 (18)	0–8 (6)	***0.001*****
	Mean ± SD	18.67 ± 3.34	4.10 ± 3.15	
Pain	Min-Max (Median)	5-8 (8)	0–2 (1)	***0.001*****
	Mean ± SD	7.80 ± 0.77	1.07 ± 0.96	
Walking	Min-Max (Median)	1-8 (5)	0–4 (2)	***0.001*****
	Mean ± SD	5.07 ± 2.28	1.80 ± 1.42	
DLA	Min-Max (Median)	4-6.5 (6)	0–2 (2)	***0.001*****
	Mean ± SD	5.80 ± 0.92	1.23 ± 0.92	

Table 2: Assessments before and after treatment.
VAS: visual analogue score; SD: standard deviation; DLA: daily living activities
***p < 0.01: Wilcoxon signed-rank test*

Simple osteophytectomi was performed in 60% (n = 12) of the knees (Fig. 3 and 4).

The mean VAS was 8.20 ± 0.68 prior to treatment and 3.33 ± 0.72 after treatment; the values were 18.67 ± 3.34 and 4.10 ± 3.15 for leg measurements, 7.80 ± 0.77 and 1.07 ± 0.96 for pain, 5.07 ± 2.28 and 1.80 ± 1.42 for walking, and 5.80 ± 0.92 and 1.23 ± 0.92 for daily living activities (DLA), respectively. All decreases were statistically significant (p = 0.001 for p < 0.01 in all cases) (Graph. 1).

Statistically significant difference was not detected between osteophytectomi performed and nonperformed individuals.

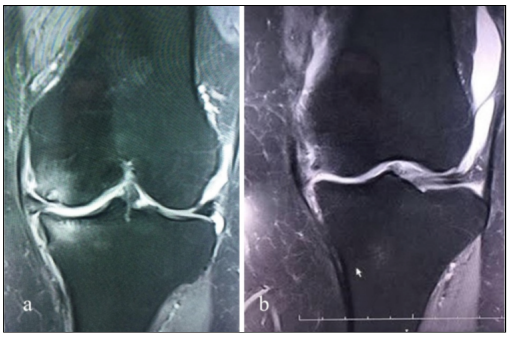
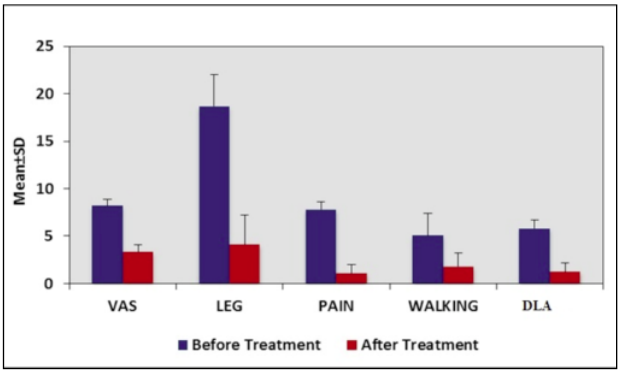


Figure 4: Preoperative and postoperative MRI of the same patients as in Figure 2 and 3. Coronal T2 MRI showin preoperative subchondral eudema and schlerosis (a), and coronal T2 MRI taken at postoperative 6. month showing relief of eudema and schlerosis.



Graphic 1: Mean VAS and Lequesne Scores.

Discussion

OA affects almost 12% of adults in the United States and creates an economic burden of more than 15 billion dollars[8]. Although total knee arthroplasty improves quality of life and provides a generally high level of patient satisfaction, it is not always without complication. Unfortunately, OA can be associated with early or late infection, venous thromboemboli, neurovascular injury, septic and aseptic loosening, reflex sympathetic dystrophy, periprosthetic fractures, arthrofibrosis, wound complications, and even amputation[9-14].

Therefore, treatment methods that provide symptomatic relief and reversal of some aspects of gonarthrosis without the requirement for foreign materials, but rather using the body's own regenerative capacity, would form an innovative therapeutic approach to this debilitating and progressive condition.

Although subchondral bone is increasingly believed to play an important role in the disease process, there is still an ongoing debate about its role in the pathogenesis of OA. The area underlying the calcified cartilage, which is composed of subchondral bone plate and subchondral trabecular bone, is involved in the pathogenesis of OA. Subchondral bone has two essential functions: stress absorption and maintenance of the cartilage nutrient supply. Pan et al.[16] reported the penetration of small molecules into calcified cartilage from the subchondral bone, where the subchondral bone plate provides a direct link between articular cartilage and subchondral bone.

In 1994, Arnoldi discussed the theory that decreased bone blood flow perfusion with decreased interstitial fluid flow in the subchondral bone results in ischemia and eventual bone death[17]. There are two potential outcomes of venous stasis in subchondral bone. First, decreased perfusion in subchondral bone results in decreased nourishment to the overlying cartilage[18]. Second, the mechanical strength of the subchondral bone could be negatively affected due to ischemia. In addition, venous stasis may lead to a loss of osteocyte viability, which stimulates a remodeling process. Subchondral bone and cartilage are complementary structures with dynamic stress-bearing features. Stiffened and less pliable subchondral bone could transmit increased loads to the overlying cartilage leading to secondary cartilage damage[19].

Therefore, one of the current authors (B.K) proposed a technique using subchondral drilling to decrease the increased venous pressure to reconstitute the circulation, promote formation of new healthy subchondral bone instead of sclerosed bone and thus help reverse the ischemic process.

In recent years, emphasis has been given to subchondral bone marrow eudema-like lesions and subchondral bone cysts, which are presumed to play a role in the pathology of osteoarthritis[20]. Subchondral cyst-like lesions are generally seen in patients with gonarthrosis. These lesions appear as well-defined rounded areas of fluid-like intensity with no evidence of epithelial lining on histological examination.

There are two theories regarding the formation of subchondral cysts:

1) they are due to the leakage of synovial fluid through fissured or ulcerated cartilage causing the eventual development of cysts;

2) subchondral cysts develop from bone mar-

row oedema-like lesions due to traumatic bone necrosis after the impacting of two opposing articular surfaces. The second theory is supported by the fact that cysts are often observed in areas of the knee with concomitant bone marrow eudema-like lesions that have areas of necrosis and features of bone trauma detectable on histological examination, and which in turn may be caused by decreased venous outflow with a subsequent cascade of osteoarthritis[21,22,23].

Pain in osteoarthritic joints has been associated with increased intraosseous pressure[24,25]. Thus, drilling the subchondral bone may relieve pain by decreasing the pressure and hence increase the circulation.

Chondrogenic bone marrow-derived mesenchymal stem cells are usually prepared as a buffy coat fraction of bone marrow. However, whole bone marrow retains the supportive chondrogenic components in marrow plasma and involves marrow adipocytes, which are also important in the formation of chondrogenesis[26]. In our patients, we used whole bone marrow injections.

Joint lavage in OA has numerous beneficial effects. It helps to remove cartilage debris, microcrystals, and degrading enzymes and cytokines involved in chondrolysis and disruption of intra-articular adhesions[27,28].

In releasing the medial collateral ligament in our patients, the main rationale was to unload the medial knee compartment, which in turn results in a reduced adduction moment and a reduction in the external rotation restraint in extension[29].

Biological treatment solutions to gonarthrosis without using foreign materials could decrease the need for prosthetic surgery and its related complications, as well as the need for further attempts at revision (Fig. 3).

We introduced a new biological method for treating patients with moderate to advanced gonarthrosis, and the results are promising. However, further studies with control groups and a longer follow-up are necessary .

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Ethical Approval
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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