Original Research Article

Ultrasound Guided Platelet Rich Plasma Injection in Post Traumatic Knee Meniscus lesion

Abstract

Background: Orthobiologics have gained a lot of attention as a potential meniscal injury therapy option in recent years. There are several techniques for biologically enhancing meniscal healing, such as the use of platelet-rich plasma (PRP), cytokines, growth factors, and fibrin clots.The aim of this study was to evaluate the efficacy of PRP injection guided by ultrasound on functional and clinical improvement in patients with post traumatic knee meniscal injury grade 2.

Methods: This study was carried out on forty patients with evidence of post traumatic knee intramural meniscal lesion grade 2 on magnetic resonance imaging (MRI). Patients were treated with three injections, two weeks apart of 4 ml of autologous PRP injected at the site of knee meniscal lesion under continuous ultrasound guidance.

Results: There were significant improvement as regard pain assessed by Visual Analogue Scale (VAS), active range of motion (ROM), knee joint line tenderness grading 4 months after treatment compared to before treatment. There was significant improvement as regard symptoms, Activities of daily living (ADL), pain, sport and recreation function and knee related quality of life (QOL) subscales of KOOS 4 months after treatment compared to before treatment.

Conclusions: Peri-meniscal PRP injection under ultrasound guidance in patients with post traumatic knee meniscal lesions grade 2 with persistent pain appears to be an effective method for pain relief. Peri-meniscal PRP injection is able to achieve improvement in clinical and functional scores after 4 months follow up. Musculoskeletal ultrasonography is a

fundamental tool for peri-meniscal areas injections to guarantee its accuracy and maximizes its benefits.

Keywords: Ultrasound, platelet rich plasma, post traumatic knee, meniscus tear

Introduction:

The menisci, which are major load-sharing elements of the knee joints, are fibro-cartilaginous elements present between the tibial plateau and the femoral condyles. Meniscal tears occur in 66 out of every 100000 people each year, making it the most frequent knee pathology[1].

A twisting action at the knee when the foot is on the ground is often linked to acute meniscal tears. The joint swelling associated with a meniscus tear is more likely to manifest in a delayed manner (>24 hours); mechanical symptoms including popping, clicking, and occasionally a sense of the knee giving way, which tend to wax and wane with levels of activity [2].

Joint imaging is necessary for a precise diagnosis of meniscal tears. Magnetic resonance imaging (MRI), which is presently the diagnostic tool of choice in the examination of menisci tears, has practically displaced knee arthrography. MRI has been shown to be more than 90% accurate in detecting meniscal tears [3].

Meniscal injuries may be categorised into four classes (0–3) using MRI imaging. Meniscus grade 1 lesions show mucoid degeneration but no evidence of ruptures. MRI findings compatible with a grade 2 lesions (an intrasubstance defect without superficial disruption) might be interpreted as an early-stage meniscal rupture. MRI findings consistent with a grade 3 lesions (a whole meniscal rupture with an interruption of the meniscal surface) indicate a full-blown meniscal rupture[4].

When a meniscus is injured, it is obvious that the damaged tissue cannot recover on its own; instead, healing relies on the injury location having an adequate blood supply and/or growth factors [5].

An autologous blood product called platelet rich plasma (PRP) has platelet concentrations above the normal range [6]. Due to the platelet-released growth factors, which are thought to have a variety of regeneration qualities**,** it is used therapeutically[5].

PRP has been shown in laboratory studies to have a favourable impact on meniscal cells. PRP might offer growth factors that improve meniscus repair by encouraging cellular proliferation and vascularization [6].

The efficacy of intra-articular administration in large joints, especially the knee, is improved by the use of image guidance, particularly ultrasound. Additionally, precise intraarticular knee injections guided by ultrasonography lead to better clinical results and fewer medical costs [7].

In patients with grade 2 post-traumatic knee meniscal damage, the purpose of this research was to assess the effectiveness of PRP injection assisted by ultrasonography on clinical and functional improvement.

Patients and Methods:

This prospective cohort observational study was carried out on forty patients with evidence of post traumatic knee meniscal lesion grade 2 on MRI imagingaged ≥ 18 years old. All patients who had chronic knee joint pain for over three months were included in this study if they had an MRI showing a grade 2 meniscal lesion and had not responded to a three-month regimen of conservative treatment, which included activity adjustment, including quitting sports, physiotherapy, and NSAIDs.

The patient provided written permission after being fully briefed. The study was conducted with the agreement of the Ethical Committee for Research at the Faculty of Medicine at Tanta University in Egypt.

Osteoarthritis with a Kellgren-Lawrence score > grade 2, lateral or medial displacement of the mechanical axis >10 mm, a meniscal lesions or prior knee injury, generalised inflammatory arthritis, systemic illnesses, severe infection, pregnancy, and known cancer were all excluding criteria. Extracorporeal shock wave treatment (ESWT) and corticosteroid administrations into the knee joint within the previous three months, nerve-related issues

including radiculopathy, bleeding issues or anticoagulant medication, and prior knee surgery are all causes for exclusion.

Clinical assessment:

By complete history taking: Age, sex, occupation, medical illness, side of affection, duration of the disease.

Assessment of pain by using Visual Analogue Scale (VAS): It includes a 10-cm straight line with labels such as "no pain" and "the greatest pain conceivable" placed at each end [8].

Assessment of degree of tenderness: Knee was assessed for tenderness by firm pressure over joint margin (joint line tenderness and tenderness on patellofemoral compression). According to the modified Ritche articular index, soreness was graded on a 4-point scale as follows: (0=no tenderness, 1=patient reported pain, 2=patient reported pain and grimaced, and 3=patient complained of pain, grimaced, and retracted the joint)[9].

Assessment of Range of Motion (ROM): With the patient supine, the investigator used an international goniometer to measure the ROM.The lateral femoral condyle served as the pivot point for the international goniometer, which was used to measure the ROM. The greater trochanter and lateral malleolus were the locations of the goniometer's fixed and movable arms, respectively. Patients engaged their affected knee to its fullest extent without the aid of an investigator or the use of their upper extremities during active ROM. The patient's knee was passively manipulated from full extension to full flexion by the observer. ROM was calculated using the arc lengths between the full extension and flexion [10].

Assessment of swelling: Assessment of knee effusion (present or absent). A variety of clinical examinations have been performed to determine if knee effusion is present, including palpation examinations like the ballottement and patellar tap tests and visual assessment of swelling [11].

Functional assessment: Using Knee Injury and Osteoarthritis Outcome Score (KOOS) which were done before injection and 4 months after the last injection.They have been shown to be effective when used with people who have meniscus injuries. Patients are asked to rate their own pain, function, symptoms, and quality of life (QOL) using these tools [12].

KOOS: It assesses the long- and short-term effects of knee injuries. It has 42 components divided into 5 individually graded subscales: pain, other symptoms, sport and recreation (Sport/Rec), function in daily living (ADL), and QOL [13][14, 15].

Each question has five potential answers, each of which is graded between 0 (No Problems), 1 (Mild), 2 (Moderate), 3 (Severe) and 4 (Extreme Problems)[16].

Each subscale's (e.g. KOOS Pain) mean value for the observed items is calculated by dividing it by four (the maximum rating for a single response choice) and then multiply by 100, then the result is subtracted from 100 to transform the score to a 0–100 scale (with 100 reflecting no knee issues and zero denoting severe knee issues) [13, 16].

NSAIDs use was discontinued by all patients for seven days prior to the administration.

Ultrasound guided injection:

Sterile aseptic procedures were followed while administering the injection. By cleaning the region of the injection site with a 70% alcohol-based solution (ethanol), sterilisation was achieved. All the patients underwent ultrasound guided PRP injection at the affected knee meniscal area in the ultrasound section of Tanta University Educational Hospital's Physical Medicine, Rheumatology, and Rehabilitation Department, utilizing SAMSUNG MEDISON (UGEO H60), with linear array transducers (frequencies ranging between 6-15MHz).The knee had been positioned at 45° of flexion with the patient supine for visualization of the anterior horns and mid zone and fully extended with the patient prone for visualization of the posterior horns.(143)The transducer is positioned longitudinally over the joint line and is always pointed perpendicular to the meniscus in order to inspect the menisci [17].

The transducer (6-15 MHZ) was placed across the articular line from the long axis of the tibio-femoral bone. Using a freehand approach, a needle was then pushed into the meniscus wall while being directly guided by sonography (Once the needle hit the meniscus wall, it was withdrawn by 1 mm and an injection was administered while strictly adhering to aseptic administration procedure) [18].

Post injection:

We applied the ice pack for ten to fifteen minutes. After the operation, we advised the patient to cease using all anti-inflammatory drugs for 4 months, with the exception of acetaminophen. All patients were permitted to bear their full weight, however it was advised to delay physical therapy and vigorous exercise for at least four weeks following the last injection. [4].

Patients were assessed clinically, functionally 4 months after the last injection.

Statistical analysis

With the aid of the IBM SPSS software package version 20.0, data were input into the computer and analysed. Number and percentage were used to describe qualitative data. The normality of the distribution was examined using the Kolmogorov-Smirnov test. The range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR) were used to characterise quantitative data, and the paired T test or marginal homogeneity test was used to compare them. At the 5% level, significance of the findings was determined.

Results:

Most of the patients were male with sport related injury being the most common cause of knee injury. Table1

Table 1: Patient characteristics of the patients (n=40)

	NO (%)
Gender	
Male	31 (77.5)
Female	9 (22.5)
Age (years)	

Mean ± SD	30.33 ± 9.17
BMI (kg/m^2)	
Mean ± SD	23.85±0.83
Cause of knee injury	
Sport related injury	25 (62.5)
Football	23 (92.0)
Wrestling	2 (8.0)
Activities with rapid stepping on an uneven surface and or twisting	15 (37.5)
Occupation	
Student	17(42.5)
Manual worker	14 (35.0)
Housewife	9 (22.5)
Disease duration (months)	
Mean ± SD.	7.38 ± 2.83
Side of knee injury No. (%)	
Right	24 (60.0)
Left	16 (40.0)

Most of our patients were posterior horn medial meniscus degeneration. Table 2

Table 2: MRI assessment of the patients before injection (n=40)

	No. (%)
Meniscal lesions (grades)	
Grade 2 meniscal lesion	40 (100.0)
Location	
Medial Meniscus (post horn)	38 (95.0)
Lateral Meniscus	2(5.0)

Table 3

Table 3: Comparison between clinical assessment of the patients before injection and 4 months after the last injection (n=40)

	Before injection	After injection	Test of Sig.	p
Pain by VAS				
Min. – Max.	5.0 – 9.0	1.0 – 5.0	t=31.416*	<0.001*
Mean ± SD.	6.73 ± 1.04	2.75 ± 1.01		
Median (IQR)	7.0 (6.0 – 8.0)	3.0 (2.0 – 3.0)		
Active ROM				
Extension				
Min. – Max.	170.0 – 180.0	175.0 – 180.0	t=17.423*	<0.001*

Mean ± SD.	174.50 ± 3.36	178.12 ± 2.45		
Median (IQR)	175.0 (170.0–175.0)	180.0 (175.0–180.0)		
Flexion				
Min. – Max.	105.0 – 120.0	120.0 – 130.0	t=10.140*	<0.001*
Mean ± SD.	114.13 ± 4.79	126.13 ± 3.10		
Median (IQR)	115.0 (110.0–120.0)	125.0 (125.0–130.0)		
Knee joint tenderness grading	**No. (%)**	**No. (%)**		
0	0(0%)	6(15.0%)	MH= 58.50*	<0.001*
1	4(10%)	34(85.0%)		
2	29(72.5%)	0(0.0%)		
3	7(17.5%)	0(0.0%)		

MH: Marginal Homogeneity Test, t: Paired t-test, p: p value for comparing between Before and after injection
*: Statistically significant at $p \leq 0.05$

There was significant improvement as regard pain, symptoms, activities of daily living (ADL), sport and recreation function and QOL before injection and 4 months after injection.

Table 4

Table 4: Comparison between functional assessment of the patients as regard Knee Injury Osteoarthritis Outcome Score (KOOS) before injection and 4 months after the last injection (n=40)

	Before injection	After injection	t	p
Pain subscale				
Min. – Max.	22.23 – 63.89	58.34 – 86.12	17.846*	<0.001*
Mean ± SD.	42.78 ± 11.53	73.58 ± 8.0		
Median (IQR)	41.67 (33.34–52.78)	75.0 (68.09–78.80)		
Symptoms				
Min. – Max.	25.0 – 50.0	46.43 – 82.15	25.057*	<0.001*
Mean ± SD.	39.65 ± 7.27	66.41 ± 8.57		
Median (IQR)	40.29 (33.15–46.43)	67.86 (60.72–73.22)		
ADL				
Min. – Max.	20.59 – 64.71	36.77 – 79.42	13.567*	<0.001*
Mean ± SD.	44.52 ± 10.65	68.39 ± 12.74		
Median (IQR)	45.59 (36.77–50.0)	75.74 (57.36–77.95)		
Sport &recreation function				
Min. – Max.	10.0 – 55.0	50.0 – 80.0	25.868*	<0.001*

Mean ± SD.	31.37 ± 11.82	69.25 ± 6.75		
Median (IQR)	30.0 (20.0–40.0)	70.0 (65.0–75.0)		
QOL				
Min. – Max.	12.50 – 56.25	50.0 – 75.0	20.941*	<0.001*
Mean ± SD.	34.27 ± 12.06	67.96 ± 6.82		
Median (IQR)	31.25 (25.0–43.75)	68.75 (62.50–75.0)		

t: Paired t-test, IQR: **Inter quartile range,** p: p value for comparing between **Before** and **after injection**,*: Statistically significant at $p \leq 0.05$

Discussion

Analgesics, activity moderation, physical therapy, and intra-articular injections are some of the more conservative treatments for meniscal lesions in addition to surgical procedures including meniscectomy and meniscal repair/reconstruction. Another less intrusive method for managing meniscal tears is intra-articular injections, which are more often made up of hyaluronic acid, corticosteroids, and PRP [19, 20].

Growing interest has been shown in Orthobiologics' potential to treat meniscal disease in recent years. Even though the majority of research focused on improving meniscal healing, a few studies also evaluated the effectiveness of Orthobiologics injections as the only therapy for meniscal tears [21].

An autologous blood product called PRP has platelet concentrations above the normal range. PRP might offer growth factors that improve meniscus repair by encouraging cellular proliferation and vascularization [22].

Activated platelets are a source of growth factors like fibroblast growth factor, platelet-derived growth factor, transforming growth factor beta, insulin-like growth factor, and vascular endothelial growth factor (VEGF), that could control meniscus cellular proliferation.VEGF may encourage vascularization of the meniscus' avascular white-white region, and transforming growth factor beta could entice and stimulate a variety of cell types,

such as bone-marrow-derived stem cells or fibroblasts to distinguish meniscus cells in the surrounding structures [22, 23].

Clinical evaluation of the affected knee joint before injection has found that, pain assessed by VAS was ranged from 5.0 – 9.0 with a mean of 6.73 ±1.04, tenderness grading of Knee joint line 72.5 % were grade 2, 17.5 % were grade 3and 10% were grade 1. As regard active ROM of our patients (flexion degree) ranged from 105.0 – 120.0 with mean of 114.13 ± 4.79. while (extension) ranged from 170.0 – 180.0 with mean of 174.50 ± 3.36.

Also, functional assessment was done using KOOS that consists of 5subscales. Pain subscale of KOOS ranged from 22.23 – 63.89 with mean of 42.78 ± 11.53, symptoms subscale ranged from25.0 – 50.0 with mean of 39.65 ± 7.27, ADL subscale ranged from 20.59 – 64.71 with mean of 44.52 ± 10.65, sport& recreation function subscale ranged from 10.0 – 55.0 with mean of 31.37 ± 11.82 and quality of life subscale ranged from 12.50 – 56.25 with mean of 34.27 ± 12.06.

Functional affection of patients with meniscal injuries explained by **Tornbjerg et al.**[24] who found that,in individuals with traumatic meniscal injury, rising levels of synovitis were slightly related to worse performance during vigorous activity (i.e., sport/Rec function).

Radiological assessment of our patients was done by MRI at start of study before injection that was found that 95.0% of our patients were posterior horn medial meniscus and 5% were lateral meniscus,

Also, this agreed with **Lento** and **Akuthota**[25] who stated that,because of its close relationship with the medial collateral ligament, the medial meniscus is more prone to damage. With the exception of ACL injuries, the movable lateral meniscus is less likely to rupture.

Due to the substantial load carrying that affects the posterior section of the medial meniscus, its posterior root is most often affected. The medial meniscus is also more susceptible to

damage and degeneration over time since it is often exposed to more stresses than the lateral meniscus [26].

Regarding clinical assessment of our patients 4 months after the last injection, there were significant improvement of pain assessed by VAS, tenderness grading of Knee joint, active ROM (flexion degree and extension angle).

Our findings were in line with those of **Elnemr et al**. [27], who examined the impact of a 6-monthly intra-articular administration of PRP on knee pain in meniscal repair patients who presented with knee pain within four months of surgery. They found a significant reduction in VAS score (1-3) versus baseline values (7 - 10).

This was also in conflict with **Urzen** and **Fllerton** [28], who detailed a case report of a 43-year-old male with a bucket handle meniscal rupture at PHMM that was validated by an MRI. The patient claimed that the pain was gone while he slept, walked, and went about his normal activities after receiving 3 injections of 7ml PRP at 6, 16, and 27 weeks following the accident. He also reported a considerable drop in VAS from 8 to 3 along with less occurrences of knee locking.

In contrast to our improved clinical results, some studies as **Li Dai et al.**[29] and **Kaminski et al. [30]** studied the augmentation effect of PRP injection after arthroscopic meniscal suture repair and concluded that there were no significant difference of VAS after 12 and 24 months follow up between PRP and non PRP group.

As regard functional assessment of our patients 4 months after the last injection, there were significant improvement of and pain, symptoms, ADL, sport and recreation function and QOL subscales of KOOS.

n the PRP-treated group than in the non PRP treated group.

Additionally, **Pujol et al. [31]**evaluated whether PRP might be used during open meniscal repair surgery for grade 2 or 3 meniscal injuries and found that Functional outcomes include

IKDC, and KOOS scores were somewhat greater in the PRP-group compared to the control group.

This was consistent with **Betancourt et al**[32] who examined the results of an US-guided administration of leukocyte-poor PRP in a case study involving a 29-year-old woman with a medial meniscus tear grade 3 that was confirmed on MRI at the 30-month follow-up. The results showed improvements in the VAS and KOOS pain scores, with the VAS decreasing from 70 mm to 40 mm and the KOOS increasing from 39 to 63.1.

However, our results disagreed with **Griffin et al.**[33]who examined the use of PRP in arthroscopic meniscal correction in subsequent meniscectomy and functional outcome measures, especially IKDC over the period of 3 years and discovered no difference in reoperation incidence or functional outcome measures between the PRP and non-PRP groups.

Our results regarding clinical and functional improvement of our patients 4 months after the last injection can be explained as follow:

Tumour necrosis factor (TNF)-α, IL-1β, IL-6, IL-8, IL-10, and proteoglycan, are all present in higher amounts in the synovial fluid of the knee joint after any trauma. Meniscal tissue exposed to IL-1 and TNF-α has reduced matrix synthesis and glycosaminoglycan (GAG) content, resulting in the activation of catabolic pathways including matrix metalloproteinases, nitric oxide, and prostaglandin E2 [34].

As a result, the following is the suggested mechanism of action of PRP in healed menisci: (a) it provides the injury site with a variety of growth factors, such as vascular endothelial growth factor, platelet-derived growth factor, and transforming growth factor beta 1; these growth factors are known to enhance angiogenesis, chemotaxis, collagen matrix formation, and cellular proliferation and differentiation [35], (b) by lowering the hyperplasia of the synovial membrane and adjusting the quantity of cytokines, it may also have an impact on joint homoeostasis, (c) PRP's anti-inflammatory actions on the whole joint have an impact on

the meniscal tissue's healing process as well as the health of the undamaged articular cartilage and meniscal tissue, and (d) direct activation of synoviocytes known to contribute to meniscal healing and overall joint health[34, 36].

These processes, which have no impact on the structure of the cartilage tissue, result in a temporary improvement in clinical outcomes. The stronger responsiveness to GFs and larger proportion of alive and functional cells in less deteriorated joints may account for the superior clinical outcomes seen in individuals with less severe cartilage damage [37].

Thus, reduction of inflammatory mechanisms might be the predominant mechanism of PRP action than tissue regeneration itself. Also reduced inflammatory cell chemotaxis toward synovium and periarticular tissue lead to decreased pain and increased mobility after PRP injection [38].

Further studies on larger samples, different dose injection and longer follow-up periods are required to detect the efficacy of PRP injection in long- term benefits (functional and radiological). Further prospective randomized studies with larger patients numbers are required to comparePRP with different treatment modalities.

Conclusions:

Peri-meniscal PRP injection under ultrasound guidance in patients with post traumatic knee meniscal lesions grade 2 with persistent pain appears to be an effective method for pain relief. Peri-meniscal PRP injection is able to achieve improvement in clinical and functional scores after 4 months follow up. Musculoskeletal ultrasonography is a fundamental tool for peri-meniscal areas injections to guarantee its accuracy and maximizes its benefits.

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