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Assessment Autologous Bone Marrow Derived Cells with Core Decompression as Treatment Option for Avascular Necrosis of the Femoral H

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avascular necrosis of the head of femur, bone marrow derived cells, cell therapy, hip.

ABSTRACT
Background: Avascular necrosis of the femoral head (AVN) is a progressive pathological process resulting from disruption of blood supply to the femoral head and elevation of intraosseous pressure. Early stage AVN can be managed by various techniques, the results have been disappointing, total hip arthroplasty is frequently the only durable option for pain relief and restoration of function. The newer treatment modalities include using high stem cell concentration in the vicinity of the necrosed tissue with core decompression to prevent disease progression. Patients and methods: A single armed study done from October 2017 till February 2019, the total number of patients was 10, (5 Female 5 male). Etiology include corticosteroids use, systemic lupus erythematosus, sickle cell disease and idiopathic. The age of the patients range from 25-57 years. The procedure includes core decompression with autologous bone marrow derived mononuclear cell injection inside the hip joint space. Results: The results showed improvement in the Harris hip score from 48.7±6.6 to 88.00±4.6 ($p<0.001$) in seven patients. With radiological proof by magnetic resonance imaging. Conclusions: This single arm short term study showed that core decompression with autologous bone marrow derived cell therapy is safe and effective method and it is a form of minimal manipulative treatment and merits such treatment in larger and longer term study.

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INTRODUCTION

Avascular necrosis of the femoral head (AVN) is a progressive pathological process resulting from disruption of blood supply to the femoral head and elevation of intraosseous pressure. The pathophysiology of avascular necrosis (AVN) is unclear in spite of attempts to provide a proper model. However, there are several recognized conditions and environmental insults that can predispose patients to AVN. Traumatic causes include fracture head or neck of the femur, nontraumatic causes include sickle cell anemia, endocrine conditions like Cushing syndrome, auto immune disease like systemic lupus erythematosus, use of corticosteroids, alcoholism, organ transplantation and others.

Although these factors may increase a patient's risk for developing AVN, others propose that the disease results from a clotting disorder or genetic abnormality that leads to vascular compromise.

In idiopathic cases the underlying abnormality may be a coagulation factor gene defect. Symptoms can vary widely, depending on the stage at presentation, In the earlier stages of AVN, patients may note an insidious onset of pain, without a clear cause or inciting event, and will often have a normal range of motion; however, this can be limited by pain, especially with internal rotation of the hip. With progression of the disease, this insidious groin discomfort may be followed by a sudden onset of severe pain, Late-stage disease is marked by mechanical difficulties with reduced motion and painful movements. The diagnosis of AVN is usually done by clinical and radiological signs; early stage disease needs better resolution like in MRI (magnetic resonance imaging) or computed tomography. Late-stage disease can be seen by plain X-ray. radiological features are important in staging the disease for proper treatment .[1]

Usually AVN affects patients aged 20-40 years with the average presenting age is 38 years. [2] Early stage AVN can be managed by various techniques, (core decompression, osteotomy, and medical treatments), the results have been disappointing, with up to 40% of patients progressing to total hip arthroplasty, however advanced stages 3 or more according to Steinberg classification .[3] total hip arthroplasty is frequently the only durable option for pain relief and restoration of function .[4] The newer treatment modalities include using high stem cell concentration in the vicinity of the necrosed tissue with core decompression to prevent disease progression. [5].

Patients and Methods

Patient's characteristics:

A single armed study done from October 2017 till February 2019, the total number of patients was 10, while the number of femur head was 17. Female patients were 5 and male patients 5.

Etiology include corticosteroids, systemic lupus erythematosus, sickle cell disease and idiopathic. The age of the patients range from 25-57 years. The stage of the disease were early in 7 cases, 3 cases were advanced according to Steinberg score. (Table1) Bilateral femoral head involved in 7 cases. Steinberg classification for avascular hip necrosis begins from stage zero with normal joint without pain or radiological

evidence of necrosis, to stage 6 with advanced degenerative changes.

Table 1:Steinberg classification for avascular necrosis of the femoral head.

Stage	**0**
No symptoms	**Normal X-ray**
MRI non diagnostic	
1	
	Mild pain in the affected hip Pain with internal rotation Normal X-ray MRI diagnostic
2	
	worsening or persistent pain Increased sclerosis or cysts in the femoral head
3	
	Subchondral collapse producing a crescent sign
4	
	Flattening of the femoral head
5	
	Normal joint space Joint space narrowing with/without femoral head involvement
6	
	Advanced degenerative changes

Procedure:

Under general anesthesia after getting patient consent, a 2-3 mm incision is made in the skin over the posterior iliac crest using a disposable bone marrow aspiration needle with multiple site aspiration to withdraw around 60 cc of bone marrow to be concentrated into 6 cc which is sufficient for one hip joint.

An incision is made over the lateral aspect of the femur at the level of vastus ridge just above the level of lesser trochanter 6 mm trochar is advanced with a 3 mm guide wire the site of the avascular area was penetrated and using 3.2 mm of cannulated drill bit over the guide wire the lesion was drilled under screen. The 4 ml of bone marrow cells was injected to the site from anterior approach. After the procedure all patients are discharged home and allowed to weight-bear as tolerated with crutches for 2 weeks.

RESULTS

Table 2 showed the results of our study, clinical response was remarkable including reduction in pain and improvement in joint mobility very early after the procedure, and one year from the start, the Harris hip score showed improvement in 7 cases out of ten (70%). The score improved from 48.7±6.6 to 88.00±4.6 ($p<0.001$). Also the AS scores for Quality of Life Score for Chronic Hip Disease was assessed and found at 9 The score is 10 in normal and 1 in severe limitation.The radiological evaluation using MRI significantly correlated. As the lesion converted from Mitchell's grade C to grade B after the procedure by 6 months.

The HHS and the AS score for Quality of Life Score for Chronic Hip Disease. The cellular concentration was 1x10 8 bone marrow derived mononuclear cells in the whole product in a volume of 4-10 cc.

Table 2. Patient's characteristics and response.

No.	Age	Sex	Dx	involvement	HH score
1	57 y	Male	idiopathic	unilateral	from 44 to 90
2	57 y	Female	SCD	bilateral	from 52 to 86
3	50 y	Male	steroids	bilateral	NS
4	35 y	Male	idiopathic	bilateral	from 43 to 86
5	30 y	Male	idiopathic	bilateral	from 53 to 85
6	48 y	Male	idiopathic	bilateral	from 45 to 85
7	30 y	Female	SLE	bilateral	NS
8	30 y	Female	idiopathic	unilateral	from 43 to 90
9	30 y	Female	SLE	bilateral	from 42 to 88
10	25 y	Female	SLE	unilateral	NS

DISCUSSION

We found that bone marrow derived cell injection injection at the site of the avascular necrosis of the head of the femur in early stage disease showed decreased in the pain scale from 8 to 1 in all patients after the procedure and in seven patients at one year time.

Marked MRI Improvement was observed in seven patients out of ten in 6-month time after the procedure. The Mitchell's grade regressed from C to B in seven patients.

Using autologous bone-marrow mononuclear cells implantation is a safe and effective procedure. Our results are promising and comparable with those of previous smaller studies comparing the use of bone marrow derived cells with core decompression to core decompression alone, there was a significant improvement in Harris Hip Scores between the CDBM core decompression groups [6-8]

A large review of 11 studies with 507 participants showed that core decompression with bone marrow cell injection was more effective than core decompression alone and increased Harris hip score[9].

Regarding pathophysiology it is known that there is an increase in the fatty tissue inside the intertrochanteric portion of the osteonecrotic hip with a significant reduction in stem cell pool [10].

One of the important facts in the clinical outcome of the bone marrow procedure for avascular hip necrosis is the concentration of the bone marrow cells near the necrotic area; we observed that in most procedures that were done they mentioned the use of 10 cc syringes with steady pressure aspirate [11].

We should point to the following facts that are very important to gain best cellular content:

1-High concentration of stem cells is usually yielded in the first few cubic centimeters aspirated, as more peripheral blood cells usually follow.

2-Multiple punctures with larger volume syringes are more preferable than small volume ones with single site aspirates.

In our study we used a mean of 1x10 8 mononuclear cells in the total volume injected.

The data showed that the total number of MSCs present in 1 cm^3 of a femoral head was on average of 700 ± 264 MSCs per cm^3. Since the femoral head has an average volume of 50 cm^3, a total of 35,000 MSCs may be considered as a useful approximation of the number of MSCs present in a femoral head [12].

It is a very important task to clarify the precise factors in the pathophysiology and healing process as there is a multitude of variables including type of cells (bone marrow or mesenchymal cells, osteoblasts or others) source (bone marrow, adipose, others) concentration, timing disease stage, and procedure that need to be discussed in future work[13,14].

CONCLUSION

This single arm short term study showed that core decompression with autologous bone marrow derived cell therapy is safe and effective method and it is a form of minimal manipulative treatment and merits such treatment in larger and longer term study.

CONFLICT OF INTEREST

No financial interest or any conflict of interest exists.

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Abbreviations:

SCD=sickle cell disease, SLE=systemic lupus erythematosus, NS=non-significant.