ISSN: 0976-3031

Available Online at http://www.recentscientific.com

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 8, Issue, 6, pp. 17943-17947, June, 2017

International Journal of Recent Scientific Research

DOI: 10.24327/IJRSR

Research Article

EVALUATION OF ORTHOBIOLOGICS FOR MANAGEMENT OF AVASCULAR NECROSIS OF HEAD FEMUR: AN INNOVATIVE SURGICAL TECHNIQUE

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ARTICLE INFO

Article History:

Received 17th March, 2017
Received in revised form 21th April, 2017
Accepted 28th May, 2017
Published online 28th June, 2017

Key Words:

Aseptic osteonecrosis; Femoral head; Bilateral core decompression; Stem cell.

ABSTRACT

In this prospective study, total 13 patients of idiopathic avascular necrosis of head femur with 20 affected hips were managed by core decompression and autologous bone marrow derived stem cell infusion. Bone marrow aspiration was followed by mononuclear cell separation and then subsequently injecting the same up to the necrotic area of the femur head. These patients were followed up clinico-radiologically at 3rd, 6th, 12th, and 24th weeks and at one year post operatively. In this study, we observed significant improvement in pain at one year follow-up as per VAS. Improvement of trendelenburg gait and range of movement at final follow-up were significant. Harris hip score during follow-up improved significantly. Core decompression and stem cell infusion is one of the less traumatic viable alternate treatment options for management of idiopathic avascular necrotic head femur.

INTRODUCTION

The aseptic osteonecrosis (avascular necrosis) of the femoral head (AVN) is a condition that results due to the reduction in an already precarious blood supply. It is a debilitating disease with multiple etiological risk factors (Lavernia *et al*., 1999; Mont *et al*., 1998). Gluco-corticoids and alcohol abuse are amongst the most widely recognised risk factors for non-traumatic osteonecrosis of the femoral head (Steinberg, 1995). Intra-osseous hypertension (Wang *et al*., 1981) and abnormalities of the blood supply (Steinberg, 1995) are the most accepted theories of the pathogenesis of the disease. Clotting disorders and genetic abnormalities causing a vascular compromise have also been considered as potential causes.

With progression of disease, the femoral head collapses, leading to hip pain and disability (Jones *et al*., 2003; Hernigou *et al*., 2004; Hernigou *et al*., 2003; Cheng *et al*., 2004). The advanced stage of the disease is hallmarked by painful restriction of the range of hip motion leading to degenerative arthritis (Houdek *et al*., 2014). If AVN is identified during the early stages the joint is amenable to salvage by a variety of hip preservation techniques. However, if the disease has progressed to an advanced stage, total hip arthroplasty (THA) is the only viable option for pain relief and restoration of function (Houdek *et al*., 2014).

Though there are several techniques to halt the progression of the disease process (including medical treatments, core decompression and osteotomies), then too approximately 40% of the patients still require a THA eventually (Hungerford, 1983). The results of these head preserving surgeries have been inconsistent which has led to innovative therapeutic methods like stem cell infusion or growth factor administration (Li *et al*., 2016). Core decompression was first described by Arlet and Ficat in 1964 with an aim to improve repair in the osteonecrotic segment. It is the most commonly used technique for early stage AVN but its efficacy has been debatable (Yan *et al*., 2009).

Several studies have advocated the use of stem cells citing its various benefits like promoting bone formation and neovascularization. The bone marrow mesenchymal stem cells have powerful capabilities of self-proliferation and multi potent cell differentiation. It is believed that stem cells implanted in the necrotic area of the femoral head differentiate into osteoblasts and vascular endothelial cells which promote bone repair and regeneration (Yan *et al*., 2009; Lau *et al*., 2014).

The purpose of present study was to assess the clinic-radiological outcome of patients with avascular necrosis of the head of femur managed by core decompression and autologous bone marrow derived stem cell infusion.

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MATERIALS AND METHODS

This prospective study was carried out in the Department of Orthopaedic Surgery of our institution in patients presenting at the outpatient department. A total of 13 patients of idiopathic avascular necrosis of head of femur with a total of 20 hips were managed by core decompression and stem cell infusion from January 2014 to January 2016.

All adults above the age of 18 years with early stage AVN of the hip (upto Ficat Arlet Stage 2) and giving consent for the procedure were included in the study.

Patients less than 18 years and with Ficat Arlet stage 3 or 4 were excluded. Patients with other causes of hip arthritis, the cases with AVN secondary to alcohol intake, steroid intake or bleeding disorders were also excluded from the study.

An eligibility questionnaire was filled out by the included patients and a written consent was taken. All the patients were examined thoroughly after a detailed history and the specific parameters were noted (Table-1). The patients were then evaluated for their fitness for surgery and anaesthesia as per our institution norms.

Table 1 List of different parameters taken from the enrolled patients.

- Demographic data
- Occupation of the patient
- Side of involvement
- Symptoms duration
- Need for painkillers per day
- Tenderness at the hip joint
- Trendelenburg gait and limp
- Limb length discrepancy
- Range of motion in both hips
- Pre-operative Harris Hip Scores
- All patients were subjected to radiological examinations with X ray pelvis with both hip-AP: radiological staging as per Ficat Arlet Classification was done.
- An MRI was done to assess the condition of the head and to confirm the extent of necrosis of head femur.

Surgical Technique

All patients were operated under regional anaesthesia. All surgeries were performed by the same surgeon in the supine position. In the present study approximately 120 ml bone marrow was harvested from the iliac crest and mononuclear cells were concentrated to a final volume of 6 ml (Figure-1). By the time the aspirate was concentrated using the centrifuge, an approximately 5 cm incision was given on the lateral aspect of hip to reach the area of trochanteric flare. 2 holes with 4 mm Cannulated drill were made into the head by gentle tapping and twisting movement up to the necrotic area under image guidance. Once the correct position was confirmed, the inner core was removed and a hollow was obtained. At this stage a biopsy sample was also obtained that was sent for histo-pathological evaluation to confirm the diagnosis. The stem cell concentrate soaked into sterile gelfoam strips was then introduced sequentially upto the necrotic core of the femur head. This prevents undue run off the aspirate and maintained sustained delivery over a longer time period. The defect on the lateral aspect of the shaft was sealed using bone wax after removing the hollow trochar shell.

Post Operatively

Non weight bearing range of motion exercises were started as soon as possible as per the patient's pain tolerance. All the patients were kept non-weight bearing for 3 weeks post operatively. This was followed by partial weight bearing for the next three weeks and then full weight bearing was allowed at six weeks post operatively.

Follow Up

The patients were followed up at 3 weeks, 6 weeks, 12 weeks, 24 weeks and at one year period post operatively. At each follow up, the following points were noted for patients:

- Limb length discrepancy if any
- Trendelenburg gait
- The daily anaelgesic need if any
- Range of motion at the hip joints
- Harris hip Score

Radiological evaluation using X-rays of pelvis with both hip - AP was done at 06 month and 01 year and MRI done at 1 year follow up post operatively.

Statistical analysis

Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA) for Windows program (15.0 version). The continuous variables were evaluated by mean, median and mode value when required. For comparison of the means between the two groups, analysis by Student's t-test, Tukey-Kramer Multiple Comparisons Test (ANOVA) with 95% confidence interval was used. A p-value < 0.05 or 0.001 was considered as significant.

RESULTS

A total of 13 patients with 20 hips were included in our study and were evaluated. The biopsy confirmed the diagnosis. A total of nine (69.2%) males and four (30.8%) females were included with an average age of 32.6 years (18-54 years). Seven patients (53.8%) underwent a bilateral core decompression and bone marrow derived mononuclear cells infusion. The average duration of symptoms before surgery was 11.7 months (2 - 24 months). Eight (61.5%) of the thirteen patients needed at least two or more painkillers every day at the time of presentation while the other five needed one painkiller on a daily basis. The average pre-operative and final Harris Hip score (HHS) was 61.9 ± 2.73 and 78.6 ± 2.77 respectively.

Ten (76.9%) patients at the time of presentation were with an average shortening of 01 cm (0.5-1.3 cm). None of the patients required any shoe raise. The trendelenburg gait was found to be positive in ten (76.9%) patients at the time of presentation whereas a total of three (23.1%) patients had a trendelenburg gait at the final follow up. Based on radiological studies, seven (53.8%) patients were at the Ficat Arlet stage 1 and thirteen (100%) at stage 2 at the time of presentation. There was no worsening of Ficat Arlet staging in any patient at one year follow up.

Based on radiological studies, seven (35%) hips were at the Ficat Arlet stage 1 and thirteen (65%) at stage 2 at the time of presentation. All patients underwent a core decompression

followed by stem cell infusion as described in the technique above.

Table 2 Average Harris Hip Scores

Average Harris Hip Score	Pre-OP	Follow up at 6th months	Follow up at one year	P- value
Males (9)	61.22 ± 2.89	70.78 ± 2.96	78.0 ± 2.72	P< 0.0001*
Females (4)	63.5 ± 2.67	71.25 ± 2.87	80.25 ± 2.86	P< 0.0001*
Total	61.9 ± 2.73	70.9 ± 2.81	78.6 ± 2.77	P< 0.0001*

Tukey-Kramer Multiple Comparisons Test (ANOVA); Significant*

Table -2 details the preoperative and follow-up average range of movements and Table-3 the average Harris respectively [Figure-2, Graph-1].

Table 3 Average range of motion at the hip joint

Movement	Pre-OP	Follow up at 6th months	Follow up at one year	P-value
Flexion	67.4 ± 2.45	98.8 ± 3.51	102.1 ± 3.22	P< 0.0001*
Extension	1.6 ± 0.23	6.45 ± 0.67	6.5 ± 0.89	P< 0.0001*
Adduction	16.5 ± 1.62	22.5 ± 1.71	24.3 ± 1.22	P< 0.0001*
Abduction	19.3 ± 1.26	26.2 ± 1.65	28.9 ± 1.13	P< 0.0001*
Internal Rotation	12.3 ± 1.39	17.2 ± 1.01	19.45 ± 1.07	P< 0.0001*
External Rotation	27.8 ± 1.41	30.9 ± 2.12	33.4 ± 2.18	P< 0.0001*

Tukey-Kramer Multiple Comparisons Test (ANOVA); Significant*

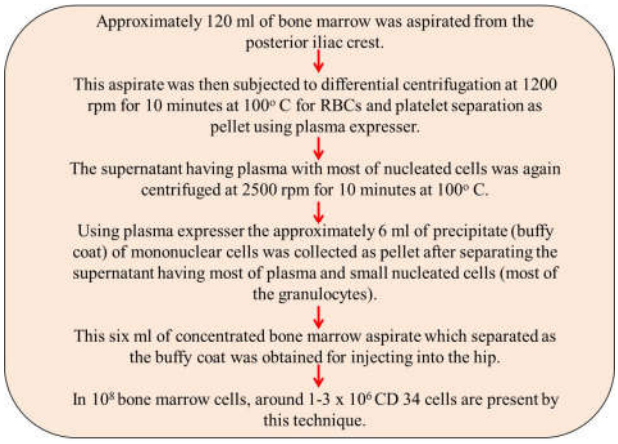


Figure1 Differential centrifugation method to separate the mononuclear cells

None of the case had any complication in the peri-operative period. All patients had significant pain relief at the final follow up of one year with an average of 63% pain relief as per the Visual Analogue Scale (VAS). Only two (15.6%) patients required analgesics on SOS basis at the final follow up of one year. The post-operative MRI at one year showed revascularization of the necrotic area with lesser oedema.

DISCUSSION

AVN of the femoral head presents frequently in the age group 20-40 years (Lavernia *et al*., 1999; Mont *et al*., 1998). In early stages of AVN, patients usually present with pain without any noticeable cause without any limitation of range of movement. As the disease progresses, patients develop more pain and mechanical restriction leading to a poor quality of life. Even though many joint preserving surgeries have been tried, none have provided with consistent results. As a result, most late stages AVN end up in a Total Hip arthroplasty eventually (Steinberg, 1995; Wang *et al*., 1981; Jones *et al*., 2003).

Core decompression is a technique used in early stages of AVN which helps in relieving pain and delays the progression of disease. It involves drilling into the femoral head and removing the necrotic area. Several studies all over the world have supplemented this with other techniques like autologous bone transplant (Hernigou *et al*., 2003), autologous bone marrow derived mesenchymal cells (BMMC) transplant (Hernigou *et al*., 2004), quadratus femoris muscle pedicle grafting (Hernigou *et al*., 2006), liquid PRP infiltration (Cheng *et al*., 2004) and human BMP (Houdek *et al*., 2014) etc.

This study was conceived to evaluate the outcome of patients with early stage AVN managed by core decompression and autologous BMMC infusion. The pre and mid-term post-operative functional outcome were assessed and are discussed. In this study, 13 patients with 20 hips were included. Trendelenburg gait was found to be positive in 06 (45.9%) patients at the time of presentation while only a total of 03 (23.1%) patients had a trendelenburg gait at the final follow up. All patients had a significant pain relief at the final follow up of one year with an average of 63% pain relief as per the Visual Analogue Scale (VAS). Significant improvement in range of movement and Harris hip score was observed during the subsequent follow-up visits.

In 1995, Steinberg in a landmark study on 300 hips assessed the safety and outcome of core decompression and cancellous bone grafting in early stage AVN and found it to have better results than those managed conservatively. This was especially significant for those with small necrotic lesions in early stage AVN. Again in 2001, Steinberg *et al*., in a study on over 400 hips found similar results with the same procedure. Bellot *et al*. (2005) in a series of 32 cases of femoral head AVN treated by core decompression and assessment done by using the Pstel-merle-d'Aubigne functional score and the radiological assessment by the ARCO (Association of Research Classification Osseous) stage and Koo index found that stage III and IV AVN hips had unfavourable outcomes and concluded them to be a contraindication for this technique. Even in stage I and II, those with a higher Koo index had a poor outcome and hence they concluded that though early disease is ideal for decompression, it alone was insufficient to guarantee success in all cases.

Hernigou and Beaujean, 2002, in their study on 189 cases managed by core decompression and injecting mesenchymal cells reported excellent results in patients who presented in the pre-collapse stage. More than half the patients managed similarly in stages III and IV eventually needed a THA. They also showed that the etiology and the amount of stem cells injected had a significant role in the eventual outcome. Those with steroid exposure, alcohol use and history of organ transplantation had an inferior outcome. Several studies have also prospectively compared the outcome of patients managed by core decompression versus core decompression and bone marrow transplantation. Zhao *et al*. (2012) in their study on a 100 patients (50 managed by core decompression group and 50 managed by core decompression and stem cell infusion) with femur head AVN found that those managed supplemented with stem cell infusion had greater improvement in the average Harris Hip Score. In a meta-analysis by Sen *et al*. (2015), papers published in over 40 years since 1966 concluded that the concurrent use of bone morphogenic proteins or stem cells may provide an enhanced benefit over decompression alone.

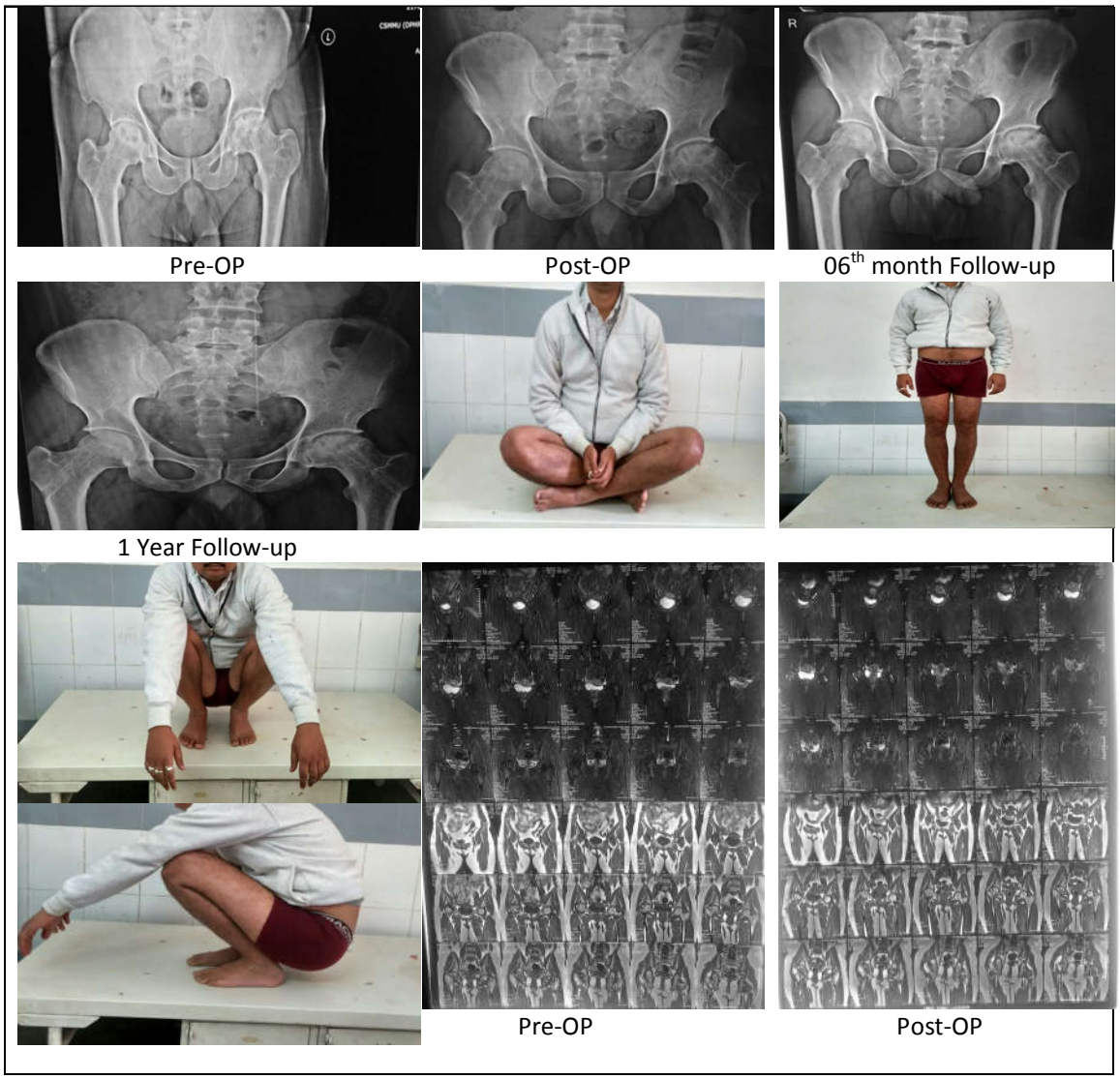
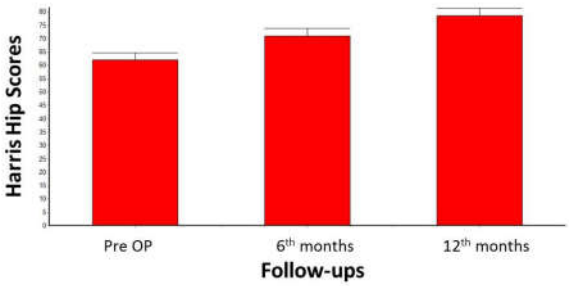


Figure 2 Management of AVN patient through innovative technique showing good clinico-radiological profile. The post-operative at one year MRI showed revascularization of the necrotic area with lesser oedema.



Graph 1 Average Harris Hip Scores.

Those with collapse of the femoral head would eventually progress to a stage requiring a THR. Sen *et al*., (2015) found a statistically significant difference in HHS for the stem cell treated patients compared to core decompression only at 12 months follow up (83.65 ± 8.04 vs. 76.68 ± 13.86, $p < 0.05$) [14]. At 24 months, overall HHS was not significantly improved between the two groups (82.42 ± 9.63 vs. 77.39 ± 16.98, $p = 0.09$), but the pain and deformity domains of the HHS were still in favour of the stem cells therapy group ($p < 0.05$).

Wang *et al*. (1981) also performed a Kaplan Mayer's survival analysis with progression to ARCO stage 3 as the end point, and found a significantly longer ($p < 0.05$) time to progression to ARCO stage 3 in the stem cells group compared to core decompression [52.2 months (43.35 - 60.96) vs 26.5 months (13.2 - 39.74). In their case series, Wang *et al*. (1981) reported a 22% rate of progression to higher ARCO stage (for hips in ARCO stage 1 or 2 before stem cell treatment) at an average follow up of 27 months. Wang *et al*. (1981) examined 3 patient reported outcomes: Lequesne index, VAS and WOMAC. The stem cell treatment group had improved Lequesne index compared to core decompression group.

Our present observations relies on studies previously done by Hernigou and Beaujean (2002), Zhao *et al*. (2012), Sen *et al*. (2012), Wang *et al*. (1981), showing that the core decompression along with stem cells shows better outcome as compare by using core decompression alone. Though we have

not performed only decompression, in present study, we also observed significant improvement of clinical parameters while radiological deterioration remained non progressive. This was confirmed by MRI studies. Current data provides a number of interesting approaches to treat musculoskeletal pathologies using orthobiologics. However, in order to realize the full therapeutic potential of stem cells, a number of open questions have to be answered. Besides the necessity of establishing further data about native stem cell function and pathways, basic research in the understanding of native tendon, bone, and cartilage regeneration also has to be continued. In the near future, an interdisciplinary approach with biologists, bioengineers, and clinicians will be essential to achieve the clinical application of these mononuclear stem cells. Being a single centric with limited number of patients, short follow-up duration, as a case series and comparing out the results with historical control group are the limitation of the study.

CONCLUSION

Core decompression and stem cell infusion is one of the less traumatic viable alternate treatment options for management of idiopathic avascular necrosis head femur. However, in order to realize the full therapeutic potential of stem cells further multicentric studies will be needed.

References

1. Arlet J, Ficat P. (1964) Forage-biopsie de la tкte fιmorale dans l'ostuıcrose primitive. Observations histopathologiques portant sur huit forages. *Rev Rhum Mal Osteoartic* ;31:257.
2. Bellot F, Havet E, Gabrion A, Meunier W, Mertl P, de Lestang M, (2005). Core decompression of the femoral head for avascular necrosis. Revue de chirurgie orthopedique et reparatrice de l'appareil moteur. 91(2):114-23.
3. Campion DR, (1984). The muscle satellite cell: a review. *Int Rev Cytol*, 87:225-251.
4. Cheng EY, Thongtrangan I, Laorr A, Saleh KJ, (2004). Spontaneous resolution of osteonecrosis of the femoral head. *J Bone Joint Surg Am*, 86-A: 2594-2599.
5. Hernigou P, Bachir D, Galacteros F, (2003). The natural history of symptomatic osteonecrosis in adults with sickle-cell disease. *J Bone Joint Surg Am*, 85-A:500-504.
6. Hernigou P, Beaujean F, (2002). Treatment of osteonecrosis with autologous bone marrow grafting. *Clinical orthopaedics and related research*, 405:14-23.
7. Hernigou P, Habibi A, Bachir D, Galacteros F, (2006). The natural history of asymptomatic osteonecrosis of the femoral head in adults with sickle cell disease. *J Bone Joint Surg Am*, 88:2565-2572.
8. Hernigou P, Poignard A, Nogier A, Manicom O, (2004). Fate of very small asymptomatic stage-I osteonecrotic lesions of the hip. *J Bone Joint Surg Am*, 86-A: 2589-2593.
9. Houdek MT, Wyles CC, Martin JR, Sierra RJ, (2014). Stem cell treatment for avascular necrosis of the femoral head: current perspectives. *Stem Cells and Cloning : Advances and Applications*, 7:65-70. doi:10.2147/SCCAA.S36584.
10. Hungerford DS, (1983). Pathogenesis of ischemic necrosis of the femoral head. *Instr Course Lect*, 32:252-26.
11. Jones LC, Mont MA, Le TB, *et al*., (2003). Procoagulants and osteonecrosis. *J Rheumatol*, 30:783-791.
12. Kondo M, Wagers AJ, Manz MG *et al*., (2003). Biology of hematopoietic stem cells and progenitors: implications for clinical application. *Annu Rev Immunol,* 21:759-806.
13. Lau RL, Perruccio AV, Evans HM, Mahomed SR, Mahomed NN, Gandhi R, (2014). Stem cell therapy for the treatment of early stage avascular necrosis of the femoral head: a systematic review. *BMC Musculoskeletal Disorders*, 15:156. doi:10.1186/1471-2474-15-156.
14. Lavernia CJ, Sierra RJ, Grieco FR, (1999). Osteonecrosis of the femoral head. *J Am Acad Orthop Surg*, 7:250-261.
15. Li D, Li M, Liu P, Zhang Y, Ma L, Xu F, (2016). Core decompression or quadratus femoris muscle pedicle bone grafting for nontraumatic osteonecrosis of the femoral head: A randomized control study. *Indian J Orthop*, 50:629-35.
16. Mauro A, (1961). Satellite cells of muscle skeletal fibers. *J Biophys Biochem*, 9:493-495.
17. Mont MA, Jones LC, Einhorn TA, Hungerford DS, Reddi AH, (1998). Osteonecrosis of the femoral head. Potential treatment with growth and differentiation factors. *Clin Orthop Relat Res*, 355:S314-S335
18. Moss FP, Lebond CP, (1971). Satellite cells as the source of nuclei in muscles of growing rats. *Anat Rec*, 170:421-435.
19. Sen RK, Tripathy SK, Aggarwal S, Marwaha N, Sharma RR, Khandelwal N, (2012). Early results of core decompression and autologous bone marrow mononuclear cells instillation in femoral head osteonecrosis: a randomized control study. *The Journal of arthroplasty*, 27(5):679-86.
20. Steinberg A, (2001). Hip joint prostheses. United States patent application US 09/902,701. 2001.
21. Steinberg ME, (1995). Core decompression of the femoral head for avascular necrosis: Indications and results. *Can J Surg*, 38 (1):S18-S24.
22. Wang GJ, Lennox DW, Reger SI, Stamp WG, Hubbard SL, (1981). Cortisone-induced intrafemoral head pressure change and its response to a drilling decompression method. *Clin Orthop Relat Res*, 159:274-8.
23. Yan Z, Hang D, Guo C, Chen Z, (2009). Fate of mesenchymal stem cells transplanted to osteonecrosis of femoral head. *J Orthop Res*, 27:442-446.
24. Zhao D, Cui D, Wang B, Tian F, Guo L, Yang L, Liu B, Yu X, (2012). Treatment of early stage osteonecrosis of the femoral head with autologous implantation of bone marrow-derived and cultured mesenchymal stem cells. *Bone*, 50(1):325-30.

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