Intractable Bone Marrow Edema Syndrome of the Hip

FUQIANG GAO, MD; WEI SUN, MD; ZIRONG LI, MD; WANSHOU GUO, MD; NEPALI KUSH, MD; KOJI OZAKI, MD

abstract

There is a need for an effective and noninvasive treatment for intractable bone marrow edema syndrome of the hip. Forty-six patients with intractable bone marrow edema syndrome of the hip were retrospectively studied to compare the short-term clinical effects of treatment with high-energy extracorporeal shock wave therapy vs femoral head core decompression. The postoperative visual analog scale score decreased significantly more in the extracorporeal shock wave therapy group compared with the femoral head core decompression group (P<.05). For unilateral lesions, postoperative Harris Hip Scores for all hips in the extracorporeal shock wave therapy group were more significantly improved than Harris Hip Scores for all hips in the femoral head core decompression group (P<.05). Patients who underwent extracorporeal shock wave therapy also resumed daily activities significantly earlier. Average overall operative time was similar in both groups. Symptoms disappeared significantly sooner in the extracorporeal shock wave therapy group in patients with both unilateral (P<.01) and bilateral lesions (P<.05). Hospital costs were significantly lower with extracorporeal shock wave therapy compared with femoral head core decompression. The intraoperative fluoroscopy radiation dose was lower in extracorporeal shock wave therapy than in femoral head core decompression for both unilateral (P<.05) and bilateral lesions (P<.01). On magnetic resonance imaging (MRI), bone marrow edema improved in all patients during the follow-up period. After extracorporeal shock wave therapy, all patients remained pain-free and had normal findings on posttreatment radiographs and MRI scans. Extracorporeal shock wave therapy appears to be a valid, reliable, and noninvasive tool for rapidly resolving intractable bone marrow edema syndrome of the hip, and it has a low complication rate and relatively low cost compared with other conservative and surgical treatment approaches. [Orthopedics. 2015; 38(4):e263-e270.]

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Bone marrow edema syndrome of the hip is a recently identified clinical entity that has been described as transient osteoporosis or algodystrophy hip.\textsuperscript{1,2} It was once mistaken for an early, reversible stage of nontraumatic avascular necrosis. The diagnosis is one of exclusion together with the presence of typical magnetic resonance imaging (MRI) findings. An MRI scan is the most specific diagnostic modality in the early diagnosis of bone marrow edema syndrome of the hip because it highlights its characteristic appearance.\textsuperscript{2}

Clinical symptoms are characterized by acute and worsening hip pain that typically resolves spontaneously in approximately 6 to 9 months. Treatment usually consists of avoiding load on the hips as well as the use of nonsteroidal anti-inflammatory drugs, bisphosphonates, and prostacyclin, which can improve local hemodynamic characteristics.\textsuperscript{1,2} Unfortunately, in some cases, conservative treatment approaches do not relieve symptoms. In these cases, the disease becomes protracted and intractable, causing a great deal of discomfort. Various treatments have been proposed in an attempt to shorten the natural course of the disease, which is invariably associated with severe and long-lasting disability.\textsuperscript{1}

In general, the therapeutic approach to bone marrow edema syndrome of the hip is based on its suspected etiology and ranges from various symptomatic therapies\textsuperscript{1,2} to core decompression,\textsuperscript{3} which has been shown to provide symptom relief within 4 weeks.\textsuperscript{1,2} Because it is considered a fully reversible disease,\textsuperscript{2} there is controversy regarding whether treatment should be conservative or invasive. Marrow core decompression is an invasive treatment and can result in complications, including wound infection, hematoma formation, reflex sympathetic dystrophy, and bone fractures associated with bone tunnel drilling.\textsuperscript{4} Therefore, there is a need for an effective noninvasive treatment.

Extracorporeal shock wave therapy has been effective in treating many orthopedic disorders, including osteonecrosis.\textsuperscript{3,5} The exact mechanism by which shock wave therapy works remains unknown. It is one of the most frequently used physical therapies, along with pulsed electromagnetic fields, and has been shown to activate many cellular processes critical to neovascularization and tissue regeneration; pulsed electromagnetic fields appear to be able to control inflammatory processes and facilitate bone reparative processes.\textsuperscript{1,5-8} Previous reports showed that extracorporeal shock wave therapy may provide a vasoactive effect analogous to that induced by pulsed electromagnetic fields.\textsuperscript{5,7} The authors’ longitudinal study evaluated the efficacy of high-energy extracorporeal shock wave therapy in reducing pain and slowing the progression of bone damage in patients with intractable bone marrow edema syndrome of the hip.

**Materials and Methods**

All patients treated for bone marrow edema syndrome of the hip at the authors’ hospital between March 2009 and September 2013 were included in this retrospective study. The patients included 24 men (52.2%) and 22 women (47.8%). The average age was 42.3 years (range, 18-61 years). All patients had been treated symptomatically with nonsteroidal analgesics and limited weight bearing in combination with the administration of alendronate sodium tablets (70 mg orally weekly; Merck & Co, Inc, Beijing, China) and alprostadil (10 μg intravenously guttae quaque die; Beijing Tide Pharmaceutical Co, Ltd, Beijing, China). The duration of conservative treatment before extracorporeal shock wave therapy is at least 3 months. The diagnosis was based on typical clinical findings, recurring severe hip pain, and bone marrow edema on MRI (a hypointense area on T1-weighted sequences and a hyperintense area on T2-weighted sequences), after exclusion of the differential diagnoses for bone marrow edema.\textsuperscript{9}

The two treatment groups included patients with both unilateral and bilateral lesions (Table 1). In the nonoperative group, patients underwent high-energy extracorporeal shock wave therapy, as shown in Figure 1. The operative group was surgically treated with femoral head core decompression with a lateral approach to the hip. Under fluoroscopy, a K-wire was introduced 2 to 5 cm inferior to the greater trochanter, then drilled at least 10 times into the affected part of the femoral head in a radial fashion. All patients used crutches for approximately 4 to 6 weeks after treatment. Patients were evaluated both before and after treatment with a visual analog scale, Harris Hip Score, and MRI (to assess bone marrow edema). Using a radiation dosimeter (ALOKA PDM-112; ALOKA Co, Ltd, Tokyo, Japan), measurements were carried out with tissue-equivalent anthropomorphic phantoms to quantitatively determine radiation exposure at various locations from the C-arm for both treatment procedures. On follow-up examination 6 months after treatment, a history was taken with regard to pain before and after treatment. The time necessary for complete recovery was noted based on a structured interview. Harris Hip Scores and a visual analog scale were used to assess functional and health status on the day of examination. Pelvic radiographs and lateral views of the affected hip were obtained to exclude avascular necrosis and other pathology. Follow-up examinations were scheduled at 1, 3, 6, and 10 months. Clinical assessment included pain history, severity and duration of symptoms, the progress of treatment, intraoperative fluoroscopy radiation dose, operative time, hospital costs, time when symptoms disappeared, and MRI findings. Preoperative and postoperative visual analog scale scores and Harris Hip Scores before therapy were retrospectively calculated based on a Harris Hip Score assessment form that is routinely completed before surgery by all patients with hip disease.

**Shock Wave Treatment**

Shock wave treatment was applied with an Electromagnetic Shock Wave Emit-
ter (Dornier Compact DELTA II; Dornier MedTech, Co, Ltd, Munich, Germany), with a penetration depth of 0 to 150 mm and a focus diameter of 4 mm. Shock waves were focused around (on the margins of) the femoral head under radiographic guidance. The treatment area was prepared with a coupling gel to minimize the loss of shock wave energy at the interface between the head of the device and the skin.

All extracorporeal shock wave therapy procedures were performed once without general or regional anesthesia by experienced physicians. Settings were as follows: 2 series of 3 treatments, 3 to 4 levels, and 2000 to 3000 impulses, each administered at 0.50 mJ/mm². After extracorporeal shock wave therapy, patients were instructed to walk on crutches and to avoid bearing weight on the affected limb for 4 to 6 weeks. All patients received alendronate sodium tablets (70 mg orally weekly for 14 days) and alprostadil (10 μg intravenously guttae quaque die for 14 days).

### Statistical Analysis

Preoperative visual analog scale scores, intraoperative fluoroscopy radiation dose, operative time, hospital costs, postoperative visual analog scale scores, postoperative Harris Hip Scores, and time when symptoms disappeared were compared between treatment groups with Student’s t test for independent samples. Each variable was compared with reference to the appropriate statistical method selected. Mean values were determined for all patients, and 95% confidence intervals were determined. The level of significance was set at P<.05. All data analyses were performed with SPSS version 16.0.0 software (SPSS, Chicago, Illinois).

### RESULTS

All of the patients had clinical recovery within 12 weeks, and MRI findings were normal within 6 months after surgery. Preoperative visual analog scale scores and preoperative Harris Hip Scores did not differ significantly between the extracorporeal shock wave therapy and femoral head core decompression groups for either unilateral or bilateral lesions (P>.05). The postoperative visual analog scale score decreased significantly more in the extracorporeal shock wave therapy group compared with the femoral head core decompression group (P<.05 for both unilateral and bilateral lesions). For unilateral lesions, postoperative Harris Hip Scores for all hips in the extracorporeal shock wave therapy group were more significantly improved than Harris Hip Scores for all hips in the femoral head core decompression group (P=.005), but this was not the case for bilateral lesions (Table 2; left, P=.042; right, P=.912).

### Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Unilateral lesion</th>
<th>Bilateral lesion</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Patients</td>
<td>Female</td>
<td>Mean±SD Age, y</td>
</tr>
<tr>
<td>Extracorporeal shock wave therapy</td>
<td>12 (12)</td>
<td>41.7%</td>
<td>41.1±10.2</td>
</tr>
<tr>
<td>Femoral head core decompression</td>
<td>16 (16)</td>
<td>37.5%</td>
<td>43.9±14.8</td>
</tr>
<tr>
<td>t</td>
<td>1.638</td>
<td>-.372</td>
<td>0.106</td>
</tr>
<tr>
<td>P</td>
<td>.174</td>
<td>.593</td>
<td>.751</td>
</tr>
</tbody>
</table>

**Figure 1:** Extracorporeal shock wave therapy equipment used in the current study (Dornier Compact DELTA II; Dornier MedTech, Co, Ltd, Munich, Germany).
Patients resumed daily activities significantly earlier in the extracorporeal shock wave therapy group. Average overall operative time was similar in both treatment groups (no statistical difference; \( P > .05 \)).

All retrospectively collected data assessing pain relief were dichotomized using 6 months of impairment as the cutoff point. The time when symptoms disappeared was significantly earlier in the extracorporeal shock wave therapy group for both unilateral lesions (\( P = .007 \)) and bilateral lesions (\( P < .05 \)). Hospital costs were significantly lower in the extracorporeal shock wave therapy group compared with the femoral head core decompression group for both unilateral and bilateral lesions. The intraoperative fluoroscopy radiation dose was much lower in the extracorporeal shock wave therapy group compared with the femoral head core decompression group for both unilateral lesions (\( P = .012 \)) and bilateral lesions (\( P < .000 \); Table 2).

### Side Effects

No clinically detectable neurovascular, systemic, or device-related adverse effects were observed in the extracorporeal shock wave therapy group. Only minor complications occurred during therapy, such as transient soft tissue swelling or minor haematoma formation and there was 1 case of wound infection. No infection, bone fractures, or sympathetic atrophy occurred.

### Case Reports

#### Patient 1

A 53-year-old saleswoman had bone marrow edema syndrome of the right hip. Extracorporeal shock wave therapy combined with alendronate produced rapid improvement in both pain and bone marrow edema. The visual analog scale score decreased from 8 points preoperatively to 3 points postoperatively. The patient was able to walk immediately after extracorporeal shock wave therapy treatment. Her pain was significantly alleviated. In addition to the visual analog scale score, the Harris Hip Score decreased from 89.2±9.5 to 83.5±7.8 for both unilateral and bilateral lesions (\( P < .05 \); Table 2).

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean±SD Surgical Time, min</th>
<th>Mean±SD Intraoperative Fluoroscopy Radiation Dose, mSv</th>
<th>Mean±SD Hospital Costs, Ren Min Bi</th>
<th>Mean±SD Postoperative Visual Analog Scale Score</th>
<th>Mean±SD Postoperative Harris Hip Score</th>
<th>Mean±SD Time When Symptoms Disappeared, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unilateral lesion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extracorporeal shock wave therapy</td>
<td>31.7±9.6</td>
<td>1.38±0.97</td>
<td>2103.9±192.2</td>
<td>3.9±1.7</td>
<td>89.2±9.5</td>
<td>21.1±1.1</td>
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<tr>
<td>Femoral head core decompression</td>
<td>34.3±8.9</td>
<td>2.79±1.98</td>
<td>3023.6±217.8</td>
<td>5.6±2.9</td>
<td>82.4±11.5</td>
<td>3.8±2.9</td>
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<tr>
<td>( t )</td>
<td>-1.611</td>
<td>-3.219</td>
<td>-6.790</td>
<td>-3.102</td>
<td>4.712</td>
<td>-3.265</td>
</tr>
<tr>
<td>( P )</td>
<td>.169</td>
<td>.012</td>
<td>.000</td>
<td>.009</td>
<td>.005</td>
<td>.007</td>
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<tr>
<td><strong>Bilateral lesion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Extracorporeal shock wave therapy</td>
<td>73.5±7.8</td>
<td>1.17±0.69</td>
<td>3957.0±98.1</td>
<td>4.5±1.8 (left)</td>
<td>86.7±9.3 (left)</td>
<td>1.7±1.8 (left)</td>
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<tr>
<td>Femoral head core decompression</td>
<td>77.9±9.3</td>
<td>2.88±1.95</td>
<td>4656.2±355.7</td>
<td>6.9±2.5 (left)</td>
<td>82.4±8.6 (left)</td>
<td>4.0±2.7 (left)</td>
</tr>
<tr>
<td>( t )</td>
<td>-0.951</td>
<td>-5.729</td>
<td>-3.973</td>
<td>-2.713 (left)</td>
<td>3.440 (left)</td>
<td>-2.784 (left)</td>
</tr>
<tr>
<td>( P )</td>
<td>.386</td>
<td>.000</td>
<td>.010</td>
<td>.017 (left)</td>
<td>.024 (left)</td>
<td>.019 (left)</td>
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</table>

All retrospectively collected data assessing pain relief were dichotomized using 6 months of impairment as the cutoff point. The time when symptoms disappeared was significantly earlier in the extracorporeal shock wave therapy group compared with the femoral head core decompression group for both unilateral lesions (\( P < .05 \)) and bilateral lesions (\( P < .000 \); Table 2).
improvements in the visual analog scale score and Harris Hip Score, MRI showed a significant reduction in edema between pretreatment (Figure 2) and 2.5 months (Figure 3) posttreatment.

**Patient 2**

A 44-year-old female teacher had bone marrow edema syndrome of the left hip that was completely cured after extracorporeal shock wave therapy. After 2 months, the patient had returned to work. The typical appearance on MRI is seen in the pretreatment images (Figures 4A-B); after 3 months, MRI showed significant resolution of edema (Figure 4C).

**DISCUSSION**

Bone marrow edema syndrome is a rare condition of unclear etiology that is characterized by hip pain, limited osteopenia on plain radiography, and characteristic MRI findings. Although the etiology and pathogenesis of bone marrow edema syndrome are not currently known, different mechanisms have been proposed, including microvascular injury, venous obstruction and secondary localized hyperemia, abnormal mechanical stress, metabolic causes, neurogenic compression, and endocrine causes. One hypothesis is that a local ischemic episode caused by multiple triggers may initiate a chain of events resulting in bone marrow edema. Ischemic events in the small vessels proximal to the nerve roots may cause the disease, and restoration of blood flow in the nerve roots and nerve regeneration may be responsible for its clinical course, which usually lasts up to 9 months. Angiographic and scintigraphic studies showed that the nutrient arteries of the femoral head were dilated and perfusion in the affected area was higher than that in the unaffected contralateral side, suggesting that ischemia is the most likely cause. Indeed, several authors have identified transient bone ischemia as a primary cause. Edema in the hip area surrounding the femur may also favor the theory of ischemia as the underlying mechanism.

In some cases, conservative treatment approaches do not relieve symptoms. In these cases, the disease...
becomes protracted and intractable, causing significant pain. In attempting to shorten the clinical course of the disease, which is invariably associated with severe and long-lasting disability, various treatments have been proposed. Core decompression has been reported to alter the natural course of the disease and to immediately relieve pain, significantly shortening the time to recovery compared with conservative treatment. The early ischemic changes seen in bone marrow edema syndrome justify core decompression as an alternative to conservative treatment. However, although this treatment mode appears to be very effective, some authors consider it too invasive for a self-limiting disease with a variable clinical course. In general, surgical core decompression is usually used as a last resort; it is probably best reserved for patients with severe pain that is difficult to control. Marrow core decompression is an invasive treatment, with possible complications that include wound infection, hematoma formation, reflex sympathetic dystrophy, and bone fractures associated with bone tunnel drilling. Therefore, there is a need for an effective and noninvasive treatment.

Extracorporeal shock wave therapy has been shown to be effective in treating many orthopedic disorders, including osteonecrosis. There is currently little research addressing its use in bone marrow edema syndrome of the hip. The authors’ study shows that extracorporeal shock wave therapy can relieve pain, significantly shortening the time to recovery compared with conservative treatment. However, the exact mechanism through which extracorporeal shock wave therapy operates remains unknown. It is one of the most frequently used physical therapies, along with pulsed electromagnetic fields, that seem to be able to control inflammatory processes and facilitate bone reparative processes; extracorporeal shock wave therapy activates many cellular processes that are critical to neovascularization and tissue regeneration. The results of animal experiments have shown extracorporeal shock wave therapy to induce the ingrowth of neovascularization; it is also associated with increased expression of angiogenic growth factors, including endothelial nitric oxide synthase, vessel endothelial growth factor, bone morphogenetic protein-2, and proliferating cell nuclear antigen, and it promotes cell proliferation and osteogenesis. Vessel endothelial growth factor may be involved in the positive effects of extracorporeal shock wave therapy because it is a specific mitogenic factor for vascular endothelial cells; vessel endothelial growth factor stimulates the proliferation of endothelial cells, promotes neovascularization, and increases vascular permeability. The increased expression of bone morphogenetic protein-2 identified in femoral heads treated with extracorporeal shock wave therapy is a key finding because bone morphogenetic protein-2 is a key mediator of bone development and repair through its capacity to mobilize osteoprogenitor cells, promoting osteoblastic differentiation processes and resulting in bone formation. Finally, endothelial nitric oxide synthase promotes neovascularization.

The response to local mechanical stimulation with shock waves (eg, in osteonecrosis) may reflect the systemic effects of angiogenesis, osteogenesis, and anti-inflammation acting in the hips. Neovascularization may play a role in the improvement of blood supply to the femoral head and may promote bone regeneration in bone marrow edema syndrome and osteonecrosis. Early studies suggested that extracorporeal shock wave therapy can provide an effect similar to that of vasoactive drugs. Previous studies showed that extracorporeal shock wave therapy was more effective than core decompression and nonvascularized fibular grafting. However, no comparative studies examining the treatment of bone marrow edema syndrome with extracorporeal shock wave therapy and femoral head core decompression have been reported.

Based on the results of the current study, the therapeutic effect of extracorporeal shock wave therapy was greater than that of femoral head core decompression. Extracorporeal shock wave therapy produced results comparable to those of femoral head core decompression in bone marrow edema syndrome of the hip. Furthermore, the authors observed a significant reduction in the mean visual analog scale score at short-term follow-up only in the extracorporeal shock wave therapy group. In addition, mean Harris Hip Scores showed statistically significant improvement from pretreatment values at all follow-up time points in the extracorporeal shock wave therapy group. During follow-up, all hips with bone marrow edema syndrome of the hip that were treated with extracorporeal shock wave therapy alone showed visible improvement on radiographs and MRI. These patients also showed overall clinical improvement. The benefits of extracorporeal shock wave therapy are supported by the finding that the grade of patients’ edema did not worsen but rather improved. Clinical improvement was obvious in most patients after the first week of treatment. Thus, extracorporeal shock wave therapy shows rapid efficacy in the management of intractable bone marrow edema syndrome of the hip.

Comparison of the results of the current study with those of other studies examining extracorporeal shock wave therapy is limited because of differences in the type of equipment used, treatment...
and evaluation protocols, inclusion criteria, and number of patients treated.

Limitations

There are limitations associated with this study. The sample sizes were small, and the follow-up time was relatively short. Because bone marrow edema syndrome of the hip is relatively uncommon in the author’s setting, it would have been difficult to perform a randomized, controlled trial. Further studies are needed with larger cohorts of patients using a homogenous classification system and standardized treatment protocols to further assess the efficacy of extracorporeal shock wave therapy in the management of bone marrow edema syndrome of the hip.

Conclusion

The findings indicate that extracorporeal shock wave therapy is a valid, reliable, and noninvasive tool for rapidly treating intractable bone marrow edema syndrome of the hip. It has a low complication rate and a relatively low cost compared with other conservative and surgical treatment approaches. Extracorporeal shock wave therapy is an innovative technology that is applicable to orthopedics, but it is still new. Further studies would be worthwhile because this treatment has the potential to resolve patient suffering quickly.

References


