Case Report

Efficacy of keishibukuryogan in muscle injury of lower extremity: Evaluation of therapeutic response and prediction of the outcome by magnetic resonance imaging

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Abstract

We evaluated the outcome of 10 patients (age range: 13-62 years; 8 males and 2 females) with acute traumatic muscle injury of lower extremity who were treated with only Kampo medicine keishibukuryogan and no analgesic. The therapeutic response was determined by the influence on daily life and comparing local pain using a visual analogue scale (VAS). For a more objective evaluation of the therapeutic response, magnetic resonance imaging (MRI) findings were also used. The results showed to be markedly effective in 5 cases, effective in 2 cases, and ineffective in 3 cases. In the 7 cases in markedly effective or effective, pain relief was associated with attenuation of MRI signal intensities reflecting edema and hematoma of the injured area. In addition, the therapeutic outcome was analyzed in relation to the MRI findings obtained at first presentation; pain tended to be alleviated more rapidly in cases shown as having muscular contusion on the initial MRI, while pain and MRI high signal intensity areas tended to persist in cases shown as having injury of musculo-tendinous junction. In 2 of the 3 cases in ineffective, the initial MRI had shown rupture of muscle tissue. Keishibukuryogan was effective against traumatic muscle injury of lower extremity and MRI was useful for evaluating responses to the treatment and predicting the therapeutic outcome.

Key words muscle injury, hematoma, keishibukuryogan, evaluation, magnetic resonance imaging.

Introduction

Kampo medicine is now commonly used in routine clinical practices. Their efficacy has been attracting close attention and is recognized by various specialties. This also applies to the field of orthopedic surgery for the treatment of chronic, painful diseases.*1) Kampo medicine is of value particularly in elderly patients from the viewpoint of avoiding adverse reactions to NSAIDs and other Western drugs.

The indications of Kampo medicine are not confined to only cases of chronic diseases but also of acute traumatic injury.*2) In this study, we evaluated the outcome of 10 patients treated with keishibukuryogan (KBG), without using any analgesic, for acute traumatic muscle injury by comparing symptoms and magnetic resonance imaging (MRI) findings before and after treatment. In addition, we determined whether or not the MRI findings obtained at first presentation would enable
prediction of the therapeutic outcome of these patients.

**Subjects and Methods**

The study included 10 patients with muscle injury of lower extremity caused by trauma. There were 8 males and 2 females with a mean age of 41.2 years (range, 13-62 years). Table 1 lists the cause of injury and the diagnosis in individual cases. During the initial visit, muscle injury was diagnosed on the basis of local symptoms/signs and diagnostic imaging findings. MRI was used for diagnostic imaging, and the images were interpreted by one orthopedic surgeon and 2 radiologists. Each patient was informed that injury could be treated by KBG, TJ-25 (Tsumura Co., Tokyo, Japan). The daily dose for adult is 7.5 g, and it was administered on the first day of the visit orally three times a day before each meal. The therapeutic response was evaluated through analysis of influence on daily life and changes in local pain. The influence on daily life at 4 weeks after the start of treatment was rated on a 4-category scale: markedly effective (pain almost absent and capable of practicing exercise and waking normally), effective (no disorder in walking despite pain during exercise), ineffective (interference with daily life due to pain), and worsened (more intense pain than that at the start of treatment or development of new adverse events). Local pain was evaluated with a visual analogue scale (VAS) during the first visit and at 2 and 4 weeks after the treatment. MRI was performed during the initial visit and at 4 weeks after the treatment, and the findings after treatment were compared with those before treatment. In addition, we determined whether or not the therapeutic outcome would differ depending on the MRI findings obtained during the first visit through analyzing the data on pain and MRI findings. All participants provided informed consent before participating in this study. The ethical committee of the Ohtawara Red Cross Hospital approved this study protocol.

**Results**

The results showed the therapy to be markedly effective in 5 cases, effective in 2 cases, and ineffective in 3 cases. None of the patients showed worsening of their condition. Of the 5 cases rated as markedly effective, 3 was diagnosed as having muscular contusion, had pain relief rapidly during the first 2 weeks after the treat-

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Gender</th>
<th>Age</th>
<th>Diagnosis of condition</th>
<th>Side of injury</th>
<th>Location of damaged muscle</th>
<th>Cause of injury</th>
<th>Evaluation after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>37</td>
<td>rupture</td>
<td>Left</td>
<td>biceps femoris</td>
<td>Baseball</td>
<td>ineffective</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>20</td>
<td>contusion</td>
<td>Left</td>
<td>semitendinous</td>
<td>traffic accident</td>
<td>markedly effective</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>62</td>
<td>contusion</td>
<td>Left</td>
<td>semitendinous</td>
<td>fall backwards while walking</td>
<td>markedly effective</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>34</td>
<td>musculo-tendinous junction injury</td>
<td>Right</td>
<td>gastrocnemius</td>
<td>stepped forwards during sotball</td>
<td>ineffective</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>41</td>
<td>rupture</td>
<td>Right</td>
<td>gastrocnemius</td>
<td>stepped forwards during tennis</td>
<td>ineffective</td>
</tr>
<tr>
<td>6</td>
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<td>52</td>
<td>musculo-tendinous junction injury</td>
<td>Right</td>
<td>gastrocnemius</td>
<td>running</td>
<td>markedly effective</td>
</tr>
<tr>
<td>7</td>
<td>Male</td>
<td>50</td>
<td>contusion and hematoma</td>
<td>Left</td>
<td>gastrocnemius</td>
<td>colliding against the catcher’s knee during baseball</td>
<td>markedly effective</td>
</tr>
<tr>
<td>8</td>
<td>Male</td>
<td>13</td>
<td>contusion</td>
<td>Right</td>
<td>vastus medialis</td>
<td>stepped on a foot and fall backwards</td>
<td>markedly effective</td>
</tr>
<tr>
<td>9</td>
<td>Male</td>
<td>56</td>
<td>musculo-tendinous junction injury</td>
<td>Right</td>
<td>vastus medialis</td>
<td>fall forwards while walking</td>
<td>effective</td>
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<tr>
<td>10</td>
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<td>47</td>
<td>contusion</td>
<td>Right</td>
<td>gastrocnemius</td>
<td>twist right ankle while walking</td>
<td>effective</td>
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</tbody>
</table>
ment, and regained the ability to walk normally. Figure 1 shows changes in VAS rating for all cases. In the 7 cases rated as markedly effective or effective, MRI showed almost complete disappearance or attenuation of the high signal density area at the site of injury. In particular, cases initially diagnosed of musculo-tendinous junction tended to show persistence of pain and signal changes on MRI as compared to cases initially showing muscular contusion. In the 2 cases rated as ineffective, the patients were diagnosed as having muscle rupture on the basis of MRI findings during the first visit, and MRI after treatment still showed high signal intensity areas at the site of injury.

![VAS graph](image)

Figure 1 Changes in VAS rating for all cases

**Case presentation**

**[Case No.3]** A 62-year-old female, rated as markedly effective

She fell backwards while walking and hit her left thigh on the ground directly. Immediately after being injured, she found it difficult to walk. On the same day, she visited the Critical Care Center, Ohtawara Red Cross Hospital.

**History of present illness:** The entire left thigh was swollen, and intense spontaneous pain and tenderness were prominent in the left ischial tuberosity. She complained of very intense pain rated at 100 on the VAS, also complained of pain during active contraction and resistant motions and during passive motions. No fracture sign was revealed by plain X-ray. MRI performed on the day of injury revealed an inhomogeneous high-signal intensity area in the semitendinous muscle of the left thigh on short-T1 inversion recovery (STIR) and T2 images (Figure 2-A,C). In addition, an extensive high-signal intensity area, suggesting edema, was noted in the femoral subcutaneous tissue on STIR image (Figure 2-A). On the basis of these findings, she was diagnosed as having semitendinous muscle contusion accompanied by extensive superficial edematous changes caused by direct external force.

**Course of treatment:** Following treatment with KBG, the VAS score for local pain improved rapidly (100 → 32 → 5). Two weeks after the treatment, this case regained

![MR images](image)

Figure 2 **[Case No.3]** A 62-year-old female, rated as markedly effective. She fell backwards while walking and hit her left thigh on the ground directly. MRI showed inhomogeneous high-signal intensity area in the semitendinous muscle of the left thigh, and also an extensive high-signal intensity area, suggesting edema, was noted in the femoral subcutaneous tissue on STIR (A) and high-signal intensity area was noted on T2 axial images (C). After 4 weeks treatment, the high-signal intensity and the extensive subcutaneous tissue edema disappeared (B,D).
the ability to walk normally without any assistive device. When MRI was performed after 4 weeks treatment, the high-signal intensity and the extensive subcutaneous tissue edema disappeared (Figure 2-B,D).

[Case No.7] A 50-year-old male, rated as markedly effective

During a baseball game, he was making a slide to the home base, became entangled with the catcher and was injured after colliding against the catcher’s knee. Immediately after injury, the man began to complain of pain in the posterior plane of his left thigh and had difficulty walking. One hour after injury, he visited our critical care center.

History of present illness: He felt spontaneous pain and tenderness in the posterior plane of his left thigh, accompanied by mild swelling. Like in Case 1, this patient had pain during active contraction, resistant motions, and passive motions. MRI, performed on the day following injury, revealed high signal intensity areas in the subcutaneous and gastrocnemius muscle layers on STIR images, suggesting a contusive change in the gastrocnemius muscle (Figure 3-A). At that time, the man was diagnosed as having contusion of the left gastrocnemius muscle. In the deeper muscle layer, sagittal MRI revealed a distorted ductal structure and axial MRI disclosed a circular high-signal intensity area (Figure 3-C,D). On the basis of the form of these abnormal areas and the patient's age, he was suspected of having intravenous thrombus. Ultrasonography and contrast-enhanced CT, however, ruled out thrombus. Combining these findings with the high-signal intensity area noted on both T1 and T2 images obtained soon after injury, the patient was finally diagnosed as having hematoma within muscle layers.

Course of treatment: Like in Case 1, KBG was prescribed, referring to the local findings and the finding of lingual vein dilation. After the start of treatment, the VAS score for his left femoral pain improved rapidly (90→24→9). When MRI was performed 4 weeks after injury, the hematoma within the muscle layers, seen immediately after injury, had disappeared almost completely (Figure 3-B,E,F).

[Case No.10] A 47-year-old male, rated as effective

He twisted his right ankle joint while walking. At that time, he did not fall but began to complain of intense pain in the right crus, having difficulty walking. He visited our critical care center 2 hours after injury.

History of present illness: Spontaneous pain and tenderness were noted on the medial side of the central and posterior planes of his right crus, accompanied by mild

![Figure 3](image-url) [Case No.7] A 50-year-old male, rated as markedly effective. During a baseball game, this case, who was making a slide to the home base, became entangled with the catcher and was injured after colliding against the catcher’s knee. MRI showed high signal intensity areas in the subcutaneous and gastrocnemius muscle layers on STIR sagittal images (A). In the deeper muscle layer, sagittal MRI revealed a distorted ductal structure and axial MRI disclosed a circular high-signal intensity area on T1 (C) and T2 (D) axial images, diagnosed as having hematoma within muscle layers. MRI which performed 4 weeks after treatment, the hematoma had disappeared almost completely (B,E,F).
swelling. He had pain during active contraction, resistant motions, and passive motions. MRI, performed on the day following injury, revealed a high-signal intensity area along the right gastrocnemius transition area on STIR sagittal and T2 axial images (Figure 4-A,C), allowing a diagnosis as musculo-tendinous junction injury of right gastrocnemius.

**Course of treatment:** KBG was prescribed. Following treatment, the VAS score for his left crus pain improved (80→60→26), but the score rose slightly again at 4 weeks after the start of treatment. Although the patient had no difficulty walking or other activities during daily life, he complained of slight pain while running. MRI, performed 4 weeks after treatment, revealed a high-signal intensity area remaining in the injured muscle layer and the surrounding tissue, although its intensity had decreased (Figure 4-B,D).

**Case No.5** A 41-year-old female, rated as ineffective

**History of present illness:** When she intensely stepped forwards with her left foot during a tennis game, she felt pain on the posterior plane of her crus, and she was unable to walk unassisted. She came to our critical care center for a consultation.

**Clinical findings:** A depressed area was palpable on the medial side of the posterior plane of left crus, accompanied by intense spontaneous pain, tenderness and swelling. Because of pain, plantar-flexion of the ankle joint was difficult. MRI, performed on the day of injury, revealed a nodular low-signal intense area suggestive of a rupture in the left gastrocnemius muscle on the STIR sagittal (Figure 5-A) and T2 axial images as well as a surrounding high-signal intensity area suggestive of hematoma (Figure 5-C). On the basis of these findings combined with clinical findings, this case was diagnosed as having a partial rupture of the left gastrocnemius muscle.

![Figure 4](image4.png) **Figure 4** **Case No.10** A 47-year-old male, rated as effective. He twisted his right ankle joint while walking. MRI revealed a high-signal intensity area in musculo-tendinous junction of right gastrocnemius on STIR sagittal (A), T2 axial (C) images. 4 weeks after treatment, revealed a high-signal intensity area remaining in the injured muscle layer and the surrounding tissue, although its intensity had decreased (B) (D).

![Figure 5](image5.png) **Figure 5** **Case No.5** A 41-year-old female, rated as ineffective. When she intensely stepped forwards with her left foot during a tennis game, she felt pain on the posterior plane of her crus. MRI revealed a nodular low-signal intense area suggestive of a rupture in the left gastrocnemius muscle on the STIR sagittal (A) and T2 axial images (B) as well as a surrounding high-signal intensity area suggestive of hematoma. MRI, performed at 4 weeks, revealed persistence of a high-signal intensity area around the injured muscle (B) (D).
**Course of treatment:** Treatment was started with KBG. The VAS score improved (90→65→32), but the patient continued to complain of pain and show limping after 4 weeks of treatment. MRI, performed at 4 weeks, revealed persistence of a high-signal intensity area around the injured muscle (Figure 5-B,D).

**Discussion**

**Types of muscular injury:** Muscular injury is defined as “a condition characterized by rupture of myofibrils or fascia.” Muscular injury takes place not only as simple tissue injury but also as various types.\(^3,4\) Injury of musculo-tendinous junction has a higher incidence than any other muscular injury during sports. There are two mechanisms for its onset. With one pattern, rupture occurs due to excessive extensive force to the muscle tissue due to twisting of the trunk while the joint near the injured site is kept in a fixed position. With the other pattern, muscular tissue is injured by the inherent muscular force used during intense stamping of the feet. Muscular injury caused by inherent muscular force in the absence of any evident external force, and that muscular injury caused by excessive extension due to indirect external force is sometimes confused with this condition. In all of these conditions, simultaneous generation of intense muscular contraction and high tension to the musculo-tendinous junction causes detachment of the tendon from the muscle due to the difference in the potential of extension, resulting in the onset of these injuries. Muscular contusion occurs not only due to a hitting (against humans or objects) during sports but its onset due to a fall is not rare. External force directly applied to the tissue can induce local contusive changes, and these changes are seen not only in muscular layers but also in superficial soft tissue, often accompanied by an intense external appearance of swelling. The type of tissue injured and the course of treatment vary depending on whether the injured tissue was exposed to direct external force or indirect external force. So, a distinction between these two forces is important.

**MRI-based diagnosis of muscular injury:** The diagnosis of muscular injury is relatively easy if the patient is consulted about the circumstances at the time of injury (cause of injury, position of extremities, etc.) and is checked for local signs. MRI is the most objective and noninvasive method of testing that also has a high level of reliability.\(^5,6\) MRI allows not only diagnosis of this kind of injury but also evaluation of therapeutic responses. For muscular injury by athletes, MRI is useful also as a means of determining the timing of resumption of sport activity.\(^7\) For MRI-based diagnosis of muscular injury, STIR or T2 imaging is used. STIR exerts fat-suppressing effects and can visualize edema (depicted as a low-signal area) and hematoma (a high-signal area) on T1 images, thus enabling more definite depiction of the injured site and its scope. In the present study, the MRI findings obtained during the first visit were compared with findings obtained during the course of treatment, to determine whether or not the course of treatment would vary depending on the initial classification of muscular injury. Regarding “muscular contusion,” both observation of the external appearance of the injured site and MRI immediately after injury revealed marked edematous changes of subcutaneous tissue due to direct external force in addition to muscular injury in the deep layers tissue, and the subcutaneous tissue changes appeared to be severer than the deeper tissue changes visually. The pain score using VAS during the first visit tended to be high in such cases. After treatment began, the severity of symptoms decreased relatively rapidly, and the final outcome was favorable. Regarding injury of musculo-tendinous junction, on the other hand, the pain score using VAS during the first visit tended to be comparable to or lower than that in cases of muscular contusion, and the high-signal intensity area on MR images tended to be confined to a narrow area. However, limping due to pain was also seen even 2 weeks after the start of treatment, and pain tended to persist at 4 weeks after the start of treatment although the activities of daily life were not disrupted. In 2 out of the 3 cases in which therapy was rated as ineffective, muscular tissue rupture had been found by MRI during the first visit, and limping due to pain could be seen even at 4 weeks after the start of treatment. These results suggest that prediction of the course of treatment is possible to some extent on the basis of findings from MRI during the first visit and that KGB should be indicated in cases of muscular contusion or injury of musculo-tendinous junction. Also in cases in which hematoma has been formed in...
deeper tissue, Case No.7, Kampo therapy seems applicable as a means of facilitating absorption of hematoma. However, in patients who have muscular ruptures, conventional methods of treatment based on Western medicine, e.g., adequate external fixation, seem to be necessary.

**Efficacy of KBG against muscular injury:** An important finding from the cases presented in this study pertains to efficacy of KBG against muscular injury. According to past reports on the time course of muscular injury usually seen following conservative treatment, the mean length of time needed for alleviation of symptoms is 6–8 weeks, and it was 12 weeks or more according to a report on cases with hamstring injury. According to our clinical experience, 3–4 weeks are necessary until unassisted walking can be resumed even in cases in which external fixation (with splint, etc.), load-free crutches and/or NSAIDs were used. In the cases in which the therapy was rated as effective among the cases presented in this study, crutches were used for several days after the first visit, but no initial fixation was needed, and the patient regained the ability to walk almost completely unassisted 2 weeks after the start of treatment. Signal changes on MRI also vary among different reports. According to some reports, signal changes in the injured site remained to be seen even 10 weeks or more after injury. Because no method for objective evaluation of Kampo medicine for the treatment of muscular injury is available, it is difficult to compare the results from the present study with those in previous studies. However, if we refer to the findings shown in the above-mentioned reports, we may say that Kampo treatment by KBG in our cases resulted in alleviation of symptoms and improvement in MRI signals.

KBG is a representative herbal mixture aimed at improving blood flow. In general it is often used for patients with climacteric syndrome or dismenorrhea, accompanied by excessive sensitivity to cold.8,9)

It has also been used for treatment of injury (bruise, etc.). This herbal mixture is composed of five herbs (Cassia Bark, Tuckahoe, Tree Peony Bark, Peach Kernel, and Peony Root). When used in patients with muscular injury, it seems likely that the analgesic and spasmyolytic actions of Peony Root and the coagulation-suppressing and anti-thrombotic actions of Tree Peony Bark and Peach Kernel exerted efficacy. Tree Peony Bark also has an action for pain relief that might be closely related to rapid improvement of the pain in our cases.10-15 Although it appears at a glance to be irrational to use drugs promoting blood flow during the early stage of injury, early absorption of deep hematoma is useful for reducing pain and preventing callus-induced myositis. In Case No.3, MRI had revealed edematous changes in subcutaneous tissue during the first visit, and treatment with KBG resulted in alleviation of such changes. We may therefore say that utilization of the bodily water-adjusting effects of Cassia Bark and Tuckahoe are valuable and that in cases of muscular contusion these herbs promoted absorption of muscular layer hematoma and contributed to alleviation of subcutaneous tissue edema.16,17)

Thus, KBG can be an important option for treatment of contusion, injury of musculo-tendinous junction and hematoma. Additionally, it is noteworthy that there is no adverse event arising from the use of KBG. It is very significant for cases in which NSAIDs are difficult to use (e.g., patients with asthma or gastric disorder). From the viewpoint of Kampo medicine, KBG is usually applied for the patients with a specific condition ‘Oiketsu’ (blood stasis). Acute traumatic muscle injury itself is considered to be ‘Oiketsu’. Therefore, it is reasonable that the patients who suffered from muscle injury were effectively treated with KBG. We plan to apply Kampo medicine positively from now on and continue evaluation of its efficacy.

**Conclusion**

Acute muscular contusion may be adequately treated even with KBG medicine alone. MRI is useful for evaluating responses to the treatment and predicting the therapeutic outcome.

**References**


2) Hijikata, Y., Miyamae, Y., Takatsu, H., Sentoh, S.: Two kampo medicines, jidabokuippo and hachimijigohan


