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博士学位論文

FLEXOR ACTIVITY BY INTRAMEDULLARY PRESSURE IN RABBIT FEMORAL BONE: An experimental study on thigh pain after total hip arthroplasty

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【ABSTRACT】

Thigh pain often appears after total hip arthroplasty (THA) using a cementless femoral component. It is known that sensory nerve endings exist in the medullary cavity of the bone. The purpose of this study was to investigate, in a rabbit model, whether the pressure on the femoral bone applied from inside the medullary cavity of the femoral bone causes flexion withdrawal reflex.

We loaded pressure on the inside of the medullary cavity of the femoral bone and observed whether muscle activity occurs. The pain resulting from pressure was evaluated by hind limb flexor activity produced by the flexor reflex. An integrated waveform was used to evaluate the degree of muscle activity. For the laboratory-animal models, we prepared the medullary cavity of the rabbits in two ways. In the rabbits with slight reaming, the flexor reflex appeared in low pressure. However, in rabbits with greater reaming, the flexor reflex did not appear, even under high pressure. This suggests that the pain was induced when the sensory nerve endings remained in the inside of the medullary cavity of the femoral bone and the sensory nerve endings were stimulated by the stress.

Key words　cementless total hip arthroplasty, thigh pain, flexor reflex, rabbit femoral bone, intramedullary pressure

INTRODUCTION

Thigh pain often appears after total hip arthroplasty (THA) using a cementless stem. The incidence of thigh pain reported in the literature ranges from 1.9%-40.4% [1,2,3,4,5].

Two potential mechanisms have been suggested: (1) thigh pain arising from inadequate fit or fixation of the stem within the femoral canal and (2) thigh pain arising from excessive stress concentration in the femur due to change in the femoral flexural and torsional rigidity caused by the stem within the femoral canal [6]. The etiology of thigh pain is often multifactorial and can be categorized generally into factors related to micromotion at the bone-stem interface, excessive stress transfer to the bone, prosthetic stem characteristics, host bone morphology, and endosteal/periosteal irritation. These factors are likely interrelated and may stimulate the final common pain mediators, the endosteum and periosteum [1].

Because the increase in flexural rigidity and bone stress near the stem tip is thought to contribute to thigh pain [7,8,9], we assumed that pressure inside the medullary cavity of the bone near the stem is one factor responsible for thigh

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pain. It is thought that the stimulated area is the endosteum or periosteum [1]. However, it has not been experimentally demonstrated that the pressure inside the medullary cavity of the femoral bone causes the pain.

The purpose of this study was to investigate whether the pressure on the femoral bone of a rabbit applied from inside the medullary cavity of the femoral bone causes flexion withdrawal reflex.

Materials and Methods

Ten Japanese white rabbits weighting approximately 3 kg were used for this study. The rabbits were anesthetized with halothane. Tracheostomy was done to provide artificial ventilation, and the head was fixed in a stereotaxic frame. The cranial bone of the animal was partially removed and suction decerebration was carried out; then, the spinal cord was transected at the most rostral level of the cervical cord and halothane anesthesia was terminated. Throughout the experiments, body temperature was kept at 36 ℃ with a radiating heat lamp and heartbeat was monitored with electrocardiography. All experiments were performed under the guidelines for animal experiments stipulated at our facility, and the procedures were the same as in our previous study [10].

One hind limb and bilateral fore limbs were strapped to the experimental table. The skin was incised along the greater trochanter, the muscle was released from the greater trochanter, and then the greater trochanter was resected. A balloon catheter (8 Fr) was placed in the isthmus of the cavity of the femoral bone.

Bipolar needle electrodes were placed in the muscle bellies of the flexor of the hip and the knee, and the derived muscle activities were observed by an electrodiagnostic system (Counterpoint, Dantec Medical, Skovlunde, Denmark), as in our previous study [11]. An integrated waveform was used to evaluate the degree of muscle activity. We confirmed the appearance of muscle activity due to pain reflex from applying a stimulus to the hind limb of the rabbits. After that, we applied pressure inside the medullary cavity of the femoral bone and observed whether muscle activity appeared. The pressure was applied by expansion of the balloon using the injection syringe. Normal saline solution was used to load the pressure. The load pressure was measured with a pressure sensor (PG-10KU, Kyowa Electronic Instruments, Tokyo, Japan) and recorded by personal computer (Fig. 1).

For the laboratory-animal models, we prepared the medullary cavity of the rabbits in two ways; in Group A, the medullary cavity of the femoral bone of the rabbit was slightly reamed, the reaming was only as large as the size that the balloon could enter (N=5), in Group B, reaming was extensively done from the medullary cavity to cortical bone of the femoral bone (N=5).

In Group A rabbits, we applied low pressure (~ 25 kPa) inside the medullary cavity of the femoral bone and observed whether muscle activity appeared. In Group B rabbits, at first, we applied low pressure (~ 25 kPa) inside the medullary cavity of the femoral bone and observed whether muscle activity appeared. Next, we applied high pressure (~ 200 kPa) inside the medullary cavity of the femoral bone and observed whether muscle activity appeared.

Statistical evaluation of the difference between the two groups was performed using Fisher's exact test for a two by two contingency table.

RESULTS

Before applying the pressure inside the medullary cavity

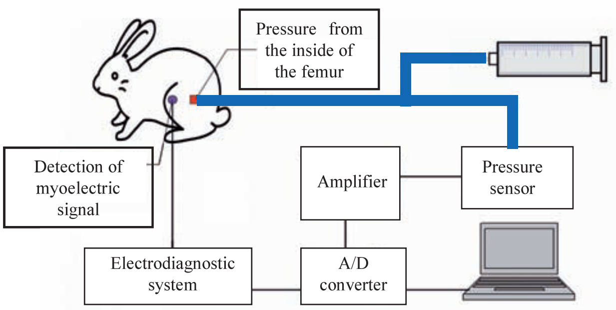

Fig. 1 Pressure was applied by expansion of the balloon by using the injection syringe. Normal saline solution was used to load the pressure. The load pressure was measured with a pressure sensor. The derived muscle activities were observed by an electrodiagnostic system. Both the pressure and the muscle activities were recorded.

of the femoral bone, we confirmed that the rabbits were fully recovered from anesthesia, by observing that hind limb muscle contraction was elicited by the pinch test. Before applying a stimulus to the hind limb of the rabbits, stable slight spontaneous electromyogram activities were observed. When we applied the stimulus to the hind limb of the rabbits, the flexor reflex appeared, and the flexor electromyogram activities increased. After recovering to the original stable slight spontaneous electromyogram activities again, we applied the pressure inside the medullary cavity of the femoral bone.

In all Group A rabbits, the flexor electromyogram activities appeared with low pressure (~ 25 kPa) (Fig. 2). As soon as the pressure was increased to 25 kPa, the flexor electromyogram activities increased. However, the flexor electromyogram activities decreased gradually, although the pressure was kept for about 30 seconds (Fig. 2). After the pressure was decreased to zero and after a brief interval, the flexor electromyogram activities recovered to the original stable slight spontaneous electromyogram activities again (not shown in Figure). The relation between the applied pressure and the flexor electromyogram activities was similar in all five Group A rabbits. After the flexor electromyogram activities recovered to the stable slight spontaneous electromyogram activities, a similar low pressure was repeated in each rabbit from Group A and we observed similar flexor electromyogram activities. In some cases, the flexor electromyogram activities appeared with the pressure of approximately 15 kPa. We confirmed the same results more than three times in each rabbit. Because we observed the flexor electromyogram activities with low pressure in Group A, we did not apply high pressure.

In Group B, we did not observe the flexor electromyogram activities with low pressure. Even though high pressure (~ 200 kPa) was applied for about 1 minute, we did not observe a significant change in the flexor electromyogram activities. A representative example from Group B with high pressure is shown in Figure 3. The same results were observed in all five Group B rabbits. We observed the same results more than three times in each rabbit.

Throughout all the experiments, body temperature and heartbeat were kept constant.

Under low pressure, the appearance ratio of the flexor reflex in Group A was significantly greater than that in Group B, as determined using Fisher's exact test for a two by two contingency table, P = 0.00794.

DISCUSSION

In this study, we experimentally demonstrated for the first time that the pressure on the femoral bone of a rabbit applied from inside the medullary cavity of the femoral bone caused flexion withdrawal reflex. It is known that somatic sensory nerves are distributed in the bone, and that sensory nerve endings exist in the medullary cavity of bone [12]. Our results suggest that the sensory nerve ending of the

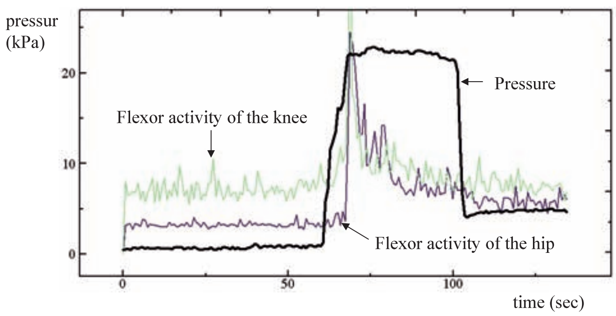

Fig. 2 In Group A rabbits, the flexor reflex appeared with low pressure (~ 25 kPa).
Heavy line: Pressure
Thin dark line: Flexor activity of the hip
Thin light line: Flexor activity of the knee

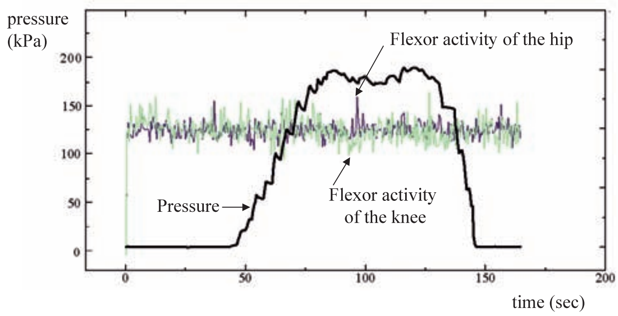

Fig. 3 In Group B rabbits the flexor reflex did not appear, even under high pressure (~ 200 kPa).
Heavy line: Pressure
Thin dark line: Flexor activity of the hip
Thin light line: Flexor activity of the knee

medullary cavity of the femoral bone is a factor of thigh pain.

The incidence of thigh pain using the cementless stem is more frequent than that of the cemented stem. The difference of fixation is thought to be a reason for difference of incidence. Maloney et al. reported that 96% of the patients who had cemented stem reported no or slight pain postoperatively, whereas 24% of the patients who had cementless stem reported mild to severe pain [13). However, some patients with obviously loosened cemented stems do not experience pain [14). As another reason for the different incidence of thigh pain, we suspect the effects of the heat from cement. Huiskes calculated a necrotic map for the hip and concluded that a larger layer of bone became necrotic in areas adjacent to a concave cement surface [15). We hypothesize that sensory nerve endings that exist in the medullary cavity of bone become necrotic by the heat from cement, and this may be one reason for the less frequent incidence of thigh pain with cemented stem.

According to Seike, the rate of sensory nerve impulses from the medullary branch of tibial nerves increases proportionally to intraosseous pressure in the range from 13.3 to 17.3 kPa, in the tibia of dogs [16). However, the increase of the rate of sensory nerve impulses may not mean that pain occurs. In its classic form, the flexor reflex is elicited most powerfully by stimulation of pain endings [17). In this study, we observed flexor reflex associated with pressure. This suggests that the pain occurred as a result of pressure. In this study, we observed the flexor reflex with a low pressure of approximately 25 kPa. This pressure of approximately 25 kPa does not indicate a threshold value. In this experiment, the muscle activities appeared with pressure of approximately 15 kPa in some cases. The pressure that caused the flexor reflex is a low pressure as in a report from Seike.

The bone-stem interface stresses are about 10 MPa when a load of 3000 N is applied to the head of the stem[18). Therefore, we thought that a low pressure of about 25 kPa might be loaded on the femoral bone from the stem. If the sensory nerve endings exist in the medullary cavity of the femoral bone (between the stem and cortical bone) after THA, thigh pain may occur in all cases. This is clinically contradictory. We assumed that, during reaming of the medullary cavity, most sensory nerve endings are removed because they are very soft. However, if the sensory nerve endings remain or are regenerated inside the medullary cavity of the femoral bone, pain will be caused.

It has been suggested that thigh pain arises from inadequate fit or fixation of the stem within the femoral canal. Engh et al. reported that in patients with radiographically stable stems, a potential source of thigh pain might be micromotion of the tip of the stem[19). The incidence of thigh pain in stems that are stable by fibrous fixation ranges from 28% to 34%, whereas stems of similar design that are stable with bony ingrowth have an incidence of approximately 8% to 10%[4,20). Whiteside reported that 53% of the patients with a loose distal fit had pain one year postoperatively, whereas 3% of those with a tight distal fit had pain one year postoperatively[5). Campbell et al. reported that thigh pain correlated with femoral stem subsidence greater than 2 mm and distal periosteal reaction[2). This suggests that stem instability seems to be a factor for thigh pain[2). The coupling between bone and the cementless stem is achieved through contact stresses between the two, and the contact regions change under load. Because these contact regions are three-dimensional, and wrap around the implant, the contact stresses change substantially while walking and during stair climbing [21). Viceconti et al. reported that the peak shear stress ranged between 2 and 170 MPa when micromotion of the stem occurred [22). When loosening and micromotion occurs in the stem, pain might be caused by the the following mechanism: the sensory nerve endings remained or were regenerated inside the medullary cavity of the femoral bone near the stem (no stress and no pain), next, the contact regions changed under load and the sensory nerve endings came in contact with the stem, and the sensory nerve endings were stimulated by the stress from loosening and micromotion.

Huiskes reported that subsidence of the stem was not associated with thigh pain[18). In addition, Barrack et al. reported six patients with thigh pain who were found to have rigid fixation and histological proof of good bone ingrowth[23). It has been suggested that excessive stress concentration is a factor for thigh pain. This excessive stress concentration is caused by changes in the femoral flexural and torsional rigidity caused by the stem within the femoral canal[6]. The structural rigidity of a particular stem is determined by the choice of stem material, stem geometry, and the stem diameter required for rigid fixation. The differences between the stiffness of femoral bone mechanical properties (ie, Young's modulus of bone elasticity = 12 GPa) and the material qualities of stems (Ti-6Al-4V = 117 GPa, cobalt-chronium = 210 GPa) may contribute to thigh pain[24]. Namba et al. observed reduced stress concentration around the stem tip with the titanium stem compared with the cobalt chrome stem, in their Finite Element analysis[8]. Skinner and Curlin described the flexural rigidity of the stem relative to the bone [7,25]. In their study of 101 hips, there was a trend toward less thigh pain with more flexible stems. Vresilovic et al. reported that thigh pain was significantly (P = 0.014) influenced by stem size in their series of 297 hips with a 12% incidence of symptoms at 1 year[6]. Arkibeck et al. reported that thigh pain was related to a larger stem size (p = 0.06) in their series of 78 hips with a 9% incidence of symptoms at a mean of ten years[26]. Lavernia et al. reported that patients receiving larger versus smaller stems irrespective of material composition were more likely to report thigh pain at 1 year and 2 years postoperatively; however, this difference was not statistically significant[27]. The general trend indicated increasing incidence of thigh pain as stem size increased.

In this experiment, the excessive stress was not replicated. We applied pressure of 200 kPa that was approximately one fiftieth of the excessive stress. After this experiment, we applied excessive stress to the cortical bone from inside the medullary cavity of the femoral bone, but the flexor reflex did not appear before fracture. So, we could not determine the reaction from the sensory nerve endings when thigh pain occurs from excessive stress. When thigh pain occurs from excessive stress, it may be the reaction from periosteal sensory nerve endings or other parts on the outside of the femoral bone, without endosteal involvement.

Domb et al. reported on the use of strut cortical allografting for the treatment of recalcitrant enigmatic thigh pain following THA patients with a well-fixed cemented or cementless stem[9]. The cortical struts were placed on the lateral cortex based at the stem tip corresponding to where the patients experienced their thigh pain in all case. While proof of the periosteum as the pain modulator is lacking, clinical reports of treatment of thigh pain with cortical strut grafting may be successful in part by the denervation of the periosteum during the exposure and graft placement [9]. We propose that the use of strut cortical allografting is an ideal treatment based on two reasons. (1) With the use of strut cortical allografting, the flexural rigidity of the femoral bone increases at the stem tip and excessive stress concentration in the femoral bone is reduced. (2) Denervation of the sensory nerves around the femoral bone may occur during operation.

The limitation of this experiment is that loading conditions did not simulate change in the pressure during walking. Because we wanted to observe the reaction from the sensory nerve endings inside the medullary cavity of the femoral bone by the direct irritation, we applied the pressure only once.

We suggest that the sensory nerve endings of the medullary cavity of the femoral bone are involved in thigh pain, based on the observation of the reaction from the sensory nerve endings inside the medullary cavity of the femoral bone. However, the reaction from the sensory nerve endings of other areas was not evaluated in this study. Thigh pain also may be the reaction from the sensory nerve endings of other regions. The mechanisms proposed from this study are likely to be one of many factors responsible for thigh pain.

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