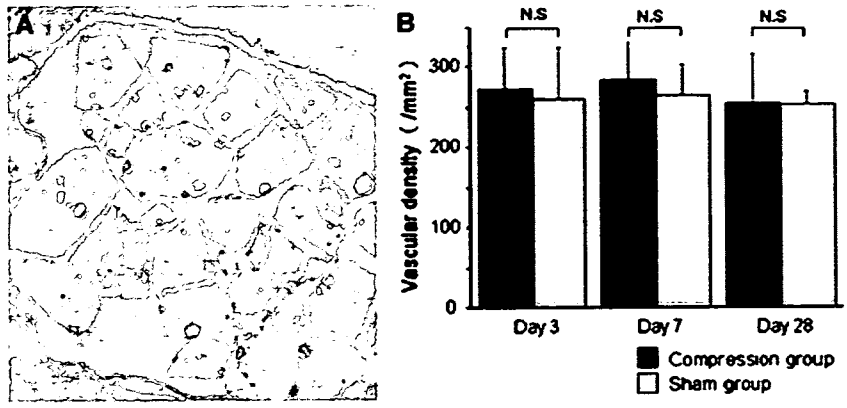

Fig. 5 **a** Photomicrographs demonstrating Factor VIII-immunoreactive blood vessels in the cauda equina of sham-operated rat at day 3 after surgery. Blood vessels are visible after immunostaining for factor VIII. *Scale bar* 200 μm. **b** Histogram presenting vascular density in the cauda equina. There were no significant differences between the compression and sham-operated groups at any time point. Results are the mean ± standard deviation of vascular density

sham-operated rats. These findings suggest that single-level compression of the cauda equina by insertion of a silicone block can reduce walking capacity and induce VEGF expression in cauda equina and DRG.

In the subacute phase, e.g., day 7 after compression, no increase in VEGF-IR cells was observed. VEGF expression in cauda equina and DRG thus appeared to be induced not only by acute compression, but also by chronic, continuous compression of cauda equina. In this study, cauda equina compression was induced by placing a silicone block into the L5 epidural space. When the block was inserted into the epidural space, acute compression of the cauda equina occurred. This limits the interpretation of the data since the onset of clinical spinal canal stenosis is much more gradual. The increase in VEGF-IR cells at day 3 might have been a direct effect of the compression being acute. However, the increase in VEGF expression at 14 or 28 days after cauda equina compression might have been due to chronic, continuous compression of the cauda equina, since the increase in VEGF expression at day 3 had disappeared by day 7, and was observed again at day 14 and day 28. These findings suggest that chronic cauda equina compression induces VEGF expression in compressed cauda equina and related DRG. In this animal model, the L5 DRG was not directly compressed, but the nerve root proximal to the L5 DRG was indirectly compressed by silicone block with decrease of spinal canal volume. Some early studies showed that VEGF expression in DRG is induced by axonal injury, and that VEGF is axonally transported and released at the site of axonal injury [21, 22]. The expression of VEGF we observed in DRG might have resulted from compression of the nerve root proximal to DRG, and VEGF may have acted at the site of compression of cauda equina. However, in our immunohistochemical examination, axons in the cauda equina did not show immunoreactivity for VEGF. Therefore, further studies are needed to explain the axonal transport of VEGF. Vascular density in the cauda equina was not increased at any of the time points examined after cauda equina compression. VEGF expression alone was observed in the compressed part of cauda equina and DRG, and was not followed by angiogenesis. It is possible that a longer period of observation associated with significant recovery of walking ability is needed to detect angiogenesis. In our animal model, cauda equina blood flow might have been reduced during walking exercise, since walking time was significantly decreased. However, cauda equina blood flow was not examined in this study. More severe compression might thus be needed to reduce blood flow enough to induce angiogenesis. On the other hand, while VEGF was originally discovered as an angiogenic factor, recent studies have indicated that it also has direct neurotrophic effects on the central and peripheral nervous systems. VEGF stimulates axonal outgrowth and enhances the survival of superior cervical and DRG neurons [21, 22], promotes neurogenesis in vitro and in vivo [7], and improves neuronal function and decreases degeneration after experimental spinal cord injury [26]. Another study suggested that endogenous VEGF has effects on neurons [12]. Therefore, expression of VEGF itself might be related to neuronal adaptation to cauda equina compression, via angiogenic as well as neurotrophic effects. Additional studies are needed to clarify the roles played by VEGF in the compressed cauda equina.

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ORIGINAL ARTICLE

The effects of a 5-HT2A receptor antagonist on blood flow in lumbar disc herniation : application of nucleus pulposus in a canine model

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Abstract Blood vessel clots are found around the nerve root in patients with lumbar disc herniation. Thrombosis formation in the experimental application of nucleus pulposus to the nerve root has been shown in histological studies. In addition, reduction of blood flow and nerve conduction velocity are induced by the application of nucleus pulposus, which mimics lumbar disc herniation. In patients with lumbar disc herniation, nerve root block, which is thought to increase nerve blood flow, improves radiculopathy. 5-HT_{2A} receptor antagonists are used in chronic arterial occlusive diseases to improve blood flow and have been reported to work as well as nonsteroidal anti-inflammatory drugs in improving radiculopathy due to lumbar disc herniation in clinical studies. This study investigated the effects of a 5-HT_{2A} receptor antagonist on blood vessel diameter and blood flow in a canine experimental model of lumbar disc herniation. A total of 13 dogs were used. The animals were divided into three experimental groups and surgery was performed 1 week before measurements. In the nucleus pulposus group (NP; $n = 5$), the nucleus pulposus was applied to the nerve roots from the ventral side. In the sham group ($n = 5$), nucleus pulposus was not applied. In the naïve group ($n = 3$), the animals did not undergo surgery. Measurements of vessel diameter and blood flow were done before and after administration of saline and drugs. The diameters and blood flow volume of the observed blood vessels were measured on video-recordings every 10 min for 65 min. In all groups, vessel diameter and blood flow did not change before or after administration of saline. In the NP and sham groups, vessel diameter and blood flow increased significantly after administration of 5-HTRA compared with the naïve group. 5-HTRA improved blood vessel diameter and blood flow in the nerve roots inflamed by the application of nucleus pulposus but not in the intact nerve roots. 5-HTRA might be a potential agent to improve blood flow in the nerve roots of patients with lumbar disc herniation.

Keywords Nerve root · Blood flow · 5-HT · Disc herniation

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Introduction

Lumbar disc herniation is the one of the most common diseases that induces low back pain and radiculopathy. Many studies have investigated the mechanisms of radicular pain due to lumbar disc herniation and both mechanical and chemical factors [9, 18, 19, 29] have been implicated. Serotonin is one of the chemical factors that play a role in inducing pain in the peripheral nerves and affecting blood vessels. Recently, a clinical study showed that a 5-HT_{2A} receptor antagonist (5-HTRA) provided the same symptom relief as nonsteroidal anti-inflammatory drugs in patients with lumbar disc herniation [11]. In the clinical studies, 5-HTRA has been shown to improve circulation and is used to treat circulatory disorders associated with diabetes as well as chronic arterial occlusive diseases [8]. In addition, 5-HTRA is used to treat intermittent claudication due to lumbar spinal stenosis and has been shown to improve blood flow in the nerve root in experimental cauda equina compression [24]. It is also expected to improve blood flow in the nerve roots in the orthopaedic field [24].

It is reported that blood vessel clots are found around symptomatic nerve roots in patients with lumbar disc herniation [5]. In the canine experimental disc herniation model, there is thrombosis formation in nerve roots exposed to nucleus pulposus [13, 20]. It has also been found that blood flow decreased after nucleus pulposus was applied to nerve roots, which is related to a reduction in nerve conduction velocity [13, 18, 31]. This study focused on blood flow to the nerve roots in lumbar disc herniation. Our aim was to assess the effect of 5-HTRA on blood flow in a canine experimental model of lumbar disc herniation.

Materials and methods

A total of 13 female beagle dogs (15 months old) with an average body weight of 10.6 ± 0.4 kg (range 10.5–11.5 kg) were used in this study (Table 1). The experimental protocol was approved by the local animal ethics committee and conformed to Fukushima Medical University Guidelines, the Japanese Government Animal Protection and Management Law (No. 15), and the Japanese Government Notification on Feeding and Safekeeping of Animals (No. 6). All the dogs were anesthetized with an intra-muscular injection of 25 mg/kg body weight of ketamine hydrochloride (Ketalar 50 mg/ml; Parke -Davis, Morris Plains, NJ, USA) and 10 mg/ml body weight of pentobarbital sodium (Nembutal 50 mg/ml; Abbott Laboratories, Chicago, IL, USA). After endotracheal intubation, anesthesia was maintained by inhalation of nitrous oxide (3 l/min), oxygen (3 l/min), and halothane (1%, SIC Chemicals Ltd., Bristol, UK).

The animals were divided into three experimental groups: the nucleus pulposus group (NP; $n = 5$), the sham group ($n = 5$), and the naïve group ($n = 3$). In the NP group, the dogs were placed prone and a partial laminectomy of the caudal part of the sixth lumbar vertebrae was performed. The dura mater was gently retracted and the dorsolateral portion of the annulus fibrosus of the L6/L7 intervertebral disc was incised using an 18-gauge needle. This procedure resulted in visible leakage of nucleus pulposus into the epidural space to the nerve roots on the ventral side. In the sham group, the procedure was the same as the NP group but nucleus pulposus was not leaked to the nerve roots. In the naïve group, the animals did not undergo surgery.

Table 1 Animals' condition

No	Breed	Age (months)	Sex	Weight (kg)
1	Beagle	15	Female	11.5
2	Beagle	15	Female	11
3	Beagle	15	Female	11
4	Beagle	15	Female	10.5
5	Beagle	15	Female	10.5
6	Beagle	15	Female	11
7	Beagle	15	Female	10.5
8	Beagle	15	Female	11
9	Beagle	15	Female	10
0	Beagle	15	Female	10.5
11	Beagle	15	Female	10.5
12	Beagle	15	Female	10
13	Beagle	15	Female	10

Analysis was conducted 7 days after the initial operation, applying the same operational procedures (e.g., animal posture, anesthesia, and preoperative and postoperative management) as in the initial operation. A catheter was inserted and placed in the left cervical artery for continuous monitoring of blood pressure. Another catheter was placed in the abdominal aorta from the right femoral artery. This catheter was used for injection of ink, saline, and 5-HTRA. Preliminary experimental tests showed that the catheter was between the first and third lumbar arteries when its tip was placed on the same level as the distal bone edge of the twelfth rib. After insertion of the catheter, the ligamentum flavum between the laminae of the seventh lumbar and first sacral vertebrae were removed, and the cauda equina was exposed. The second or third sacral nerve root was identified just caudal to the compression site. The blood vessels were observed using a microscope equipped with a video-camera (Digital HI-SCOPE Video System; Hirox Co. Ltd., Tokyo Japan) at 400× magnification [22, 24–26] (Fig. 1).

Sarpogrelate hydrochloride (5-HT_{2A} receptor antagonist; 5-HTRA) (Mitsubishi Pharma Co. Tokyo, Japan) was used. In a clinical situation, the maximum serum concentration is 0.54 μg/ml after 100 mg sarpogrelate hydrochloride oral administration in adults. According to our previous paper, 0.05 μg/ml 5-HTRA was effective in improving blood flow in compressed nerve roots [24]. Therefore, we chose 0.05 μg/ml of 5-HTRA for this study. Saline was used for a vehicle of 5-HTRA. Blue ink was used to measure blood flow velocity. From the catheter in the abdominal aorta, 3 ml of blue ink (Pilot Co. Ltd., Tokyo, Japan) was injected manually for 1 s. When the ink flowed through the observed blood vessel, the color of the vessel changed from red to blue for 3 s. After confirming a flow of ink from the catheter to the observed blood vessels, recordings of the blood vessels were performed for 65 min. In all groups, intra-arterial saline (0.2 ml/min) was injected for 5 min using a catheter. After the administration of saline, the blood vessels were observed for 15 min. After 15 min, 5-HTRA (0.2 ml/min) was injected for 15 min and then the blood vessels were observed for 30 min without injection. Ink was injected before 5-HTRA and every

Fig. 1 The observed blood vessel on the monitor. *N* nerve root, *B* blood vessel. *Bar* = 100 μm

10 min thereafter (Fig. 2). The measurements of vessel diameter, blood flow velocity, and blood flow volume index in the observed blood vessels were performed by a blinded investigator using a video recording. The diameter of the blood vessels (μm) was measured for each ink injection using a monitor-connected video system equipped with a distance-measuring device. When two points were chosen, the distance-measuring device measured the distance between the two points automatically. Two points on the edge of blood vessel were chosen and measured three times at each time point. The average data of the diameter were used at each time point. The time (s) of the color changes from red to blue after injection of blue ink was measured using the iMovie software (Macintosh version) installed in a computer. The blood flow velocity (mm/s) was calculated by formula using time and distance (Fig. 3). The blood flow volume index was defined as (1/2 diameter)^2 × (blood flow velocity) [22, 24–26]. The values of the diameter and blood flow volume index served as the baseline (100%) before injecting saline. All recordings of the diameter of vessels and the blood flow volume index were expressed as a percentage of baseline values.

Statistical analysis

Comparisons of the differences of the diameter of the blood vessels and blood flow index among each group over the entire observed time were evaluated by repeated measure ANOVA. Data were expressed as means ± SD. A value of $P < 0.05$ was considered significant. The diameter and ink speed were measured three times at each time point;

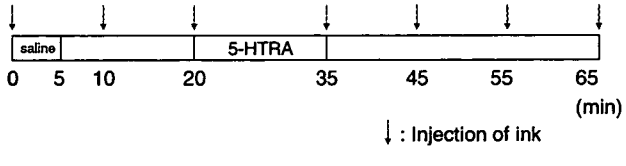

Fig. 2 Time course of injection. Saline was injected for 5 min, and 5-HTRA was injected for 15 min at 15-min intervals. The blood vessels were observed for 65 min. Blue ink was injected before 5-HTRA and every 10 min to measure the blood flow speed

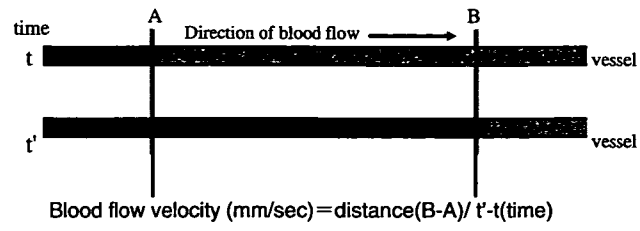

Fig. 3 The time (s) was measured using ink color changes ($t' - t$). The distance from *A* to *B* was 0.82 mm on the monitor. The blood velocity (mm/s) was then calculated

therefore, intra-observer reliability (*R*) was evaluated by one-way ANOVA. *R* was calculated using a formula of *R* = (mean square between samples − mean square within samples)/mean square between samples + (times of measurement − 1) × mean square within samples. *R*-values of more than 0.8 were considered to be "good" and more than 0.9 to be "great". The *R*-value was determined to be 0.939 and 0.896 for blood vessels and ink speed, respectively. Because intra-observer reliabilities of the diameter of blood vessels and blood speed in this study were great and good, the average data of three measurements were used.

Results

Throughout the observation period, neither paralysis nor dysfunction of the bladder was observed in any dog. The average body weight was 11 ± 0.4 kg when the analyses were performed. No wound infections occurred.

The blood pressure was not significantly different between pre and post administrations of 5-HTRA or saline in each group. The observed blood vessels were defined and we recorded seven vessels in the NP group, eight vessels in the sham group, and four vessels in the naïve group.

Diameter of blood vessels

The diameters of the blood vessels did not change after administration of saline in any group and there were no significant differences in diameters among groups (Table 2). In the NP and sham groups, the vessel diameter increased after injection of 5-HTRA (Fig. 4). In the naïve group, the diameter did not change after administration of 5-HTRA. In the NP and sham groups, changes in blood vessel diameter during and after administration of 5-HTRA (from 20 to 65 min) were significantly higher than in the naïve group ($P < 0.0001$ and $P = 0.0182$, respectively). In particular, the diameter in the NP group was significantly increased compared with the sham group ($P = 0.0027$) (Table 3; Fig. 5)

Table 2 Diameter of blood vessels (%) during and after administration of saline

Group	Pre	10 min	20 min	*P* value vs. naïve	*P* value vs. sham
NP	100 ± 0	100.4 ± 15.5	103.5 ± 9.5	0.3047	0.1337
Sham	100 ± 0	98.4 ± 4.2	99.9 ± 6.5	0.8184	
Naïve	100 ± 0	101.4 ± 2.1	98.6 ± 1.4		0.8184

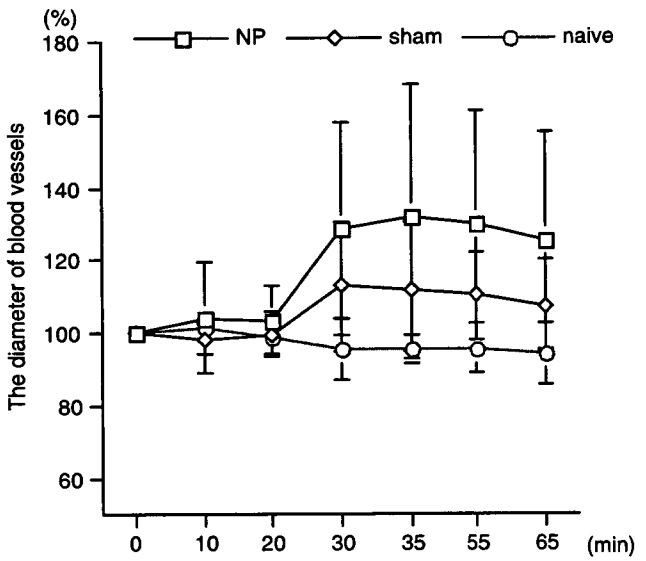

Fig. 4 The diameter of blood vessels after administration of 5-HTRA. In the NP and sham groups, changes in blood vessel diameter during and after administration of 5-HTRA (from 20 to 65 min) were significantly higher than in the naïve group ($P < 0.0001$ and $P = 0.0182$, respectively)

Blood flow volume

Blood flow did not change after administration of saline in any group and there were no significant differences in blood flow among groups (Table 4). In the NP and sham groups, blood flow increased after injection of 5-HTRA (Fig. 2). In the naïve group, blood flow did not change after administration of 5-HTRA. In the NP and sham groups, the changes in blood flow during and after administration of 5-HTRA (from 20 to 65 min) were significantly higher than in the naïve group ($P < 0.0001$ and $P = 0.0007$, respectively). In particular, blood flow in the NP group was significantly increased compared with the sham group ($P = 0.0278$) (Table 5).

Discussion

In the present study, vessel diameter and blood flow did not change before and after administration of saline in any group. This fact demonstrated that saline as a vehicle and ink to measure the blood flow velocity did not affect the blood vessel reaction in this experimental setting. In addition, all animals received saline before treatment; thus, blood vessels could be compared before and after administration of 5-HTRA both within each group and in each animal.

The blood vessels in the naïve group in this study did not change before or after administration of 5-HTRA. It is known that normal blood vessels keep their tension due to a balance of vasoconstrictor and vasodilator effects that occurs in smooth muscle and endothelial cells in blood vessels. There are seven groups of 5-HT receptors with 14 subtypes; the 5-HT1 and 5-HT2 receptors are associated with blood vessels. Nitric oxide, which is an important vasodilator [30], is produced in normal endothelial cells, mediated by the 5-HT1 receptor on endothelial cells, and affects vascular smooth muscle [2, 14, 28]. This vasodilator effect, and the vasoconstriction mediated by the 5-HT2A receptor on smooth muscle, maintains the tension in normal blood vessels. This tension can be maintained in various situations and may explain why, in this study, intact blood vessels in the naïve group did not change after the administration of 5-HTRA.

However, in the pathological lesions observed previously, blood vessels are vasoconstricted after administration of serotonin in canine coronary arteries [27]. It is known that vasospasm can be induced by serotonin through the 5-HT1 or 5-HT2 receptor [1, 3, 4, 10] and that 5-HTRA inhibits vasoconstriction by serotonin in the caudal artery in rats [6]. In the present study, the diameter and blood flow of blood vessels increased after administration of 5-HTRA in animals that underwent surgery. Surgery and surgical procedures such as the spread of blood around nerve roots could affect the nerve root, even though nucleus pulposus was not leaked in the sham group. Serotonin is released from platelets when inflammation and bleeding occur. In

Table 3 Diameter of blood vessels (%) during and after administration of 5-HTRA

Group	20 min	35 min	45 min	55 min	65 min	*P* value vs. naïve	*P* value vs. sham
NP	103.5 ± 9.5	128.5 ± 29.1	131.6 ± 36.6	129.7 ± 31.3	125.4 ± 29.6	<0.0001	0.0027
Sham	99.9 ± 6.5	114.2 ± 18.6	111.9 ± 18.7	111.4 ± 12.4	109.0 ± 12.8	0.0182	
Naïve	98.6 ± 1.4	95.6 ± 8.3	95.5 ± 4.0	95.7 ± 6.9	94.1 ± 8.2		0.0182

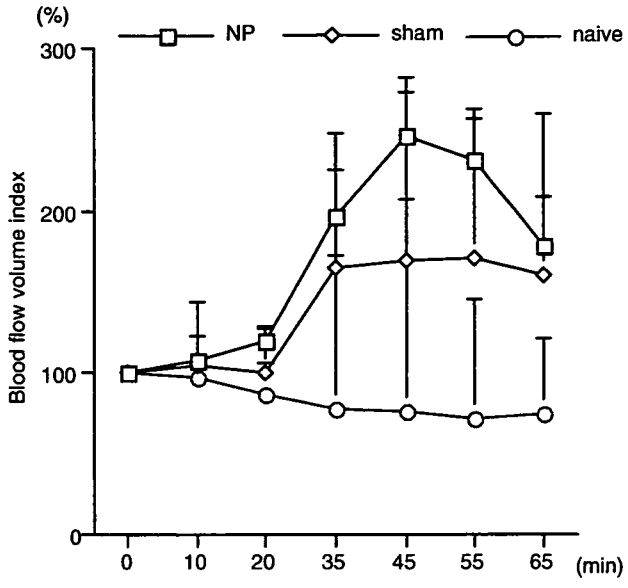

Fig. 5 Blood flow after administration of 5-HTRA. In the NP and sham groups, the changes in blood flow during and after administration of 5-HTRA (from 20 to 65 min) were significantly higher than in the naïve group ($P < 0.0001$ and $P = 0.0007$, respectively)

the NP and sham groups, the local concentration of serotonin might increase around the surgical area. However, in the NP group, the changes in vessel diameter and blood flow were highest compared with the sham and naïve groups. We could not determine whether serotonin was included in the nucleus pulposus or not under these inflammatory conditions. However, a previous study showed that plasma 5-hydroxyindoleacetic acid (5-HTAA), a metabolite of 5-HT, increased in animals in which the nucleus pulposus was harvested compared with sham animals [12]. This fact suggests that serotonin is associated with inducing symptoms seen in a lumbar disc herniation. The NP group in this study may have experienced increased inflammation and serotonin release compared with the sham group. We have also reported previously on the compression of the cauda equina in the canine model and showed that blood flow in the compressed nerve roots decreased with the dysfunction of endothelial cells after administration of serotonin, whereas blood flow in normal nerve roots did not decrease [25]. In addition, this reduction of blood flow was prevented by the 5-HTRA, indicating that this blood vessel reaction is associated with the 5-HT2A receptor [24]. The NP group in this study might have a dysfunction of endothelial cells compared with the sham group. This could explain why the effect of 5-HTRA was enhanced in the NP group rather than in the sham group.

In addition, 5-HT2A receptors are located on platelets, and serotonin can cause platelets to aggregate; thus the release of serotonin from aggregating platelets increases further platelet aggregation mediated by 5-HT2A. In a clinical situation, blood vessel clots are found around the nerve root in patients with lumbar disc herniation. Thrombosis formation in the experimental application of nucleus pulposus to the nerve root has been shown in histological studies [13, 20]. Therefore, 5-HTRA may prevent platelet aggregation and decrease the release of serotonin from platelets in patients with lumbar disc herniation.

There is no strong evidence regarding how much blood flow reduction influences the neuropathic pain. However, blood flow and nerve conduction velocity in the nerve root decrease after application of nucleus pulposus [13, 21, 31]. In addition, in the clinical setting, nerve root block is useful for improving radicular pain and maintains more duration than that of a local anesthetic effect. This is considered by the effect of blood flow increase. In an experimental study, intraradicular blood flow increased after nerve root infiltration [32]. Therefore, decreasing blood flow is associated with the dysfunction of the nerve root, and increasing blood flow might contribute to improving radiculopathy. In this

Table 4 Blood flow index (%) during and after administration of saline

Group	Pre	10 min	20 min	*P* value vs. naive	*P* value vs. sham
NP	100 ± 0	107.5 ± 47.2	120.0 ± 20.1	0.0773	0.2576
Sham	100 ± 0	104.6 ± 6.7	100.6 ± 25.5	0.4064	
Naïve	100 ± 0	97.7 ± 12.9	87.2 ± 18.2		0.4064

Table 5 Blood flow index (%) during and after administration of 5-HTRA

Group	20 min	35 min	45 min	55 min	65 min	*P* value vs. naïve	*P* value vs. sham
NP	120.0 ± 20.1	196.6 ± 94.1	245.8 ± 130.1	231.6 ± 74	178.5 ± 47.0	<0.0001	0.0278
Sham	100.6 ± 25.5	161.2 ± 77.0	165.2 ± 97.1	167.2 ± 79.9	155.9 ± 93.1	0.0007	
Naïve	87.2 ± 18.2	78.7 ± 25.3	75.8 ± 11.7	72.4 ± 13.1	74.5 ± 10.2		0.0007

study, blood flow increased after administration of 5-HTRA, and thus this compound might improve radiculopathy due to lumbar disc herniation.

There are some limitations to this study. The same blood vessel cannot be investigated before and after application of nucleus pulposus using this method. Therefore, the blood flow in this study did not show results before and after the leakage of the nucleus pulposus. According to a previous paper, blood flow in the nerve root was reduced 1 week after application of nucleus pulposus in a canine model [21]. Thus, the baseline of blood flow in the NP group could decrease after application of nucleus pulposus and the increased blood flow in these results suggests that changes in blood flow recover to normal levels. In either case, 5-HTRA is effective in improving blood flow. In addition, we investigated the treatment effect only 7 days after application of nucleus pulposus. A previous study in a canine model showed that blood flow decreases and nerve conduction velocity is reduced 7 days after application of nucleus pulposus, but these variables recover at 1 month after application of nucleus pulposus [21]. It is not clear if the effect of 5-HTRA will continue over a chronic period. This might be a limitation of this experimental model. Another limitation is the choice of the observed blood vessel. Because of difficulty of this procedure, we could find only one or two blood vessels on the monitor in one animal when the magnification was 400×. Even though blood vessels were observed, if we could not define the ink flow in the observed blood vessels on the monitor, we cannot measure blood flow. If we could observe two blood vessels fortunately, we could analyze two blood vessels in one animal. Thereby, the number of observed blood vessels was different in each group, which might affect the results.

Serotonin has effects not only in blood vessels but also in the nervous system. Serotonin is a neurotransmitter that inhibits and/or moderates pain in the central nervous system, whereas in the peripheral nervous system, serotonin induces pain. 5-HT1 and 5-HT3 receptors are known to be related to pain in peripheral nerves. In addition, it is reported that 5-HT2A receptors are expressed on dorsal root ganglion (DRG) neurons [17]. It has been reported that 5-HTRA is effective in the reduction of pain behavior in some experimental studies [7, 15, 16, 23]. However, we could not investigate pain behavior in this study. The improvement of blood flow may be directly or indirectly related to neuropathic pain relief. Thus, it is difficult to explain the relationship between pain behavior and blood flow. Based on the role of 5-HT2A receptors on blood vessels and in the peripheral nervous system, 5-HRTA may effect to improve blood flow and pain individually or interactively.

Conclusion

The present study, which focused on blood flow, found that 5-HTRA improves blood flow. 5-HTRA might be a potential agent to improve radiculopathy due to lumbar disc herniation.

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Original article

Correlation between inflammatory cytokines released from the lumbar facet joint tissue and symptoms in degenerative lumbar spinal disorders

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Abstract

Background. Lumbar facet joint tissue has inflammatory cytokines. However, no reports have shown whether inflammatory cytokines in the facet joint leads to pain. This study was designed to characterize the correlation between inflammatory cytokines released from facet joint tissue and symptoms in degenerative lumbar spinal disorders. The purpose of this study was to seek involvement of inflammatory facet joint for radiculopathy in lumbar spinal canal stenosis with clinical and anatomical studies.

Methods. Lumbar facet joint cartilage and synovial tissues in 40 cases of posterior lumbar surgery were harvested to measure tumor necrotizing factor-α (TNFα), interleukin-1β (IL-1β), and interleukin-6 (IL-6) during operation. The visual analogue scale (VAS) and Roland-Morris disability questionnaire (RDQ) were used to examine the correlation between cytokine concentration and symptoms. Coloring agent was injected into facet joints of fresh cadavers to find leakage of pigment from the facet joint into the spinal canal.

Results. Inflammatory cytokines were detected in the joint tissues in the lumbar spinal canal stenosis (LSCS) and lumbar disc herniation (LDH) groups. A positive reaction rate of IL-1β was significantly higher in the LSCS group than in the LDH group. IL-1β-positive cases in the LSCS group showed higher VAS scores for leg pain and higher RDQ scores. Intraspinal canal tissues including lumbar nerve root were stained by injection of methylene blue into the facet joints.

Conclusions. IL-1β in facet joint cartilage in LSCS was associated with leg pain and a decline of quality of life. Inflammatory cytokines produced in degenerated facet joint may leak into the intraspinal space through the lateral part of the ventral facet joint capsule. These results suggest the involvement of inflammatory cytokines in degenerated lumbar facet joints regarding the genesis of pain production.

Introduction

Much attention has been focused on the involvement of chemical factors in radiculopathy caused by lumbar disc herniation. It is, meanwhile, reported that osteoarthritic (OA) changes in a facet joint cause pain in degenerative lumbar spinal disorders.[1–6] Moreover, some reports demonstrate that inflammatory cytokines such as tumor necrosis factor-α (TNFα), interleukin-1β (IL-1β), and interleukin-6 (IL-6), as well as inflammatory mediators such as prostaglandins also can be found in the facet joint tissues in degenerative lumbar disorders.[7,8] On the other hand, based on clinical examination of limb joints with OA, local OA joints showed long-lasting, severe inflammatory symptoms and findings similar to those of inflammatory arthritis, such as rheumatoid arthritis (RA).[9–11] Based on these observations, OA produces symptoms similar to those of inflammatory arthritis including RA, resulting in possible involvement of inflammation in the joint cartilage and synovial tissue during joint destruction and pain.[9,12–14] According to these findings, a facet joint with the same anatomy as the limb joints might exhibit painful symptoms due not only to mechanical factors such as arthropathic changes but also to chemical factors due to arthritis. Nevertheless, there have been no reports suggesting that inflammation due to chemical factors, such as inflammatory cytokines, in the lumbar degenerated facet joint also cause pain in degenerative lumbar spinal disorders. The purpose of this study was to determine the involvement of the inflammatory facet joint in lumbar spinal canal stenosis, in addition to mechanical compression, using clinical and anatomical methods.

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Materials and methods

Patient information

A total of 40 patients who underwent posterior lumbar spinal surgery due to degenerative lumbar spinal disorders were enrolled in this study. Informed consent was obtained from all patients. There were 24 men and 16 women in the study group. More particularly, there were 11 cases in the lumbar disc herniation (LDH) group and 29 in the lumbar spinal canal stenosis (LSCS) group. The average age of the patients subjected to operation was 50 years (range 30–66 years) for the LDH group and 67 years (range 48–84 years) for the LSCS group, with no significant difference between the two groups. The average duration of illness for the LDH group was 13 weeks, whereas the duration for the LSCS group was a significantly longer period of 132 weeks.

We determined the number of responsible levels from clinical symptoms, physical findings, neurological findings, various imaging findings including magnetic resonance imaging (MRI), and selective nerve root blocks. The symptoms of all LDH cases were due to radiculopathy caused by a single-disc disorder; therefore, we observed no cases of cauda equina syndrome in the LDH group. The responsible level of the LSCS group amounted to 65.5% for single-disc involvement and 35.5% for multiple-disc involvement. It was found that radiculopathy accounted for 55.2% and cauda equina syndrome/mixed type (i.e., combination of radiculopathy and cauda equina syndrome) for 44.8% in the LSCS group. In cases in which the symptoms appeared in bilateral lower extremities, the side where the facet joint tissue had more severe symptoms was used. Also, in cases in which the responsible level was found at multiple intervertebral levels, the facet joint tissue was chosen where the problem seemed to be most significant according to neurological findings and selective nerve root block.

Determining the quantity of inflammatory cytokines and comparing cytokine levels and clinical symptoms

The cartilage and synovial tissues were harvested with surgical knives and punches from the facet joints at the responsible level during operation. The collected tissues were immediately cooled to –80°C and were kept at that temperature for preservation. Each tissue was homogenized by ice application to prepare a suspension. The tissues were subject to centrifugal separation with 15000 rpm for 30 min at 4°C, and its supernatant was collected to measure the properties. In each tissue, the levels of TNFα and IL-1β were measured as indexes of inflammatory cytokines by enzyme-linked immunosorbent assay (ELISA), and the IL-6 level was measured by chemiluminescent enzyme immunoassay (CLEIA) using human TNFα kit (Japan Immunoresearch Laboratories, Gunma, Japan), human IL-1β EASIA kit (BioSource Europe, Nivelles, Belgium), and human IL-6 kit (Fujirebio, Tokyo, Japan), respectively. The measuring instrument was the EMax Microplate Reader (Molecular Devices, Sunnydale, CA, USA). The detection sensitivities for TNFα, IL-1β, and IL-6 were 5 pg/ml, 10 pg/ml, and 4 pg/ml, respectively, because the serum concentrations of these cytokines in healthy adults were less than those at each detection sensitivity by the supply companies. Each value for these cytokines beyond the sensitivity was regarded as "positive," and each value within the sensitivities were regarded as "negative." The inflammatory cytokine levels for each collected tissue and the correlation with the visual analogue scale (VAS) for low back pain, leg pain, and leg numbness and the Japanese version of the Roland-Morris disability questionnaire (RDQ) were statistically examined. For statistical examination, Student's *t*-test and the Kruskal-Wallis test were used; significant difference was set at less than 5% risk.

Assessing facet joint osteoarthritis on MRI

MRI studies for all patients in both groups were performed on the same 1.5 T imaging system. Each study included T1-weighted and T2-weighted sagittal images. One experienced orthopedic surgeon reviewed all MR images and was masked to any clinical and prior imaging data. Four grades of osteoarthritis of the facet joints were defined using criteria by Weishaupt et al.[15]: grade 0, normal facet joint space (2–4 mm); grade 1, narrowing of the facet joint space (<2 mm) and/or small osteophytes and/or mild hypertrophy of the articular process; grade 2, narrowing of the facet joint space and/or moderate osteophytes and/or moderate hypertrophy of the articular process and/or mild subarticular bone erosions; grade 3, narrowing of the facet joint space and/or large osteophytes and/or severe hypertrophy of the articular process and/or severe subarticular bone erosions and/or subchondral cysts.

Two weeks later, the same person evaluated the facet joints on MRI using the same grading to assess intraobserver variability. Weighted kappa statistics were used to describe intraobserver agreement for MRI. The value of weighted kappa coefficients for intraobserver agreement for MRI here was considered to be "good" when the score was >0.8.

Anatomical study of joint fluid leakage from degenerated lumbar facet joints

A total of 24 lumbar facet joints from three fresh male cadavers — ages 63, 65, and 85 years — were used for

the macroscopic study. None of the cadavers had undergone any lumbar surgery during their lifetimes. The causes of death were colon cancer, heart failure, and pneumonia, respectively. According to lumbar plain radiographic examination, degeneration changes were observed in lumbar facet joints in all cases.

The bodies were placed in prone position, and a medial skin incision was made on the lumbar part. Paravertebral muscles were detached, and dorsal capsules of bilateral L1/2, 2/3, 3/4, 4/5 facet joints were exposed. Agar jelly was injected into the subdural and epidural space through inter-raminal space. This jelly injection procedure was to prevent cauda equina avulsion and to keep the nerve and connective tissue structures in the spinal canal fixed when the vertebral body was removed. Methylene blue was injected into the lumbar facet joints using a 20-gauge needle and syringe under direct vision to detect any leakage of the coloring agent toward the intraspinal canal tissue including the lumbar nerve root. The methylene blue volume injected into each facet joint was 0.5 ml in this study because the dosage of contrast medium for lumbar facet joint block is generally 0.5 ml, and it is reported that the lumbar facet joint capacity is approximately 1–2 ml.[16] A block of lumbar spine was then removed in one piece and kept frozen. Each lumbar vertebral body was cut in a level of each facet joint and a slice section was prepared.

Extraarticular leakage of the coloring agent was classified into four categories to discuss the extent of its leakage. Specifically, leakage localized in the joint cartilage and joint capsule was defined as type C (cartilage); staining of the joint cartilage, joint capsule, and subsequently ligamentum flavum was defined as type F (flavum); staining of the ligamentum flavum and further soft tissue in epidural space was defined as type E (epidural tissue); and staining of nerve roots was defined as type R (root). By definition, types C and F are localized in the joint, and types E and R are subject to extraarticular leakage. All experiments in this study were approved by the Fukushima Medical University Investigation Review Committee.

Results

Correlation between inflammatory cytokine concentration and clinical symptoms

Each inflammatory cytokine concentration in the synovial and cartilage tissue was examined in the LDH and LSCS groups. The collected volumes of cartilage tissue and synovial tissues in the LDH group were 201 ± 105 mg and 123 ± 121 mg, respectively, and those in the LSCS group were 287 ± 208 mg and 200 ± 151 mg, respectively. There was no significant difference in collection volume of either tissue between the two groups.

In both groups, the positive reaction rate of inflammatory cytokines in each tissue was determined. In the LDH group, no TNFα was detected from either the cartilage or synovial tissues. The positive reaction rate of TNFα for cartilage tissue was 0% and for synovial tissue it was 3.7% (1/27 cases) in the LSCS group. Whereas this value for IL-1β expressed in cartilage tissue in the LDH group was 11.1% (1/9), the positive reaction rate was 34.5% (10/29) in the LSCS group. As for IL-1β, the synovial tissue had a positive rate of 0% in the LDH group, but the value was 38.5% (10/26) in the LSCS group. IL-1β had significantly higher positive reaction rates in the LSCS group than in the LDH group ($P < 0.05$). The detection rate of IL-6 was higher for both tissues in both groups than the detection rates for TNFα or IL-1β ($P < 0.05$). The positive reaction rates in the cartilage and synovial tissues in the LDH group were 90.0% (9/10) and 90.9%(10/11), respectively; and they were 100% for all the cases in both tissues in the LSCS group (Fig. 1). More specifically, the highest positive rate was obtained for IL-6, followed by IL-1β and

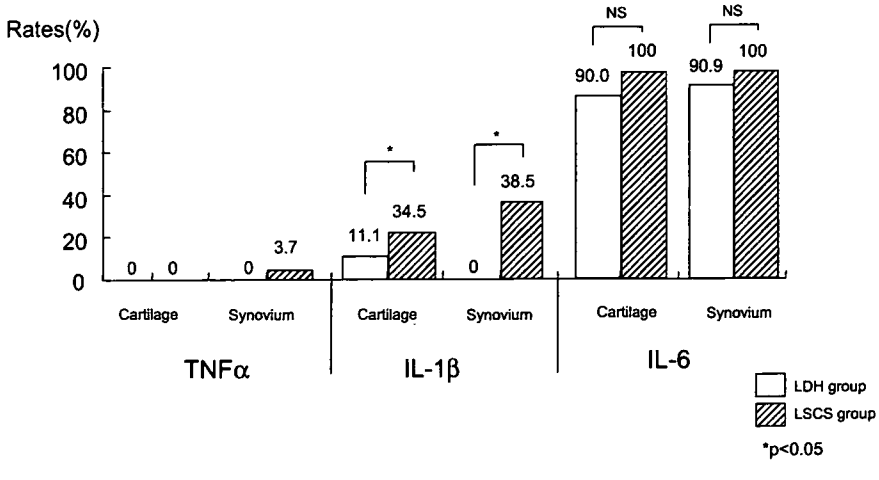


Fig. 1. Positive reaction rates for each inflammatory cytokine in the lumbar disc herniation (*LDH*) and lumbar spinal canal stenosis (*LSCS*) groups. The positive reaction rate was the greatest for interleukin-6 (IL-6), followed by IL-1β, and tumor necrosis factor-α (TNFα) for both tissues in both groups. The IL-1β-positive rate was significantly higher in the LSCS group than in the LDH group. IL-6 was observed at a high rate for both tissues in both groups

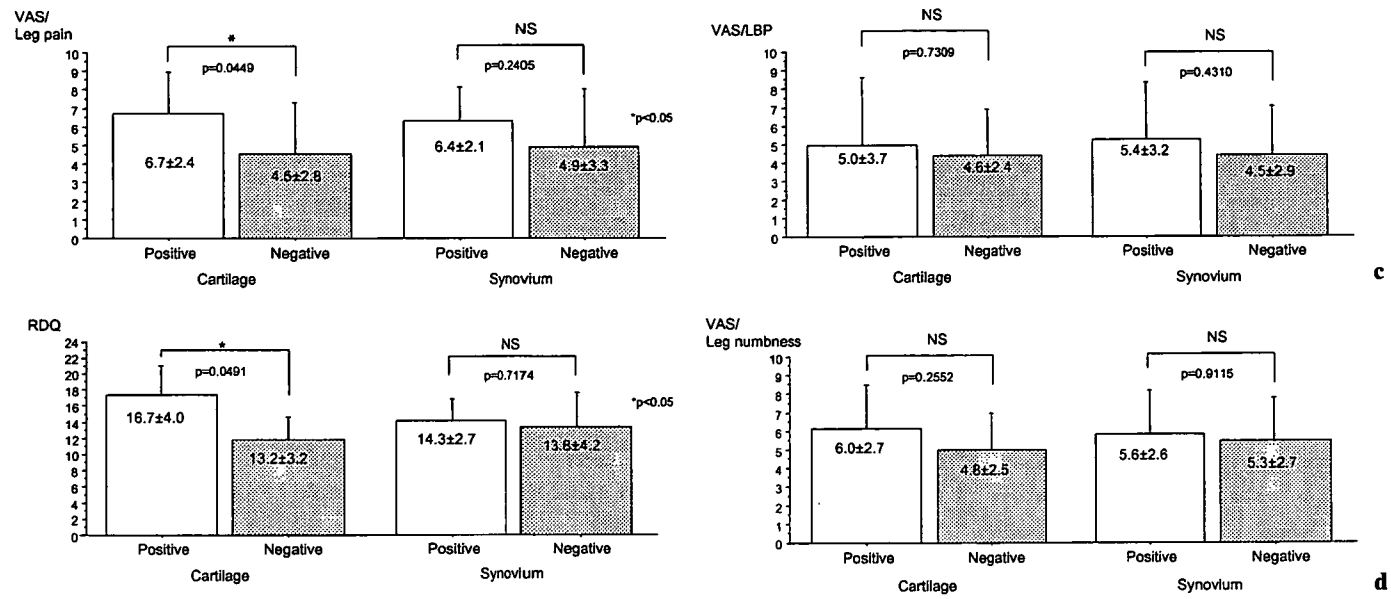


Fig. 2. As for IL-1β, the LSCS group was divided into a positive group and negative group to explore the extent of clinical symptoms. With regard to cartilage tissue, the IL-1β-positive group showed a significantly higher Visual Analogue Scale (VAS) score for leg pain (**a**) and the Roland-Morris disability questionnaire (RDQ) (**b**) compared to the IL-1β-negative group. On the other hand, IL-1β expression in synovial tissue indicated no statistically significant difference in the VAS for leg pain or the RDQ between the IL-1β-positive group and the IL-1β-negative group. The VAS value for low back pain (*LBP*) and leg numbness indicated no significant difference in the tissues between the two groups (**c**, **d**)

TNFα for both tissues in both the LDH and LSCS groups.

Moreover, for IL-1β, the LSCS group was divided into a positive group and negative group to discuss the extent of clinical symptoms. In the LSCS group, the IL-1β-positive group in the facet joint cartilage at the responsible level had VAS for leg pain and RDQ values of 6.7 ± 2.4 and 16.7 ± 4.0, respectively. In contrast, the IL-1β-negative group had VAS and RDQ values of 4.5 ± 2.8 and 13.2 ± 3.2, respectively. There was a statistically significant difference between the two groups (Fig. 2a,b). The IL-1β-positive group had VAS for low back pain and leg numbness and RDQ values of 5.0 ± 3.7 and 6.0 ± 2.7, respectively, and the IL-1β-negative group had values of 4.6 ± 2.4 and 4.8 ± 2.5, respectively. There was no statistically significant difference between the groups, as there was for cartilage tissue (Fig. 2c,d). Specifically, as for the cartilage tissue, the IL-1β-positive group showed significantly higher VAS for leg pain and RDQ scores than the IL-1β-negative group. In addition, the VAS for low back pain and leg numbness indicated no significant difference between these two groups for both tissues. Thus, lumbar spinal canal stenosis provided an association of IL-1β that was found in the facet joint cartilage with leg pain and diminished quality of life.

Assessing facet joint osteoarthritis on MRI and its IL-1β production

The weighted kappa coefficient for intraobserver agreement for MRI was 0.85. The degree of OA change of the lumbar facet joints at the responsible level was grade 2 or 3 in all cases of the LSCS group (Fig. 3). IL-1β-positive cases in cartilage tissue numbered 4 of 12 (33.3%) in grade 2 and 6 of 17 (35.3%) in grade 3. There were no cases of OA change of grade 0 or 1 in facet joints in the LSCS group. In contrast, some degree of OA change was seen in all of the lumbar facet joints in the LDH group. The degree of OA change for most cases was grade 1 in the LDH group. The degree of OA change for the only case that was IL-1β-positive in the cartilage in the LDH group was grade 2.

Leakage of coloring agent inside the facet joint from the intraspinal canal space

In the anatomical study with fresh cadavers, methylene blue, which was injected into the facet joints from the dorsal joint capsule, was used and stained the joint cartilage, ventral capsule, and ligamentum flavum in all three cases (Table 1). The injection of methylene blue into the left L4/5 facet joint in case 2 was incomplete because the joint space was too narrow to put the needle into capsule owing to severe OA changes. The epidural space, including the vertebral foramen, dura

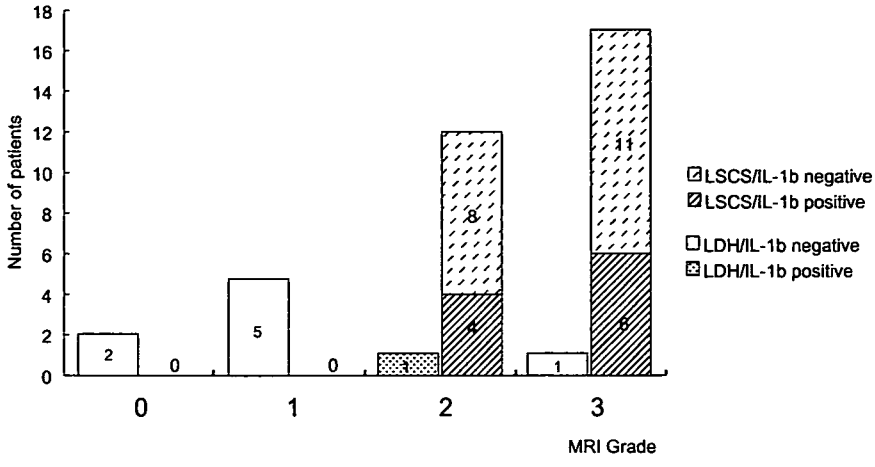
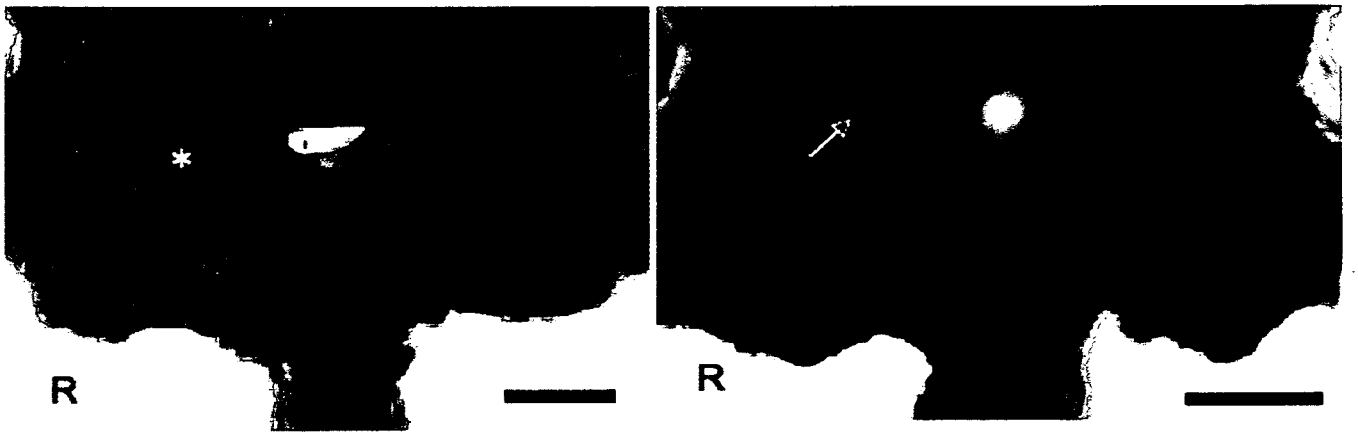


Fig. 3. Assessment of facet joint osteoarthritis (OA) by magnetic resonance imaging (MRI) and IL-1β production. The degree of OA change of the lumbar facet joints in the level was grade 2 or 3 in all cases in the LSCS group. Cartilage tissue was IL-1β-positive in 4 of 12 (33.3%) grade 2 cases and in 6 of 17 (35.3%) grade 3 cases



a b

Fig. 4. **a** Bilateral L4/5 facet joint of case 1. Methylene blue injected from the dorsal joint capsule into the facet joint stained joint cartilage, the ventral joint capsule, and the lateral part of the ligamentum flavum. The epidural space, including the foraminal space, dura mater, and nerve root, were also stained (*asterisk*). **b** Bilateral L4/5 facet joint of case 3. Not only the ventral joint capsule and lateral part of the ligamentum flavum but also the dura mater and epidural space were stained (*arrow*). Elderly patients and the lower level of the lumbar spine showed considerably more cartilage degeneration. *Bar* 1 cm

Table 1. Classification of leakage

Type	Description
C (cartilage)	Coloring agent is localized in the joint cartilage and joint capsule
F (flavum)	Staining of joint cartilage, joint capsule, and ligamentum flavum
E (epidural tissue)	Staining of ligamentum flavum and soft tissue of epidural space
R (root)	Staining of nerve roots

By definition, types C and F are localized in the joint, and types E and R are subject to extra-articular leakage

mater, and nerve roots, was also stained. The most lateral part of the ventral joint capsule, including the ligamentum flavum, was stained by methylene blue injected from the posterior capsule in type F; this was also found in types E and R, which shows that connective tissues in the epidural space and nerve root were also stained by methylene blue (Fig. 4). Considerable cartilage degeneration (e.g., reduction of cartilage, uneven cartilage surface, subchondral bone exposure) was more marked in the more elderly case than in the younger cadavers; and more severe coloring agent leakage was found at the lower lumbar vertebral level, especially the L4/5 level, than at the upper level. It suggests that inflammatory cytokines produced in degenerated facet joints may

leak into the intraspinal space through the most lateral part of the ventral facet joint capsule.

Discussion

In recent studies, inflammatory cytokines produced in the cartilage or synovial cells might involve the development of OA and the genesis of pain.[17,18] However, it is still unknown if inflammatory mediators (e.g., cytokines) modify inflammation in a complicated manner or if chemical factors are involved in osteoarthritis. In a previous study, it was reported that inflammatory cytokines are released from lumbar facet joints with OA changes in degenerative lumbar spinal disorders.[7] Nevertheless, there have been no reports that inflammation in the lumbar facet joint due to chemical mediators such as inflammatory cytokines causes pain and a declining quality of life (QOL). This study found that the LSCS group had a higher positive reaction rate of inflammatory cytokines than did the LDH group. Specifically, the LSCS group is characterized by a higher positive reaction rate of IL-1β in the lumbar facet joint cartilage and synovial tissue. The concentrations of IL-1β and IL-6 in lumbar facet joint cartilage and synovial tissue were higher in the LSCS group than in the LDH group.

Pain seriously affects QOL. There are various methods for evaluating pain, with the VAS approach being widely used as a measurement of the extent of pain. Because low back pain-related functions are affected primarily by the extent of leg pain, a greater extent of low back and leg pain worsens low back pain-related functions.[19] The Roland-Morris disability questionnaire is one of the most widely used indexes of low back pain-related functions.[20–22] In this study, those with IL-1β-positivity at the responsible level of the lumbar facet joint in the LSCS group showed significantly higher VAS for leg pain and RDQ scores than those with no IL-1β expression. This result indicates that IL-1β in the facet joint cartilage was associated with leg pain and declining QOL in the LSCS group.

There were no statistically significant differences between IL-1β expression and the VAS for low back pain and leg numbness. The reason for this result seems to be that low back pain may not be related to chemical mediators such as inflammatory cytokines derived from the facet joint. Instead, repeated mechanical stress or trauma and spinal deformity by secondary overload on a degenerated facet joint may be a more important factor for low back pain in degenerated lumbar disorders. Although the correlation between IL-1β and leg numbness is still uncertain, the influence on lumbar nerve roots by inflammatory cytokines from degenerated facet joint cartilage would induce nerve root injury, which causes leg pain more than leg numbness.

It is largely agreed that the first stage of OA results from mechanical stress against cartilage due to aging, genetic factors, and environmental factors, followed by secondary synovitis. Also, it is thought that the presence of synovial inflammation, which is often associated with the OA process, is believed to be a secondary phenomenon related to the destruction of cartilage and the release of cartilage breakdown products in the synovial fluid.[11] That would be why IL-1β in facet joint cartilage was more associated with leg pain and a declining QOL than that in synovial tissue in the series of this study.

The reason IL-1β was not detected at a high rate in either tissue in the LDH group and was not as closely associated with symptoms is thought to be due to the fact that the LDH group comprised younger subjects, and there is likely less degeneration in their facet joints. Moreover, the inflammation associated with symptoms might be derived not from facet joint tissues but from herniated nucleus pulposus.

IL-6 was highly detected in both groups but was not significantly associated with symptoms. IL-6 has been known to be both a proinflammatory and antiinflammatory cytokine that controls and maintains inflammation not only in an acute state but also a chronic state, even when the inflammation has subsided.[23,24] It is thought that IL-6 might not be closely related to symptoms or QOL because continuous local inflammation in the facet joint tissues would help produce IL-6 even after inflammation has subsided in the LSCS group. Therefore, inflammatory cytokines that express in the lumbar facet joint at a responsible level contribute to leg pain and the declining QOL because of the pain-related function.

In this MRI study of lumbar facet joint, the degree of facet joint degeneration for the cases in the LSCS group was "moderate" or "severe." This suggests that inflammatory cytokines might be produced in highly degenerated facet joint tissues, which should be different from that in normal or less degenerated facet joint tissues in LSCS and from that in the LDH group.

An anatomical study with fresh cadavers was performed to identify how inflammatory cytokines in degenerated lumbar facet joints could be transmitted to the intraspinal space, even to the nerve root. As a result, a coloring agent was injected from the dorsal capsule into the facet joint. It stained not only joint cartilage, the ventral capsule, and the lateral part of the ligamentum flavum but also the extraarticular epidural space, dura mater, and lumbar nerve roots. It is suggested that inflammatory cytokines, which can be produced in facet joint cartilage and synovial tissue, may leak out of the facet joint capsule, especially into the intraspinal space through the lateral part of the ventral facet joint capsule, owing to OA changes in the lumbar facet joint.

It has been reported that the ends of the ventral facet joint capsule in the lumbar spine are attached to the ridge of facet joint surface, whereas the ends of the posterior facet joint capsule are attached over the ridges of the facet joint surface.[25] These authors also reported that the thickness of the ventral joint capsule was thicker than that of the posterior capsule at every lumbar level because the ventral capsule and ligamentum flavum become united and cannot be distinguished from each other. These findings support the belief that a degenerated ventral joint capsule, which would be even thicker together with the ligamentum flavum, may be torn minutely at the most lateral part by mechanical stress because a degenerated lateral ventral joint capsule may not have enough tissue margin to be stretched but be structurally defective. Therefore, it is possible that inflammatory cytokines produced in the facet joint leak into the intraspinal space through the lateral part of the ventral joint capsule tear and affect the lumbar nerve root through an inflammatory process.

Conclusions

These results in this study indicate the possible involvement of inflammation of the lumbar facet joint in clinical symptoms. Moreover, we explored the possibility that inflammation of a degenerated lumbar facet joint may cause the radiculopathy that is involved in the etiology of lumbar spinal canal stenosis.

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厚生労働科学研究費補助金(長寿科学総合研究事業)
高齢者の腰痛症に係る効果的な診断、治療、リハビリテーション等の確立
分担研究報告書

電気生理学的手法を用いた新たな高齢者腰痛診断法の確立

分担研究者:四宮 謙一 東京医科歯科大学大学院医歯学総合研究科整形外科学 教授

研究要旨:従来我々は腰痛患者の表面筋電図を測定し、腰痛と腰背部筋活動との関係を考察することで腰痛を客観的に評価する方法を検討してきた。結果、腰背筋の筋活動および筋疲労と腰痛には大きな相関を認め、筋活動を抑え、筋疲労を減少させるためには良好な姿勢と体幹の安定が重要であるとの考察を得た。腰痛の客観的評価は、治療方針の確認、変更を容易にし、治療を無駄に長引かせることを防ぎ、また、患者の治療に対するモチベーションを上げることで治療効果にも好循環をもたらすと考えられた。

続いて、高齢者の代表的腰椎変性疾患の腰部脊柱管狭窄症に注目をおいた。高齢者の腰部脊柱管狭窄症では複数の高位において狭窄を認めることも多く、多椎間の手術が患者に身体的負担を負わせることは少なくない。責任病巣を絞って最小侵襲で手術を行うために、神経機能評価のための検査法の開発が望まれる。我々は非侵襲的脊髄機能診断法の開発を目指し、誘発磁界測定によって脊髄障害を体表面から診断できることを報告した。今回、神経磁界測定の腰椎疾患への応用を目指し新たに仰臥位型の磁束計を開発し、腰椎部での伝導性神経活動を測定したので報告する。

A. 研究目的

本研究の目的は、腰椎部での馬尾神経活動を神経誘発磁界の測定を行うことで非侵襲的に評価することである。

B. 研究方法

対象は健常成人5名。測定は、仰臥位にて腓骨頭後方において総腓骨神経を電気刺激し、仰臥位測定が可能な105channel超伝導量子干渉素子(SQUID)磁束計を用いて腰椎背側(L2-L4)の皮膚上から、神経誘発磁界を測定した。刺激は、強度 5～7mA、持続時間 0.3ms の矩形波で行い、4,000～6,000 回の加算平均を行った。

C. 研究結果

総腓骨神経刺激後、10ms 前後より、脊柱管の左側では腹側から背側に噴き出す磁界が、右側では吸い込まれる磁界が記録され、頭側に伝搬した。その後、磁界分布が反転し刺激後 12.5ms 前後には脊柱管の左側では背側から腹側に吸い込まれる磁界が、右側では噴き出す磁界が観察され同様に頭側に伝搬した。等磁場線図では、四重極子パターンを呈する磁界が、尾側から頭側に向けて脊椎正中に沿って伝搬する様子が観察できた。磁界のピークから計算される伝導速度は約 60m/s であり、生理学的神経伝導速度に一致していた。

D. 考察

総腓骨神経からの神経の信号は坐骨神経、腰仙椎神経叢および神経根を経由し、腰部脊柱管内の馬尾神経を上行する。今回測定された磁界は、神経軸索活動に伴って発生する四重極子パターンに一致し、また、磁界活動の中心が L2-L4 脊椎正中を上行したことより、脊柱管内の馬尾神経活動による磁界と考える。馬尾の磁界の伝搬を詳細に記録した報告は世界で初めてである。今回、新たに仰臥位型磁束計を開発したことにより、これまで不可能であった非常に微弱な腰椎部での磁界伝搬の計測に成功したが、詳細な電流源の解析を行うには更に Signal/Noise 比を向上させる必要があった。今後、より感度が高くノイズの少ないセンサーの開発が必要と考えられた。

E. 結論

今回、世界で始めて健常者における腰部馬尾神経の詳細な誘発磁界測定に成功した。今後、装置や条件の改良を行うことで、腰部脊柱管狭窄症などの腰椎疾患の患者への臨床応用が可能であると考える。

F. 研究発表

1. 論文発表

なし

2. 学会発表

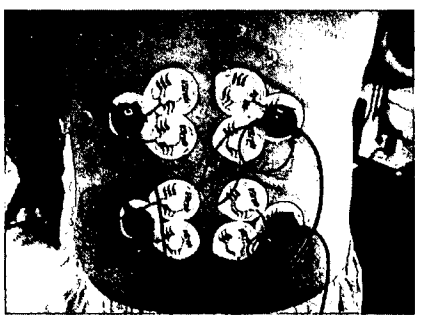
平成19年11月 第15回日本腰痛学会発表
『表面筋電計を用いた腰痛患者の腰背筋活動評価』

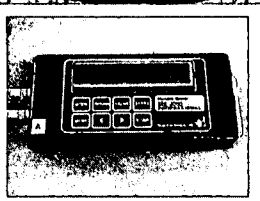
H. 知的財産権の出願・登録状況
(予定を含む)

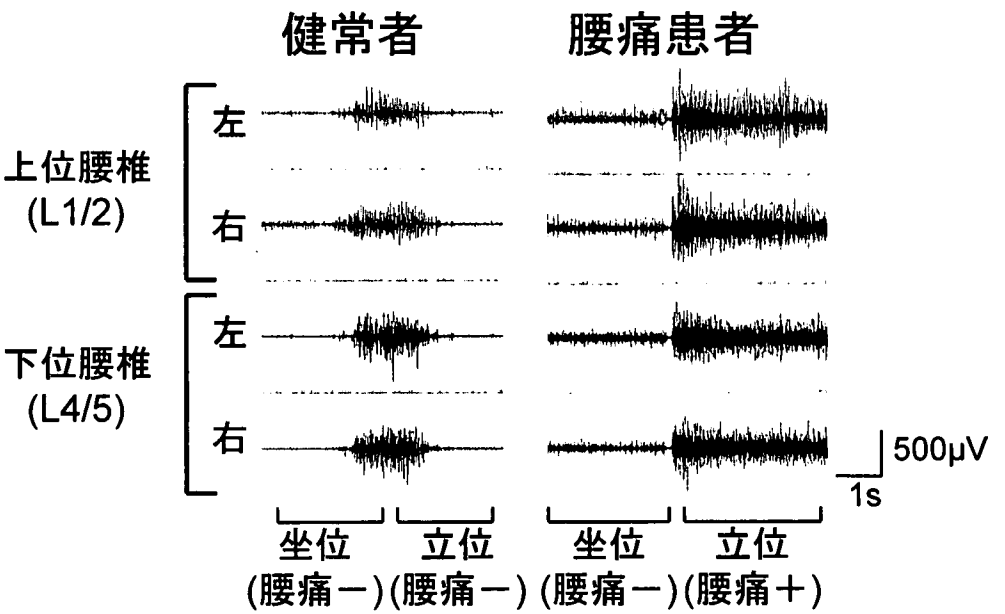
1. 特許取得
   なし
2. 実用新案登録
   なし
3. その他
   特になし

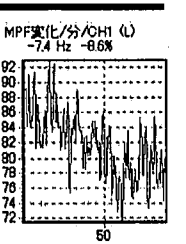
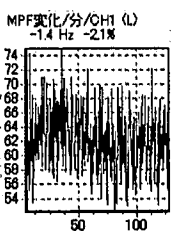
腰背筋筋電図を用いた腰痛の他覚的評価

ポータブル表面筋電計







		MPF変化／分	
	腰痛患者 女性5名、男性1名 平均65歳	-3.9%	
	対象群 女性2名、男性3名 平均55歳	0.6%	

腰痛を有する患者では腰背筋の筋疲労度が大きい。

腰痛の改善には

1，脊柱の安定（体幹筋力強化、杖・コルセットの使用）により腰背筋の安静、筋の疲労軽減、腰痛の軽減が得られる。

2，脊柱のalignment改善は腰背筋の負荷を軽減し、腰痛の軽減が得られる。

3，筋力トレーニングの指導、患者のモチベーションの継続が重要