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Original article

Impacts of triamcinolone acetonide on femoral head chondrocytic structures in lumbosacral plexus block

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ABSTRACT

Objective: To investigate impacts of triamcinolone acetonide (TRI) on femoral head chondrocytic (FHC) structures when used for lumbosacral plexus block (LPB). *Methods:* A total of 32 6-month-old New Zealand white rabbits were selected (averagely weighing 2.75–3.25 kg) and added TRI into nerve block solution for LPB. The rabbit were randomly divided into four groups: group A1: 2.5 ml × 2 times, group A2 2.5 ml × 4 times, group B1 5 ml × 2 times, and group B2 5 ml × 4 times; the time interval among the injection was 5 days, and the structural changes of FHC were the observed using 50/100/200 light microscope; the modified Mankin pathological scoring was also performed for the evaluation. *Results:* There exhibited significant microscopic changes of FHC structures between the rabbits performed LPB and the normal rabbits, among which group B2 exhibited the most serious FHC damages, and the Mankin pathological score in group B2 was much higher than those in the other three groups, and the scores of the experimental group were higher than the control group. *Conclusions:* The addition of TRI in LPB can damage the FHC structures, and large-dose (5 ml/once) and long-course (four times) will result in more serious injuries.

1. Introduction

Chronic pain always seriously affects patients' daily activities and quality of life (Dueñas et al., 2016), and the morbility increases in recent years (Gordon and Bloxham, 2016; Abbas et al., 2017). Since prolonging the peripheral nerve block may reduce the pain (Liu et al., 2015a; YaDeau et al., 2008), nerve blockade is often performed as therapeutic or palliative interventions for pain relief, especially for chronic pain (Luo et al., 2016; Hayek and Shah, 2014).

Nowadays, interventional procedures of nerve block are a widely accepted modality for pain management in adults (Shah et al., 2016), which would reduce the adverse reactions systemically (Wardhan, 2015; Ali et al., 2017). A meta-analysis compared nerve block with physical therapy and intra-articular injection which focused on shoulder pain, and revealed that among the 591 patients, nerve block is of priority than physical therapy and not less useless than intra-articular injection (Chang et al., 2016). Another study focused on coccygodynia and draw the conclusion that ganglion impair block appears to be more effective than conservative therapy in resistant patients, 82% of the patients achieve at least 50% relief of pain after the first treatment, and the relief lasts for a median duration of 6 months (Gunduz et al., 2015).

Nerve block used in the treatment of chronic pain has already been developed maturely, and achieves good effects for osteoarthritis of knee joint, hip osteochondritis, and early femoral head necrosis, and a single-injection of femoral nerve block has been recommended as a routine therapy (Cien et al., 2015), which is also suggested in mild neurological deficit (Jonayed et al., 2016).

At the same time, the value of glucocorticoid has been demonstrated, such as dexamethasone is helpful to prolong pain block duration (YaDeau et al., 2015). A meta-analysis found that the addition of dexamethasone into local anesthetics prolongs brachial

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plexus block (Choi et al., 2014). Even low-dose dexamethasone (1–2 mg) would prolong the analgesia duration and motor blockade (Yine et al., 2015; Zhao and Ashraf, 2016; Liu et al., 2015a,b; Ghafar et al., 2017).

The addition of triamcinolone acetonide (TRI) when performing nerve block can achieve very good effects in nerve block therapies. Nerves have internal axonal motions, and this motion can transport glucocorticoids into joints so as to play the roles of anti-inflammation, analgesia, and joint pain relief. However, it has not been reported whether the treatment of distal articular cartilages can cause damages. This study used one optical microscope to observe the articular cartilage, aiming to see if the articular cartilage was affected. The study is reported as follows.

2. Materials and methods

2.1. Animals

A total of 32 6-month-old New Zealand white rabbits, weighing 2.75–3.25 kg, with the average as 2.95 kg, were selected and then divided into four groups (n = 8, gender-unrestricted). This study was carried out in strict accordance with the recommendations in the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health. The animal use protocol has been reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) of Guizhou Provincial Orthopaedic Hospital.

2.2. Experimental methods preliminary experiment

Three rabbit were firstly shaved the right waist fur, and then placed in the left lying position; the needling site was positioned 1.5 cm laterally away from the right side of the spinous process of spine-iliac connection, and then one needle punctured 2–2.5 cm so as to break through the intertransverse ligament and enter the intergroove of right greater psoas muscle. After confirmed the position accuracy using X-ray, 1 ml of iohexol was then injected, and then computed tomography (CT) was performed to check the distribution of the contrast agent within the intergroove of right greater psoas muscle, and the depth was also recorded. Another three rabbits were then selected and performed the positioning using the same method, with the depth referring to the average depth obtained in the first time experiment, during which period the sense of breaking through should also be reviewed; 2.5 ml and 5.0 ml of Methylthioninium Chloride (MC) were then injected, respectively. The rabbits were then euthanized using propofol and dissected so as to inspect the location and distribution of MC. Once it was confirmed distributing within the intergroove of right greater psoas muscle, and the distribution of lumbosacral plexus block (LPB) can be seen, it can confirm the consistency of the two positioning methods (Fig. 1).

The rabbits of hte two groups were placed in the left lying position, positioned, and then medicated into the intergroove of right greater psoas muscle; the muscle strength of lower extremities were then observed and classified according to the human muscular strength classification. The final concentrations for LPB were as follows: lidocaine 0.5%, VB12 50 μg/ml, TRI 2 mg/ml. The doses and injection times of hte four groups: group A1: 2.5 ml × 2 times, group A2 2.5 ml × 4 times, group B1 5 ml × 2 times, and group B2 5 ml × 4 times, with the injection interval is 5 days.

2.3. Detection indexes

One optical microscopy was sued to observe the right femoral head chondrocytic (FHC), and the modified Mankin pathologic scoring was used to evaluate each group; group A1 and A2, B1 and B2, A1 and B1, and A2 and B2 were performed statistical X2 analysis.

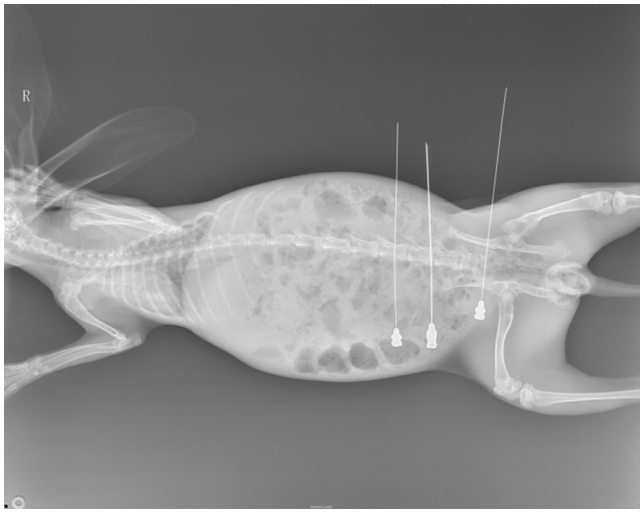

Fig. 1. The needle clearance of the body surface was determined by metal needle under the C arm.

2.4. Statistical analysis

SPSS 16.0 software was used for statistical analysis. The counting data were analyzed using the *t* test; the measurement data were expressed as mean ± standard deviation, using the chi-square test, with $\alpha = 0.05$ and $P < 0.05$ considered as a statistical difference and $P < 0.01$ as a statistically significant difference.

3. Results

3.1. Determination of insertion point of puncture needle

The needling site was positioned 1.5 cm laterally away from the right side of the spinous process of spine-iliac connection, and then one needle punctured 2–2.5 cm so as to break through the intertransverse ligament and enter the intergroove of right greater psoas muscle. CT exhibited the contrast agent distributing paraspinally, and partially entering the retroperitoneum. After injecting 2.5 ml and 5 ml of MC, it can be seen than MC distributed up to the L2 level and down to the pelvic ilium. After treatment, the muscle strength of hte two 2.5 ml groups was in class II-III, and that of the two 5 ml groups was in class II or so. All the rabbits can only walk with their legs dragging. No statistically significant difference can be seen among the groups under optical microscope.

3.2. Microscopic results

FHC tissue exhibited normal structures, smooth surface, uniform thickness, normal chondrocytic size, shape, number, and arrangement; no cartilage growth or ossification exhibited abnormality; the epiphyseal plate thickness was normal and uniform, the chondrocytic size, shape, number, and arrangement were normal, and no cartilage growth or ossification exhibited abnormality; the chondrocytic column was arranged regularly; the trabecular thickness and morphology were normal and closely connected; the osteoblasts and osteoclasts' size, shape, number, and arrangement were normal; the structure of bone marrow was normal, and the cell proportion and component composition showed no abnormality (Fig. 2).

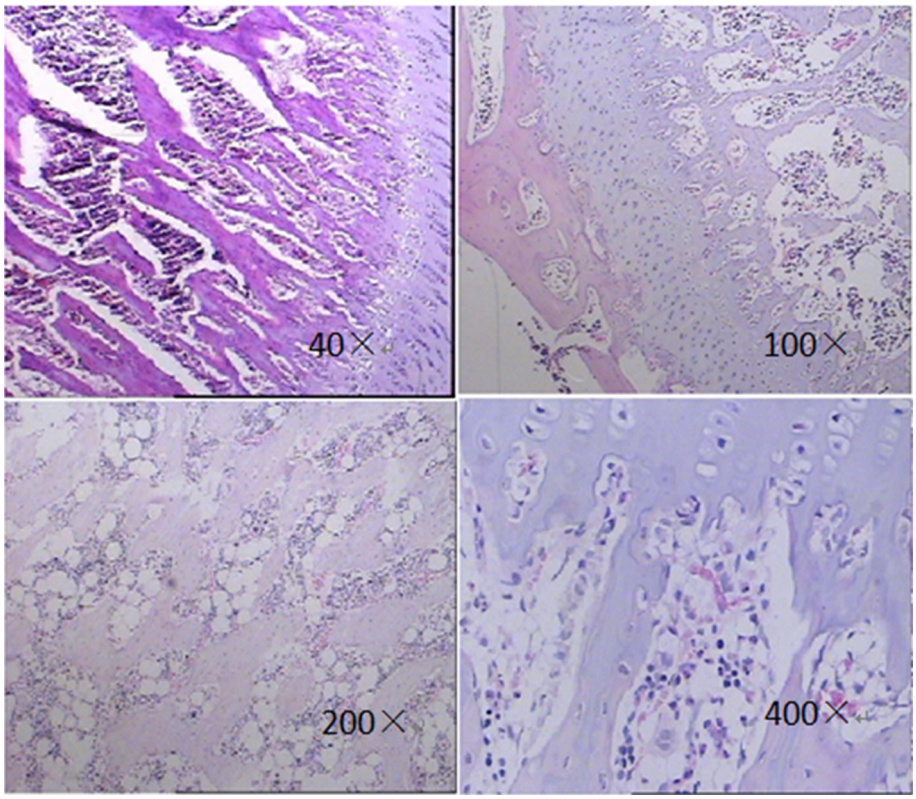

Fig. 2. FHC surface in group A0.

3.3. Effect of TRI on caput femoris cartilage in different doses and medicine times

Group A1: Exhibited normal FHC tissue, smooth surface, but partial thickness was mildly thinned; the chondrocytic size, shape, number, and arrangement showed no abnormality, and no cartilage growth or ossification exhibited abnormality; the epiphyseal plate thickness was moderately thinned, the chondrocytic size, shape, number, and arrangement were normal, and no cartilage growth or ossification exhibited abnormality; the chondrocytic column was arranged regularly; most trabecular thickness and morphology were normal and closely connected, but a small part of trabecular bone exhibited mild atrophy, and the connection was moderately loose; the osteoblasts and osteoclasts' size, shape, number, and arrangement were normal; the structure of bone marrow was normal, and the cell proportion and component composition showed no abnormality; the structure and thickness of cortical tissue were normal, and the bone cells' size, shape, number, and arrangement showed no abnormality (Fig. 3).

Group A2: FHC tissue exhibited normal structures, smooth surface, but partial thickness was mildly thinned; the chondrocytic size, shape, number, and arrangement were normal; no cartilage growth or ossification exhibited abnormality; the epiphyseal plate thickness was moderately thinned, the chondrocytic size, shape, number, and arrangement were normal, and no cartilage growth or ossification exhibited abnormality; the chondrocytic column was arranged regularly; most trabecular thickness and morphology were normal and closely connected, but a small part of trabecular bone exhibited mild atrophy, and the connection was moderately loose; the osteoblasts and osteoclasts' size, shape, number, and arrangement were normal; the structure of bone marrow was normal, and the cell proportion and component composition showed no abnormality; the structure and thickness of cortical tissue were normal, and the bone cells' size, shape, number, and arrangement showed no abnormality (Fig. 4).

Group B1: FHC tissue exhibited normal structures, smooth surface, uniform thickness, normal chondrocytic size, shape, number, and arrangement; no cartilage growth or ossification exhibited abnormality; the epiphyseal plate thickness was normal and uniform, the chondrocytic size, shape, number, and arrangement were normal, and no cartilage growth or ossification exhibited abnormality; the chondrocytic column was arranged regularly; the trabecular thickness and morphology were normal and closely connected; the osteoblasts and osteoclasts' size, shape, number, and arrangement were normal; the structure of bone marrow was normal, and the cell proportion and component composition showed no abnormality (Fig. 5).

Group B2: FHC tissue exhibited normal structures, smooth surface, but partial thickness was severely thinned; the chondrocytic size, shape, number, and arrangement were moderately abnormal; no cartilage growth or ossification exhibited abnormality; local epiphyseal plate thickness was slightly thinned, the chondrocytic size, shape, and number were normal while the arrangement was slightly disordered; no cartilage growth or ossification exhibited abnormality; the chondrocytic column was slightly disordered; the trabecular thickness and morphology were normal and closely connected; the osteoblasts and osteoclasts' size, shape, number, and arrangement were slightly disordered; the structure of bone marrow was normal, and the cell proportion and component composition showed no abnormality (Fig. 6).

3.4. Pathological scoring results

The Mankin pathological scores in group A0, A1, A2, B1, and B2 were 0.46 ± 0.25, 1.75 ± 0.46, 1.83 ± 0.74, 2.0 ± 1.20, and 4.25 ± 0.89, respectively; the scores in all the experimental groups

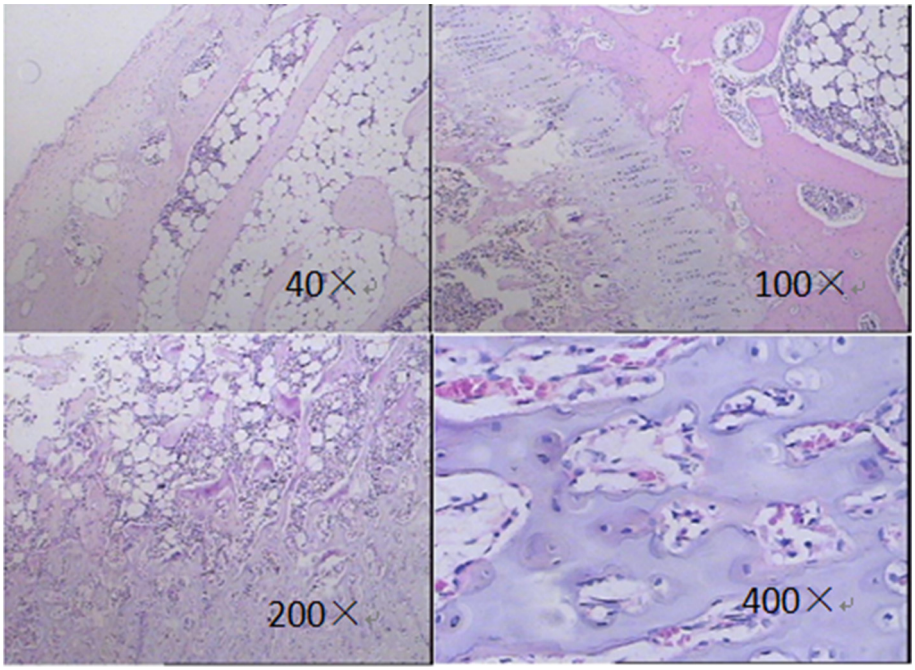

Fig. 3. FHC results in group A1.

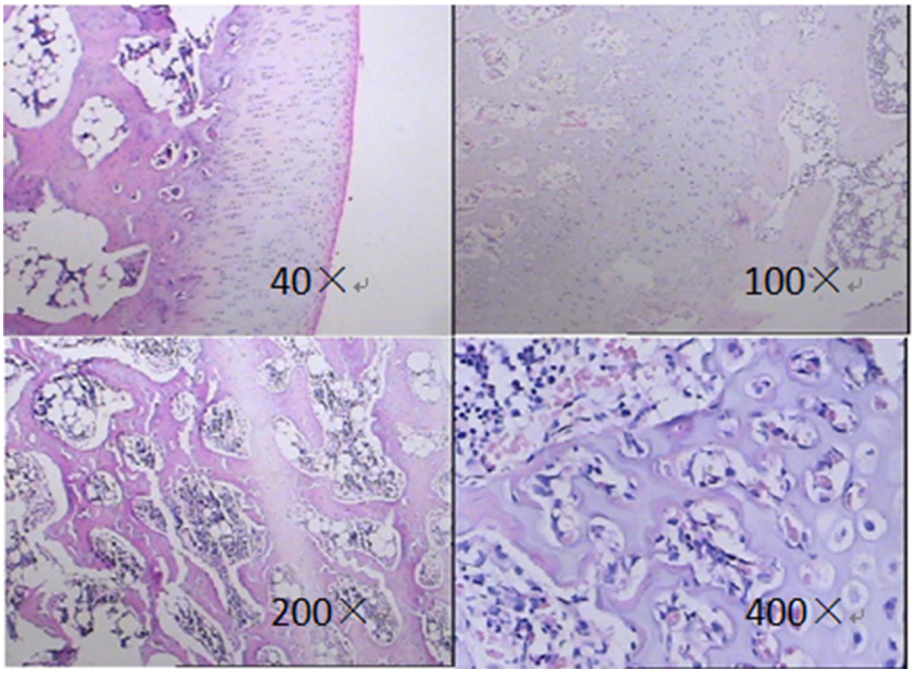

Fig. 4. Pathological results of FHC in group A2.

were higher than the control group (group A0), and the differences were statistically significant ($P < 0.05$). With the increasing of the injection dose and frequency, the scores in group A1, A2, B1, and B2 were also increased, and that in group B2 was significantly higher than the other three groups, and the differences were statistically significant ($P < 0.05$).

4. Discussion

Nerve block has achieved good results in treating chronic pain, and it is being used increasingly as a therapy for chronic pain (Mallinson et al., 2013; Jamal et al., 2017). For example, nerve block has recently emerged as a novel alternative treatment in chronic knee pain (Safi et al., 2015; Yasar et al., 2015); furthermore, mixing injections of corticosteroids in neuroleptics has increasingly been used in clinical practice. The mechanisms of nerve block treatment toward chronic pain include blocking the vicious cycle of pain, suppressing central sensitization, improving the blood circulation of pain, promoting the absorption of inflammatory mediators, and significantly reducing the inflammatory cytokines inside knee articular cavity fluid when applied in lumbosacral plexus and branch nerve block; furthermore, it can relieve muscle spasms and improve muscle nutrition (Yasar et al., 2015). One study reported

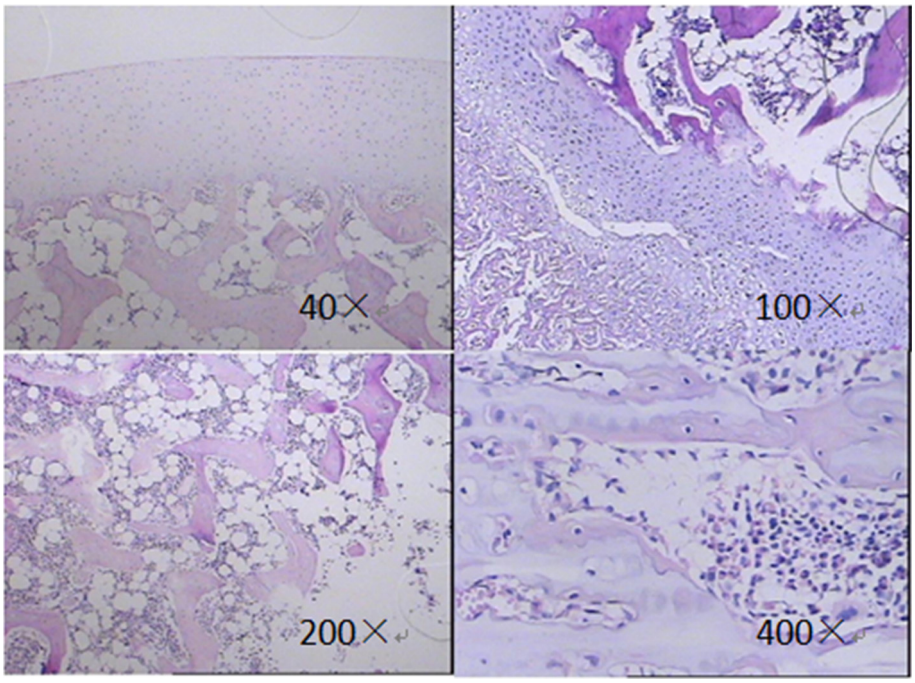

Fig. 5. Pathological results of FHC in group B1.

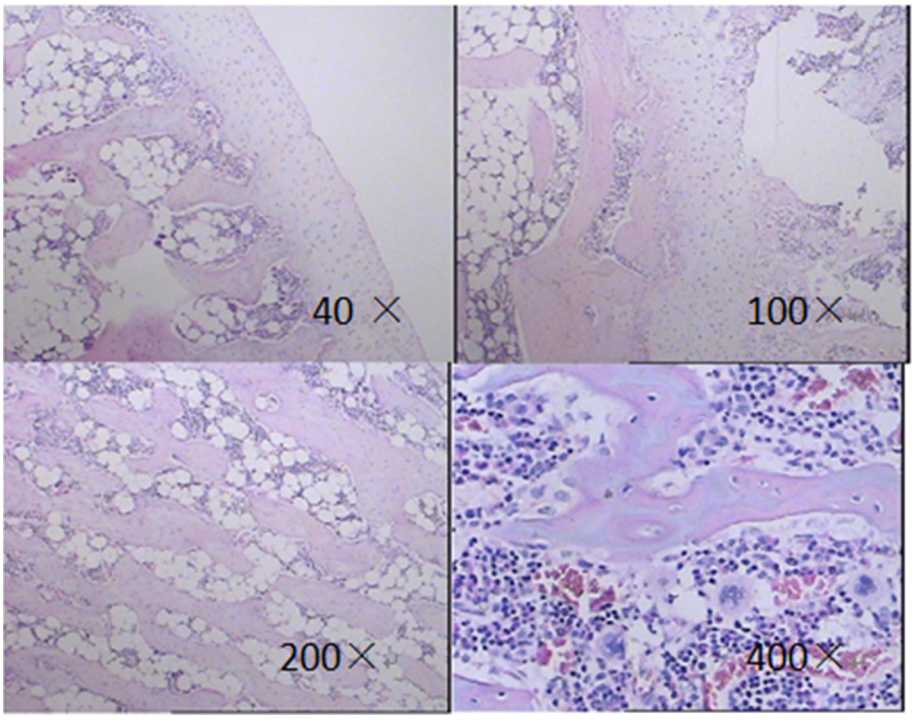

Fig. 6. Pathological results of FHC in group B2.

that a mixture of local anesthetic and corticosteroid (bupivacaine 0.25% with methyl-prednisolone 20–120 mg) for the treatment of refractory cancer-related pain in the brachial plexus territory was acceptable and effective (Huang et al., 2015; Baheti, 2015; Zinboonyahgoon et al., 2015). Meanwhile, perineural dexamethasone addition to local anesthetic solutions in brachial plexus block also significantly improves the pain while without increasing complications (Knezevic et al., 2015), and also prolongs the duration of analgesia (Abdallah et al., 2015; Sindhu et al., 2017).

Back pain always relates with facet joints, vertebral body, intervertebral disk, and paraspinal structures including nerves and ganglion roots (Khaliq et al., 2016; Santiago et al., 2014), and glucocorticoids have been considered to be able to help to relief the pain; since we know in SARS, high-dose oral corticosteroids cause femoral head necrosis (Zhao et al., 2013; Griffith et al., 2005), so if glucocorticoids in lumbosacral plexus nerve block would cause damages in femur should be considered. It's still unknown whether it can cause damages to the articular cartilage

inside the innervation area, the dose and frequency of application still needs to be considered (Wang et al., 2015; Williams et al., 2014). Magnetic resonance imaging (MRI) studies reveal that damages would have occurred in early phase after the start of steroid administration (Kubo et al., 2016). Not only bone but also cartilage is severely affected by glucocorticoids (Hartmann et al., 2016; Shamsudin et al., 2017). Damages of hormones on cartilage is caused when hormones contact with cartilage, they will damage the cartilage matrix, particularly the matrix metalloproteinases, thus increasing the apoptosis of chondrocytes. When performing nerve block, glucocorticoids added into nerve tissue fluid can reach the distal tissue via axonal motions. When the drugs reach the subchondral bone, they can reach the inner side of cartilage tissue via osmosis, and then result in cartilage injuries (Iwaniak et al., 2015).

The results suggest that after LPB, FHC exhibits pathological abnormalities, indicating that the addition of TRI into tissue fluid for nerve block can affect articular cartilage. It's speculated that the inflammatory and analgesic effects of the added glucocorticoids during nerve block toward distal tissue are transported around inflammatory tissues via nerve axonal motions, thus reducing inflammation and edema at lesions, and promoting the absorption of inflammatory mediators. Meanwhile, TRI can reach the articular cartilage by an unknown route, and then cause cartilage damages. It can also be seen from this study that the higher the dose, as well as the longer the duration, the severer the damages. Therefore, the optimal doses and duration still need further refinement so as to achieve the maximum benefits.

Limitation

This study was an animal study, and the results may lack sample size, which need further study to confirm our results.

Conflict of interest

All authors have no conflict of interest regarding this paper.

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