The Anti-inflammatory Effects of Osthole on Sciatica of Rat Experimental Lumber Disc Herniation Model given by Epidural Catheterization

INTRODUCTION:
Lumbar disc herniation (LDH) commonly induces sciatica and low back pain, which seriously influences the patients’ quality of life. The mechanical compression is considered to be the only reason of sciatica for a long time. However, recent studies suggest that the severity of symptoms in LDH patients is often associated with mechanical compression but also remarkable inflammation around the nerve root. Inflammatory factors such as prostaglandins (PGs), nitric oxide (NO), cytokines including interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) play very important roles in the pathophysiological changes of sciatica induced by LDH.

At present, many drugs have been developed to treat sciatica induced by LDH. Duhuo Jisheng Decoction, one of traditional Chinese medicine formulas, is used to treat LDH and shows good curative effect. Duhuo (Radix Angelicae Pubescentis) is the monarch drug in the decoction and formulas, is used to treat LDH and shows good curative effect. Duhuo Jisheng Decoction, one of traditional Chinese medicine formulas, is used to treat LDH and shows good curative effect. Therefore, osthole may be a promising drug in treatment of sciatica induced by LDH.

MATERIALS AND METHODS:
1. Development of a rat model of sciatica induced by LDH and a new method of epidural catheterization
Forty-two male Sprague-Dawley rats were randomly divided into 3 groups: nucleus pulposus (NP) group (n=30), sham group (n=6), and blank group (n=6). NP group: The L5 dorsal root ganglion (DRG) and a part of dura sac were exposed by a L5 hemilaminectomy and LS-L6 facetectomy on the left side. Autologous NP (about 0.4 mg) was harvested from the tail and placed to the L5 DRG and epidural space. PE-0503 catheter was put into epidural space cranially where the catheter tip was in epidural space and around L4-5.Dehydroepiandrosterone (DHEA) was administered epidurally on day 2 or 6 day after surgery. But when administered on 13 or 28 day after surgery, the tip of the catheter was in epidural space and around L4-5.

2. The effects of osthole on sciatica induced by LDH given by epidural catheterization

Thirty-six male Sprague-Dawley rats were randomly divided into 6 groups. NP group: Autologous NP was harvested from the tail and placed to the L5 DRG and epidural space. Epidural catheterization was performed. Vehicle group: 50 µL osthole was administered epidurally on day 2 after the same procedures of NP group, T2, T6, T13, and T20 groups. 2% osthole was administered epidurally on day 2, 6, 13, and 20 after the same procedures of NP group, respectively. 2% osthole was administered epidurally on day 2, 6, 13, and 20 after the same procedures of NP group, respectively.

RESULTS:
Fig. 1 is showing that 50% PWT on each time point after surgery were significantly lower than on 1 day before surgery in NP group (P<0.05) and were significantly lower than blank group and sham group (P<0.05). The tip of the catheter was in epidural space and around L4 nerve root. The methylene blue was spread of cranial L1 nerve root and caudal L6 nerve root (Fig. 2).

After osthole administration of day 2 and 6, 50% PWT (Fig. 3) were significantly higher than the day of osthole administration (P<0.05) and recovered to the same level as 1 day before surgery (P>0.05). It was also significantly higher than vehicle and NP group (P<0.05).

Cell numbers for the expression of COX-2 and NOS (Fig. 4) in NP and vehicle groups were significantly higher than that in blank and sham groups (P<0.05). In the osthole group, it was lower than that in NP and vehicle groups (P<0.05), but slightly higher than that in sham group and blank group (P<0.05).

DISCUSSION:
A new rat model of sciatica induced by LDH was developed and mechanical allodynia maintained 28 days at least. The epidural catheterization had no influences on measurement of 50% PWT. The position of the catheter tip and the extension of the drug were reliable. 50 µL 2% osthole could completely inhibit the mechanical allodynia in the rat model of sciatica induced by LDH when it was administered epidurally on day 2 or 6 day after surgery. But when administered on 13 or 20 day after surgery, its analgesic effect was transient. The effects of 50 µL 2% osthole epidural administration on day 6 after surgery on the rat model of sciatica induced by LDH was related to inhibiting the expression of COX-2 and NOS in DRG.

CONCLUSION:
The current studies indicate that its anti-inflammatory effect is associated with suppression of the content of PGs, NO and the activity of NOS when osthole epidural administration on the early stage after surgery on the rat model of sciatica induced by LDH.

ACKNOWLEDGEMENT:
NSFC-Guangdong combined funding (u0732001) provided support for this study.

REFERENCES: