Original Article

Tashinone II A-sulfoacid-natrum elevates the pain threshold through inhibiting nuclear factor kappa B pathway in neuropathic cancer pain

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Abstract

OBJECTIVE: The purpose of this study was to evaluate the effects of Tashinone II A-sulfoacid-natrum on the pain threshold and potential molecular mechanism for neuropathic cancer pain. **METHODS:** Forty-five male Balb/c mice were divided into control group model group and experiment group with each 15. The sciatic nerve muscle plexus of experiment and model group were given injection containing S180 sarcoma cell 2×10^6 mL for each mouse. Mice in the experiment group were given Tashinone II A-sulfoacid-natrum 25 mg/kg once a day intraperitoneal injection. Moreover, mice in the control group were given physiological saline 25 mg/kg, once a day intraperitoneal injection. The mechanical withdraw threshold and thermal withdraw latency were recorded before S180 sarcoma cell injection and in the time point of day 3, 6, 9, 12, and 14. After 14 days treatment, the mice were treated to death and the sciatic nerve CX3CR1 and nuclear factor kappa B (NF-κB) mRNA was tested by quantitative polymerase chain reaction. **RESULTS:** Compared with control group, the mechanical and thermal pain threshold of experiment group was significant decreased ($P < 0.05$). However, compared with the model group, the mechanical, and thermal pain threshold of experiment group was significant elevated in time point of day 3, 6, 9, 12, 14 for mechanical pain threshold and day 9, 12 14 for thermal pain threshold ($P < 0.05$); the pain threshold for the experiment and model group was decreased in the first 9 days and then elevated gradually. Compared with control group, the CX3CR1 and NF-κB mRNA relative expression in mice sciatic nerve of experiment group was significant elevated ($P < 0.05$); but compared with model group, the CX3CR1 and NF-κB mRNA relative expression of experiment group was significant decreased ($P < 0.05$). **CONCLUSION:** Tashinone II A-sulfoacid-natrum can elevates the mechanical and thermal pain threshold through inhibiting the NF-κB in neuropathic cancer pain rat.

Key Words: Mice, molecular mechanism, neuropathic cancer pain, signal pathway, tashinone II A-sulfoacid-natrum

Introduction

Neuropathic pain is usually caused by damage or disease affecting the somatosensory nervous system which may be associated with abnormal sensations called dysesthesia or pain from normally nonpainful stimuli (allodynia). Neuropathic pain may also result from disorders of the peripheral nervous system or the central nervous system (brain and spinal cord). It was reported that more than 7% of the European population is affected by neuropathic pain, and in 5% of them it may be severe.[1,2] But the exact mechanism of neuropathic pain was not clear. Some researchers believed that the altered expression of ion channels, changes in neurotransmitters and their receptors as well as altered gene expression in response to neural input is important for the neuropathic pain.[3] Neuropathic pain in cancer arises following injury to peripheral or central neurons, in a similar manner to such pain arising from a noncancer injury.[4]

Recently, report showed that tashinone II A-sulfoacid-natrum can reduced the neuropathic pain in mice.[5] However, its mechanism was not clear. Here, we discuss the effects of tashinone II A-sulfoacid-natrum on the pain threshold and potential molecular mechanism for neuropathic cancer pain.

Methods

Forty-five male Balb/c mice were divided into control group model group and experiment group with each 15. The sciatic nerve muscle plexus of experiment and model group were given injection containing S180 sarcoma cell 2×10^6 mL for each mouse.[6] Mice in the experiment group were given tashinone II A-sulfoacid-natrum 25 mg/kg once a day intraperitoneal injection. Moreover, mice in the control group were given physiological saline 25 mg/kg, once a day intraperitoneal injection. The mechanical withdraw threshold and thermal withdraw latency were recorded before S180 sarcoma cell injection and in the time point of day 3, 6, 9, 12, and 14. After 14 days treatment, the mice were treated to death and the spine cord CX3CR1 and nuclear factor kappa B (NF-κB) mRNA was tested by quantitative polymerase chain reaction.

Statistics

All values are expressed by mean ± standard deviation. The significance of differences was analyzed by an ANOVA test and an unpaired Student's *t*-test to compare between groups. The data were analyzed using the GraphPad Prism software 5.0 (http://www.graphpad.com/scientific-software/prism/). A significant value was considered at $P < 0.05$.

Results

The mechanical pain threshold comparison

Compared with control group, the mechanical pain threshold of experiment group was significant decreased ($P < 0.050$); but compared with the model group, the mechanical pain threshold of experiment group was significant elevated in time point of day 3, 6, 9, 12, and day 14 ($P < 0.05$); and the pain threshold for the experiment and model group was

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decreased in the first 9 days and then elevated gradually, Figure 1.

The thermal pain threshold comparison

Compared with control group, the thermal pain threshold of experiment group was significant decreased ($P < 0.05$); but compared with the model group, the thermal pain threshold of experiment group was significant elevated in time point of day 9, 12, and day 14 ($P < 0.05$); and the pain thermal pain threshold for the experiment and model group was decreased in the first 9 days and then elevated gradually, Figure 2.

CX3CR1 and nuclear factor kappa B mRNA expression sciatic nerve

Compared with control group, the CX3CR1 and NF-κB mRNA relative expression in mice sciatic nerve of experiment group was significant elevated ($P < 0.05$); but compared with model group, the CX3CR1 and NF-κB mRNA relative expression of experiment group was significant decreased ($P < 0.05$), Figure 3.

Discussion

Neuropathic pain is defined by the International Association for the Study of Pain as pain that arises as a direct consequence of a lesion or disease affecting the somatosensory system.[7,8] Neuropathic pain is usually caused by damage or disease affecting the somatosensory nervous system which may be associated with abnormal sensations called dysesthesia or pain from normally nonpainful stimuli (allodynia).[9] It was reported that more than 7% of the European population is affected by neuropathic pain, and in 5% of them it may be severe.[1,2] However, the exact mechanism of neuropathic pain was not clear.[8,10,11] Hence, it is urgent to develop novel mechanism-based therapeutic agents that are highly efficacious and well tolerated to improve relief of neuropathic pain.[12] Neuropathic pain is difficult to treat with only 40–60% of the patients achieving partial relief.[13] Favored treatments are certain antidepressants (tricyclic antidepressant and serotonin-norepinephrine reuptake inhibitors), anticonvulsants (pregabalin and gabapentin), and topical lidocaine.[14] But the efficacy is not satisfaction. Recently, report showed that tashinone II A-sulfoacid-natrum can reduced the neuropathic pain in mice.[5] However, its mechanism was not clear. In our present study, we evaluate the effects of tashinone II A-sulfoacid-natrum on the pain threshold and potential molecular mechanism for neuropathic cancer pain model mice. We find that the mechanical and thermal pain threshold was significant decreased by intraperitoneal injection of tashinone II A-sulfoacid-natrum. The CX3CR1 and NF-κB mRNA relative expression in mice sciatic nerve was significant decreased ($P < 0.05$) compared to model group which indicated that tashinone II A-sulfoacid-natrum can elevates the mechanical and thermal pain threshold through inhibiting the NF-κB and CX3CR1 expression in neuropathic cancer pain mice.

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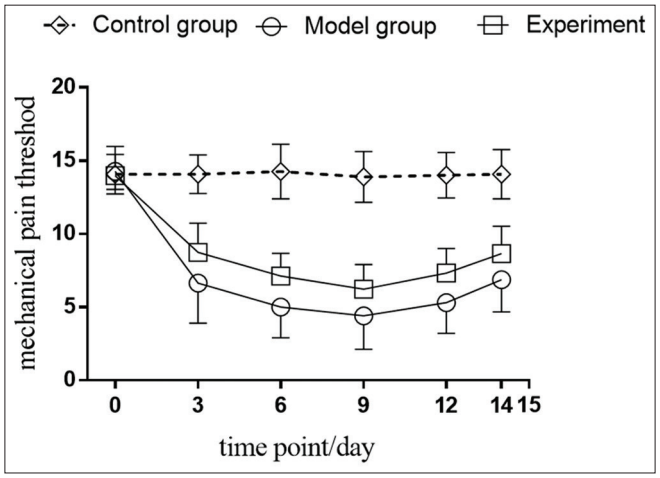

Figure 1: The mechanical pain threshold comparison for the three groups

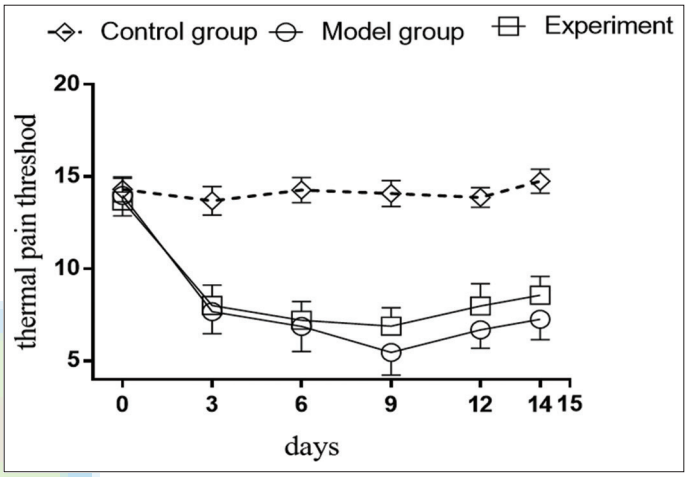

Figure 2: The thermal pain threshold comparison for the three groups

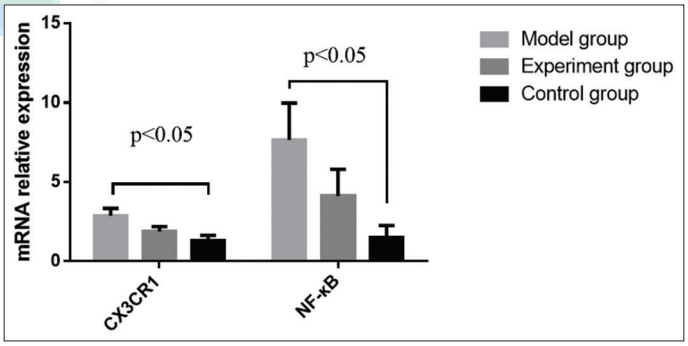

Figure 3: CX3CR1 and nuclear factor kappa B mRNA expression sciatic nerve

Conflicts of interest

There are no conflicts of interest.

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