Short information preclinical study

Neuropathic pain

Buchheit T. et al.
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Intrathecal administration of conditioned serum from different species resolves Chemotherapy-Induced neuropathic pain in mice via secretory exosomes

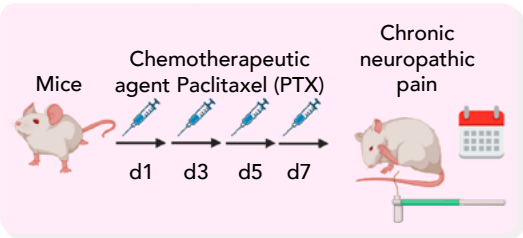
- ACS provides long-lasting relief of peripheral neuropathic pain and restores nerve conduction velocity.
- ACS exosomes are thought to play a crucial role in long-lasting pain relief and tissue regeneration.
- ACS is known for its healing successes, which are attributed to growth factors. There is now an additional explanatory approach for the long-lasting resolution of pain and inflammation.

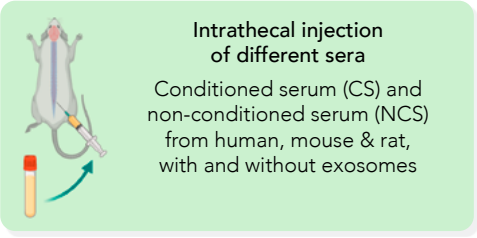
PAIN FROM PERIPHERAL NEUROPATHY

Peripheral neuropathy often occurs in the hands and feet, e.g. after chemotherapy. Other causes include diabetes or damage to the nervous system. Tingling, sensory disturbances and impaired tactile sensation, pain transmission and temperature sensation are the main symptoms. The nerve endings in the hands and feet have been damaged and the transfer of substances and information between nerve cell and tissue is disturbed. Peripheral neuropathy and the accompanying neuropathic pain cannot yet be treated in a satisfactory manner. Regular exercise training is recommended as a prophylactic measure.

STUDY DESIGN

In this study, mice were first treated with the chemotherapeutic agent paclitaxel (PTX). PTX, a cytostatic drug from the taxane group, causes typical neuropathic pain. PTX is used, for example, for breast cancer and non-small cell lung cancer. After chemotherapy, the experimental animals received an injection into the spinal cord (intrathecal) of various sera (human, mouse, rat). The animals in the verum group each received an injection of conditioned serum (CS/Orthokine®). The animals in the control group received an injection of non-conditioned serum (NCS).





The researchers decided to use NCS as a control in order to gain new insights into the clinical effect of the technology used. In the preparation of CS, the blood sample was stored at 37° Celsius for 24 hours. For NCS, the blood sample was not stored but centrifuged immediately to obtain serum. CS not only contains large amounts of inflammation resolving and growth-promoting messenger substances but also nanoparticles, so-called exosomes. To further investigate their influence, the exosomes were removed from the serum by ultracentrifugation in another experiment. Sera with and without exosomes were injected intrathecally into the test animals.

RESULTS

Neuropathic pain is improved significantly and long-lasting by a single injection of CS into the spinal cord of the test animals. No analgesic effect could be achieved with NCS (Fig. 1).

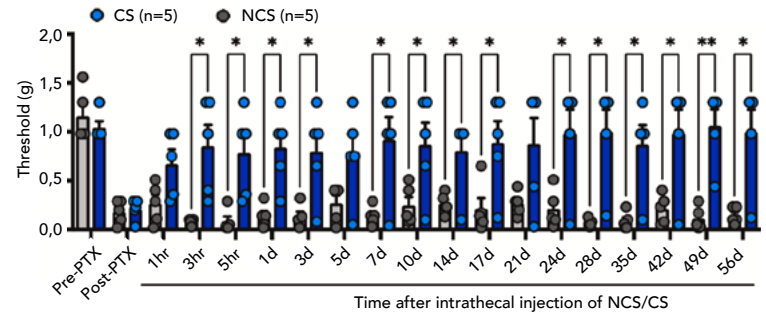


Fig. 1

Treatment with ACS (Orthokine®) terminates chemotherapy-induced glial activation in the spinal cord and also restores nerve conduction (Fig. 3). Compared to the control (NCS), the therapeutic serum contains significantly higher concentrations of anti-inflammatory and growth-promoting messengers, including IL-1Ra, TIMP-1, TGF-β1 and resolvins.The pain relief induced by therapeutic ACS/Orthokine® was largely cancelled after removal of exosomes from CS by ultracentrifugation (Fig. 2).

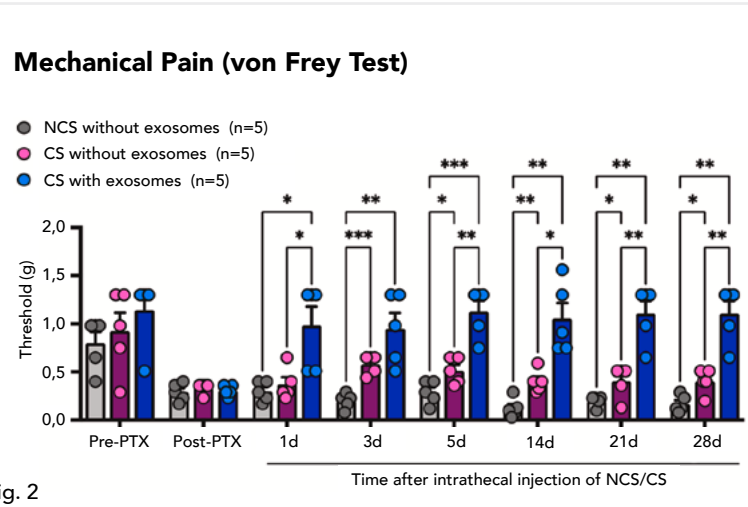


Fig. 2

Quantification of exosomes showed that the conditioned serum contained a significantly greater number than the control (NCS). This suggests that exosomes play a crucial role in the effect of the therapeutic serum. Exosomes are nanovesicles that contain signaling substances and can also cross the blood-brain barrier. The fact that CS from mice, rats and humans produced the same therapeutic effect in mice suggests an evolutionarily conserved mechanism of action.

PTX also causes motor function disorders. Measurement of nerve conduction velocities showed that CS treatment not only relieves pain but also restores nerve function. This did not happen with NCS treatment (Fig. 3).

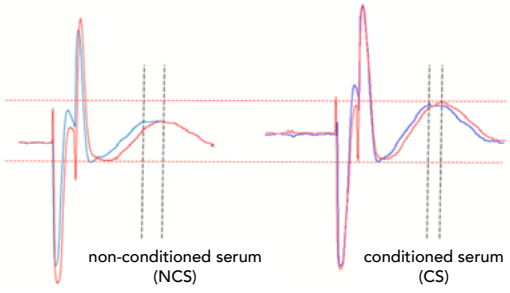


Fig. 3

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