

CROATIAN INTERNATIONAL PUBLICATIONS

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Filipović B, Matak I, Bach-Rojecky L, Lacković Z. Central action of peripherally applied botulinum toxin type A on pain and dural protein extravasation in rat model of trigeminal neuropathy. *PLoS One*. 2012;7(1):e29803.

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BACKGROUND: Infraorbital nerve constriction (IoNC) is an experimental model of trigeminal neuropathy. We investigated if IoNC is accompanied by dural extravasation and if botulinum toxin type A (BoNT/A) can reduce pain and dural extravasation in this model.

METHODOLOGY/PRINCIPAL FINDINGS: Rats which developed mechanical allodynia 14 days after the IoNC were injected with BoNT/A (3.5 U/kg) into vibrissal pad. Allodynia was tested by von Frey filaments and dural extravasation was measured as colorimetric absorbance of Evans blue-plasma protein complexes. Presence of dural extravasation was also examined in orofacial formalin-induced pain. Unilateral IoNC, as well as formalin injection, produced bilateral dural extravasation. Single unilateral BoNT/A injection bilaterally reduced IoNC induced dural extravasation, as well as allodynia (lasting more than 2 weeks). Similarly, BoNT/A reduced formalin-induced pain and dural extravasation. Effects of BoNT/A on pain and dural extravasation in IoNC model were dependent on axonal transport through sensory neurons, as evidenced by colchicine injections (5 mM, 2 μ l) into the trigeminal ganglion completely preventing BoNT/A effects.

CONCLUSIONS/SIGNIFICANCE: Two different types of pain, IoNC and formalin, are accompanied by dural extravasation. The lasting effect of a unilateral injection of BoNT/A in experimental animals suggests that BoNT/A might have a long-term beneficial effect in craniofacial pain associated with dural neurogenic inflammation. Bilateral effects of BoNT/A and dependence on retrograde axonal transport suggest a central site of its action.

Jotanovic Z, Mihelic R, Sestan B, Dembic Z. Role of interleukin-1 inhibitors in osteoarthritis: an evidence-based review. *Drugs Aging*. 2012 May 1;29(5):343-58.

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Osteoarthritis (OA), the most common chronic musculoskeletal disease, represents a leading cause of disability in the elderly population worldwide. At present, there is no aetiological treatment for OA patients. Also, current therapeutic regimens for OA are only partially effective, and that is the main reason for most physicians' complaints. Therefore, one of the biggest challenges in the future will be to find the most appropriate therapy or therapies for OA. Currently, there are three basic modalities of treatment: non-pharmacological, pharmacological and surgical. Regarding pharmacological treatment, numerous molecular pathways involved in the pathophysiology of OA have been investigated as potential therapeutic targets. In preclinical and clinical trials, many compounds and agents have been tested, and some of them have already shown positive effects on the progression of knee and/or hip OA. One such possible pharmacological treatment of OA is anticytokine therapy. Interleukin-1 (IL-1), as a main inflammatory and catabolic cytokine in the pathophysiology of OA, represents one of the possible treatment targets. For specific inhibition of IL-1 production or activity, various treatment strategies could be used. These include the inhibition or modification of IL-1 action through the application of IL-1 receptor antagonist proteins, soluble IL-1 receptors, monoclonal antibodies against IL-1 or against IL-1 receptor I, blocking the formation of active IL-1 β , blocking the IL-1 cellular signalling pathways, or using gene therapy. All the above mentioned treatment strategies for specific inhibition of IL-1 production or activity have been investigated in numerous preclinical and clinical studies. Some of these investigations led to the discovery of new potential drugs for the treatment of OA. However, the results of treatment with these drugs were not entirely satisfactory, and further research is required to achieve the desired goals of therapy.

Džumhur A, Zibar L, Wagner J, Simundić T, Dembić Z, Barbić J. Association studies of gene polymorphisms in toll-like receptors 2 and 4 in croatian patients with acute myocardial infarction. *Scand J Immunol*. 2012 May;75(5):517-23.

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The aim of the study was to assess the frequency of SNP896A/G in the Toll-like receptor (TLR) 4 gene and SNP1350T/C in the TLR2 gene in patients with acute myocardial infarction (AMI) and to analyse the association of these SNPs with risk factors for atherosclerosis and clinical aspects of AMI in a sample of the Croatian population. We included 240 participants in the study: 120 AMI patients and 120 sex- and age-matched healthy blood donor controls. The SNP1350T/C variant in the TLR2 gene showed a lower frequency in the AMI patient group than in the control group ($P=0.033$). The frequency of SNP896A/G variants in the TLR4 gene between the patients and the controls did not differ ($P=0.286$). Significantly, fewer people had SNP1350T/C in the TLR2 gene ($P=0.003$) among the participants with arterial hypertension than those without it. The frequency of SNP896A/G in TLR4 was the same in hypertensive patients compared with normotensive subjects ($P=0.088$). SNP1350T/C in TLR2 was less frequent in the AMI patients and in those with hypertension. Thus, SNP1350T/C in TLR2 might play a protective role against AMI and arterial hypertension. The frequency of SNP896A/G in the TLR4 gene was not associated with AMI and arterial hypertension. Other risk factors for atherosclerosis and clinical aspects of myocardial infarction were not associated with the genotype distribution of the examined genes.

Hauser G, Tkalcic M, Pletikosic S, Grabar N, Stimac D. Erythrocyte sedimentation rate - Possible role in determining the existence of the low grade inflammation in Irritable Bowel Syndrome patients. Med Hypotheses. 2012 Jun;78(6):818-20.

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Irritable Bowel Syndrome (IBS), the most prevalent functional gastrointestinal disorder, is best described by the presence of recurrent symptoms of abdominal pain, diarrhea and/or constipation. It has been thought that IBS is stress-related disorder with no known structural abnormalities, e.g. infectious, biochemical or metabolic causes. But, recent evidence suggests that inflammation within the gastrointestinal tract may be of great importance in the pathogenesis of IBS. Our question is could the conventional and widely available general biological markers of inflammation

such as erythrocyte sedimentation rate (ESR) be indicator of microscopic inflammatory process in some IBS patients? We hypothesize that mild inflammation in IBS patients could be detected by meaning of a sensitive but cheap and ubiquitous test - ESR. Furthermore we assume that ESR would be related with the disease severity index and decreased general and disease-specific health-related quality of life (HRQoL). A pilot study has been conducted with 86 outpatients (65% female) with IBS, average age 47.76 (SD=13.68). The preliminary results were partly in favor of our hypothesis. They showed that IBS patients with higher ESR expressed lower disease-specific HRQoL (e.g. they expressed more bowel symptoms, social and emotional disturbances related to disease). No significant correlations were found between ESR and the disease severity as well as general HRQoL.

Vuk T, Barišić M, Očić T, Dogić V, Bingulac-Popović J, Sarlija D, Balija M, Jukić I. Management of complaints in blood establishments: thirteen years of experience at the Croatian Institute of Transfusion Medicine. Blood Transfus. 2012 Mar 29:1-9.

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BACKGROUND: The aim of the study is to present the results and experience in the management of complaints in a transfusion service in order to draw attention to the importance of this segment of quality management and to stimulate publication of other studies on the topic.

MATERIALS AND METHODS: This study is based on data from the Croatian Institute of Transfusion Medicine obtained by analysis of complaints recorded during a 13-year period (1998-2010). The distribution of the types and frequencies of complaints is presented, along with the level of their justifiability and criticality. The dynamics of the complaints is analysed overall and within particular categories. In addition, corrective actions and other factors that may have influenced the trends observed are discussed.

RESULTS: During the study period, 817 complaints were received, most of which (40.9%) referred to the positive direct antiglobulin test in red cell concentrates, followed by blood product issuing and distribution (12.9%) and blood product quality (9.4%). Of the 817 complaints, 177 (21.7%) were assessed as serious and 645 (78.9%) as justified based on the testing performed.

CONCLUSION: Data collected by systematic recording and analysis of complaints provide a basis for problem identification, implementation of corrective and preventive actions, and improvement of product and service quality, and, thereby, customer satisfaction.