to improve the pain management practices in the hospital, with an initial emphasis on pain assessment.

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A6

Promising effects of donepezil when added to patients treated with gabapentin for neuropathic pain

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Aims: The clinical relevance of adding the acetylcholinesterase inhibitor donepezil to existing gabapentin treatment in patients with post-traumatic neuropathic pain was explored in this open-label study. The two drugs have previously shown synergism following co-administration in nerve-injured rats [1,2].

Methods: The study comprised two consecutive periods of minimum six weeks: (1) titration of gabapentin until highest tolerable dose or maximum 2400 mg daily; and (2) addition of donepezil 5 mg once daily to the fixed gabapentin dose. Efficacy and tolerability were assessed by ratings of pain intensity, questionnaires for pain and health-related quality of life, and reporting of adverse events and analgesic rescue medication. Pain scores were also analyzed using mixed-effects analysis (i.e. incorporating inter-subject variability) with the software NONMEM.

Results: Eight patients commenced treatment with donepezil upon the gabapentin titration period, of which two withdrew due to adverse events. Addition of donepezil reduced pain by >35% in four of six patients compared to gabapentin monotherapy. Mixed-effects analysis revealed that pain scores were significantly lower during co-administration ($p < 0.05$ combination vs. monotherapy). Donepezil was well tolerated in combination with gabapentin. At the end of study, three patients wished to continue combination therapy with gabapentin and donepezil.

Conclusion: Donepezil may provide additional analgesia to neuropathic pain patients with insufficient pain relief from gabapentin as monotherapy. Further confirmation in controlled clinical trials is justified. Mixed-effects analysis was sensitive enough to detect statistically significant effects, showing its usefulness in small-scale trials and/or when data is associated with high variability.

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A7

A pediatric patients' pain evaluation in the emergency unit

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Aims: Helsinki University Hospital for Children and Adolescents treats 0- to 16-year old pediatric and surgical patients. The patients arrive to the emergency unit by ambulance, referral or by decision of the triage nurse. The most common reason for visit is pain. VAS pain scale should be used, but pain is not evaluated properly. The aim of this study was to review literature on evaluation and treatment of pain in pediatric emergency unit.

Methods: A search from Cinahl and Finnish Medic-database covering last 10 years was performed using: pain, child, trauma, documentation, evaluation, emergency and assessment as keywords.

Results: Multiple pain scales are used in pediatric emergency units. A scale possibly useful for us is the CEM, College of Emergency Medicine tool. Non-medical procedural pain treatment: physical methods (e.g. cold, warm, massage), emotional support and cognitive-behavioral methods (e.g. relaxation, mental imagery and information) was found to be as useful in children. The aim of cognitive-behavioral methods is to decrease fear, stress and pain and improve self-determination. Non-medical treatment was found to be cost efficient and decrease the need of analgesics. It was also found that a child in pain should be raised in triage. Educated staff usually means that children get pain medication quicker.

Conclusions: Research on the effects of systematic use of a pain scales on pain treatment, pain and fear in pediatric patients would be interesting.

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B2

Proteomic analysis of cerebrospinal fluid gives insight into the pain relief of spinal cord stimulation

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Aims: Neuropathic pain is caused by a lesion or disease of the somatosensory nervous system affecting approximately 2% of the population. Current pharmacological treatments are ineffective for more than 50% of the patients and often give much adverse effects. Spinal cord stimulation (SCS) is an alternative cost-effective treatment with high efficacy, prolonged pain relief, few side effects. We have compared the cerebrospinal fluid (CSF) proteomes from neuropathic pain patients during pain relief induced by SCS and during pain sensation without SCS, to gain further insights into the mechanisms behind the obtained analgesia.

Methods: Paired CSF samples were taken from SCS-responsive neuropathic pain patients after the SCS had been turned off for 48 h and when the SCS had been used normally for three weeks. Thus, each patient acted as their own control. The corresponding pro-

teomes for each patient were relatively quantified using a mass spectrometry based shotgun approach.

Results: In total, 419 unique proteins were simultaneously identified and relatively quantified. A panel consisting of seven proteins, 5 up-regulated and 2 down, were found to be significantly regulated by SCS in two complementary statistical tests ($P \leq 0.01$). The most up-regulated protein in the SCS linked panel is a known modulator of nicotinic acetylcholine (ACh) receptor activity. Interestingly, it has a striking tertiary structural similarity and biological functionality as pain modulating prototoxins found in snake venoms.

Conclusions: Our findings reveal possible insights into the mechanism of spinal cord stimulation and the obtained pain relief.

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B3

The DQB1(∗)03:02 HLA haplotype is associated with increased risk of chronic pain after inguinal hernia surgery and lumbar disc herniation

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Abstract: Neuropathic pain conditions are common after nerve injuries and are suggested to be regulated in part by genetic factors. We have previously demonstrated a strong genetic influence of the rat major histocompatibility complex on development of neuropathic pain behavior after peripheral nerve injury. In order to study if the corresponding human leukocyte antigen complex (HLA) also influences susceptibility to pain, we performed an association study in patients that had undergone surgery for inguinal hernia ($n = 189$). One group had developed a chronic pain state following the surgical procedure, while the control group had undergone the same type of operation, without any persistent pain. HLA DRB1genotyping revealed a significantly increased proportion of patients in the pain group carrying DRB1(∗)04 compared to patients in the pain-free group. Additional typing of the DQB1 gene further strengthened the association; carriers of the DQB1(∗)03:02 allele together with DRB1(∗)04 displayed an increased risk of postsurgery pain with an odds risk of 3.16 (1.61–6.22) compared to noncarriers. This finding was subsequently replicated in the clinical material of patients with lumbar disc herniation ($n = 258$), where carriers of the DQB1(∗)03:02 allele displayed a slower recovery and increased pain. In conclusion, we here for the first time demonstrate that there is an HLA-dependent risk of developing pain after surgery or lumbar disc herniation; mediated by the DRB1(∗)04–DQB1(∗)03:02 haplotype. Further experimental and clinical studies are needed to fine-map the HLA effect and to address underlying mechanisms.

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B4

On the pharmacological effects of two lidocaine concentrations tested on spontaneous and evoked pain in human painful neuroma: A new clinical model of neuropathic pain

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Aims: Spontaneous and evoked pains are key symptoms of patients with neuropathic pain and there is a current discussion on the predictive value of evoked pain read outs for the reduction of spontaneous pain. Here we describe a new clinical model of neuropathic pain that may be useful for evaluation of new drugs. We also report the effects of lidocaine in this model as reference values.

Methods: In a randomized double-blind experiment, the analgesic effects of local lidocaine were investigated separately for spontaneous pain and for stimulus-evoked allodynia and hyperalgesia in sixteen patients with painful neuromas after traumatic nerve injuries in the upper extremities. The patterns of sensory changes were compared before and after treatment with lidocaine (0.1% or 0.5%, 1 ml), with 1–2 weeks interval, injected close to the neuroma. Spontaneous and evoked pains were assessed using a visual analogue scale (VAS) and quantitative/qualitative sensory testing.

Results: Lidocaine dose-dependently reduced spontaneous and evoked pain scores by more than 90% with maximum effects between 1 and 5 min for evoked pain and between 3 and 15 min for spontaneous pain. While evoked pain normalized rapidly reaching about 50% of the control level 20 minutes after the injection spontaneous pain levels were lower than 25% at this time. Moreover, in 4 patients the reduction of ongoing pain lasted 24 h whereas evoked pain had returned to baseline levels in all the patients after 1 h.

Conclusion: Differential analgesic effects of local lidocaine on spontaneous and evoked pain suggest that different mechanism underlie these two key clinical symptoms. Thus, clinical trials assessing localized traumatic neuropathic pain should investigate both aspects of pain separately with the proposed model allowing testing of new drugs systemically or locally administered.

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