CROATIAN INTERNATIONAL PUBLICATIONS

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Mlinac K, Fabris D, Vukelic Z, Rozman M, Heffer M, Bognar SK. Structural analysis of brain ganglioside acetylation patterns in mice with altered ganglioside biosynthesis. Carbohydr Res. 2013;382C:1-8.

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Gangliosides are sialylated membrane glycosphingolipids especially abundant in mammalian brain tissue. Sialic acid O-acetylation is one of the most common structural modifications of gangliosides which considerably influences their chemical properties. In this study, gangliosides extracted from brain tissue of mice with altered ganglioside biosynthesis (St8sia1 null and B4galnt1 null mice) were structurally characterized and their acetylation pattern was analyzed. Extracted native and alkali-treated gangliosides were resolved by high performance thin layer chromatography. Ganglioside mixtures as well as separated individual ganglioside fractions were further analyzed by tandem mass spectrometry. Several O-acetylated brain ganglioside species were found in knockout mice, not present in the wild-type mice. To the best of our knowledge this is the first report on the presence of O-acetylated GD1a in St8sia1 null mice and O-acetylated GM3 species in B4galnt1 null mice. In addition, much higher diversity of abnormally accumulated brain ganglioside species regarding the structure of ceramide portion was observed in knockout versus wild-type mice. Obtained findings indicate that the diversity of brain ganglioside structures as well as acetylation patterns in mice with altered ganglioside biosynthesis, is even higher than previously reported. Further investigation is needed in order to explore the effects of acetylation on ganglioside interactions with other molecules and consequently the physiological role of acetylated ganglioside species.

Lukic A, Lukic IK, Malcic I, Batinic D, Milosevic D, Rozmanic V, Saraga M, Subat-Dezulovic M, Metlicic V, Malenica B, Jelusic M. Childhood-onset systemic lupus erythematosus in Croatia: demographic, clinical and laboratory features, and factors influencing time to diagnosis. Clin Exp Rheumatol. 2013;31(5):803-12.

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OBJECTIVES: Childhood-onset systemic lupus erythematosus (cSLE) presents with diverse clinical features and often with non-classical symptoms that may delay diagnosis and increase risk of morbidity and mortality. This paper aims to analyse incidence, and clinical and laboratory features of cSLE in Croatia between 1991 and 2010, and to identify factors influencing time to diagnosis.

RESULTS: Medical records at three university-based tertiary care centres were analysed retrospectively for 81 children with cSLE (68 girls). Mean age at onset was 13.4±2.8 yr (interquartile range 3), and annual incidence varied from 1-15 per million at risk. The most frequent clinical and laboratory features were musculoskeletal symptoms (80%) and increased erythrocyte sedimentation rate (96%). The most frequent immunological laboratory findings were the presence of antibodies against histones (86%), double-stranded DNA (73%), and Sm protein (64%), as well as low levels of C3 complement (69%). Haematuria was present in 58% of children, proteinuria in 56%, and biopsy-confirmed lupus nephritis in 43%. Median time from symptom onset to diagnosis was 2 months (range 0-96). Time to diagnosis was inversely associated with ECLAM score ($p<0.001$), but it showed no association with age, gender, clinical features or distance from the nearest paediatric centre.

CONCLUSIONS: This is the first large-scale, in-depth study of clinical and laboratory features of cSLE in Croatia. Among all demographic, laboratory and clinical fe-

atures examined, ECLAM score alone was inversely associated with time to diagnosis. This highlights the need to improve detection of children with fewer symptoms early in the course of the disease, therefore serious consequences for prognosis could be avoided.

Flego V, Ristic S, Devic Pavlic S, Matanic Lender D, Bulat-Kardum L, Kapovic M, Radojcic Badovinac A. Tumor necrosis factor-alpha gene promoter -308 and -238 polymorphisms in patients with lung cancer as a second primary tumor. Med Sci Monit. 2013;19:846-51.

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Background Lung cancer is the most common second primary cancer. We investigated whether the TNF-alpha-308 and TNF-alpha-238 polymorphisms were associated with the susceptibility and severity of lung cancer as the second primary cancer (LC2). Material and Methods This study included 104 patients from the group LC2. The control subjects included 2 groups. The first control group (LC1) comprised 201 unrelated patients with lung cancer as a first primary cancer. The second control group (HC) comprised 230 healthy blood donors, matched for sex and age to the study group. Results The frequencies of the TNF-alpha-238 polymorphism GG genotype and the G allele were higher in the LC2 group than in the LC1 group, but the differences did not reach significance (p=0.054 and p=0.057, respectively). Similar differences were found in the TNF-alpha-238 polymorphism GG genotype and G allele between the LC2 group and the HC group (p=0.054 and p=0.057, respectively). In terms of the different types of lung cancer, patients with a second primary NSCLC (non-small cell lung cancer) more frequently had TNF-alpha-238 polymorphism GG genotypes and G alleles than patients with a first primary NSCLC (the differences approached statistical significance: p=0.060, p=0.064, respectively). All (100%) patients of group LC2 (n=104) had the GG genotype and the G allele. GG genotype was exclusive and no A allele was found in group LC2. Conclusions TNF-alpha-238 polymorphism GG genotype and the G allele could have a promotional effect on the development of NSCLC in the group of patients with LC2.

Ivancev B, Carev M, Pecotic R, Valic M, Pavlinac Dodig I, Karanovic N, Dogas Z. Remifentanil reversibly abolished phrenic long term facilitation in rats subjected to acute intermittent hypoxia. J Physiol Pharmacol. 2013;64(4):485-92.

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The aim was to investigate whether intravenous infusion of remifentanil would depress phrenic long term facilitation (pLTF) evoked by acute intermittent hypoxia (AIH) in adult, male, urethane anaesthetized Sprague-Dawley rats, bilaterally vagotomized, paralyzed and mechanically ventilated. The experimental group received a remifentanil infusion (0.5 μg/kg/min i.v., n=12), whereas the control group (n=6) received saline. Rats were exposed to AIH protocol. Phrenic nerve amplitude (PNA), burst frequency (f) and breathing rhythm parameters (Ti, Te, Ttot) were analyzed during 5 hypoxias and at 15, 30, and 60 minutes after the final hypoxia, and compared to baseline values. At the end of the experiment, the infusion of remifentanil was stopped and phrenic nerve activity was compared to baseline values prior to remifentanil infusion. In the control group, peak phrenic nerve activity (pPNA) significantly increased at 60 min (T60, increase by 138.8±28.3%, p=0.006) after the last hypoxic episode compared to baseline values, i.e. pLTF was induced. In remifentanil treated rats, there were no significant changes in peak phrenic nerve activity at T60 compared to baseline values (decrease by 5.3±16.5%, p>0.05), i.e. pLTF was abolished. Fifteen minutes following cessation of remifentanil infusion, pPNA increased by 93.2plusmn;40.2% (p<0.05) and remained increased compared to pre-remifentanil-infusion values for more than 30 minutes, i.e. pLTF could be observed after cessation of the remifentanil infusion. In conclusion, the short acting μ-opioid receptor agonist, remifentanil, reversibly abolished phrenic long term facilitation in urethane anesthetized rats.