

ARCHIVES OF THE HUNGARIAN MEDICAL ASSOCIATION OF AMERICA



The official publication of the Hungarian Medical Association of America, Inc.

HMAA

Várgesztes Meeting

2024

ABSTRACTS

INVESTIGATION OF INFLAMMASOME ACTIVITY IN RODENT MODELS OF DUCHENNE MUSCULAR DYSTROPHY

Artúr Tóth, Zsófia Gulyás-Onódi, Petra Lujza Szabó, Dániel Kucsera, Péter Pokreisz; Christopher Dostal, Karlheinz Hilber, Gavin Y. Oudit, Bruno K. Podesser, Péter Ferdinandy, Zoltán Varga, Attila Kiss (1 Department of Pharmacology and Pharmacotherapy, HCEMM-SE Cardiometabolic Immunology Research Group, Semmelweis University; 2 Center for Biomedical Research, Medical University of Vienna)

Keywords: inflammasomes, cardiomyopathy, muscular dystrophy, inflammation

Aims: Duchenne muscular dystrophy (DMD) is an inherited, X-linked disease characterized by severe muscle loss. Affected young boys die prematurely due to respiratory and heart failure. Given that the inflammation of the muscle is a therapeutic target, our aim was to elucidate whether inflammasomes, multiprotein complexes of the innate immune response, play roles in the pathomechanism.

Methods: We investigated skeletal and heart muscle samples from dystrophin-deficient rodent models: mdx mice and DMD(mdx) rats, at early (3 month old) and late (10 month old) stages. The expression of inflammasome proteins was assessed by immunoblotting. The control groups consisted of time- and age-matched wild-type animals.

Results: The inflammasome adaptor protein (ASC) showed significant expression in the skeletal muscle ($p=0.003$; and 0.017 , respectively) of mdx mice at early and late time points. Meanwhile, the effector cytokines of the inflammasomes (IL-1 β) were more augmented in rat skeletal muscle ($p=0.049$; and 0.03 , respectively). Only tendentious changes were detected in heart muscle.

Conclusions: The different phenotypes of the models can cause the altered inflammasome activation patterns. The skeletal muscle was more prone to inflammation than the heart muscle in both species, highlighting the potential limitations of the anti-inflammatory therapies regarding heart failure.

Support: EU-Horizon-2020 (No 739593); MTA-Lendület (LP2021-14); NKFIH (FK134751); 2020-4.1.1.-TKP2020; Austrian Science Fund (P35542-B)

THE EFFECTIVENESS OF PHENOBARBITAL IN NEONATAL SEIZURES CAUSED BY HYPOXIC-ISCHEMIC ENCEPHALOPATHY

Barna Péter Hegyi, Ünőke Méder (Pediatric Center, Semmelweis University)

Keywords: neonatal seizure, hypoxic-ischemic encephalopathy, phenobarbital, amplitude-integrated EEG

Aims: Neonatal seizures are the most common neurological emergencies in the Neonatal Intensive Care Unit. Hypoxic-ischemic encephalopathy (HIE) is the leading cause, but stroke, intraventricular haemorrhage, sepsis, metabolic disorders and developmental brain malformations are also known risk factors. Electrographic seizures without clinical symptoms can only be detected by EEG or an amplitude-integrated EEG (aEEG). Current guidelines recommend phenobarbital (PHB) as first line treatment regardless of the aetiology, however significant differences in effectiveness have been reported due to heterogenous sample groups or lack of EEG. We aimed to evaluate the 24-hour effectiveness of PHB in neonates with moderate or severe HIE by using amplitude-integrated EEG.

Methods: Our single center retrospective observational study included neonates born between 2013-2018 with moderate or severe HIE treated with therapeutic hypothermia at the Pediatric Center, Semmelweis University. aEEG background pattern and seizure activity was evaluated for 84 hours. The primary outcome was the 24-hour electrographic seizure cessation rate of PHB treatment.

Results: We enrolled 267 neonates, 54 of whom received phenobarbital based on clinical symptoms. 32 patients had electrophysiological convulsions at a median of 7,2 (5,1-14,2) hours of life and received phenobarbital treatment (median 20 mg/kg) at a median 10,8 (6,8-28,2) hours. 26 (81%) of the treated patients had seizures during the following 24 hours. 16 (50%) neonates received a second dose phenobarbital while 13 (41%) patients required second line treatment.

Conclusions: Phenobarbital provided 24-hour electrographic seizure cessation in only 6 (19%) neonates with moderate or severe HIE treated with therapeutic hypothermia.