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BACKGROUND: The extent of lung hypoplasia in neonates with congenital diaphragmatic hernia (CDH) can be assessed from gas exchange. We examined the role of preductal capillary blood gases in prognosticating outcome in patients with CDH. METHODS: We retrospectively reviewed demographic data, disease characteristics, and preductal capillary blood gases on admission and within 24 h following admission for 44 high-risk outborn neonates. All neonates were intubated after delivery due to acute respiratory distress, and were emergently transferred via ground ambulance to our unit between 1/2000 and 12/2014. The main outcome measure was survival to hospital discharge and explanatory variables of interest were preductal capillary blood gases obtained on admission and during the first 24 h following admission. RESULTS: Higher ratio of preductal partial pressure of oxygen to fraction of inspired oxygen (PcO2/FIO2) on admission predicted survival (AUC = 0.69, P = 0.04). However, some neonates substantially improved PcO2/FIO2 following initiation of treatment. Among neonates who survived at least 24 h, the highest preductal PcO2/FIO2 achieved in the initial 24 h was the strongest predictor of survival (AUC = 0.87, P = 0.002). Nonsurvivors had a mean admission preductal PcCO2 higher than survivors (91 ± 31 vs. 70 ± 25 mmHg, P = 0.02), and their PcCO2 remained high during the first 24 h of treatment. CONCLUSION: The inability to achieve adequate gas exchange within 24 h of initiation of intensive care treatment is an ominous sign in high-risk outborn neonates with CDH. We suggest that improvement of oxygenation during the first 24 h, along with other relevant clinical signs, should be used when making decisions regarding treatment options in these critically ill neonates.

Šimić I1,2, Potočnjak I1, Kraljičković I2, Stanić Benić M4, Čegec I1, Juričić Nahal D2, Ganoci L1,2, Božina N1. CYP2D6 *6/*6 genotype and drug interactions as cause of haloperidol-induced extrapyramidal symptoms. Pharmacogenomics. 2016; 13:1385-9.

1University of Zagreb School of Medicine, Zagreb, Croatia, 2Division of Clinical Pharmacology, Department of Internal Medicine, University Hospital Centre Zagreb, Zagreb, Croatia, 3Clinical Unit of Clinical Pharmacology & Toxicology, Croatia.
A 66-year-old male Caucasian, received 1 mg of haloperidol orally and rapidly developed severe iatrogenic extrapyramidal symptoms. Treatment was immediately discontinued, and the side effects resolved. Haloperidol is mainly metabolized by Phase I CYP2D6 and to the lesser extent by CYP3A4 and by Phase II UGT2B7 enzymes. Genotyping was performed revealing CYP2D6*6/*6, CYP3A4*1/*1, and UGT2B7 -161 C/T genotypes, implicating poor, extensive and intermediate metabolism, respectively. Of the CYPs, haloperidol is metabolized by CYP2D6 and CYP3A4 primarily. It was the introduction of ciprofloxacin which was a trigger for the development of adverse drug reaction due to inhibition of CYP2A4, which was in presented patient main metabolic pathway for haloperidol since he was CYP2D6 poor metabolizer. Presented case report highlights the importance of genotyping. Pharmacogenetics testing should be considered when drug toxicity is suspected, polymorphic metabolic pathways used and drugs concomitantly applied.

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INTRODUCTION: β-Catenin is a central effector molecule of the canonical wingless-related integration site (Wnt) signaling pathway. It is important for maintenance of stem cell homeostasis and its aberrant activation has been implicated in a wide array of malignant hematological disorders. There are few reports suggesting its dysregulation in Philadelphia chromosome-negative (Ph-) myeloproliferative neoplasms (MPNs).

METHODS: We analyzed β-catenin mRNA expression in bone marrow (BM) aspirates of 29 patients with primary (PMF) and 4 patients with secondary, post Ph- MPN, myelofibrosis (SMF) using quantitative real-time polymerase chain reaction (qRT PCR). The control group consisted of 16 BM aspirates from patients with limited-stage aggressive non-Hodgkin lymphoma without BM involvement. We compared relative gene expression with clinical and hematological parameters. RESULTS: Relative expression of β-catenin differed significantly among groups (P = .0002), it was significantly higher in patients with PMF and SMF than in the control group, but did not differ between patients with PMF and SMF. A negative correlation was found regarding hemoglobin level in PMF (P = .017). No association according to Janus kinase 2 (JAK2) V617F mutational status or JAK2 V617F allele burden was detected. CONCLUSION: Our results show for the first time that β-catenin mRNA expression is increased in patients with PMF and SMF and its upregulation might potentiate anemia. A number of inflammatory cytokines associated with PMF are capable of mediating their effects through increased β-catenin expression. Accordingly, β-catenin can induce expression of a number of genes implicated in processes of cell cycle control, fibrosis, and angiogenesis, which are central to the PMF pathogenesis. Therefore, β-catenin might represent an interesting new therapeutic target in these diseases.
on brain edema formation via a still unknown mechanism. The aim of this study was clarifying the mechanisms of action of NPs on BK signaling, and their interactive effects after ischemic brain injury. We used a mouse model for stroke, the middle cerebral artery (MCA) occlusion. Brain lesion and edema were measured by microcomputerized tomography volumetric measurements. To determine the effects of NPs on the BK signaling pathway in the MCAs we measured changes in vessel diameter and membrane potentials in endothelial cells. To determine the effects of NPs on BK signaling pathway in isolated astrocytes and neurons, membrane potentials and intercellular Ca2+ concentrations were measured. Urodilatin inhibited and when applied together with BK, reduced the formation of the ischemic lesion via activation of G-Protein-Signaling Protein Type 4 at the cellular (astrocytes, neurons) and blood vessel (endothelial cells and isolated MCA) level as well as in vivo experiments. The results of this study show the existence of a natural antagonist of BK in the brain, and the possible use of NPs in the treatment of stroke.