Special Section: Update in Hepatic Encephalopathy- Part III

The current issue of the Journal of Clinical and Experimental Hepatology presents the third and last series of peer reviewed review articles based on their research and clinical experience as a Special Section: “Update in Hepatic Encephalopathy- Part III”. The International Society for Hepatic Encephalopathy and Nitrogen Metabolism (ISHEN) organized 17th ISHEN Symposium that took place in Gurugram, India from 9th to 11th March 2017 where experts discussed various aspects of HE, from nomenclature to etiology, pathogenesis, classification, diagnosis, treatment and to outcome and the current section represents a consolidated effort at presenting the consensus on pathogenesis, monitoring and management of hepatic encephalopathy (HE).

Singh and Anand¹ discuss new insights on the residual cognitive defects after neurological recovery in acute liver failure (ALF). Structural damage and persistent neurological abnormalities seen after ALF are more likely to be related to cerebral edema, raised intracranial tension and cerebral hypoxemia, while neurocognitive dysfunctions are likely related to the critical illness. Evaluation of cerebral injury in ALF using Magnetic Resonance imaging with or without spectroscopy, PET (positron emission tomography) scan and EEG (electroencephalography) reveals structural abnormalities as well as cognitive impairment, which may take months to resolve.^{2,3} Weissenborn⁴ reviews the importance of minimal or covert encephalopathy which affects motor speed, attention and reasoning and are affected by a multitude of factors in cirrhosis, neuroinflammation, hyperammonemia,⁵ hyponatremia,⁶ sepsis⁷ and co morbidities like diabetes⁸ and alcohol intake. Fluid and Duarte-Rojo⁹ describe the prognostic usefulness of minimal or covert HE by analyzing >100 large-scale validation cohort studies which confirm MHE or covert HE as predictors of overt hepatic encephalopathy, decreased quality of life (QOL), and mortality.^{10,11} DeMorrow¹² reviews the role of bile acid signaling in key pathogenic features of HE development and includes discussion of some possible explanations of potential downstream consequences of aberrant bile acid signaling. The role of Farnesoid X receptor (FXR) immunoreactivity,¹³ intestinal microbiota¹⁴ and Takeda G-protein coupled receptor (TGR5) expression¹⁵ is also explained lucidly.

Lattanzi et al.¹⁶ present the available data on the synergistic effect of HE and sarcopenia, which affects patients with advanced cirrhosis and worsens their outcome. The brain-muscle-liver axis is de-ranged and muscle tissue becomes the main alternative organ for ammonia

metabolism via glutaminase by incorporating it into glutamine.¹⁷ Ammonia itself impairs muscle protein synthesis in part through the up-regulation of myostatin production.¹⁸ Myostatin, a member of the TGF β superfamily, is a powerful catabolic signal that inhibits protein synthesis and satellite cells proliferation and differentiation through SMAD 2/3 signaling.

Aamann, et al.¹⁹ define the concepts of frailty, sarcopenia and malnutrition in cirrhosis review the role of optimizing muscle mass in patients with HE using exercise as a potential strategy to decrease ammonia levels. Further studies measuring the impact of exercise training on HE, using animal as well as human studies, are warranted.²⁰ Finally Ridola et al.²¹ describe the methodology for designing randomized controlled trials in three different settings in HE: 1) management of hospitalized patients with episodic HE; 2) secondary prophylaxis in patients following an episode of HE; and 3) management of minimal/covert HE.

This is the final and Part III compilation of “Update in Hepatic Encephalopathy”. The Editors believe that the resulting compilation of reviews is extremely informative and hope the readers will share this appreciation.

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