

Units/wk	Patients		Controls	
	Duration (yr)*	Age started (yr)*	Duration (yr)*	Age started (yr)*
>0	30 (23–36)	17 (16–18)+	30 (23–36)	16 (15–18)
>40	20 (14–27)	22 (18–30)+	22 (16–30)	19 (17–25)
>80	12 (6–19)	29 (21–38)+	13 (7–22)	25 (18–33)
>120	3 (0–12)	32 (24–41)++	4 (0–10)	28 (21–37)
>160	0 (0–7)	33 (27–41)+++	0 (0–7)	30 (24–39)

\*: median (interquartile range). +:  $p < 0.001$ , ++:  $p = 0.02$ , +++:  $p = 0.017$  by Mann-Whitney test for patients vs controls.

## 532

**IMPACT OF INVASIVE ASPERGILLOSIS ON SHORT-TERM MORTALITY IN PATIENTS WITH SEVERE ALCOHOLIC HEPATITIS**

T. Gustot, E. Maillart, M. Bocci, R. Surin, J. Schreiber, V. Lucidi, D. Degré, V. Donckier, F. Jacobs, C. Moreno. *Erasme Hospital Université Libre de Bruxelles, Brussels, Belgium*

E-mail: tgustot@ulb.ac.be

**Introduction:** Alcoholic hepatitis (AH), in its severe form, is a lethal disease in the short-term. Although infections are frequent complications of AH, the incidence of invasive aspergillosis (IA), and its impact on short-term survival remain unknown.

**Methods:** We retrospectively analyzed 82 patients prospectively followed for biopsy-proven severe AH (modified Discriminant Function (mDF)  $>32$ ) from June 2006 to December 2011 with a follow-up of 3 months after biopsy. AH were treated in 58 patients with corticosteroids, 4 with corticosteroids and pentoxifyline (PTX), 1 with PTX alone and 20 did not received specific treatment. Demographic, bacteriological and therapeutic data were collected. The diagnosis of IA was based on the revised criteria of EORTC/Mycoeses Study Group and the AspICU except for host factors.

**Results:** Forty cases of IA classified as proven ( $n=5$ ), probable ( $n=8$ ) or possible ( $n=1$ ) were diagnosed (17%) after a median delay of 34 [0–79] days after AH diagnosis. The sites of infection were the lungs ( $n=10$ ) and the central nervous system ( $n=2$ ) and was disseminated in 2. *Aspergillus fumigatus* was isolated in 10 cases (71% of IA): 5 in bronchoalveolar lavage (BAL), 4 in bronchial secretions and 1 in a brain biopsy. Diagnosis of other IA was based on radiological signs and galactomannan detection. Patients with IA were younger, had higher total bilirubine, creatinine and Prothrombin Time at day 28 ( $p < 0.01$ ) and were more frequently admitted in ICU. 12 patients with IA received corticosteroids but 2 did not receive any treatment for AH. The occurrence of IA was similar in non-responders to corticosteroids vs responders as defined by the Lille score. The 3-month mortality was higher in patients with IA than without IA (93 vs. 50%,  $p < 0.01$ ). Multivariate logistic regression analysis showed that age  $\geq 53$ y, a Lille score  $\geq 0.45$  and the presence of IA were associated with a higher risk of mortality at 3 months.

**Conclusions:** IA is a frequent complication of corticosteroid-treated severe AH, carrying a high risk of mortality. Systematic screening for IA should be recommended in these patients while further studies are needed to identify high risk population requiring antifungal prophylactic treatments.

## 533

**METADOXINE ADDED TO STEROID THERAPY IMPROVES SIX-MONTH SURVIVAL IN PATIENTS WITH SEVERE ALCOHOLIC HEPATITIS**

M.F. Higuera-de la Tijera<sup>1</sup>, A.I. Servín-Caamaño<sup>2</sup>, A. Serralde-Zuñiga<sup>3</sup>, J.M. Abdo-Francis<sup>1</sup>, J. Cruz-Herrera<sup>2</sup>, J.L. Pérez-Hernández<sup>1</sup>. <sup>1</sup>Gastroenterology, Liver Clinic, <sup>2</sup>Internal Medicine, Hospital General de México, <sup>3</sup>Fundación Mexicana para la Salud A.C. (FUNSALUD), Mexico, Mexico

E-mail: fatimahiguera@yahoo.com.mx

**Introduction and Aim:** Severe alcoholic hepatitis (SAH) implies 50% mortality at 2 months. Studies show that therapy with steroids has reduced mortality to 35% at 6 months. However, mortality is still high. A recent study has demonstrated that *in vitro* steroid-treatment resistance is high and correlate with adverse clinical outcome. It is need to explore new therapeutic alternatives to improve survival rate in patients who fail to respond to steroid therapy.

Oxidative stress and depletion of mitochondrial glutathione are important implied factors in liver injury. Metadoxine (MTD) has shown to inhibit hepatic lipid accumulation. In tissues, ion pair molecules can be separated forming N-oxide molecules that work as rotating traps capable of capturing reactive oxygen species.

The aim of this study was to evaluate the impact on mortality rate at six months of MTD added to steroid therapy in patients with SAH. Also, risk factors implicated in increased mortality in the next six months were analyzed.

**Patients and Methods:** Randomized clinical trial, open label, conducted in Mexico's General Hospital (Registry Key DIC/10/107/03/043). We randomized 70 patients with SAH criteria, 35 received prednisone (PDN) 40mg/day and 35 received PDN 40mg/day plus MTD 500mg three times daily. The duration of treatment in both groups was 30 days.

**Results:** In the group supplemented with MTD significantly improved the following parameters: At the end of treatment, survival was better (74.3% vs. 45.7%  $P=0.02$ ); there was less development or progression of complications such as encephalopathy (28.6% vs. 60.0%  $P=0.008$ ) and hepatorenal syndrome (31.4% vs. 54.3%  $P=0.05$ ). Survival was also higher at 6 months follow-up (48.6% vs. 20%  $P=0.003$ ). Cox regression shown that relapse in alcohol consumption is strongly associated with 6-month mortality (HR 8.4; 95% CI 2.8 to 25.4).

**Conclusions:** MTD added to steroid therapy improves survival at six months in patients with SAH. Relapse in alcohol consumption is the main independent risk factor associated with mortality within the first 6 months of follow-up.

Acknowledgment: This work was supported by 'Estimulo Angeles Espinosa Yglesias 2010'.

## 534

**MUSCLE GLUTAMINE SYNTHASE REGULATES THE SEVERITY OF HYPERAMMONEMIA, HEPATIC INFLAMMATION, BRAIN SWELLING AND SURVIVAL IN ACETAMINOPHEN HEPATOTOXICITY**

M. Jover-Cobos<sup>1</sup>, N.A. Davies<sup>1</sup>, D. Adebayo<sup>1</sup>, A. Habtesion<sup>1</sup>, L.A. Baker<sup>2</sup>, N. Shah<sup>1</sup>, Y. Sharifi<sup>1</sup>, R. Mookerjee<sup>1</sup>, R. Jalan<sup>1</sup>. <sup>1</sup>Institute for Liver and Digestive Health. Liver Failure Group, University College London, Division of Medicine, <sup>2</sup>Royal Veterinary College, London, UK  
E-mail: m.cobos@ucl.ac.uk

**Introduction and Aim:** In patients with liver failure, urea synthesis is diminished. Glutamine is a multifunctional amino-acid that is important in regulating ammonia metabolism, gut integrity, protein synthesis and immune function. The main organs expressing the enzyme, glutamine synthase (GS), which is responsible for its generation are the liver and the muscle. The aim of this study was to determine the effect of knocking-out muscle GS (GS-KO) in