liver abnormalities. Anti-PG-PS IgA antibodies were elevated in spite of normal H2BTs. A multivariate analysis of studied parameters showed that the significant decrease of ALT (average variation vs. placebo, p 0.03) and of anti-PG-PS IgA antibodies (average variation vs. placebo, p 0.03) values after probiotic treatment was independent from changes of BMI z score and visceral fat. TNF-α, and US bright liver parameters remained fairly stable. The baseline t test (T0 placebo vs T0 probiotic) was not significant for all variables evaluated (ALT, BMI z score, US visceral fat, TNF-α, US ROI ratio, anti-PG-PS IgA antibodies).

**Conclusion:** Results of the present pilot study confirm that lactobacillus rhamnosus strain GG deserves consideration as a therapeutic tool for improving hypertransaminasemia but not bright liver in hepatopatic obese children who are unable to follow slimming diets and/or to change lifestyle. Further studies on a larger scale are therefore warranted.

## CO3

## A COHORT OF ITALIAN CHILDREN WITH PORTAL HYPERTENSION COMPLICATIONS TREATED BY TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT (TIPS)

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**Introduction:** Therapy of Portal Hypertension (PH) is primarily directed at the management of its complications including gastrointestinal bleeding (GI), ascites and hypersplenism.

Transjugular Intrahepatic Portosystemic Shunt (TIPS) is a radiological procedure which consists of placement of a shunt between a hepatic vein and the portal vein (PV) to decompress the portal venous system (PVS). In paediatric patients TIPS is an underutilized procedure because of concerns about technical practicability and absence of clear indications, benefits and risks on its placement. The aim of our study is to report data on the use of TIPS in children to manage the severe complications of PH.

**Methods:** Patients were selected among the children referred to Paediatric Liver, Gastrointestinal and Transplantation Unit, Ospedali Riuniti, Bergamo (Italy) in the last five years. Children were considered eligible candidates for TIPS placement if they developed complications of PH including gastrointestinal bleeding from oesophageal or intestinal varices and ascites unresponsive to medical and endoscopic treatment. TIPS procedure was performed under general anaesthesia in all patients. An expanded polytetrafluoroethylene-covered Viatorr-Gore stent-graft was employed to create a porto-systemic shunt. Follow-up assessments were performed by means of physical examination, laboratory investigations and an abdominal ultrasound every 3-monthly for the first year and 6-monthly thereafter, or whenever symptoms were noted.

**Results:** 14 patients were considered candidates for the TIPS procedure but one of them had a low porto-systemic gradient (PSG) so the shunt was not placed. TIPS placement was attempted in 13 patients. The median age was 9.4 years (2.2–18) and the median weight 29.0 kg (11.5–96). Patients were affected by different illnesses, three of them had a portal cavernoma (PC) and four had already undergone a liver transplantation (LTX). The indications for the TIPS procedure were intractable ascites in 5 patients and GI bleeding in 8 patients. The median of PSG gradient before TIPS was 20.5 mmHg (16–35). We successfully placed a shunt in 12/13 patients (92.3%), in one with a PC TIPS procedure failed. No patients had peri- and postprocedural complications. The median PSG after shunt placement significantly reduced up to 10 mmHg (5–15) ($p<0.00001$). Clinical success was achieved in 10/12 patients (83.3%). Median ammonia levels before and after the procedure were 44 (28–96) and 68 μMol/L ($p=0.02$) respectively but no patient developed overt hepatic encephalopathy. The median follow-up period was of 14 months (range 2–67). Three patients had shunt dysfunction (2 thrombosis and 1 stenosis) resolved by angioplasty and restating in all. In 4 patients TIPS was placed as a bridge to LTX after a median follow-up of 6 months (1.5–33). At the last follow-up TIPS was patent in 100% of patients.

**Conclusions:** TIPS placement is an effective means of lowering portal venous pressure and controlling recurrent variceal bleeding and intractable ascites. In experienced hands TIPS procedure is feasible and has no procedural complications. PC is not a contraindications for a TIPS procedure but its presence can reduce the success rate for TIPS placement. The use of a covered stent can improve the shunt patency. TIPS should be considered as a valuable treatment option both in children with severe PH as a bridge to LTX and in children with compensated liver disease as a long-term treatment of PH.

### Reference

Lorenz JM. Placement of tranjugular intrahepatic portosystemic shunt in children. Tech Vasc Interv Radiol 2008;11(4):235–40. Review.

## CO4

## THERAPEUTICAL IMPLICATIONS IN THE STUDY OF MUTATION OF THE CYP450 3 A5*3 IN THE METABOLISM OF TACROLIMUS IN PAEDIATRIC LIVER TRANSPLANTATION: THE EXPERIENCE OF A SINGLE MEDICAL CENTRE

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**Background and aim:** The aim of this study is to evaluate the influence of CYP3A5 polymorphism on pharmacokinetics and pharmacodynamics of Tacrolimus on a population of paediatric patients after liver transplant (LT).

**Methods:** Ninety-two LTs were performed on 86 pediatric patients in Turin between October 1999 and December 2009. Eighty patients, treated ab initio with Tacrolimus, were analyzed retrospectively. The allelic variants *1 and *3 of the cytochrome P450 were studied on samples of donor peripheral blood. The concentration of the drug in relation to the dose given in the first 3 weeks post LT, expressed as a concentration/dose (C/D) ratio, were measured as a pharmacokinetic parameter. A statistical analysis of the data was obtained by the t-test and the ANOVA (analysis of variations) test.

**Results:** The frequency of genotype *3/*3 was 70% according to the literature. Genotype *1/*3 was present in 30% of our patients. The relation between the ratio C/D and the donor's genotype showed that the metabolic capacity of the grafts that expressed *1/*3 is significantly higher ($p<0.001$) than those that expressed *3/*3. Moreover, when a comparison of the pro kg dose to be administered to the two groups to obtain the target concentration was made, it was observed that grafts with genotype *1/*3 needed a significantly higher dose ($p<0.05$) than those expressing *3/*3.

**Conclusions:** The CYP3A5 polymorphism influences both the metabolic capacity of the graft and Tacrolimus pharmacokinetics. These data are useful to optimize LT paediatric patients' immunosuppressive therapy and to avoid the toxic effects of Tacrolimus.

## CO5

## EARLY DETECTION OF LYMPHOPROLIFERATIVE DISORDERS (PTLD) IN PAUCISYMPTOMATIC PEDIATRIC LIVER TRANSPLANT RECIPIENTS BY ADENOTONSILLAR HISTOLOGY

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**Objectives and Study:** PTLD is a severe complication of transplantation linked in most cases to EBV infection. Prevalence in pediatric liver transplant recipients is 5–7% and mortality over 50%. In most cases PTLD is recognized at the stage of lymphoma because less aggressive variants are