ESPGHAN 50th ANNUAL MEETING

of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition

Abstracts

10–13 May 2017

Prague · Czech Republic

Prague Congress Centre (PCC)

www.espghancongress.org

G-eP-046

Thalidomide-induced peripheral neuropathy in children with nflammatory bowel disease

Matteo Bramuzzo[1], Gabriele Stocco[2], Marcella Montico[3], Serena Arrigo[4], Angela Calvi[5], Paola Lanteri[6], Stefano Costa[7], Salvatore Pellegrini[8], Giuseppe Magazzù[9], Jacopo Barp[10], Silvia Ghione[11], Paolo Lionetti[12], Giovanna Zuin[13], Massimo Fontana[13], Teresa Di Chio[14], Giuseppe Maggiore[15], Marzia Lazzerini[16], Marianna Lucafò[17], Chiara Udina[17], Maria Chiara Pellegrin[17], Andrea Chicco[2], Marco Carrozzi[18], Giuliana Decorti[17], Alessandro Ventura[19], Stefano Martelossi[19]

[1]Gastroenterology and Nutrition Unit Institute for Maternal and Child Health, Irccs "burlo Garofalo," Trieste , Italy
[2]University of Trieste, Department of Life Sciences, Trieste, Italy
[3]Institute for Maternal and Child Health Irccs "Burlo Garofolo", Trieste, Italy
[4]Gaslini Children Hospital, Pediatric Gastroenterology and Endoscopy Unit, Genoa, Italy
[5]Institute "giannina Gaslini", Paediatric Gastroenterology Unit, Genoa, Italy
[6]Institute "giannina Gaslini", Neuropsychiatry Unit, Genoa, Italy
[7]University of Messina, Paediatric Gastroenterology and Cystic Fibrosis Unit, Messina, Italy
[8]Policlinico Universitario G Martino, Messina, Italy
[9]University of Messina, Celiac Regional Centre, Pediatric Gastroenterology and Cystic Fibrosis Unit, Messina, Italy
[10]University of Florence, Meyer Children Hospital, Department of Sciences for Woman and Child Health, Florence, Italy
[11]Meyer Children's Hospital, Gastroenterology and Nutrition, Florence , Italy
[12]University of Florence, Meyer Children's Hospital, Neurofarba Department, Gastroenterology and Nutrition, Firenze, Italy
[13]Children's Hospital "v. Buzzi" Milan, Paediatric Department, Milan, Italy
[14]University of Pisa, Paediatric Gastroenterology and Hepatology, Pisa, Italy
[15]Department of Medical Science, University of Ferrara, Ferrara, Italy
[16]Institute for Maternal and Child Health, Irccs "burlo Garofolo", Clinical Epidemiology and Public Health Research Unit, Trieste, Italy
[17]University of Trieste, Department of Medical, Surgical and Health Sciences, Trieste, Italy
[18]Institute for Maternal and Child Health, Irccs "Burlo Garofolo", Paediatric Neurology, Trieste, Italy
[19]Institute for Maternal and Child Health, Irccs "Burlo Garofolo", Paediatric Department, Trieste, Italy

Objectives and study: Thalidomide is effective in inducing and maintaining remission in children with inflammatory bowel disease (IBD) refractory to standard treatments. However long-term thalidomide use may be limited by the development of thalidomide-induced peripheral neuropathy (TPN). Our study aimed to investigate the risk factors and the outcome of TPN in children with IBD.

Methods: Within a retrospective multi-centre cohort study we evaluated prevalence and evolution of TPN in children treated with thalidomide 1.5-2.5 mg/Kg/day and regularly followed-up with clinical and electrophysiological neurological assessment. To detect predisposing factors to TPN, the clinical history of patients who developed TPN and of patients who didn't was compared. Genotyping of variants in *ABCA1* (rs363717), *ICAM1* (rs1799969), *PPARD* (rs2076169), *SERPINB2* (rs6103), and *SLC12A6* (rs7164902) genes, previously associated with TPN, and in *CYP2C19* (rs4244285), which may influence thalidomide conversion to an active metabolite, was performed by TaqMan assays (Thermoscientific).

Results: One hundred forty-two patients were identified: 64% had Crohn's disease, 35% ulcerative colitis and 1% IBD-unclassified. Mean age at thalidomide start was 14 years. TPN was found in 72.5% of patients: 38.7% had clinical and electrophysiological alterations, 26.8% had exclusive electrophysiological anomalies, 7.0% had exclusive neurological symptoms. Median TPN-free period of treatment was 16.5 months; the percentage of TPN-free patients was 70.0% and 35.6% at 12 and 24 months of treatment respectively. TPN was a sensory neuropathy in 75% and a sensorimotor neuropathy in 17% of cases. Symptoms did not interfere with daily activities. TPN was the cause of drug suspension in 41.8% patients. Clinical symptoms resolved in 89.2% of cases while instrumental alteration persisted in more than half of the patients during a short follow-up.bBaseline characteristics and previous medical history were not found to be associated with TPN. The risk of TPN increased

depending on the mean daily dose (50-99 mg/day adjusted-Hazard Ratio 2.62 95%CI 1.31-5.21; 100-149 mg/day adj-HR 6.16 95%CI 20.9-13.06; >150 mg/day adj-HR 9.57 95%CI 2.6-35.2). Single nucleotide polymorphisms in *ICAM1* (rs1799969) and *SERPINB2* (rs6103) genes were found to be protective against TPN (OR 0.15 95%CI 0.03-0.82 and 0.36 95%CI 0.14-0.88, respectively).

Conclusion: TPN developed in more than two thirds of children with IBD but was generally mild and reversible during the follow-up. Cumulative dose was the most relevant risk factor for TPN while variants in genes involved in neuronal inflammation were protective.