

## BIOLOGICAL ASPECTS REGARDING THE MANAGEMENT OF CHRONIC VIRAL HEPATITIS C IN CHILDREN

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*Abstract* - Hepatitis C virus infection has reached epidemic proportions worldwide and there is increased interest in its occurrence in children. While there are certain controversies regarding the mechanisms and management of chronic viral hepatitis C in children, in the present study we were interested in comparing, from a biological perspective, the types of responses to two different management options in chronic viral hepatitis C in children: monotherapy with pegylated interferon (PEG-IFN) and interferon associated with ribavirin, for a period of one year. The obtained results showed that in almost 49% of the patients that received monotherapy treatment a sustained virological response was present. For the patients that received combined IFN-ribavirin therapy for one year, the sustained virological response was present in almost 50% of them. These findings show that the combination of interferon and ribavirin treatment was effective in children with chronic hepatitis C, however, further studies are needed to identify the optimum management of this pediatric population.

*Key words:* chronic viral hepatitis C; management; children

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### INTRODUCTION

The discovery of hepatitis C virus (HCV) in 1989 represented a major advance in the microbiological field and since then we have gained a variety of data on virological responses, genotypes and the management of chronic viral hepatitis C (Zein et al., 2007).

Recently there is an increased interest in the features of HCV infection in the pediatric population (Farci et al., 2007; Manns et al., 2006). This could be perhaps explained by the existence of several contro-

versies in this area of research. In most cases, children with hepatitis C are asymptomatic, although on histopathological examination significant histological lesions may be present. Correlations between the symptomatology, histological/biochemical activity and severity of the disease are low and progress of the disorder is extremely silent and dependant on the integrity and reactivity of the immune system (Yeung et al., 2007). It also important to mention that HCV infection is confirmed by serological tests used for the detection of anti-HCV antibodies and by using molecular tests for the detection of RNA HCV viral nucleic acid (Vassilopoulos et al., 2002). RNA HCV

viral nucleic acid is a fundamental early marker of infection that can be detected within a few days after infective contact (Kalantari et al., 2010; Moy et al., 2009).

The various concepts of the management of hepatitis C in children have changed in time (Zein et al., 2007) and were always subject to controversies. Recently, interferon alpha therapy was suggested for the management of chronic viral hepatitis C in children (Moy et al., 2009). Currently we have modern associated therapy and management schemes, such as interferon combined with ribavirin, which presumably is followed by sustained therapeutic responses (Manns et al., 2006; Jara et al., 2008; Kalantari et al., 2010). Since very few aspects are known about the relevance of this combination (interferon + ribavirin) in the pediatric population, the objective of our study was to compare, from a biological perspective, the types of responses to two different management options in chronic viral hepatitis C in children: monotherapy with pegylated interferon and therapy with interferon and ribavirin for a period of one year.

## PATIENTS AND METHODS

The study was conducted from January 2009 to December 2012 and included 86 patients (aged between 3 to 18 years) that have been diagnosed with chronic HCV hepatitis. The inclusion criteria were biological, histological, clinical and/or imaging elements for chronic viral hepatitis C. The analyzed viral markers were anti-HCV antibodies and RNA-HCV quantitative viremia. The study was conducted according to the provisions of the Helsinki Declaration and all the patients' families signed a consent form for participation in this study.

## RESULTS AND DISCUSSION

The distribution by years for the selected cases of viral hepatitis C was the following: 25 cases in 2009, 25 cases in 2010, 30 cases in 2011 and 6 cases in 2012. Since we wanted to understand some of the mechanisms relevant to the management of viral hepatitis C, we were also interested in the manifestations ex-

hibited by the patients from the study group, which included fatigability (49%), anorexia (20%), nausea and vomiting (10%), jaundice (3%), hypocholic stool (6%) or arthralgia and myalgia (3%). Mechanistically speaking, the high rate of fatigue, which is not related to the amount of transaminase, could be the effect of cytokines or could be even caused by viral invasion of the neurological structures.

Following an assessment of the therapy eligibility criteria, either the interferon therapy (monotherapy) or the associated therapy (interferon plus ribavirin) was initiated. Thirty percent of the patients were assigned to interferon monotherapy and 20% to associated therapy (interferon with ribavirin), while the rest followed a support treatment with Ursosalk, hygienic-dietetic regime and hepatoprotectors. Our results showed that in almost 49% of the patients that received monotherapy treatment a sustained virological response was present. For the patients that have received combined IFN-ribavirin therapy for one year, a sustained virological response was present in almost 50% of them.

It is considered that hepatitis C virus infection has reached epidemic proportions worldwide and despite being less prevalent in children, it is known that it could generate significant complications in this age group as well (Zein et al., 2007). Emerging management options are currently in trials for the adults with hepatitis C with encouraging initial results, which should be extended to children (Manns et al., 2006; Zein et al., 2007; Kalantari et al., 2010). Our data showed that a sustained virological response was established in almost half of IFN monotherapy-treated patients, with a similar situation in those treated with combined therapy (interferon and ribavirin).

Ribavirin is a guanosine analog that interferes with RNA metabolism required for viral replication (Wu et al, 2003). The generically named interferons are proteins that respond to the presence of various pathogens including viruses, increasing the anti-viral defenses through various mechanisms, as they are implicated in processes such as the activation of

the macrophages or increasing the expression of major histocompatibility complex antigens (Yang et al., 1995). Regarding the relevance of these drugs in the management of chronic viral hepatitis C in children, in other studies the sustained viral response was identified in 70% patients that benefitted from combined therapy (IFN and ribavirin), while a smaller percentage was recorded among those treated by IFN monotherapy (Manns et al., 2006; Kalantari et al., 2010). A reference study by Yeung et al. (2007) in Canada described the spontaneous clearance rate of childhood hepatitis C virus infection, as well as other predictors of clearance. It seems that if this clearance occurs, it tends to occur early in infection, at a younger age, with an increased relevance for the management of the disorder in the pediatric population (Yeung et al., 2007).

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