

## Efficiency of Chronic Hepatitis C Therapy with Pegylated Interferon and Ribavirin using Microsoft SQL Server

Vasileios PAPACHRISTOS<sup>1</sup>, Andrei ACHIMAȘ-CADARIU<sup>2,3</sup>, and Christos DRACOU LIS<sup>4</sup>

<sup>1</sup> General Pediatric Hospital “Aglaia Kyriakou”- Athens, Str. Thivon si Livadias, 11527 Athens, Greece.

<sup>2</sup> Clinical Hospital CF Cluj-Napoca. 16-20 Republicii, 400015 Cluj-Napoca, Romania.

<sup>3</sup> Department of Medical Informatics and Biostatistics, “Iuliu Hatieganu” University of Medicine and Pharmacy Cluj-Napoca, 6 Louis Pasteur, 400349 Cluj-Napoca, Romania.

<sup>4</sup> General Hospital Nikaia – Athens, 3 Dim Mantouvalou, 18454 Nikaia, Pireus, Athens.

E-mails: dr\_papachristosvasilis@yahoo.com; aachimas@umfcluj.ro

\* Author to whom correspondence should be addressed; Tel.: +302132009354

Received: 15 October 2012/Accepted: 28 October 2012/Published online: 24 November 2012

### Abstract

*Aim:* The most effective treatment for patients with chronic hepatitis C virus infection is pegylated interferon (PegIFN $\alpha$ ) and Ribavirin combination therapy. The aim of this study was to examine the effect of PegIFN and Ribavirin combination therapy in patients infected with hepatitis C virus, using the application Microsoft SQL Server. *Material and Method:* We compared the rates of sustained virological response, who is defined as the absence of HCV RNA in serum 24 weeks after the end of treatment, between patients with different genotype (1,2,3 and 4), gender (male and female) and age (patients aged 19-45 years and patients aged  $\geq 45$  years). *Results:* The majority of patients were male patients (n = 173) and only 24% (n = 47) were female patients. The number of genotype 1 and 2 patients was 80 (34.7%) and 14 (6.1%), respectively, and the number of genotype 3 and 4 was 108 (46.9%) and 28 (12.3%). SVR rates in the patients according with their HCV genotype were 48.3% (n = 25) for genotype 1, 50% (n = 5) for genotype 2, for genotype 3 were 61.5% (n = 43) and for genotype 4 were 19.1% (n = 4). *Conclusions:* In conclusion, this study show that the efficacy of PegIFN and Ribavirin combination therapy for HCV infection in patients with genotype 2 or 3, in female patients and in patients aged 19-45 years is superior to those in genotype 1 and 4, male patients and patients aged  $\geq 45$  years. The use of Microsoft SQL Server was efficient, simple, safe, not time consuming and precise. This software can be used for optimal efficiency in the process of medical analysis and reviews.

**Keywords:** Chronic hepatitis C; Database; Software; Efficacy of treatment.

### Introduction

Infection with the hepatitis C virus (HCV) represents a significant global health problem, infection affects an estimated 180 million people worldwide, which accounts 2-3% of the world's population [1]. HCV remains endemic in many countries of the world [2]. Hepatitis C continues to cause substantial morbidity and mortality worldwide [3]. Many patients remain asymptomatic for years and are only detected on health screening. About 20% of cases of hepatitis C infection develop an acute infection and 80% of those develop a chronic infection [4]. Only 20-30% of patients will progress to cirrhosis after 20-30 years [5], and from those 3% have risk of

hepatocellular carcinoma and 4-5% have risk of liver transplantation or death [6].

Patients with acute infection have an excellent replay to 6 months of standard therapy with interferon. The treatment of chronic HCV infection has 2 goals: to obtain the complete eradication of HCV (sustained virological response (SVR) who is the persistent absence of HCV RNA in serum 24 weeks after the end of treatment) and to prevent progression to cirrhosis or hepatocellular carcinoma [7]. The most efficient treatment for patients with chronic hepatitis C virus infection is pegylated interferon (PegIFN $\alpha$ ) and ribavirin combination therapy [8]. The planned duration of HCV treatment is 24 or 48 weeks according to the HCV genotype [9]. Patients infected with HCV genotype 2 and 3 show better SVR compared with the patients infected with HCV genotype 1 and 4 [10].

The aim of this study were to examine the efficiency of PegIFN and ribavirin combination therapy in patients infected with hepatitis C virus using the application Microsoft SQL Server [11]. This software is a database developed by Microsoft whose primary function is to store and retrieve data as requested by other software applications.

It is important in the era of technology all information collected about the patient, and not only, to be recorded in data bases for fast and effective use. In the last 10 years the technological evolution of application and databases has reached a point where we can handle a large data volume quickly and remotely (Web applications).

The relational databases are leading to quick search of information. Programming languages create graphical windows application that is very easy for the users.

The aim of this study was to examine the effect of PegIFN and Ribavirin combination therapy in patients infected with hepatitis C virus, using the application Microsoft SQL Server.

## **Material and Method**

410 patients with chronic hepatitis C were diagnosed at the Department of Hepatology, Nikaia Hospital, Athens. From those only 230 were treated with PegIFN and ribavirin combination therapy (81 were genotype 1, 14 were genotype 2, 108 were genotype 3 and 28 were genotype 4). Patients with genotype 1 and 4 were treated for 48 weeks and patients with genotype 2 and 3 for 24 weeks. They were excluded from the treatment if they had neutropenia (neutrophils < 1500/mm<sup>3</sup>), thrombocytopenia (platelets < 90000/mm<sup>3</sup>), anemia (hemoglobin < 12 per deciliter), decompensate liver disease, serum creatinine level more than 1.5 times the upper limit to normal, alcohol or drug dependence. A liver biopsy was performed in 178 of the patients before the treatment, and all biopsy were assigned a fibrosis score based on the Metavir score (F0= no fibrosis, F1= portal fibrosis without septa, F2= portal fibrosis with few septa, F3= numerous septa without cirrhosis, F4= cirrhosis) [12].

The primary efficacy end point was sustained virological response (SVR), defined as undetectable HCV RNA in serum 24 weeks after the end of treatment. For patients with at least 24 weeks of follow-up, the last observed HCV RNA level was used in assessments of efficacy. Even if the treatment was prematurely discontinued because of side effects or non-compliance, patients could be considered to have an SVR on the bases of their serum result of HCV RNA results at the 24 week follow-up.

All information about the patients were collected by the application Microsoft SQL Server. The specific application was created with the programming language Visual Basic [13].

The Visual studio is a complete development environment model (IDE) in many languages where Visual Basic is the most popular [14] with applicability in:

1. Create users
2. Auxiliary files
3. Printing
4. Statistics
5. Patients table
6. Patients history
7. Patients test results

The database used by the application is Microsoft SQL Server. It is a database based on SQL architecture server- client. Based on SQL means that uses the ANSI version of the Structural Query Language, or SQL Server [15]. Server-client means that SQL Server is designed to store data in a central location and delivers them, on request, to various other locations (customers). Statistical calculation (or report) were obtained using the Crystal Report manager.

## Results

The data were collected with the Microsoft SQL Server application. We collected information about: demographic data, blood count values, AST values, ALT values, viral load, genotype of HCV, fibrosis type, if the patients have started therapy with PegIFN and Ribavirin, SVR (Figure 1).

We can always add new patients in the database with automatically update of statistical results. This application gives as the descriptive statistic parameters by pushing the button < Report >. If we want to see the therapy efficacy in different age groups we use the button < Report 2 >, if we want to see the therapy efficacy in different types of fibrosis we use the button < Report 4 > (Figure 2).

230 patients started treatment with PegIFN and Ribavirin. The majority of patients were patients aged 19-45 years (n= 183, 79.5%) and 21.5% patients aged  $\geq 45$  years (n= 47), 76% were male patients (n= 173) and only 24% (n= 47) were female patients. The number of genotype 1 and 2 patients was 80 (34.7%) and 14 (6.1%), respectively, and the number of genotype 3 and 4 was 108 (46.9%) and 28 (12.3%). All the patients had a high viral load ( $> 106$  IU/mL). A liver biopsy was performed in 178 of the patients, from those 32 (18%) had fibrosis1, 71 (39%) had fibrosis2, fibrosis3 had 44 (24.7%) and fibrosis4 had 31 (18%) of patients.

SVR rates in the patients according with their HCV genotype were 48.3% (n= 25) for genotype 1, 50% (n= 5) for genotype 2, for genotype 3 were 61.5% (n= 43) and for genotype 4 were 19.1% (n= 4). The numbers of patients that stop the therapy were 14 (5 of genotype 1, 6 of genotype 3, 3 of genotype 4 and none of genotype 2). We also observed the impact of age in the efficacy of the treatment for genotype 1,2,3 and 4, respectively. Figure 3 shows SVR rates according to age for all the group of genotypes (SVR rates for patients aged 19-45 years was 47.5% (n=57) and for patients aged  $> 45$  was 45.2% (n=19)). The female patients was a minority in our study but their SVR rate was 64.1% , while the SVR rate of the male patients was only 46.3%.

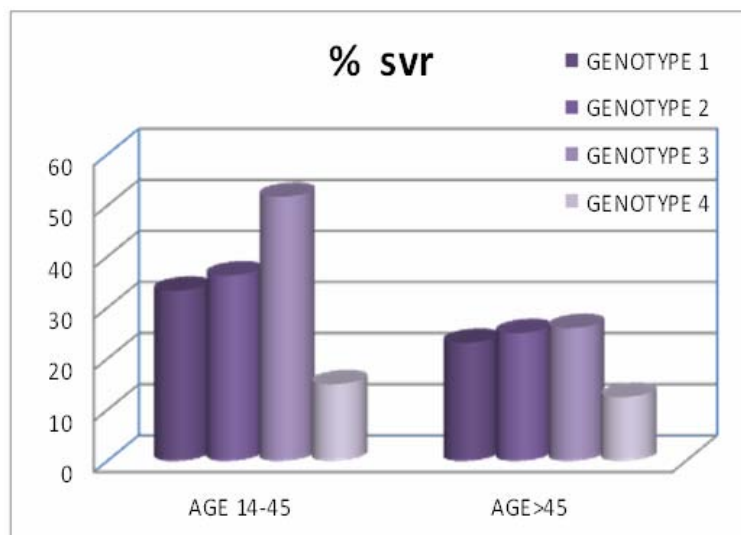
The screenshot shows a web-based data entry form for chronic hepatitis C patients. The form is organized into several sections. The top section is for patient identification, including fields for SURNAME, FIRST NAME, FATHER'S NAME, AGE, GENDER (with a dropdown menu), ADDRESS, POST CODE, and COUNTRY. Below this is a section for therapy details, with checkboxes for 'THERAPY WITH PEGASIC AND RIBA-RON', 'STOP OF THERAPY', and 'REAL COMPLIANCE OF THERAPY'. There are also dropdown menus for 'GENOTYPE', 'GENOTYPIC 2', and 'STEP', and a text input for 'GENOTYPIC 4'. The bottom section contains laboratory test results with input fields for: 'Viral load cells (IU/mL)', 'Red blood cells (10<sup>12</sup>/mm<sup>3</sup>)', 'Hemoglobin (g/dL)', 'Platelets (10<sup>9</sup>/mm<sup>3</sup>)', 'AST (U/L)', 'ALT (U/L)', and 'Viral Load (IU/mL)'. At the very bottom, there are four buttons labeled 'Report 1', 'Report 2', 'Report 3', and 'Report 4', and a red 'STOP' button on the right side.

Figure 1. Database screenshot for patients with chronic hepatitis C

*Report 2*

	Age between 19 and 45	Age upper 45
THERAPY WITH PEGASIS AND RIBAVIRIN	103	46
BREAK OF THERAPY	0	4
NON-COMPLIANCE OF THERAPY	11	13
SVR	57	39

**Figure 2.** Statistics parameters in two age groups



**Figure 3.** SVR rate according to age for all the groups of genotype

## Discussion

It is important that all medical data collected to be recorded in data bases for fast and effective use. Our data was collected by the application Microsoft SQL Server, created with the programming language Visual Basic, application that allows a rapid assessment of descriptive

statistical parameters.

In this study we found that the SVR rates, after the combination therapy with PegIFN and ribavirin, was 48.3% for genotype 1, 50% for genotype 2, 61.5% for genotype 3 and 19.1% for genotype 4. The response rate to combination therapy is higher in genotype 2 and 3 than in genotype 1 and 4, the SVR rates in our study being comparable with the SVR rates from previous studies [16].

While in another study the response rate to combination therapy is worse in female than in male patients we have shown better SVR rates in female (64.1%) than in male patients (46.3%) [17].

In the present study we found a significant difference in SRV rate between the two age groups of patients according to HCV genotype and also a significant difference in the response rate to combination therapy between the two age groups, which proves that both genotype and younger age they are predictors of SVR rates in patients treat with PegIFN and Ribavirin.

## **Conclusions**

In conclusion, this study show that the efficacy of PegIFN and Ribavirin combination therapy for HCV infection in patients with genotype 2 or 3, in female patients and in patients aged 19-45 years is superior to those in genotype 1 and 4, male patients and patients aged  $\geq 45$  years. The use of Microsoft SQL Server was efficient, simple, safe, not time consuming and precise. This software can be used for optimal efficiency in the process of medical analysis and reviews.

## **List of abbreviations**

SVR = Sustained virological response.

## **Conflict of Interest**

The authors declare that they have no conflict of interest.

## **References**

1. Rosen HR. Clinical practice. Chronic hepatitis C infection. *N Engl J Med* 2011;364(25):2429-38.
2. Alter MJ. Epidemiology of hepatitis C virus infection. *World J Gastroenterol* 2007;13(17):2436-41.
3. Moorman AC, Gordon SC, Rupp LB, Spradling PR, Teshale EH, Lu M, et al. Baseline characteristics and mortality among people in care for chronic viral hepatitis: the chronic hepatitis cohort study (CHeCS). *Clin Infect Dis* 2012 Sep 18. doi:10.1093/cid/cis815.
4. Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. *Lancet*. 2011;378(9791):571-83.
5. Thomas DL, Seeff LB. Natural history of hepatitis C. *Clin Liver Dis* 2005;9(3):383-98.
6. Alazawi W, Cunningham M, Dearden J, Foster GR. Systematic review: outcome of compensated cirrhosis due to chronic hepatitis C infection. *Aliment Pharmacol Ther* 2010;32:344-355.
7. Mukherjee S. Natural History, Risk Factors and Management of Hepatitis C After Liver. *Transplantation Inflammation & Allergy - Drug Targets* 2012;11(2):124-130.
8. Fried MW, Shiffman ML, Reddy KR, Smith C, Marinos G, Gonçales FL Jr, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *New Engl J Med* 2002;347(13):975-82.
9. Harrison SA, Abdurakhmanov D, Shiffman ML, Bakulin I, Mazur W, Rodriguez-Torres M, et al. Intensified Peginterferon alpha-2a Dosing Increases Sustained Virologic Response Rates in

- Heavy, High Viral Load Hepatitis C Genotype 1 Patients With High Low-density Lipoprotein. *J Clin Gastroenterol* 2012 Aug 30.
10. Guo X, Zhao Z, Xie J, Cai Q, Zhang X, Peng L, Gao Z. Prediction of response to pegylated-interferon- $\alpha$  and ribavirin therapy in Chinese patients infected with different hepatitis C virus genotype. *Viol J* 2012;19;9:123.
  11. \*\*\*"Microsoft Releases SQL Server 2012 to Help Customers Manage "Any Data, Any Size, Anywhere"". Microsoft News Center. Microsoft. 6 March 2012. <http://www.microsoft.com/Presspass/press/2012/mar12/03-06SQLServer12PR.mspx>. (Retrieved 7 March 2012)
  12. Bedossa P, Poynald T. An algorithm for the grading of activity in chronic hepatitis C. The METAVIR cooperative study group. *Hepatology* 1996;24:289-293.
  13. \*\*\* "Description of Visual Studio 2010 Service Pack 1". Microsoft. (Retrieved 25 March 2011).
  14. \*\*\*Visual Studio 2005 SDK. "Visual Studio Development Environment Model". Microsoft. Retrieved 2008-0Lextrait, Vincent (July 2010).
  15. \*\*\* "The Programming Languages Beacon, v10.3". Retrieved 5 September 2010. 1-01.
  16. Zeuzem S, Berg T, Moeller B, Hinrichsen H, Mauss S, Wedemeyer H, et al. Expert opinion on the treatment of patients with chronic hepatitis C *J Viral Hepat* 2009;16(2):75–90.
  17. Nishikawa H, Iguchi E, Koshikawa Y, Ako S, Inuzuka T, Takeda H, et al. The effect of pegylated interferon-alpha2b and ribavirin combination therapy for chronic hepatitis C infection in elderly patients. *BMC Res Notes* 2012;5:135.