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INFECTION WITH HEPATITIS C VIRUS A REAL HEALTH PROBLEM

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Abstract. The hepatitis C virus (HCV) is the most common cause of chronic liver diseases world-wide and it is a real health problem. The Centre for Diseases Control and Prevention (CDC) estimates that only for U.S.A at least 3.9 million people have been infected with HCV as indicated by a positive HCV antibody test. The World Health Organisation (WHO) estimates that 170 million people world-wide are infected with HCV. Recently after the HCV discovery in 1989 the diagnosis tests became available. The blood screening introduced in the Regional Transfusion Centres conducted to a dramatic decline of post-transfusional hepatitis.
In Romania, the prevalence of anti-HCV (around 4.5%.) before introduction of routine screening was 10 fold higher than in west European countries. For this reason, in our country the size of phenomena is more important.
The present paper reviews the major ways of transmission of HCV infection and how we can implement primary and second prevention activities that will reduce the risks for contracting this infection and to reduce the risks for liver and other chronic diseases respectively.
The lack of vaccine and the difficulties linked to the efficiency of chronic hepatitis infection due to HCV enforce the role of preventive measures in our needs to reduce the prevalence of infection with this virus.
Key words:Hepatitis C virus, prevention activities, primary prevention, secondary prevention

Rezumat. Virusul hepatitei C (VHC) este cea mai frecventă cauză de boală în cazul hepatitei cronice şi reprezintă o reală problemă de sănătate publică. Centrul de Control şi Prevenţie al Bolilor (CDC Atlanta) estimează, pe baza testelor ce evidenţiază anticorpii anti-VHC, numai pentru Statele Unite, că 3.9 milioane persoane sunt infectate cu acest virus. Conform datelor Organizaţiei Mondiale a Sănătăţii (OMS), în lume trăiesc aproximativ 170 milioane persoane infectate.
De la descoperirea virusului, în 1989, s-au pus la punct numeroase teste de diagnostic. Screening-ul sângelui efectuat în Centrele de Recoltare şi Conservare ale Sângelui (CRCS) a dus la scăderea dramatică a hepatitei post-transfuzionale.
In România, înainte de introducerea screening-ului în CRCS, prevalenţa anti-VHC era de 4.5%, de cel puţin 10 ori mai mare decît în ţări din vestul Europei. Deci, pentru ţara noastră amploarea fenomenului este mult mai mare.
Lucrarea de faţă îşi propune să treacă în revistă principalele căi de transmitere ale infecţiei cu VHC şi cum pot fi introduse şi aplicate măsurile de prevenţie primară pentru a reduce riscul contractării infecţiei dar şi a măsurilor de prevenţie secundară, pentru a reduce riscul evoluţiei spre boli cronice hepatice.
Lipsa unui vaccin şi eficienţa redusă a tratamentului antiviral cresc rolul măsurilor preventive pentru reducerea prevalenţei infecţiei cu acest virus.
Cuvinte cheie: virusul hepatitei C (VHC), activităţi preventive, prevenţie primară, prevenţie secundară.

INTRODUCTION

The hepatitis C virus (HCV) is the most common cause of chronic liver diseases world-wide. The Centre for Diseases Control and Prevention (CDC) estimates that only for U.S.A at least 3.9 million people have been infected with HCV as indicated by a positive HCV antibody test (1). The World Health Organisation (WHO) estimates that 170 million people world-wide are infected with HCV. 70% of them will develop a chronic hepatitis. It is generally believed that about 20 – 30% of people infected with this virus will develop cirrhosis over 10 to 30 years. Of those with cirrhosis, an estimated 25 - 30% or up to 5% of all persons initially infected with HCV will develop end-stage liver diseases or liver cancer (1)

The incidence of disease

In Romania, during the last 10 years, the incidence of Non-A Non-B (NANB) hepatitis has been decreased as a consequence of blood screening in Regional Blood Transfusion Centres (RBTC) . Fig 1 outlines the incidence evolution for NANB hepatitis; even if in this category the major ethiological agent is HCV, we must underline the possible role of other viruses (2).

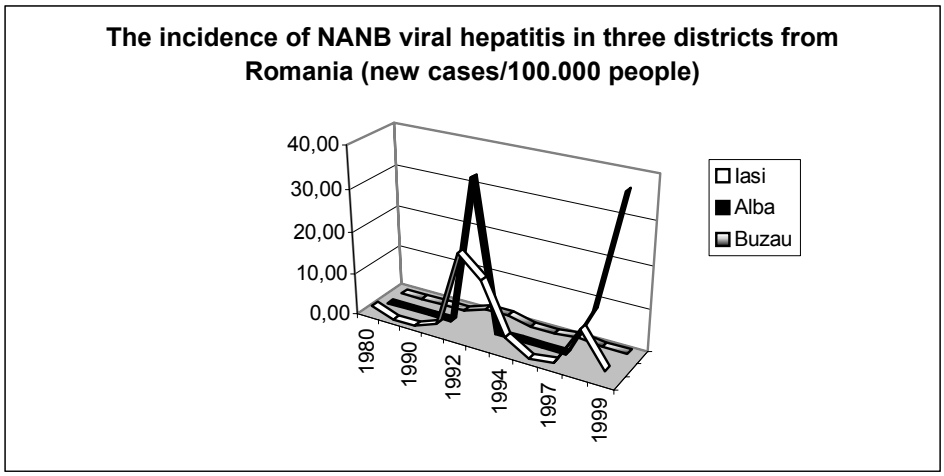

Fig. 1: Incidence by NANB viral hepatitis in some districts from Romania

The dramatic decrease of post-transfusional hepatitis (PTH) is obvious in all districts, but the new increase of incidence in Iasi and Alba, of 10.5/0000 in 1998 and 38.97/0000 in 1999 respectively, is difficult to explain. An explanation can be linked with the possible role of other NANBNC viral hepatitis (e.g. HGV-C) or the positive RNA HCV persons and negative for anti-HCV antibodies as we can see in "immunologic window" period or, in some rare cases, when the seroconversion is later than few weeks or absent (3, 4)

Prospective studies of transfusion recipients demonstrated that the rates of PTH in the 1960s exceeded 20%. In the mild-1970s, available diagnostic tests indicated that 90% of PTH was not caused by hepatitis A (HAV) or hepatitis B virus (HBV) (3). Discovery of HCV by molecular cloning in 1989 showed that NANB hepatitis was primarily caused by HCV infection. Soon after this discovery, an indirect ELISA using C100-3 antigen was introduced on the market. The major disadvantage for this test is its incapacity to reveal antibodies appearance in the first few weeks after infection. Currently, the second (ELISA-2) and, more recently, third-generation ELISA (ELISA-3) for antibodies to HCV (anti-HCV) are the most practical screening tests for HCV infection. (3, 5, 6).

In brief, the diagnosis of HCV infection can be sustained or confirmed by the recombinant immunobinding assay (RIBA) or test for HCV RNA. The first diagnosis test will be compulsory an ELISA test. RIBA detects antibodies to individuals HCV antigens (e.g. C_{22-3}, C_{33-c}, C_{100-3}) and granted increased specificity comparatively with ELISA-2 or ELISA-3. Qualitative reverse transcription-polymerase chain reaction (RT-PCR) assay for HCV RNA are simpler and cheaper than quantitative tests and sufficient for confirmation of the diagnosis of HCV infection. More than that, qualitative assays are more sensitive than quantitative tests and must be used to confirm the virus clearance after the end of the treatment (4, 5, 7).

More sensitive and specific methods to detect hepatitis B surface antigen (HBsAg) and anti-HIV antibodies have been introduced after 1990 and the screening for HCV antibodies in January 1994 in all RBTC. The prevalence of anti-HCV antibodies found in the studies before 1994 was around 4,5% (6). Later, between January 1995 and September 1997, this prevalence decreased at 2.6% (8).

In the same period, the prevalence of anti-HCV antibodies for 825 medico-sanitary staff was 8% (8). The consequences of the high prevalence of HCV infection in our region can explain the high number of chronic hepatitis cases; these findings infection, corroborate with a high alcohol consumption which represents the major risk factor for chronic hepatitis, cirrhosis and liver cancer.

The lack of vaccine and the difficulties linked to the efficiency of chronic hepatitis infection due to HCV strengthen the role of preventive medicine in our needs to reduce the prevalence of this virus infection.

HCV specific information and prevention messages should be provided to infected persons and individuals at risk by trained personnel in public and private health-care settings.

Health-education material should include: general information about HCV infection; risk factor for infection, transmission, disease progression and treatment; detailed prevention methods appropriate for the population being tested (2).

I. GENERAL INFORMATION ABOUT HCV

This virus it is an RNA virus belong to *Flaviviridae* family. HCV must enter liver cells to carry out its life cycle, as all viruses; once inside, the virus commanders the cell's ribosomes to reproduce, eventually killing host cell. There are at least six genotypes and more than 90 subtypes of HCV (9). Multiple quasispecies may co-exist in a single individual. Different subtypes have different geographical distributions and are associated with different rate of disease progression, severity and response to treatment (9, 10, 11).

In Romania, the major serotype seems to be the serotype 1, but other serotypes can be revealed with an ELISA types test (Murex HCV 1-6 serotypes): 2, 3, 4 or 6 (unpublished data).

Because it is a RNA virus that is prone to errors in its replication and mutates rapidly, HCV initiate a special infection in which the immune system cannot eradicate the virus, and it remains in the body of most people which are infected; estimates of chronic HCV range from 70 to 85% (4, 10). For unknown reasons a minority of infected persons are able to clear the virus, although they typically remain HCV antibody positive.

News in HCV domain:

- recently, in July 1999, Michail Lai and colleagues reported in Science's issue the discovery of an HCV surface protein (called E2) that inhibits the immune system's activity against the virus (12). On the other hand, the virus' genetic variability explains the difficulties that we have in the discovery of a vaccine against HCV infection;
- few months ago, in august 2000, R. Bartenschlager and co-workers reported that they devised a DNA complementary strand ("replicon") of HCV's genetic material that could be inserted into human cells to create a laboratory model of HCV infection (12).

II. TRANSMISSION OF HCV INFECTION

(1) Blood and blood products

(a) In the past, many people contracted HCV through blood transfusions. A test screen of donated blood was developed in 1990, and a more sensitive and specific tests became widely available. The risk of HCV transmission through donated blood is now very small, estimated at 0.01% or one in 100.000 transfusions (10). Before 1999, a large number of haemophiliacs were infected with HCV through pooled blood product transfusions, until new methods were developed to treat blood clotting factor preparations.

(b) Today the most common risk factor for HCV infection is the common use of shared needles or others equipment to inject drugs. Drug users acquire HCV soon after they start to inject. This way of transmission seems to increase its role in Romania in the last few years.

(c) Health-care workers are at some risk of occupational exposure to HCV, primarily through needlestick injuries,

which carry an estimated infection rate of 1.8%. In our region as we specified earlier the prevalence of anti-HCV antibodies in health-care workers was 8% (8).

(d) HCV can be transmitted through implements that can transfer blood, including tattooing and piercing equipment, acupuncture needles, manicure tools, razors, and toothbrushes (1, 3, 10, 11)

(2) Sexual transmission: although HCV can be transmitted sexually, this type of exposure is much less likely to lead to infection than previous one. Studies have shown that HCV is present in semen and vaginal secretion. According to CDC, up to 20% of HCV infections are due to sexual contact (3). This estimated rate seems to be high, given the most studies have shown a very low rate of sexual transmission; analysis of several different studies reveals an average sexual transmission rate of 1.5% among long-term, monogamous partners, although transmission risk increases among individuals with multiple sexual partners (3). Seems that HCV transmission from men to women is more efficient than opposite one.

(3) Mother to child:

(a) HCV can be transmitted from mother to child before or during birth, but such transmission is uncommon. The overall rate of vertical transmission is generally estimated to be less than 5%. Perinatal HCV transmission is more common in women with higher HCV viral loads and those coinfected with HCV and HIV with rate as high as 14-17% (13, 14). In this last case, only those co-infected mothers with detectable HCV RNA viral loads are at risk of transmitting HCV to their babies (15). Others authors consider this risk as low and infrequent (16).

(b) There is conflicting evidence about whether HCV can be transmitted through breast-feeding. Some studies have shown that HCV is present in the colostrum and breast milk, and that transmission through breast-feeding can occur, especially if the mother has a high HCV viral load; despite the results of this studies, such transmission appears to be rare (10).

(4) Others factors that may affect the rate of HCV : age, gender, income, and education level (17).

III. PREVENTION OF HCV TRANSMISSION

(1) Primary prevention activities can reduce or eliminate potential risk for HCV transmission from:

(a) blood, blood components or plasma derived products;
(b) high risk activities: injecting-drug or
(c) sex with multiple partners and
(d) percutaneous exposure to blood in health-care and other (e.g. tattooing and body piercing) settings (1, 3, 10).

Immunisation being not available, identifying persons at risk but not infected with HCV provides opportunity for counselling on how to reduce the risk of infection.

(2) Secondary prevention activities can reduce the risks of chronic diseases by identifying HCV-infected

persons through diagnostic testing and by providing appropriate medical management and antiviral therapy. Because of the huge number of persons with chronic HCV infection, identification of these cases must be a major focus of current preventing programmes (1, 3).

Identification of persons at risk for HCV infection provides opportunity for testing their infection status, to determine their disease status if infected, and antiviral treatment if appropriate. Also, for infected persons is useful to obtain information concerning how they can prevent further aggressions to their liver and prevent transmitting HCV to others.

Factors to take into consideration when making decisions regarding the development and implementation of preventive methods for special diseases include:

(a) the public health consequence of the disease;

(b) the availability of appropriate diagnostic tests and

(c) the effectiveness of available preventive and therapeutic interventions. In case of HCV we can underline that hepatitis C is a disease of major importance for public health (around 170 million people are infected world-wide).

Suitable and accurate diagnostic tests (ELISA, RIBA, qualitative and quantitative PCR) as well as behavioural and therapeutic interventions are available (e.g.interferon alfa, ribavirin, pegylated interferon).

The strategy to prevent and control HCV infection and HCV - related disease should be based on:

- Primary prevention activities:
  - screening and testing of blood, plasma, organ, tissue and semen donors;
  - virus inactivation of plasma-derived products;
  - risk-reduction counseling and services, and
  - implementation and maintenance of infection-control practices.
- Secondary prevention actions:
  - identification, counseling, and testing persons at risk, and
  - medical management of infected persons.
- Professional and public education;
- Surveillance and research to monitor HCV infection trends and the effectiveness of prevention activities and the develop improved prevention methods (1, 3).

The objectives of controlled surveillance for HCV infection are to:

- identify new cases and determine disease incidence and trends;
- determine risk factors for infection and disease transmission patterns;
- estimate disease burden, and
- identify infected persons who can be counselled and referred for medical follow-up.

Different surveillance approaches are required to achieve these objectives because of limits of diagnostic tests for HCV infection, the high percentage (up to 75) of asymptomatic patients with acute infectio as well as the long latent interval between acute infection (symptomatic or not) and chronic disease outcome (1, 3).

(1) Surveillance for acute infection with HCV

For new, symptomatic patients:

- provide the information necessary for determining incidence trends, changing patterns of transmission and persons at highest risk for infection;
- the surveillance for these cases provides the best means to evaluate the efficiency of prevention efforts and to identify missed opportunities for prevention. (1)

For unknown reasons, in our country, acute hepatitis C is registered as NANB hepatitis even the diagnosis is specific for HCV. (2).

Two kind of surveillance can be described in HCV infection: laboratory and serological:

(a) development of records of persons with anti-HCV-positive laboratory results might facilitate efforts to provide counselling and medical follow-up; these registries could be used to provide regional and national estimates of proportion of persons with HCV infection who have been identified. It is obvious that the confidentiality of results must be ensured.

(b) serologic surveys at regional and national levels can detect the variation in prevalence of HCV infection, identifies the population at high risk, monitor trend and evaluate prevention programmes.

(2) Surveillance for chronic infected patients can provide information about the extent of phenomena, its natural history and risk factors, and to evaluate the effect of therapy and prevention methods on incidence and severity of the disease (1, 3, 10, 11).

CONCLUSIONS AND PERSPECTIVES

To prevent chronic HCV infection and its consequences, prevention of new HCV infections should be the primary objective of public health activities.

In Romania, the identification of people with chronic HCV infection is difficult. The most efficient way to achieve this identification is not known yet, because the prevention effectiveness of different implementation strategies has not been evaluated. For these reasons we must initiate widespread programmes to identify, counsel, and treat persons infected chronically with HCV. These measures, combined with improvements in the efficiency of treatment, are expected to decrease the morbidity and mortality from HCV-related chronic liver diseases.

The epidemiologists and public health authorities must create a programme for monitoring the progress of these activities, to evaluate their efficiency in achieving a reduction in HCV–related chronic infection.

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