Problems in Inducing Interferon Therapy of Opiate Addicts with Chronic Hepatitis C Who Are In Substitution Maintenance Therapy with Buprenorphine/Naloxone (Suboxone®)

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Abstract: Chronic hepatitis C virus (HCV) is highly infected disease with long period of failure to recognize it, what leads to chronic liver damage and lower chances for complete cure if detected late. Intravenous opiate users (IDU) often pass the infection to other IDUs, or themselves be infected from virus carriers using the same non-sterile equipment. After the implementation of substitution treatment of opiate addicts (OST) with July 2009 year, serological tests for chronic hepatitis B and C and HIV were indispensable, as well as laboratory findings with liver function parameter analysis as a condition for starting OST. In this way we discovered 50 chronic hepatitis C positive opiate addicts out of 195 of those whom we induced in OST. Although faced with danger of the final result if not treated in time, addicts when become aware that they were chronic hepatitis C positive, they avoid further needed procedures leading to the inclusion of specific therapy with Peginterferon plus Ribavirin. The authors present the problems that chronic hepatitis C positive opiate addicts bring out as a reason they do not accept the continuation of the procedure detecting HCV genotypes, and the inclusion of specific therapy for the chronic hepatitis C treatment in the Departments for Infectious or Internal diseases. The authors present efforts of experts responsible for the chronic hepatitis C treatment to organize a multidisciplinary team, in order to coordinate Interferon therapy for each chronic hepatitis C positive IDUs.

Keywords: Chronic hepatitis C, Peginterferon plus Ribavirin, Opiate Addiction, Substitution Opiate Treatment, Buprenorphine/Naloxone, Suboxone®

Introduction
By the end of 1980s, studies from several laboratories identified that the major risk group for contracting the newly identified hepatitis C virus (HCV) infection were parenteral opiate and cocaine abusers (1). It is now well known that a history of intravenous drug use is the single strongest risk factor for acquiring HCV infection and that prevalence of HCV, particularly in intravenous drug users (IDUs) greater than 40 years of age, is over 70%. (2-4). Hepatitis C is a highly infectious disease with a long period of unrecognized chronic damage of the liver and lower chances for full healing if it is discovered too late. IDUs of opiates most commonly get the infection from other IDUs, or get infected themselves by the virus carrier by using the mutual, non-sterile equipment for intravenous injection of opiates (5).

After we introduced the substitution treatment of opiate addicts with Buprenorphine/Naloxone (Suboxone®) on the Department of Psychiatry in Tuzla, from 27th of July 2009, we made the serological tests on chronic hepatitis B and C and HIV a mandatory condition (6-8). Also, the laboratory findings with liver functions and kidney's functions are obligatory too as a term for starting the substitution opiate treatment (OST). On this way, we discovered 50 opiate addicts that were positive on HCV from 195 of those whom we regularly induced in the OST (9).

When we found the fact that the candidate for the treatment of opiate addiction is positive on chronic HCV, motivational interview for parallel treatment of this insidious chronic deadly disease with Peginterferon plus Ribavirin starts (10). The treatment could begin when IDUs become mentally and somatically stable with OST. Regarding that the treatment can be implemented only by interdisciplinary engagement of psychiatrists, specialists of infectious diseases and internist-gastroenterologist. Due to that, we formed a team on...
the University Clinical Center Tuzla for the application of interferon to chronic HCV positive opiate addicts induced to the OST with Suboxone® (9).

There is convincing evidence provided by Sylvestre and colleagues that when antiviral treatment is managed in cooperation with the staff of a methadone or buprenorphine maintenance program, compliance is maximized and outcome is comparable to that of non-opiate-maintained HCV patients (11). Former opiate addicts receiving methadone or buprenorphine maintenance treatment can comply and respond to a standard course of pegylated interferon and ribavirin for eradication of HCV infection. The ideal treatment setting for former addicts is the methadone or buprenorphine maintenance clinic, which is the primary care site for treatment of addiction, with a multidisciplinary team composed of the addiction specialist, hepatologist or infectious disease specialist, and psychiatrist. Treatment of opiate addiction with adequate doses of methadone or buprenorphine to eliminate drug craving, with appropriate increases to counteract side effects from pegylated interferon therapy, is essential to ensure maximum compliance to antiviral treatment (5). For this purpose, the process of drafting a procedure that defines a set of measures and procedures with opiate addict infected with chronic HCV needed to be defined and established in our interdisciplinary clinical environment. At this point, the part of procedure relating to the psychiatric part of the treatment is defined. The Procedure will be finished when the parts which determine the treatment of chronic HCV with Peginterferon plus Ribavirin from the perspective of Infectious Diseases and Gastroenterology be completed.

Excerpt from the Procedure: Accreditation standard: 50.66.

4.1. The way of starting the treatment

4.1.1. The treatment of addiction of opiates and the treatment of hepatitis C at opiate addicts is resting on the principle of voluntariness. It is related to the patients that are adult and have expressed a wish on their own to be treated. If it is about addicts that are younger than 18 years, with the voluntary principle, a written consent of a parent/adopter/legal guardian must exist that he/she will be included in the deciding of the important decisions during the treatment (6).

4.1.2. A patient with his supervisor physician neuro-psychiatrist / psychiatrist is making a therapy agreement. He/she is to give suggestions for including the family members/careers as a mandatory part of a teamed-up approach for control of taking the substitution medicine for the successfulness of the treatment. After the informed consent that the addict and a family member signs, the addicts who get a positive chronic HCV findings, the patient and his guardian are referred towards an extra infectology and gastroenterology interview procedure because of laboratory and histopathology determining of the genotype of the chronic HCV and the impairment of the liver's parenchyma.

4.1.3. Based on the achieved agreement, the psychiatrist makes a real written plan of the treatment with which he meets the patient and his family members/guardians in situations in which their including is being held out. About this, the competent staffs of Department for Infectious diseases and the Department for gastroenterology diseases are being introduced to.

4.1.4. Forced admission and forced hospitalization is being held out in situations when the patient is vitally threatened or when the patient is a danger to the environment and him/herself, and it is held out by the Law of protection of persons with mental disorders and („Official newspapers of Federation of Bosnia-Herzegovina, No. 37/01, 40/02) special procedure.

Types of treatment and the necessary consultations

4.2.1. As a rule, treatment of substitution treatment is done at the Department of Psychiatry according to prescribed doctrine by Institution for Health Insurance of Tuzla Canton (ZZOTK), adopted by the Tuzla Canton Minister of Health. The patient is required to come in a companion with family member every day for the first four days for dose titration of Suboxone®, when he/she take tablets sublingually in front of the physician. Patient and family member are given tablets for home application, and they are said to come on the seventh day from the first tablets application, if everything started properly during first four days. After that, each successive seventh day a urine test is done for metabolite of psychoactive substances (PAS), and if everything is neatly after a month (four weeks), the patient will be awarded, so he/she receives medication for 14 days in advance, to bring it home and to use it under the strict control of family member who signed the written consent. Again at each arrival a urine control is to be done, and if everything is tidy (no abuse of PAS and

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4.2.2. Types of treatment
Type of chronic hepatitis C treatment is determined by finding of genotype of C virus and the presence / absence of mental complications.

4.2.3. In the treatment of addicts who become pregnant during running treatment, pregnant addict who previously started the treatment without pregnancy is required to discontinue Suboxone® use, but she may be given methadone or pure buprenorphine (Subutex®) instead of. The problem is that Subutex® is not registered in Bosnia-Herzegovina. In these situations, it is necessary to obtain medication from abroad, but administration of Suboxone® has to be discontinued (6).

4.2.4. If the patient insists on a different model of treatment, which is not carried out at the Department of Psychiatry, or if there are medical indications which required it, the possibility of referral to another health facility will be considered. In the case of need for referring opiate addict(s) outside the Health Insurance Institute of Tuzla Canton, the proposal provides from Medical council.

Problems that interfere with the timely administration of Peginterferon plus Ribavirin

Stigma
Before the introduction of substitution treatment of opiate addicts with buprenorphine / naloxone (Suboxone®) at the Department of psychiatric in Tuzla, any sign that a patient positive for chronic HCV was admitted to the treatment has caused unease among psychiatrists and other members of therapeutic teams at the clinic. Taking gloves was mandatory and patients were not approached too close if it wasn’t required (12).

Since the introduction of Suboxone® therapy included, it was impossible to avoid drug addicts who were IDUs and who were already infected with chronic HCV. The stigma is slowly melting so that the Department in cooperation with the NGO "Hope" (Association of Parents and friends of addicts on psychoactive substances) in cooperation to UNDP organized the workshop for people with chronic hepatitis C and members of their families, in order to reduce to stigma, and to help addicts and their partners in the therapy be better acquainted with this dangerous and insidious disease, with the aim of starting the administration of interferon as early as possible (13).

Another type of stigma encountered in Departments for infectious diseases and Internal diseases otherwise deal with the treatment of chronic hepatitis C. The problem arises when they get opiate addicts IDUs, then, medical personnel, inadequately prepared to deal with opiate addicts, openly shows impatience and often inappropriate behavior which bothers the addicts and it is painful and difficult to tolerate. They regularly complain about the scene, inappropriate for medical workers.

Laboratory diagnosis is not in one place
To complete the set of different findings to define the current state of each addict positive for chronic hepatitis C, it is necessary to do a series of additional tests that are in Tuzla Health Care environment scattered across multiple organizational units. Patient and his / her partner forth comes a series of
unnecessary waiting(s), a series of meetings with new faces acting on a reserve, unnecessary lengthy processes of sampling, lost time, especially when the samples are taken the wrong way, so everything has to be repeated. Very often addicts when this process starts, interrupt on their own initiative, not wanting additional frustration.

Fear from liver biopsy
One of the biggest problems is the myth about the “painful” biopsy of liver, which is considered to be the reason of death cases among the addicts. That is contributed by doctors and medical staff that approach the biopsy process without adequate psychological preparation, they do it as on a „non-living thing“. During the procedure of taking liver biopsy, they have no contact with the addict, but they initiate conversations among themselves. Often, they don't target the liver, so they have to repeat the procedure. Because of that all, opiate addicts start to believe that they are not important as humans so they decide not to do the biopsy for the histopathology finding.

Lack of information between teams
Regarding that the process is held in three different Departments, the information on the level of procedure that has been reached are missing out. From the acquired findings, it can't correctly be seen what next is necessary to do with the patient to complete the process of preparation for start with interferon treatment; so the patients, because of negative experiences in the procedure they have been through, often forget what is said to them.

Our experiences on the Department of psychiatry Tuzla
On the Clinic of psychiatry in Tuzla, from July 2009 until today, we have discovered 50 of 195 opiate addicts that are positive on hepatitis C. From them, four (8%) are girls/women. The average age of the patients is 28.3 years. From them who did the findings of virus hepatitis C genotype, ten have Genotype 3, one has genotype 1 (one) and one genotype 4. Eleven of them have successfully ended the interferon treatment and on the control finding, it was objectified that the chronic hepatitis C virus of these patients is eradicated.

All other patients form this group was in different stages of laboratory examinations or preparation for taking a liver cut-out (liver biopsy).

In spite of the problems that were stated above and the lacking in work with these patients, psychiatrists are obliged to hold motivation for finishing procedures for including in the interferon therapy and to coordinate with their colleagues on other clinics, since addicts that are treated by Suboxone® are often coming for new receipts, which opens the possibility to insist on ending the preparations for including interferon as following the therapy itself.

The limitation of this study is number of the described participants.

Conclusion
Although, conflicted with the danger of the final outcome if they don't begin treatment on time, the addicts, even when they find out they are Chronic hepatitis C positive, avoid further procedure that leads to including a specific therapy with pegilated Interferon. In spite of row of problems that opiate addicts that are positive on Chronic hepatitis C state as the reasons that they are not reporting in for the continuation of the procedure of revealing the genotype of the virus or involving in a specific therapy for curing Chronic hepatitis C on clinics for infectious or internal diseases, it is mandatory to insist in continual and stubborn watching over this problem alongside the addicts, their families and the staff of other departments to insist on a reliable defining of the problem and the start of the adequate treatment.

It is necessary that the experts that are responsible for the treatment of chronic hepatitis C in opiate addicts organize a multidisciplinary team, so the treatment would be coordinated by the Interferon of every I.V. addict positive to chronic hepatitis C from the discovery of the disease to its cure. That is the way to achieve double performance, with the treatment of opiate addiction, the additional infectious and highly harmful disease, is also cured.

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Conflict of Interests
We as the authors of the manuscript declare that we have not any direct financial relation with the commercial identities mentioned in the paper that might lead to a conflict of interests or not.

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