UNIVERSITY OF MEDICINE, PHARMACY, SCIENCES AND TECHNOLOGY "GEORGE EMIL PALADE" OF TIRGU MURES

ABSTRACT OF THE PhD THESIS

PROGNOSTIC FACTORS IN CHRONIC HEPATIC DISEASES

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Chronic hepatic diseases lead in most cases to partial or even complete loss of an individuals' work capacity, with significant social and economic consequences. In this respect, there is an issue in identifying a range of prognostic factors that influence disease evolution from the point of view of investigations range and cost, treatment, rehabilitation and the removal of an active person from the work force.

The present research tries to identify, through two distinct studies, the prevalence and prognostic factors of chronic hepatic disease from the perspective of renal involvement as well as the efficiency and efficacity of the new interferon free treatments in modulating viral influence over renal function.

The purpose of the first study is to analyze the prevalence of chronic hepatic diseases, of different etiologies, in different stages of evolution and to evaluate the possible correlations with renal function impairment.

The purpose of the second study is to evaluate the correlations between serum levels of transaminases and viral load, on one side, and standard doses of α 2a or 2b peginterferon and ribavirin, in the first stage, respectively to prove the efficiency of direct antiviral agents, in the second stage.

This research subject has followed aspects linked to renal function assessment in chronic hepatic disease patients, focusing on the accuracy of the common use formulas of kidney function evaluation. At the same time, we studied the influence of renal function over the evaluation of hepatic function through common serum markers, considering the start-point and evolution values of transaminases (TGO, TGP) in parallel to serum creatinine and eGFR (the globally accepted standards).

The originality of this thesis consists of the contrast with international studies published to date. All studies included in evaluating the current level of knowledge, both

from online and offline sources, acknowledge hepatic function from the perspective of the chronic renal patients. Moreover, the majority of study groups include patients that undergo hemodialysis, patients that were included through other criteria, from the point of view of direct antiviral treatment and the adjustment of conventional treatments to renal function. Our approach evaluates patients from the opposite view. We have studied patients with diagnosed chronic hepatic disease, of different etiologies, considering ethanol, steatosis or viral cause, noting the degree of renal impairment and the laboratory estimation of it, in rapport to the different degrees of hepatic fibrosis.

By establishing statistically significant differences between the values of transaminases in hepatic patients with normal renal function compared to those with a modified function rises the point of discussion of adapting the accepted normal values of TGO and TGP by the degrees of renal impairment established by the estimated glomerular filtration rate. This element represents a definite research direction for the future and the first conclusion of its kind drawn in nationwide studies, to date.

At the same time, we bring forward the first Romanian study that aligns itself with European tendencies of contesting the precision of the Cockcroft-Gault eGFR formula in patients with hepatic disease of different etiology. The originality of our study also consists in the inclusion of all the common causes of hepatitis, in the context in which most studies follow solely patients infected with hepatitis C virus.

One other element of originality is represented by the epidemiological draw up of an important group of patients with hepatic disease and renal impairment. Also, we consider important the fact that the study was conducted in a multidisciplinary medical center, constituting a study group with populational characteristics, as age groups, gender, environment of origin, variation of etiology of hepatic disease, in comparison with most studies conducted in hepatology or nephrology oriented centers that are unable to offer population characteristics for the region that they represent.

The study on interferon free treatment comes to strengthen the importance of its efficiency in the evolution and prognosis of patients with chronic viral C hepatitis, by eliminating a proven causing factor of renal impairment.

The thesis has managed to offer an image over the prognostic importance of renal function in chronic liver disease, with clinical significance from the point of view of the complexity of hepatic patients monitoring and the accuracy of clinically established serum markers. It also brings forward elements of novelty regarding the need for new markers and calculation formulas for the evaluation of renal function and supports the efficacy of the new treatment protocols for viral hepatitis, important in the evolution and prognosis of the patients that can be included in the studied profile.