COVID-19 AND LIVER DISEASE

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Introduction. Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the agent that causes the disease called COVID-19, represents one of the greatest challenges to the infrastructure of health systems and public health in recent times [1, 2]. As of 1 June 2020, this pandemic has caused more than 300,000 deaths worldwide [3]. In Spain, the impact of COVID-19 is particularly serious, as it is, in Europe, the country with the third largest confirmed caseload, and, globally, the country with the fifth largest confirmed caseload, after the United States, Brazil, Russia and the United Kingdom [3]. In most cases, the disease follows a benign course; however, in others, the outcome may be fatal; its mortality rate in Spain is 11.1% [4]. The cause of death is usually acute respiratory failure secondary to diffuse alveolar damage; however, the liver may play a key role in two respects: as it may be affected by the infection itself or its treatment (or both) and owing to the possible implications of underlying chronic liver disease for the patient's prognosis.

The aim of the study. To review scientific publications on the effects of coronavirus infection on liver function. To study the mechanisms of pathological processes in the liver in the background of the course of coronavirus disease.

Materials and methods. Using current scientific research in the field of hepatology in COVID-19 infection. Used summaries of recommendations based on agreed documents in particular by the authoritative scientific organisations "American Association for the Study of Liver Diseases" (AASLD), "Spanish Association for the Study of the Liver" (AEEH) and "European Association for the Study of the Liver" (EASL).

Results. Today it is known that SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE-2) receptors as a gateway for infection [5]. These receptors are present on the cell surface of practically all human organs, rendering COVID-19 a systemic disease which, though it essentially manifests with respiratory symptoms, may similarly affect other vital organs, such as the liver, heart, pancreas, kidneys and bowel.

Liver impairment associated with COVID-19, understood to refer to any clinical or laboratory abnormality tied to liver function, may develop in previously healthy individuals and in individuals with pre-existing liver disease. The initial studies from China offered disparate data on its prevalence, with percentages ranging from 14% to more than 50% [6-8]. In the study that enrolled a higher number of patients the main abnormality detected was elevated aminotransferase levels, present in up to 20% of cases, followed by slightly increased bilirubin levels, in 10% of cases [9]. By contrast, elevation of other cholestasis parameters, such as gamma-glutamyl transferase (GGT) and alkaline phosphatase (AP), was relatively uncommon. Other more recent accounts have indeed reported elevated GGT levels in up to 50% of cases, but with normal AP

levels [10]. Hypoalbuminaemia, for its part, is usually a relatively common laboratory finding in patients with serious COVID-19; however, it is not accompanied by other findings suggestive of liver failure, such as hyperammonaemia, hyperbilirubinaemia, hypoglycaemia or prolonged clotting times [9].

To date, no cases of serious acute liver failure secondary to SARS-CoV-2 infection have been reported and abnormalities in transaminase levels are usually transient [8, 9]. Studies that have analysed the relationship between liver impairment and prognosis have yielded contradictory results. Whereas two cohorts of Asian patients identified a relationship between seriousness of COVID-19, need for admission to an intensive care unit (ICU), male sex and high transaminase levels [6, 9], others have not detected a higher risk of death in this subgroup [11, 12]. Although the fact that approximately one-third of patients already have liver impairment on admission could indicate a direct cytopathic effect of the virus on the liver, other pathophysiological mechanisms also present in critical haemodynamic and respiratory situations, or in situations of serious sepsis, are certainly more likely to contribute more to liver damage. This probably makes it difficult to interpret the role played by liver dysfunction in the prognosis of patients with COVID-19.

Pathophysiology of liver injury: various mechanisms related to SARS-CoV2 infection may induce liver abnormalities, both due directly to the cytopathic effect of the virus and due to the indirect effect of immune hyperactivation and drug toxicity. Recent publications have suggested that the virus may bind to ACE-2 receptors located in hepatocytes, especially in cholangiocytes where their expression is more abundant [13]. After they bind to the receptor and enter the cell, replication mechanisms are initiated that are intended to generate new viral RNA and synthesise structural proteins needed for the assembly and release of new viral particles [14]. By contrast, expression of ACE-2 receptors in hepatocytes is limited; this could explain the absence of laboratory and histology data typical of viral forms of hepatitis [15].

In some serious cases, proinflammatory immune hyperactivation has occurred; the consequences of this could be more deadly than the cytopathic effect of the virus itself [16]. The potential benefit of certain currently investigational drug treatments is predicated on this hypothesis of immune-mediated damage [17, 18]. However, the consequences for the liver of this immune dysfunction in the context of COVID-19 remain unknown.

Secondly, the toxicity induced by the drugs used to treat COVID-19 also may contribute to liver damage [19]. This is particularly important, on the one hand, in patients with pre-existing chronic liver diseases in whom the risk of toxicity is higher and, on the other hand, in liver transplant patients, due to potential interactions with routinely used immunosuppressant drugs. Among the different drug treatment options used to date, remdesivir, a nucleotide analogue, has yielded promising results in decreasing recovery time and duration of hospital stay [20]. Initially elevated transaminase levels during treatment with remdesivir were reported in up to 23% of patients, with two patients requiring suspension of the treatment for this reason [20].

Nevertheless, the preliminary results of two clinical trials have found this adverse effect in just 4.1%- 5.0% of patients, with no differences versus the placebo group [21, 22]. Other drugs used in the treatment of COVID-19, such as protease inhibitors (lopinavir) and tocilizumab, could also carry a potential risk of hepatotoxicity [23, 24].

Many complementary tests used in the diagnosis and follow-up of chronic liver disease, such as ultrasound, liver biopsy, elastography, endoscopy and liver haemodynamics, have been delayed or cancelled. In this regard, various scientific associations advocate the gradual restoration of these complementary tests; those patients with the highest risk must be prioritised. It is advisable to perform screening ultrasounds for hepatocellular carcinoma as soon as possible and to delay other complementary tests which are rarely urgent, such as elastography and liver haemodynamic. Liver biopsies, both percutaneous and trans jugular, should be initially reserved for serious cases in which the biopsy result entails a change in therapeutic strategy. Measurement of the hepatic venous pressure gradient, for its part, should be initially reserved for patients who are candidates for hepatocarcinoma resection surgery. Upper gastrointestinal endoscopy is a procedure that generates aerosols and, as a result, a procedure that carries a risk of SARS-CoV-2 transmission. Therefore, it is important to adhere to the criteria proposed at the Baveno VI consensus conference which, through non-invasive methods, allow the risk of developing oesophageal varices to be stratified.

Conclusions. It should be noted that the COVID-19 pandemic arrived at a very important time in the history of hepatology, when plans for the macroelimination (in the general population) and microelimination (in risk populations) of the hepatitis C virus (HCV) were starting to be developed. It is clear that the pandemic may have negative repercussions for the achievement of such important and ambitious goals as eradication of the infection before the year 2024. However, healthcare contact due to SARS-CoV-2 infection for many otherwise healthy patients may also facilitate opportunistic diagnoses of chronic HCV infection. Therefore, re-establishment of outpatient hepatology activity must continue to maintain simplified, universal access to antiviral treatments as an objective.

The pandemic caused by SARS-CoV-2 represents one of the greatest challenges in recent decades for healthcare professionals and systems worldwide. COVID-19 not only compromises the survival of patients suffering from this disease, but also has major repercussions for medical care for other conditions, including chronic liver diseases. In this regard, it is important to generate more and better evidence with regard to the safety and efficacy of the treatments, both in the general population and in specific subgroups, and, at the same time, adapt routine care protocols to the current situation, in which the availability of complementary tests and treatment options has been compromised.

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ГЕПАТОПРОТЕКТИВНІ ВЛАСТИВОСТІ ЕКСТРАКТУ КАПУСТИ БРОКОЛІ ТА ЇХ ПРОЯВИ ПРИ НАВАНТАЖЕННІ ОРГАНІЗМУ ІТРІЄМ

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Вступ. Останнім часом увагу вчених привертає комплекс біоактивних капусти броколі, що має антиоксидантні, протизапальні, протиракові та нейропротективні властивості; справляє коронаропротективну та гіполіпідемічну дію; демонструє протимікробний ефект. Описано здатність броколі гальмувати розвиток ліпідозу печінки та її ушкодження, індуковані введенням миш'яку лабораторним тваринам, однак гепатопротективні властивості цієї рослини потребують подальшого дослідження.

Мета роботи – вивчити вплив сухого екстракту наземної частини капусти броколі на вагові індекси та стан пероксидного окиснення ліпідів (ПОЛ) в печінці лабораторних тварин за умов навантаження організму ітрієм.

Матеріали та методи. Експерименти виконані на 22 білих щурах-самцях. За сполуку ітрію брали ітрію ацетат, який вводили тваринам з їжею протягом 10 діб у дозі 175 мг/кг маси на добу (0,25 $ЛД_{100}$). Для фармакологічної корекції застосовували сухий екстракт наземної частини капусти броколі (*Brassica oleracea L. var. italica Plenck*), одержаний на кафедрі хімії природних сполук НФаУ (м. Харків), який вводили тваринам разом з їжею щодня в дозі 25 мг/кг. Наприкінці експерименту тварин піддавали евтаназії під уретановим наркозом. Визначали вагові індекси печінки, вміст продуктів, що реагують із 2-тіобарбітуровою кислотою (ТБК-активних продуктів) та активність супероксиддисмутази (СОД) у