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REVIEW

Chronic Obstructive Pulmonary Disease and Hepatitis C

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Chronic obstructive pulmonary disease (COPD) is a preventable, treatable disease with significant extrapulmonary manifestations that could affect negatively its course in some patients. Hepatitis C virus infection (HCV), on the other hand, is associated with a number of extrahepatic manifestations. COPD patients have increased prevalence of HCV and patients with HCV, especially older ones, have increased prevalence and faster progression of COPD. HCV infection exerts long-term effects on lung tissue and is an additional risk factor for the development of COPD. The presence of HCV is associated with an accelerated loss of lung function in COPD patients, especially in current smokers. COPD could represent extrahepatic manifestation associated with HCV infection. The aim of this article was to review the literature on prevalence of HCV in COPD and vice versa, pathogenetic link and the consequences of their mutual existence.

BACKGROUND

Chronic obstructive pulmonary disease (COPD) is a preventable, treatable disease with significant extrapulmonary manifestations that could worsen the course of the disease in some patients.[1] An epidemiological study shows a prevalence of COPD in Bulgaria of 11.2% (23.7% in current smokers, 21% in former smokers, 6.6% in non-smokers)[2], which is similar to the global COPD prevalence of 11.7% among people aged >30 years[3].

The prevalence of hepatitis C in Bulgaria is 1.5%[4], whereas worldwide prevalence is 2.8%[5]. Hepatitis C virus is a small single stranded RNA virus of the *Flaviviridae* family, which is a major cause of liver cirrhosis and hepatocellular carcinoma worldwide.[6]

Hepatitis C virus (HCV) infection, in turn, is connected to a large number of extrahepatic manifestations such as mixed cryoglobulinemia, lichen planus, porphyria cutanea tarda, B-cell non-Hodgkin's lymphoma, monoclonal gammopathy, etc.[7] An increasing body of evidence supports the possibility of pulmonary involvement as extrahepatic manifestations of chronic HCV infection.[8,9]

AIM

The aim of this article was to review literature on the prevalence of HCV in COPD and vice versa, the pathogenetic link and the consequences of their mutual existence.

HCV IN COPD

The available studies on the prevalence of HCV in COPD are scant and have small sample sizes.

Erol et al. reported a prevalence of HCV infection of 8.3% in patients with COPD (n=108).[10] Forty-four point four percent of patients with HCV and COPD had risk factors for viral infection (such as blood transfusions, surgery, hemodialysis, exposure to blood or biofluids, risky sexual behavior, use of intravenous drugs, dental treatments, tattoos), while in the control group with no HCV, risk factors were found in 12.1% of patients. The two groups were matched in age, gender, smoking status and number of previous hospitalizations.

The incidence of HCV in 187 patients with COPD, according to another study, was 7.5% (95%CI

6.5-8.5), while in blood donors - 0.41% (95%CI 0.40-0.42). Patients with HCV have lower FEV_1 (34.7%) and a higher BODE index [B - body mass index, O – obstruction, D – dyspnoea, E - exercise (exercise test)] (median=6) compared to patients without HCV infection (mean FEV_1 42.7%, BODE median=4, p=0.011 and 0.027, respectively).[11]

As suggested in one of the hypotheses, chronic HCV infection leads to inflammations in the lung and is associated with development of COPD.[8]

The presence of HCV is associated with an accelerated loss of lung function in current smokers (ΔFEV_1 79.5 ml/year and ΔDLCO 4.5%/year) compared to former smokers with HCV (ΔFEV_1 54.0 ml/year and ΔDLCO 3.36%/year) and current smokers without HCV infection (ΔFEV_1 59.7 ml/year and ΔDLCO 3.50%/year), but the biggest difference is found in former smokers without HCV infection (ΔFEV_1 33.5 ml/year and ΔDLCO 2.66%/year).[8] The response to interferon treatment (negative HCV RNA) was associated with slowing in the annual decline of FEV_1 over a period of three years (from 68.4 ml/year to 57.3 ml/year) compared to patients with no response (from 65.5 ml/year to 66.1 ml/year).

The presence of HCV is also associated with worse lung function in another study - FEV_1 67 vs. 55%.[12] Lung function in this study showed correlation with the severity of liver damage according to Child (mean FEV_1 61% in Child A, 51% - Child B, 51% - Child C). However, there is no difference in the degree of obstruction (FEV_1/FVC) among patients with Child A, B and C, probably due to the decrease in FVC (presence of ascites, which hinders the movement of the diaphragm).[13]

COPD IN HCV

Studies on the prevalence of COPD in patients with HCV are also scant.

In patients with chronic HCV infection, prevalence of COPD (17.6%) and bronchial asthma (14.7%) is significantly higher compared to that in patients with hepatitis B infection matched in age, gender and smoking status (COPD 5%, bronchial asthma 1.7%).[10]

This prevalence is considerably higher in comparison with the representative study in the general population - 10.6% (15.4% male, 6% in women older than 40 years).[14] COPD patients were significantly older (60.9 vs. 46.5 years) in comparison with other characteristics. Another study found prevalence of COPD of 11.4% in patients with HCV as compared to 9.2% in patients with no HCV (n=126971, p<0.001).[15] Minakata et al. reported prevalence of COPD of 19.3% (6/31) in patients with HCV.[16]

A small study found impairment in lung function in 75% of patients with HCV (15/20). Patients with reduced FEV_1/FVC<80% ratio, suspected for COPD are 55% (11/20).[17]

However, the relative risk for COPD in HCV patients, as reported in another study, is not increased, although there is clearly a tendency for this (OR 1.69, 95%CI 0.97-2.96, p=0.066).[18] The prevalence of COPD in the same study is 14.1% (22/156).

In contrast to these results, another retrospective study found no increase in the prevalence of virus infection (hepatitis viruses A, B, and C) in patients with COPD compared to that in the control group. This low prevalence in the light of the previous studies (0.44% vs. 0.50%) could be attributed to underdiagnosis.[19]

Risk factors for COPD include smoking, occupational hazards, exposure to the environment and others, including latent viral infections.[9] Patients with HCV infection do not have increased prevalence of risk factors for COPD, despite the presence of COPD (25% vs. 33.9%, p=0.7).[10]

Interestingly, there is one study that found no increase in the prevalence of obstructive lung diseases (OLD) in HCV.[20] The authors suggested that increased prevalence of OLD (defined as prebronchodilator FEV_1/FVC <70%) may have been confounded by the strong relationship between HCV and heavy tobacco exposure. However, in this study, post-bronchodilator spirometry was not performed and the distinction between reversible (asthma) and irreversible (COPD) airflow obstruction could not be made. Moreover, smoking is a well-established risk factor for OLD, yet in this study there was no significant association between pack-years and OLD (particularly COPD) which makes the diagnosis of asthma more likely. Lastly, the low mean age (48 years) in this group also suggests significant prevalence of asthma with inability to judge the prevalence of COPD alone.

COMMON PATHOGENESIS

The exact mechanism of interaction between HCV and COPD is unclear (**Fig. 1**).

Systemic inflammation in HCV could facilitate the occurrence of COPD. COPD is characterized by increased levels of inflammatory cytokines (IL-1β, IL-6, IL-8, and TNFα) which can increase further in exacerbation.[21] There is also neutrophilic inflammation with increased local levels of IL-8, as well

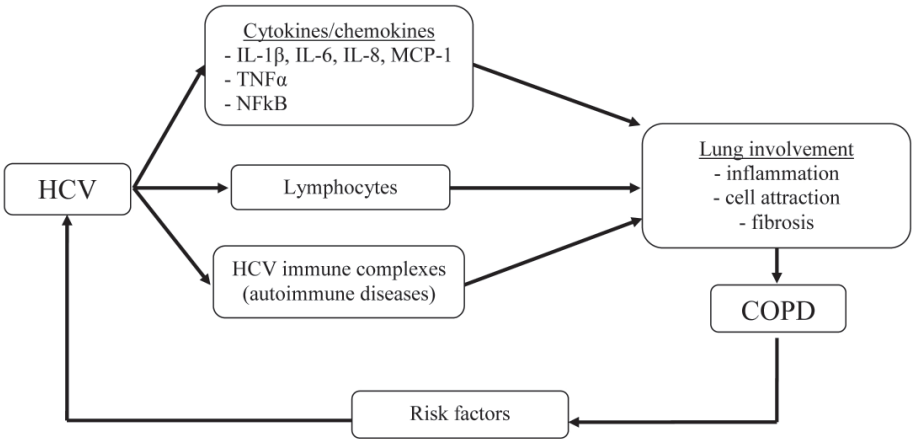

Figure 1. Association between HCV and COPD

as NF-kB and 15-lipoxygenase.[22] In addition, the bronchial epithelium in COPD expressed an increased amount of monocyte chemoattractant protein-1 and IL-8, which is a leukocyte attractant and contribute to increased levels of neutrophils in the sputum.[23]

At molecular level, the most likely link is IL-8, which is crucial in the pathogenesis of COPD. HCV increases the level of IL-8 in endothelial cells by transcriptional activation and stabilization of the mRNA[24] and the level of IL-8 in turn is correlated with the replication of HCV[25]. In addition, HCV nuclear nucleocapsid protein increases IL-8 by p-38 and gC1qR (receptor protein, which is involved in the complement system - C1).[26]

IL-8 has a chemotactic effect on inflammatory cells such as neutrophils through CXCR receptors 1 and 2, which increases pulmonary inflammation.[27] It could directly induce bronchoconstriction and contribute to bronchial hyperresponsiveness, as well as indirectly through stimulation of neutrophil attraction and activation.[28] Serum and intrahepatic cytokines, in particular IL-8 in patients with HCV, are increased.[29,30] The expression of IL-8 can inhibit the antiviral activity of IFNγ and correlates with the degree of liver fibrosis and portal inflammation in HCV.[31,32]

The number of lymphocytes in bronchoalveolar lavage (BAL) in patients with HCV is increased, which implies involvement of HCV infection in the development of lymphocytic alveolitis.[33] Thus HCV may contribute to the development of lung parenchymal destruction. Except for increased numbers of lymphocytes, other studies showed an increased number of lymphocytes and neutrophils[34] as well as increased neutrophils only[35] in the BAL of patients with HCV. An increased number of CD2+, CD3+, CD4+ and HLA-DR+ T-lymphocytes has also been reported.[33,34] However, these results are based on small sample sizes and in asymptomatic patients with no clinical and radiological data of pulmonary disease.

Cytotoxic CD8+ T-lymphocytes increase in viral infection and activate a series of inflammatory pathways which results in release of inflammatory mediators.[36] CD8+ cells are also involved in pulmonary inflammation in COPD as their number is increased and correlates inversely with lung function.[37]

CD8+ T lymphocytes contribute to dysregulation of M_2 muscarinic receptors whose main function is to inhibit the release of acetylcholine and prevent bronchoconstriction.[38] CD8+ lymphocytes increase the level of IFNγ, which reduces the expression of M_2-receptors in the parasympathetic neurons in the airways and increases bronchial hyperresponsiveness.[38,39]

Last, but not least, smoking-related diseases such as COPD are of great concern in the HIV-infected population which is commonly associated with HCV. The prevalence of COPD is higher in patients with HIV when compared to the general population.[40] HAART therapy has led to changes in HIV-related pulmonary diseases which prolong survival. COPD is emerging as a new source of morbidity and mortality in HIV-infected patients.[41,42]

SECONDARY INVOLVEMENT OF THE LUNG IN HCV

Secondary involvement of the lung in HCV is associated on one hand with the development of liver cirrhosis and portal hypertension and on the other - with the development of autoimmune diseases which are prevalent in patients with HCV.[7] Formation of immune complexes in the pulmonary

vasculature may represent another mechanism of lung involvement (**Fig. 1**). Chronic liver disease may lead to lung injury because of changes in liver metabolism due to circulating inflammatory mediators and/or changes in blood flow due to pulmonary hypertension.

Liver cirrhosis (due to HCV) could lead to hepatopulmonary syndrome (vasodilation) and portopulmonary hypertension (vasoconstriction).

Hepatopulmonary syndrome (HPS) is represented by the triad of liver disease (liver dysfunction), pulmonary vasodilation and impaired arterial oxygenation (hypoxemia).[43] The prevalence of HPS in patients with chronic liver disease is 10-15%.[44] The clinical presentation varies from asymptomatic course to shortness of breath, cyanosis and finger clubbing.[44] Platypnea (dyspnoea occurring when getting up from a lying position) and orthodeoxia (lowering of PaO_2>3 mm Hg when getting up from a lying position) are common in patients with HPS due to pulmonary vasodilation, mainly in the lower lung lobes due to gravity.[45]

Pulmonary vasodilation is a major cause of hypoxemia in HPS. It leads to a mismatch between ventilation and perfusion due to increased perfusion and unchanged ventilation, which makes impossible the diffusion of the oxygen from the alveolar space to the center of abnormally dilated capillaries and oxygenation of hemoglobin.[45] In addition, hypoxic vasoconstriction in patients with chronic liver disease and increased pulmonary blood flow also contributes to the mismatch between ventilation and perfusion.[46]

Portopulmonary hypertension (PPH) is characterized by the tetrad: increased pulmonary pressure (>25 mm Hg at rest), increased pulmonary vascular resistance (>240 dyn.s.cm^{-5}), normal wedge pressure (<15 mmHg) and portal hypertension (>10 mm Hg).[47]

In most patients with PPH, portal hypertension is preceding 4-7 years on average.[48] The pathogenesis of the structural changes is not entirely clear, but include pulmonary vasoconstriction, remodeling of the muscle layer on the wall of pulmonary arteries and in situ microthrombosis and/or thromboembolic lesions.[46] Although pathological changes are similar to those shown in primary pulmonary hypertension, PPH is characterized by increased cardiac output.[49] It is notable that HIV-HCV co-infected patients have higher prevalence of PAH, which could worsen the prognosis.[50]

Last but not least, HCV infection leads to chronic liver inflammation and liver fibrosis. It is possible that HCV plays a similar role in the lung and is involved in the pathogenesis of pulmonary fibrosis.[51]

PULMONARY COMPLICATIONS OF INTERFERON THERAPY

Interferon (IFN) therapy shows good results in HCV.[52] This discovery was followed by reports of IFN-associated pulmonary complications. Most of them are reporting of cases, which impedes determination of the prevalence. They include interstitial pneumonitis, ARDS, sarcoidosis, pulmonary hypertension and pleural effusions.[53-56] According to two large studies the frequency of IFN-associated interstitial pneumonitis is 0.2-0.3%.[57,58]

Pulmonary complications of HCV therapy without IFN are still under study.

CONCLUSION

COPD patients have increased prevalence of HCV and patients with HCV, especially older ones, have increased prevalence of COPD. COPD patients have an increased risk of acquiring HCV infection due to the chronic nature of the disease and frequent medical treatment as well as presence of classical risk factors for HCV. However, patients with HCV infection don't have increased prevalence of risk factors for COPD, despite the presence of COPD.

HCV infection has long-term effects on lung tissue and is an additional risk factor for the development of COPD. The presence of HCV is associated with an accelerated loss of lung function in COPD patients, especially in current smokers. COPD could represent extrahepatic manifestation, associated with HCV infection. The most likely pathogenetic link between both diseases is systemic inflammation.

Secondary involvement of the lung in HCV is associated on the one hand with the development of liver cirrhosis and portal hypertension, and on the other - with the development of autoimmune diseases which are prevalent in patients with HCV. Liver cirrhosis can cause hepatopulmonary syndrome and portopulmonary hypertension, which further worsen the prognosis of patients with HCV and COPD.

Interstitial pneumonitis is a well-described complication of therapy with IFN, but the association with other reported complications is questionable.

CONFLICT OF INTEREST

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REFERENCES

1. From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2016. Available from: http://www.goldcopd.org/.
2. Pavlov P, Ivanov Y, Glogovska P, et al. COPD morbidity among smokers – an epidemiological study. Thoracic medicine 2011;3(2):50-3.
3. Adeloye D, Chua S, Lee C, et al. Global and regional estimates of COPD prevalence: systematic review and meta-analysis. J Glob Health 2015;5(2):020415.
4. Bulgarian clinical practice guidelines on the diagnosis, management and treatment of chronic hepatitis C, 2015.
5. Mohd Hanafiah K, Groeger J, Flaxman AD, et al. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology 2013;57:1333-42.
6. Wasley A, Alter MJ. Epidemiology of hepatitis C: geographic differences and temporal trends. Semin Liver Dis 2000;20(1):1-16.
7. Zignego AL, Ferri C, Pileri SA, et al. Extrahepatic manifestations of hepatitis C virus infection: a general overview and guidelines for a clinical approach. Dig Liver Dis 2007;39(1):2-17.
8. Kanazawa H, Hirata K, Yoshikawa J. Accelerated decline of lung function in COPD patients with chronic hepatitis C virus infection: a preliminary study based on small numbers of patients. Chest 2003;123(2):596-9.
9. Moorman J, Saad M, Kosseifi S, et al. Hepatitis C virus and the lung: implications for therapy. Chest 2005;128(4):2882-92.
10. Erol S, Saglam L, Ozbek A, et al. Hepatitis C virus infection and chronic obstructive pulmonary disease. Hepatitis Monthly 2009;9(1):39-44.
11. Silva DR, Stifft J, Cheinquer H, et al. Prevalence of hepatitis C virus infection in patients with COPD. Epidemiol Infect 2010;138(2):167-73.
12. El-Habashy M, Eldahdouh S, Mohamed A. The impact and effect of liver insufficiency of HCV infection on patients with chronic obstructive pulmonary diseases. Egyptian Journal of Chest Diseases and Tuberculosis 2014;63:81-5.
13. Yigit I, Hacievliyagil S, Seckin Y, et al. The relationship between severity of liver cirrhosis and pulmonary function tests. Dig Dis Sci 2008;53(7):1951-6.
14. Buist A, McBurnie M, Vollmer W, et al. International variation in the prevalence of COPD (the BOLD study): a population-based prevalence study. Lancet 2007;370(9589):741-50.
15. Butt A, Khan U, McGinnis K, et al. Co-morbid medical and psychiatric illness and substance abuse in HCV-infected and uninfected veterans. J Viral Hepat 2007;14(12)890-6.
16. Minakata Y, Sugiura H, Yamagata T, et al. Prevalence of COPD in primary care clinics: correlation with non-respiratory diseases. Internal Medicine 2008;47(2):77-82.
17. Erturk A, Tokgonul A, Capan N, et al. Pulmonary alterations in patients with chronic HCV infection. Dig Liver Dis 2006;38(9):673-6.
18. Minakata Y, Ueda H, Akamatsu K, et al. High COPD prevalence in patients with liver disease. Internal Medicine 2010;49(24):2687-91.
19. Mapel D, Marton J. Prevalence of renal and hepatobiliary disease, laboratory abnormalities, and potentially toxic medication exposures among persons with COPD. Int J Chron Obstruct Pulmon Dis 2013:8;127-34.
20. Fischer W, Drummond M, Merlo C, et al. Hepatitis C virus infection is not an independent risk factor for obstructive lung disease. COPD 2014;11(1):10-6.
21. Agusti AG. Systemic effects of chronic obstructive pulmonary disease. Proc Am Thorac Soc 2005;2:367-70.
22. Zhu J, Kilty I, Granger H, et al. Gene expression and immunolocalization of 15-lipoxygenase isozymes in the airway mucosa of smokers with chronic bronchitis. Am J Respir Cell Mol Biol 2002;27:666-77.
23. de Boer WI, Sont JK, van Schadewijk A, et al. Monocyte chemoattractant protein 1, interleukin 8, and chronic airways inflammation in COPD. J Pathol 2000;190:619-26.
24. Wagoner J, Austin M, Green J, et al. Regulation of CXCL-8 (interleukin-8) induction by double-stranded RNA signaling pathways during hepatitis C virus infection. J Virol 2007;81:309-18.
25. Koo BC, McPoland P, Wagoner JP, et al. Relationships between hepatitis C virus replication and CXCL-8 production in vitro. J Virol 2006;80:7885-93.
26. Moorman JP, Fitzgerald SM, Prayther DC, et al. Induction of p38- and gC1qR-dependent IL-8 expression in pulmonary fibroblasts by soluble hepatitis C core protein. Respir Res 2005;6:105.
27. Jeffery PK. Remodeling in asthma and chronic obstructive lung disease. Am J Respir Crit Care Med 2001;164:S28-S38.
28. Fujimura M, Myou S, Nomura M, et al. Interleukin-8 inhalation directly provokes bronchoconstriction in guinea pigs. Allergy 1999;54:386-91.
29. Kaplanski G, Farnarier C, Payan MJ, et al. Increased levels of soluble adhesion molecules in the serum of patients with hepatitis C: correlation with cytokine concentrations and liver inflammation and fibrosis. Dig Dis Sci 1997;42:2277-84.

30. Polyak SJ, Khabar KS, Rezeiq M, et al. Elevated levels of interleukin-8 in serum are associated with hepatitis C virus infection and resistance to interferon therapy. J Virol 2001;75:6209-11.
31. Mahmood S, Sho M, Yasuhara Y, et al. Clinical significance of intrahepatic interleukin-8 in chronic hepatitis C patients. Hepatol Res 2002;24:413-9.
32. Shimoda K, Begum NA, Shibuta K, et al. Interleukin-8 and hIRH (SDF1-/PBSF) mRNA expression and histological activity index in patients with chronic hepatitis C. Hepatology 1998;28:108-15.
33. Kubo K, Yamaguchi S, Fujimoto K, et al. Bronchoalveolar lavage fluid findings in patients with chronic hepatitis C virus infection. Thorax 1996;51:312-4.
34. Yamaguchi S, Kubo K, Fujimoto K, et al. Analysis of bronchoalveolar lavage fluid in patients with chronic hepatitis C before and after treatment with interferon. Thorax 1997;52:33-7.
35. Idilman R, Cetinkaya H, Savas I, et al. Bronchoalveolar lavage fluid analysis in individuals with chronic hepatitis C. J Med Virol 2002;66:34-9.
36. Lukacher AE, Braciale VL, Braciale TJ. In vivo effector function of influenza virus-specific cytotoxic T lymphocyte clones is highly specific. J Exp Med 1984;160:814-26.
37. Fabbri LM, Romagnoli M, Corbetta L, et al. Differences in airway inflammation in patients with fixed airflow obstruction due to asthma or chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2003;167:418-24.
38. Adamko DJ, Fryer AD, Bochner BS, et al. CD8+ T lymphocytes in viral hyperreactivity and M2 muscarinic receptor dysfunction. Am J Respir Crit Care Med 2003;167:550-6.
39. Jacoby DB, Xiao HQ, Lee NH, et al. Virus- and interferon-induced loss of inhibitory M2 muscarinic receptor function and gene expression in cultured airway parasympathetic neurons. J Clin Invest 1998;102:242-8.
40. Raynaud C, Roche N, Chouaid C. Interactions between HIV infection and chronic obstructive pulmonary disease: Clinical and epidemiological aspects. Respiratory Research 2011;12:117.
41. Hull MW, Phillips P, Montaner JS. Changing global epidemiology of pulmonary manifestations of HIV/AIDS. Chest 2008;134:1287-98.
42. Magalhaes MG, Greenberg B, Hansen H, et al. Comorbidities in older patients with HIV: a retrospective study. J Am Dent Assoc 2007;138:1468-75.
43. Rodriguez-Roisin R, Krowka MJ. Hepatopulmonary syndrome – a liver-induced lung vascular disorder. N Engl J Med 2008;358:2378-87.
44. Lange PA, Stoller JK. The hepatopulmonary syndrome. Ann Intern Med 1995;122:521-9.
45. Yen KT, Krowka MJ, Lee AS, et al. Liver and lung: hepatopulmonary syndrome. J Crit Illness 2002;17:309-15.
46. Herve P, Lebrec D, Brenot F, et al. Pulmonary vascular disorders in portal hypertension. Eur Respir J 1998;11:1153-66.
47. Rodriguez-Roisin R, Krowka MJ, Herve P, et al. Pulmonary-hepatic vascular disorders (PHD). Eur Respir J 2004;24(5):861-80.
48. Hadengue A, Benhayoun MK, Lebrec D, et al. Pulmonary hypertension complicating portal hypertension: prevalence and relation to splanchnic hemodynamics. Gastroenterology 1991;100:520-8.
49. Kuo PC, Plotkin JS, Johnson LB, et al. Distinctive clinical features of portopulmonary hypertension. Chest 1997;112:980-6.
50. Sangal R, Taylor L, Gillani F, et al. Risk of echocardiographic pulmonary hypertension in individuals with human immunodeficiency virus-hepatitis C virus coinfection. Ann Am Thorac Soc 2014;11:1553-9.
51. Aisa Y, Yokomori H, Kashiwagi K, et al. Polymyositis, pulmonary fibrosis and malignant lymphoma associated with hepatitis C virus infection. Intern Med 2001;40:1109-12.
52. Davis GL, Balart LA, Schiff ER, et al. Treatment of chronic hepatitis C with recombinant interferon: a multicenter randomized, controlled trial. Hepatitis Interventional Therapy Group. N Engl J Med 1989;321:1501-6.
53. Abi-Nassif S, Mark EJ, Fogel RB, et al. Pegylated interferon and ribavirin-induced interstitial pneumonitis with ARDS. Chest 2003;124:406-10.
54. Fruehauf S, Steiger S, Topaly J, et al. Pulmonary artery hypertension during interferon therapy for chronic myelogenous leukemia. Ann Hematol 2001;80:308-10.
55. Rubinowitz AN, Naidich DP, Alinsonorin C. Interferon-induced sarcoidosis. J Comput Assist Tomogr 2003;27:279-83.
56. Takeda A, Ikegame K, Kimura Y, et al. Pleural effusion during interferon treatment for chronic hepatitis C. Hepatogastroenterology 2000;47:1431-5.
57. Karino Y, Hige S, Matsushima T, et al. [Interstitial pneumonia induced by interferon therapy in type C hepatitis.] Nippon Rinsho 1994;52:1905-9 (Japanese).
58. Okanoue T, Sakamoto S, Itoh Y, et al. Side effects of high-dose interferon therapy for chronic hepatitis C. J Hepatol 1996;25:283-91.

Хроническая обструктивная болезнь лёгких и гепатит С

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Хроническая обструктивная болезнь лёгких (ХОБЛ) является предотвратимой, лечимой болезнью со значительными внелёгочными проявлениями, которые могут оказать отрицательное воздействие на протекание заболевания у некоторых пациентов. С другой стороны, инфицирование вирусом гепатита С (HCV) связано с рядом внепечёночных проявлений, связанных с HCV инфицированием. У пациентов с ХОБЛ проявляется HCV, а у пациентов с HCV, особенно у пожилых, проявляется распространение и скоротечное развитие ХОБЛ. HCV инфицирование оказывает долгосрочное воздействие на лёгочную ткань и является дополнительным фактором риска развития ХОБЛ. Наличие HCV связано с ускоренной потерей лёгочной функции у пациентов с ХОБЛ, особенно у активных курящих. ХОБЛ может привести к внепечёночным проявлениям, связанным с HCV инфицированием. Целью данной статьи является дополнительный обзор литературы, связанной с распространением HCV и ХОБЛ, и с другой стороны, установление их патогенной связи и последствий их взаимного проявления.