

Original Research Article

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Progressive Decline in Pulmonary Functions in Adolescents with Chronic Hepatitis C Infection

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ABSTRACT

Chronic hepatitis C infection is considered now a multi-system disease, affecting nearly all body system. Hepatic affection of such viruses are widely evaluated while extra-hepatic manifestations (including lungs) still need more studies, especially in children and adolescents. To evaluate if chronic HCV (CHCV) infection without treatment is associated with progressive deterioration of pulmonary functions. Fifty adolescent patients with CHCV infection (12-18 years) and 50 control health subjects included in the study, with full hepatic evaluation beside pulmonary function tests (PFTs) at the start of the study. PFTs were repeated in patient group after 6 and 12 months and evaluated in comparison to start results and to control group. There was a gradual deterioration of PFT in adolescent patients with CHCV infection reached a significant levels (FEV1 89 ± 1.3 , FVC 88 ± 0.8 , FEV1/FVC 91 ± 1.1) when compared to healthy control group (FEV1 96 ± 1.9 , FVC 95 ± 1.2 , FEV1/FVC 97 ± 1.1) with P value (0.02, 0.03, 0.01) respectively. Progressive decline in pulmonary functions is observed in adolescents with chronic HCV infection, but more researches are needed to further explore such deteriorations.

Keywords

Chronic
Hepatitis B and C,
FEV1,
FVC,
Pulmonary functions.

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Introduction

Hepatitis C virus (HCV) is a worldwide major health problem, affecting nearly 200 million people, and considered to be one of the leading top ten lethal infectious agents (Elwan *et al.*, 2016). Infection by either of them can occur, but also co infection is widely recorded because of similar modes of transfer (e.g. blood products transfusion, sexual routes, drug abuse, needle injury). Co infection causes more health hazards than single infection. Liver injuries caused by such viruses are well known and widely

evaluated in researches, while extra hepatic manifestations are still evolving, including skin, kidneys, CNS, blood, cardiovascular system, endocrine, oncologic., etc. (Zignego, 1999; 2008). Pulmonary manifestations of hepatitis C viruses (HCV) are recently attack the attention of researchers, especially in adults with chronic HCV infection after treatment (Ueda *et al.*, 1992), with controversy results. Most of the studies record decline in pulmonary functions in adults with chronic HCV due to different mechanisms, either direct effect (induction

of interstitial fibrosis activation of asthma (Yamaguchi *et al.*, 1997), COPD (Silva *et al.*, 2010), or indirect effects (through induction of cryoglobulinemia (Ferri *et al.*, 2004), and side effects of therapy (Zignego, 2007).

Despite the rapid increase in number of patients with HCV worldwide, the pulmonary complications of such infections not widely investigated and explained in adults, most of reports are casa-study, and up to our knowledge, no previous research evaluate the pulmonary complications in children and adolescents chronically infected with HCV.

The aim of this study was to evaluate pulmonary functions (FEV1.FVC. FEV/FVC) in adolescents with chronic HCV infection.

Subjects and Methods

Subjects

This prospective randomized control study included 50 adolescent patients (aged 12-18 ys) with chronic hepatitis-C virus (CHCV) infection and 50 healthy subjects of matched age and sex as a control group. All subjects attended OPD clinics for hepatology and gastroenterology, Tanta University, Egypt; during the period from September 2014 till September 2015.

All subjects should be: non-smokers, with no chronic lung diseases (eg. asthma, COPD), have normal liver function tests at the begging of the study, normal liver ultrasound, and normal liver fibroscan (for CHCV patients only). Hepatitis patient group not received treatment for CHCV and had negative HBsAg and negative anti-HBc, with positive hepatitis C antibody (anti-HBc) test.

All patients were diagnosed as HCV for at least one year before start of the study.

In CHCV group, study began with 50patients, but only 34 patients completed the study (9 patients started treatment during the study period, 7 patients missed).

Written consent had been taken from all patients (or their care-givers) and underwent ethical committee

Methods

All patients and control group subjected to

- 1-Full history taking
- 2-Complete medical examination
- 3-Liver function tests
- 4-Hepatitis B surface antigen (HBsAg) and Hepatitis B core antibodies (antiHBc)
- 5-Hepatitis C antibody (anti-HCV)
- 5-Abdominal ultrasonography
- 6-Liver fibroscan for hepatitis group only
- 7-Pulmonary function tests (PFTs) by Spirometry, FEV1.FVC, and FEV1/FVC: done for all subjects at the begging of the study, then done only for patient group after 6 and 12 months. PFTs measured at the morning 9 AM-11 AM, the best of 3 reading was recorded and compared to the best predictive value depending on age (kg), height (cm) and sex.

Data of all subjects were collected, analyzed according to STATA version 11.

Results and Discussion

Data of CHCV patients who completed the study (34) and control group (50) collected in tables (1-6)

Fifty adolescent patients with chronic hepatitis C infection met the inclusion criteria at the start of the study, only 34 complete the study according to such

criteria, 50 healthy subjects of non-significant difference regarding demographic data (age, sex, height, BMI, waist: hip ratio) (Table 1) evaluated as control group.

At the start of the study, PFTs in patient group were lower (FEV1 94 %± 2.1, FVC 95 % ± 0.9, FEV1/FVC 97 ± 0.8) but non-significant, when compared to control group (FEV1 96 % ± 1.9, FVC 95 % ± 1.2, FEV1/FVC 97 ± 1.1) with P value 0.86, 0.77, 1.05 respectively (Table 2).

After 6 months from start of the study, PFTs in patient group were slightly lower (FEV1 93 %± 1.7, FVC 95 % ± 1.4, FEV1/FVC 95 ± 1.0) but non-significant, when compared to control group (FEV1 94 %± 2.1, FVC 95 % ± 0.9, FEV1/FVC 97 ± 0.8) with P value 0.89, 0.87, 1.1 respectively (Table 3).

After 12 months from start of the study, more deteriorations in PFTs in patient group (FEV1 89 %± 1.3, FVC 88 % ± 0.8, FEV1/FVC 91 ± 1.1) but non-significant, when compared to their PFTs recorded 6 months earlier (FEV1 93 %± 1.7, FVC 95 % ± 1.4, FEV1/FVC 95 ± 1.0) with P value 0.06, 0.07, 0.1 respectively (Table 4), and still not significantly lower when compared to their PFTs recorded at the start of the study, 12 months earlier, with P value 0.08, 0.07, 0.08 respectively (Table 5).

Of interest, PFTs recorded in adolescent patients at the end of our study (after 12 months) became significantly lower (FEV1 89 %± 1.3, FVC 88 % ± 0.8, FEV1/FVC 91 ± 1.1) when compared to control group (FEV1 96 %± 1.9, FVC 95 % ± 1.2, FEV1/FVC 97 ± 1.1) with P value 0.02, 0.03, 0.01 respectively (Table 6). Hepatitis C virus infection is a worldwide health problem. Due to lack of effective vaccine (up till now), beside wide scale of methods of

transmission, the disease affects more and more victims of all ages. Although the liver is the main target of the HCV, chronic HCV infection is considered a multisystem disease, affecting nearly all body organs, contributing to wide range of presentations and complications. Association between CHCV infection with pulmonary functions and diseases not sufficiently evaluated, especially in children and adolescents. The present study aimed at evaluating the progress changes in pulmonary functions in adolescents with chronic HCV infection not received interferon or ribavirin.

In adults with CHCV infection, limited studies evaluated such infection and chest, with controversy results. While Kanazawa *et al.*, reported a greater decline in FEV1 in COPD adult patients who had HCV infection in a small prospective cohort study, however, nearly half of the patients received interferon therapy which affect per-se lung functions, making a confounding effect on the result. On the other hand, Tueber *et al.*, (2002) studied 178 non-cirrhotic patients with chronic viral hepatitis and found no significant impairment of FEV1 and FVC.

Minakata *et al.*, (2010), in a large study in Japan found no significant association between both diseases, while Silva *et al.*, (2010) recorded a higher prevalence of COPD in HCV-positive individuals compared to negative ones. Up to our knowledge, this is the first study evaluated pulmonary functions in adolescent patients with CHCV.

In our single-center prospective pilot study, we selected adolescent patients with CHCV infection who not received interferon or ribavirin to concisely evaluate the effect of viral infection on pulmonary functions (FEV1, FVC, FEV1/FVC).

Table.1 Demographic data of studied groups at the start of the study

	Patient (n=34)	Control(n=50)	P value
Age (years) Mean(\pm SD)	15.4 2.1	15.2 2,6	1.3
Sex (M:F)	18:16	26:24	0.9
Heigh(cm) Mean(\pm SD)	155.7(9.77)	157.5(9.6)	1.2
BMI Mean(\pm SD)	26.89(4,97)	26.44(6.05)	2
Waist:hipratio;Mean(\pm SD)	0.93(0.006)	0.91(0.09)	1.7

P significant if < 0.05

No significant difference between patients and control group regarding demographic data at the start of the study.

Table.2 Pulmonary functions in studied groups at the start of the study

	Patient (n=34)	Control(n=50)	P value
FEV1(%):Mean(\pm SD)	94(2.1)	96(1.9)	0.86
FVC(%):Mean(\pm SD)	95(0.9)	95(1.2)	0.77
FEV1/FVC: Mean(\pm SD)	97(0.8)	97(1.1)	1.05

P significant if < 0.05 FEV1 forced expiratory volume in 1 second FVC forced vital capacity

No significant difference between patients and control group regarding pulmonary functions at the start of the study.

Table.3 Pulmonary functions in patient group after 6 months from the start of the study

	Patient (n=34)at start	Patient (n=34)after 6 months	P value
FEV1(%):Mean(\pm SD)	94(2.1)	93(1.7)	0.89
FVC(%):Mean(\pm SD)	95(0.9)	93(1.4)	0.87
FEV1/FVC: Mean(\pm SD)	97(0.8)	95(1.0)	1.1

P significant if < 0.05 FEV1 forced expiratory volume in 1 second FVC forced vital capacity

No significant difference regarding pulmonary functions at the start of the study compared to after 6 months from start in patient group.

Table.4 Pulmonary functions in patient group after 6 months and 12 months from the start of the study

	Patient (n=34)after 6 months	Patient (n=34)after 12 months	P value
FEV1(%):Mean(\pm SD)	93(1.7)	89(1.3)	0.09
FVC(%):Mean(\pm SD)	93(1.4)	88(0.8)	0.07
FEV1/FVC: Mean(\pm SD)	95(1.0)	91(1.1)	0.1

P significant if < 0.05 FEV1 forced expiratory volume in 1 second FVC forced vital capacity

No significant difference regarding pulmonary functions in patient group after 6 months when compared to pulmonary functions after 12 months from the start of the study

Table.5 Pulmonary functions in patient group at the end of the study compared to pulmonary functions at the beginning of the study

	Patient (n=34)	patient(n=34)	P value
FEV1(%):Mean(±SD)	89(1.3)	94(2.1)	0.08
FVC(%):Mean(±SD)	88(0.8)	95(0.9)	0.07
FEV1/FVC: Mean(±SD)	91(1.1)	97(0.8)	0.08

P significant if < 0.05
 FEV1 forced expiratory volume in 1 second
 FVC forced vital capacity
 No significant difference regarding pulmonary functions in patient group after 12 months when compared to pulmonary functions at the start of the study

Table.6 Pulmonary functions in studied groups at the end (after 12 months) of the study

	Patient (n=34we)	Control(n=50)	P value
FEV1(%):Mean(±SD)	89(1.3)	96(1.9)	0.02*
FVC(%):Mean(±SD)	88(0.8)	95(1.2)	0.03*
FEV1/FVC: Mean± (SD)	91(1.1)	97(1.1)	0.01*

P significant if < 0.05
 FEV1 forced expiratory volume in 1 second
 FVC forced vital capacity
 There were significant difference regarding pulmonary functions in patient group after 12 months when compared to pulmonary functions of control group.

At the beginning of our study, our patients showed lower but non-significant PFT when compared to control group, although there were no history or clinical picture of any disease can affect PFT in such patients, except CHCV infection. With serial follow up of PFT, gradual deterioration recorded, and after 12 months of follow up, PFT decrease to a significant levels compared to control group, and still lower (not significant) when compared to patients at the start of our study. Explanation of such deterioration not found in the literature, especially most recorded studies done in adults and as a case-record .Biological mechanisms can be used for explanation, as viral hepatitis infection associated with increase in cryoglobulines, which in turn can lead to development of pulmonary sarcoidosis an interstitial lung disease (28-61).

A larger study with longer period follow up are needed to evaluate the long term effects

of hepatitis virus infection on lungs of both children and adults.

Competing interest

All authors declare they have no competing interest

Abbreviations

- HBV: hepatitis B virus
- HCV: hepatitis C virus
- PFT: pulmonary function test
- FEV1: forced expiratory volume in 1 second
- FVC: forced vital capacity
- COPD: chronic obstructive pulmonary disease
- Anti-HBc: hepatitis B core antibody
- HBsAg: hepatitis B surface antigen
- Anti-HCV: hepatitis C antibody
- CHCV: chronic hepatitis C virus

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