Effect of Hepatitis C Infection and Its Clearance on the Frequency of Coronary Artery Disease in Diabetics

Hepatit C Enfeksiyonunun ve Klirensinin Diyabetik Hastalarda Koroner Arter Hastalığı Sıklığına Etkisi

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ABSTRACT

Objectives: Chronic hepatitis C (CHC) infection considered to be associated with an increased risk of coronary artery disease (CAD). However, there is not enough data concerning this association in diabetics. Thus, this study investigated the effect of chronic HCV infection and its clearance on the CAD risk in diabetics.

Materials and Methods: This was a retrospective case-control study conducted at the Mustafa Kemal University, Department of Infectious Diseases and Clinical Microbiology, Hatay, between January 2010 and January 2015. The presence of CAD and its main risk factors such as age, sex, hypertension (HT), hyperlipidaemia (HL), chronic obstructive pulmonary disease and chronic renal failure were compared between 100 HCV infected diabetic patients and 100 uninfected diabetic controls. The HCV-infected patients were further divided into a viral clearance group and a persistence group, and the CAD prevalence was also compared between these two groups.

Results: Patients with CHC were predominantly male (55% vs 39%) and predominantly older than 60 years of age (68% vs 51%) in comparison with controls. The HCV-infected group had a significantly lower prevalence of CAD, HT and HL compared with controls (p<0.001). Furthermore, no significant differences were found between groups with viral clearance and persistent viremia for the prevalence of CAD (p=0.80).

Conclusion: Our data suggested that chronic HCV infection might be a protective factor against CAD and successful HCV eradication may not increase the risk of CAD in diabetics. These findings indicate a need for additional studies to clarify the effects of HCV infection and its clearance on the risk of CAD in diabetics.

Keywords: Chronic HCV infection, coronary artery disease, diabetes mellitus

ÖZ

Amaç: Kronik hepatit C (KHC) enfeksiyonunun artmış koroner arter hastalığı (KAH) riski ile ilişkili olduğu kabul edilmektedir. Bununla birlikte diyabetik hastalarda bu ilişki ile ilgili yeterli veri bulunmamaktadır. Bu nedenle bu çalışma ile kronik HCV enfeksiyonunun ve klirensinin, diyabetik hastalardaki KAH riski üzerine etkisi araştırılmıştır.

Gereç ve Yöntemler: Bu çalışma; Mustafa Kemal Üniversitesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilimdalı, Hatay'da, Ocak 2010-2015 tarihleri arasında yapılan retrospektif bir olgu kontrol çalışmasıdır. HCV ile enfekte diyabetik olgular (n=100) ile HCV ile enfekte olmamış diyabetik kontrol grubu (n=100) arasında KAH varlığı ve yaş, cinsiyet, hipertansiyon (HT), hiperlipidemi (HL), kronik obstrüktif akciğer hastalığı ve kronik böbrek yetmezliği gibi KAH için risk faktörleri açısından karşılaştırıldı. Buna ek olarak, HCV ile enfekte diyabetik olgular viral klirens gelişen ve persistan viremisi olan olgular olarak iki alt gruba ayrıldı ve bu iki grup arasında da KAH prevalansı karşılaştırıldı.

Bulgular: CHC olguları kontrol grubuna göre çoğunluğu erkekti (%55'e karşı %39) ve ağırlıklı olarak 60 yaşından büyüktü (%68'e karşı %51). HCV ile enfekte olan grupta, kontrol grubuna kıyasla KAH, HT, HL prevalansı anlamlı olarak daha düşüktü (p<0.001). Ayrıca, viral klirens gelişen ve persistan viremisi olan olgular arasında KAH prevalansı açısından anlamlı fark bulunmadı (p=0.80).

Sonuç: Verilerimiz kronik HCV enfeksiyonunun KAH'a karşı koruyucu bir faktör olabileceğini ve başarılı HCV eradikasyonunun diyabetik hastalarda KAH riskini arttırabileceğini düşündürmektedir. Bu bulgular HCV enfeksiyonunun ve klirensinin diyabetik hastalarda KAH riski üzerindeki etkilerini açıklığa kavuşturmak için ek çalışmalara ihtiyaç olduğunu göstermektedir.

Anahtar Kelimeler: Kronik hepatit C enfeksiyonu, koroner arter hastalığı, diabetes mellitus

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Introduction

Some studies have suggested that chronic infections including chronic active hepatitis C plays a role in the pathogenesis of atherosclerosis and coronary artery disease (CAD) (1,2). However, the effect of hepatitis C virus (HCV) infection on the risk of CAD is still unclear. Even though most studies have declared that HCV increases the risk of CAD (3,4), some studies have shown no association (5,6), while others have reported that HCV could be protective against CAD (7). As diabetic patients, have higher mortality rates from CAD than non-diabetics (8), this association gains more importance in diabetics. The presence of HCV infection is known to accelerate the occurrence of both metabolic syndrome and diabetes mellitus (DM) (9). This seems to support the studies that have reported an increased risk for CAD with HCV infection. On the other hand, lower serum lipid levels have been observed in patients infected with HCV (4). HCV-related hypolipidemia could be associated with decreases in atherosclerosis (10), which may then decrease the risk of CAD. This study aimed to investigate the effect of HCV infection and its clearance on CAD risk in diabetics. To our knowledge this is the first study performed in diabetic patients concerning this issue.

Materials and Methods

Study population

We conducted a retrospective case-control study that included 200 diabetics with and without chronic hepatitis C (CHC) infection who were admitted to our clinic between January 2010 and January 2015. Of the 200 patients, 47% were male and 53% were female. The mean age of the patients was 62.8±9.8 (range: 37-88) years. Patients were classified into two groups. Group A was comprised of 100 diabetic patients with chronic HCV infection and group B had 100 uninfected diabetic patients as a control group. Among CHC patients, 90% of cases were infected with genotype 1b, while the remaining 10% were infected with genotype 4. The presence of CAD and its main risk factors such as age, sex, hypertension (HT), hyperlipidaemia (HL), chronic obstructive pulmonary disease (COPD) and chronic renal failure (CRF) were compared between the two groups.

According to the treatment results, the patients in Group A also were divided into subgroup A1 (47 patients) for those who achieved viral clearance and subgroup A2 (53 patients) for those with persistent viremia (who failed therapy or were untreated). The prevalence of CAD was also compared between these two subgroups (subgroup A1 and A2). Patients coinfected with hepatitis B were excluded from the study as well as patients who were diagnosed as having CAD before the diagnosis of the HCV infection.

Definitions

CHC was defined by the presence of the HCV antibody and the persistence of detectable HCV-RNA for at least six months. Patients who were negative for HCV antibodies were considered as HCV-uninfected. Subjects were considered diabetic if they had plasma glucose levels of ≥200 mg/dL and if they were under treatment for DM. CAD was defined as 50% or more stenosis in at least one major coronary artery as determined with anjiography. HT was defined by the presence of diagnostic codes (ICD-10 codes) for HT and the use of antihypertensive drugs. HL was defined by the presence of elevated serum cholesterol levels (total cholesterol >200 mg/dL; LDL-C >130 mg/dL) and a current prescription of cholesterol-lowering medication. CRF was defined as an estimated glomerular filtration rate less than 30 mL/min for at least three months. COPD was defined by the presence of the diagnostic code (ICD-10 code) for COPD and the use of nebulizer therapy.

Statistical Snalysis

Statistical analyses were performed using the SPSS version 23. The chi-square test (or Fisher's exact test, where appropriate) and the Student's t-test were used for statistical comparisons. A p-value <0.05 was considered significant.

Results

CHC patients were predominantly male (55% vs 39%) and were predominantly older than 60 years (68% vs 51%) in comparison with the controls. However, there were no statistically significant differences in age between the HCV-infected patients and controls (p=0.075). The HCV-infected group had a significantly lower prevalence of CAD compared with controls (p<0.001). The prevalence of HT and HL were also significantly lower in the HCV-infected group (p<0.001 for both). The HCV group had a higher prevalence of COPD and CRF, but these differences were not statistically significant (p=0.45 and p=0.47 respectively).

There were no statistically significant differences in the CAD prevalence between subjects with viral clearance (group A1) and subjects with persistent viremia (group A2) (p=0.80).

Comparisons of the characteristics of HCV negative and positive diabetic patients are shown in Table 1.

Discussion

There is much evidence that HCV infection have been associated with an increased risk of CAD (11,12,13). However, in our study we observed that HCV-infected diabetic patients had a lower prevalence of CAD in comparison with the uninfected controls. This difference that we found in our study may be due to the different study population, which, in this study, consisted entirely of diabetics.

There are two possible explanations for this difference in diabetic patients in the present study. The first is that lower sustained virologic response (SVR) rates have been reported in diabetic patients compared with non-diabetics (14). This suggests that diabetics may have higher viral load levels than non-diabetics. This hypothesis also was supported by findings of one study conducted by Hsu et al. (15), who found a relationship between high viral load levels and insulin resistance. Furthermore, one study has indicated a relationship between high viral load and lower lipid levels in patients with HCV infection (16). As a result, possible higher viral load levels and related lower lipid levels in the present study, compared with similar studies, may explain the decreased CAD risk in diabetics, which was observed in this study.

Another explanation stems from a previous report indicating that genetic polymorphisms in IL28B may influence the risk of developing DM and related complications like CAD in patients with genotype 1 CHC infection (17). Different genetic variants of IL28B

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Table 1. Comparisons of the characteristics of HCV negative and positive diabetic patients

Characteristics	HCV (+) diabetics (n=100)	HCV (-) diabetics (n=100)	p
Age (years)	63.9±8.9	61.4±10.5	0.075
Age			
37-60	32	49	-
≥60	68	51	-
Males (n)	55	39	0.023
CAD (n)	14	36	<0.001
COPD (n)	5	2	0.45
CRF (n)	11	8	0.47
HL (n)	17	56	<0.001
HT (n)	26	50	<0.001
CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, CRF: Chronic renal failure, HL: Hyperlipidaemia, HT: Hypertension, HCV: hepatitis C virus			

may explain the difference in the impact of HCV on the prevalence of CAD in diabetics.

In the present study, we also observed that the HCV-infected group had a lower prevalence of HT and HL, which is consistent with other studies (4,18). Although lower lipid levels were described in HCV-infected patients, achieving SVR has been found to be associated with a rebound increase in lipid levels (4,19). As high lipid levels are considered a risk factor for CAD, rebound increases in lipid levels may also be associated with an increased risk of CAD. Therefore, we also analysed the effect of viral clearance on the development of CAD in diabetics. However, we did not see a significant association between viral clearance of HCV and the development of CAD in diabetics.

Study Limitations

Our study has some limitations due to its retrospective nature. First, we had no information on body mass index, family history of CAD and smoking history in our study population. These are important risk factors for developing CAD. Second, we did not have information about the degree of liver fibrosis, which is a condition that may influence the risk of CAD. Finally, we could not examine IL28 B genotypes in patients.

Despite these limitations, this is the first study to investigate the effects of HCV infection on the risk of CAD in diabetics. This is also the first study to look at the effect of successful HCV eradication on the development of CAD in diabetics.

Conclusion

The results of this study have important ramifications for future research. Our findings suggest that the presence of HCV infection may reduce the risk of CAD in diabetics. Our findings also suggest that successful HCV eradication may not increase the risk of CAD in diabetics. Further prospective studies are necessary to clarify the roles of HCV and HCV eradication in the development of CAD in diabetics.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of Mustafa Kemal University Hospital (approval number: 07, date: 11/06/2020).

Informed Consent: Due to the restrospective design of the study informed consent was not obtained.

Peer-review: Externally peer-reviewed.

Authors contributions

Concept: T.B., C.K., Design: T.B., C.K., M.C., Y.O., Data Collection or Processing: T.B., C.K., Analysis: T.B., C.K., M.C., Y.O., Literature Search: T.B., C.K., Writing: T.B., C.K.

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