

Prevalence of Senv-D and Senv-H Variants of Sen Virus in Peritoneal Dialysis Patients

Periton Diyalizi Hastalarında Sen Virüsü Varyantı Olan Senv-D ve Senv-H'nin Prevalansı

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ABSTRACT

OBJECTIVE: Patients on peritoneal dialysis are at high risk of blood-borne infections due to frequent blood transfusions. We aimed to determine and compare the prevalence of SENV-D and SENV-H variants of the SEN virus (SENV) in these patients.

MATERIAL and METHOD: A total of 143 subjects, 43 on peritoneal dialysis and 100 healthy controls, were included in this point-prevalence study. SENV-D and SENV-H DNAs were detected with the polymerase chain reaction.

RESULTS: The prevalence of SENV-D was 23.2% in peritoneal dialysis patients. The prevalence of SENV-H being 20.9% in peritoneal dialysis patients was found to be higher than that of SENV-D. SENV-H prevalence was not significantly higher in our patient population compared with healthy subjects (16.0%). On the other hand, SENV-D was significantly more prevalent in all patient groups compared to healthy control subjects (5.0%). There was no association between SENV and HCV.

CONCLUSIONS: SEN virus infection, particularly SENV-D variant, has high prevalence in patients on peritoneal dialysis in Turkey. Care should be taken for SENV hepatitis and transmission of virus among these patients.

KEYWORDS: SEN virus, Peritoneal dialysis, Hepatitis

ÖZ

AMAÇ: Kan transfüzyonları sebebiyle kan ile taşınan enfeksiyonlar periton diyalizi hastalarında daha sık görülür. Bu çalışmanın amacı, bu hastalarda SEN virüslerinin (SENV) SENV-D ve SENV-H tiplerinin sıklığını tespit etmek ve birbiriyle karşılaştırmaktır.

GEREÇ ve YÖNTEM: 100 sağlıklı kontrol, 43 periton diyalizi hastası olmak üzere 143 hasta bu çalışmaya dahil edildi. SENV-D ve SENV-H DNA polimerase chain reaction yöntemi ile çalışıldı.

BULGULAR: Periton diyalizi hastalarında; SENV-D sıklığı %23.2, SENV-H %20.9 bulundu. SENV-H sıklığı sağlıklı grup (%16.0) ile karşılaştırıldığında anlamlı olarak yüksek değildi. Diğer yandan SENV-D sağlıklı grup (%5.0) ile karşılaştırıldığında anlamlı olarak yüksek bulundu. SENV ile HCV arasında birliktelik tespit edilmedi.

SONUÇ: SEN virüs enfeksiyonu ve özellikle SENV-D tipi Türkiye'deki periton diyalizi hastalarında sağlıklı gruba göre daha yüksek sıklıkla görülmektedir. SEN-V ve HCV arasında birliktelik tespit edilmemiştir.

ANAHTAR SÖZCÜKLER: SEN virus, Periton diyalizi, Hepatit

INTRODUCTION

The SEN virus (SEN-V), a blood-borne novel DNA virus, was identified as a putative non-A-to-E hepatitis virus and thought to be associated with post-transfusion hepatitis (1). SEN-V consists of eight strains known as strains A to H (2). Among these strains, D and H were found to be related more often with non-A-to-E hepatitis (3). Most studies in the literature focused on these two

strains because of their association with post-transfusion hepatitis. These two strains have been found in 30% of cases of transfusion-associated non-A-to-E hepatitis, compared to 1.8% of healthy blood donors (3).

Due to its transmission by transfusion, SEN-V DNA was detected more in conditions where transfusion is common like surgery, hemophilia, injection drug users, HIV, and haemodialysis (3-5). A prevalence of

SEN-V ranging from 13% to 68% was reported among haemodialysis patients (4-6).

The prevalence of SEN-V and D/H strains differs markedly from 2% to 25% in healthy individuals by geographic region (3,4,7).

Furthermore, coinfection with SEN-V in patients with chronic hepatitis C was reported which may suggest a specific link between SEN-V and HCV (8,9).

Patients on haemodialysis and peritoneal dialysis are at high risk of blood-borne infections due to frequent blood transfusions. Therefore it is important to define the prevalence of SENV-D and SENV-H to determine the clinical relevance of SENV infection and the risk of non-A-to-E hepatitis among these patients. Country-specific data on SENV-D and SENV-H prevalence have crucial importance since the prevalence of SEN-V depends on geographic region.

In this study, we aimed to determine and compare the prevalence of SENV-D and SENV-H variants of SEN virus in peritoneal dialysis patients. We particularly focused on demographic and virological characteristics of patients on peritoneal dialysis. We also aimed to determine whether there is an association between SEN and HCV virus in these patients.

SUBJECTS and METHODS

Patients

This was a point-prevalence study performed at the Marmara University Medical School Hospital. Patients aged 18-75 years who had been undergoing peritoneal dialysis for a minimum of 3 months were included in the study. Peritoneal dialysis was administered as continuous ambulatory peritoneal dialysis (CAPD). Additionally, healthy controls that were selected among donors at the Marmara University Blood Transfusion Center were included.

A total of 143 subjects, 43 on peritoneal dialysis and 100 healthy controls, were included in this study.

All study subjects provided informed consent before the study. This study was approved by the Marmara University Institutional Ethics Committee.

Laboratory tests

Hepatitis B surface antigen (HbsAg), HCV RNA, SENV-D and SENV-H DNAs were studied. SENV-D and SENV-H DNAs were screened with the seminested polymerase chain reaction using primers from the ORF-1 region. Randomly selected amplicons were sequenced on the ABI 310 sequencer following cycle sequencing with the big dye terminator kit.

Laboratory tests were performed at the Istanbul University Cerrahpasa Medical School Microbiology Laboratory. Patients' blood samples were centrifuged and kept frozen at -80 oC and then sent to the microbiology laboratory.

Statistical analysis

Study data were provided with descriptive statistics. χ^2 or Fisher's exact test was used for analyzing categorical data. The level of statistical significance was defined as $P < 0.05$.

RESULTS

Prevalence of SENV-D and SENV-H

SENV-H was positive in 16.0% of healthy controls. Although SENV-H positivity was higher among patients on peritoneal dialysis (20.9%), the difference was not statistically significant. SENV-D prevalence was significantly higher in patients on peritoneal dialysis compared with healthy controls (23.2% vs. 5.0%, $P = 0.001$) (Table I).

The mean duration of peritoneal dialysis was 45.8 ± 24.4 months ($n = 43$). Six out of 43 peritoneal dialysis patients (13.9%) had undergone kidney transplantation. The mean age was significantly higher in peritoneal dialysis group than the control group (48.8 ± 14.4 vs. 33.0 ± 7.8 years, $P < 0.0001$). Although the peritoneal dialysis group consisted of an almost equal number of male and female patients, almost 90% of subjects were male in the control group ($P < 0.0001$) (Table I). Similarly, the rate of positive HCV was higher in the peritoneal dialysis group (18.6% vs. 1.0%, $P < 0.0001$) but the prevalence of SENV-H and positive HbsAg was similar between the peritoneal dialysis and control groups (Table I).

No relation was found between SENV-D and HCV in the peritoneal dialysis group or control group, (Table II). In the peritoneal dialysis group, SENV-D was positive in 25.0% of HCV (+) patients and in 22.9% of HCV (-) patients ($P = 0.897$). There was also no relation between SENV-H and HCV. HCV was positive in 1 out of 25 SENV-H (+) patients (4.0%) and in 8 out of 118 SENV-H (-) patients (6.8%) ($P = 0.603$).

DISCUSSION

This study determined the prevalence of SENV-D and SENV-H variants of SEN virus in peritoneal dialysis patients in Turkey. We found a prevalence of 23.2% for SENV-D in peritoneal dialysis patients. The prevalence of SENV-H was 20.9% in peritoneal dialysis and higher than that of SENV-D. SENV-H prevalence was not significantly higher in our patient population compared with healthy subjects. On the other hand, SENV-D was

Table I. Demographics and prevalence of SENV-D, SENV-H, HbsAg, and HCV positivity among CAPD patients and healthy controls. Data are given as mean ± SD or n (%).

	Peritoneal dialysis (n=43)		Control (n=100)		P value
Age (years)	48.8 ± 14.4		33.0 ± 7.8		<0.0001
Sex					
Male	22	51.2 %	89	89.0 %	<0.0001
Female	21	48.8 %	11	11.0 %	
SENV-D (+)	10	23.2 %	5	5.0 %	0.001
SENV-H (+)	9	20.9 %	16	16.0 %	0.476
HbsAg (+)	0	0.0 %	2	2.0 %	0.350
HCV (+)	8	18.6 %	1	1.0 %	<0.0001

Table II. SENV-D status of HCV (+) and HCV (-) patients in peritoneal dialysis and control groups. Data in the table represent the number of patients.

		SENV-D (+)		SENV-D (-)		P value
Peritoneal dialysis (n=43)	HCV (+)	2	4.6 %	6	13.9 %	0.897
	HCV (-)	8	18.6 %	27	62.8 %	
Control (n=100)	HCV (+)	0	0.0 %	1	1.0 %	0.053
	HCV (-)	5	5.0 %	94	94.0 %	

significantly more prevalent in peritoneal dialysis patients than in healthy control subjects.

The hepatitis G virus (HGV), TT virus (TTV) and SENV have been suggested as the causative viruses for acute or chronic hepatitis of unknown origin (non-A to E hepatitis). There seems to be an association between SENV and transfusion-related hepatitis, but definite evidence linking HGV and TTV to acute or chronic liver disease is still lacking (10).

Although patients on peritoneal dialysis are considered to be at high risk for blood-borne infections such as SENV or HCV, there is limited number of studies on the prevalence of SENV variants in peritoneal dialysis patients.

A high prevalence of SEN virus infection in patients on maintenance haemodialysis was reported (11). Kobayashi et al. (6) found that the prevalence of SENV (D and/or H) infection was 38% in haemodialysis patients and higher than the 22% in healthy controls. In this study, the distribution of SENV-D and -H infections did not significantly differ between the patients and the controls (SENV-D prevalence was 61% and 77% for haemodialysis patients and controls; SENV-

H prevalence was 22% and 15% for haemodialysis patients and controls) (6). In a recent study performed in Slovakia, the highest prevalence of SENV was reported for haemodialysis patient as 50% (12). In patients on maintenance haemodialysis in Taiwan, the prevalence of SENV-D and SENV-H DNA was 46.5% and 27.3%, which was significantly higher than for donors (18.3% and 5.8%, respectively; $P < 0.0001$) (13). In another study, the prevalence of SENV-H was determined to be 12.8% among patients on maintenance hemodialysis, which is nearly the same prevalence as in healthy blood donors (16.8%) (14). In a study from Poland, SENV-H was present in 40% of haemodialysis patients and in 2% of control subjects ($P < 0.0001$) (15). Serin et al. determined the prevalence of SENV-D as 10% and SENV-H as 15% among 100 blood donors in the Mersin district of Turkey (16). The prevalence of SENV-D and -H in healthy blood donors in our study was 6.0% and 17.0%, respectively, being close to the findings of Serin et al. (16). The prevalence rates of SENV-D and SENV-H in our study reflect the frequency of SENV infection in peritoneal dialysis patients in the Turkish population.

TTV, which is another novel virus isolated from patients with post-transfusional hepatitis of unknown

etiology, has also been found to have high prevalence in Spain (22.7%) (17) and in Turkey (44%) (18) in patients on continuous ambulatory peritoneal dialysis.

In the present study, we also determined whether there was an association between SENV and HCV in CAPD and the healthy control group. SENV is detected frequently in patients infected with the hepatitis C virus (HCV) but there are conflicting reports on the association and interaction between SENV and HCV (19). Umemura et al. found that the frequency of SENV was equal in HCV endemic and nonendemic regions of Japan (20). On the other hand, Rigas et al. showed in their preliminary study that coinfection with SENV is frequent in chronic HCV patients, reflecting their shared mode of transmission (9). They also showed that this coinfection of SENV with HCV might adversely affect the outcome of treatment with interferon and ribavirin. Kao et al. suggested that SENV has a specific link to HCV genotype 2a and coinfection with SENV has no effect on response to therapy with interferon and ribavirin (8). In our study, we found no relation between SENV and HCV. The prevalence of SENV-D was similar in HCV positive and negative patients in both the peritoneal dialysis and control groups.

The major limitations of the study are the small sample size and the cross-sectional design of the study. Prospective and controlled studies with a large sample size should be performed to reach a more definitive conclusion for the prevalence and clinical significance of SENV in peritoneal dialysis patients.

In conclusion, we found that SEN virus infection, and particularly the SENV-D variant, has high prevalence in patients on peritoneal dialysis in Turkey in this point-prevalence study. These patients may be at high risk for SENV hepatitis. There was no relation between SENV and HCV in this study. Care should be taken regarding SENV hepatitis and transmission of virus among peritoneal dialysis patients in clinical practice.

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