ORIGINAL ARTICLE

Incidence of acute hepatitis B in patients with spinal cord injury

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Study design: Retrospective case survey.

Objective: To examine incidence and clinical characteristics of hepatitis B infection in individuals with spinal cord injury (SCI).

Setting: Inpatient clinic within a physical medicine and rehabilitation hospital specialized in rehabilitation.

Participants: A total of 161 patients with SCI.

Interventions: Patients' records were investigated and the status of hepatitis B surface antigen (HBsAg), anti-hepatitis C virus (HCV), anti-hepatitis B surface antigen positivity, alanine aminotransferase levels, duration of hospitalization and cost were recorded.

Main outcome measures: Incidence of acute hepatitis B.

Results: Six patients were diagnosed with acute hepatitis B on the first hospitalization for rehabilitation. A total of 11 patients (4.2%) were HBsAg positive with a previously established diagnosis of hepatitis B virus infection, 1 patient (0.4%) was anti-HCV positive. After a follow-up of 6 months, three of the acute hepatitis B patients progressed into chronic hepatitis B stage. In acute hepatitis B patients' initiation of the rehabilitation was delayed, duration of hospitalization was increased.

Conclusions: After SCI, patients are at high risk of acute hepatitis B infection. A high rate of chronicity may be associated with impaired immune response, secondary to neurological deficit. Screening and vaccination protocols may prevent the spread of the hepatitis B infection, healthcare losses and financial loss.

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Keywords: hepatitis B; rehabilitation; spinal cord injury; incidence.

Introduction

Traumatic spinal cord injury (SCI) is a worldwide problem that may cause loss of motor and sensory function below the level of injury and accompanied by dysfunction of the bladder and bowel. The annual incidence of traumatic SCI in Turkey is 12.7 per million population.¹ Life expectancy of SCI is 25–45 years and has increased with advances in rehabilitation.² These individuals need hospitalization, multiple surgeries and blood transfusions in the acute and chronic periods.³ For these reasons, they have a high risk of acquiring contagious infection diseases especially viral hepatitis B and C. The aim of this study was to investigate incidence of hepatitis B (hepatitis B virus (HBV)) and C (hepatitis C virus (HCV)) in patients with traumatic SCI.

Subjects and methods

Subjects

A total of 161 subjects with traumatic SCI were reviewed from the cohort of hospitalized patients who were admitted to Ankara Physical Medicine and Rehabilitation Training and Research Hospital between March 2009 and March 2010 for rehabilitation for the first time. Non-traumatic SCI patients (malignancy, infections, iatrogenic and so on) and chronic patients were excluded. There were 119 men (73.9%) and 42 women (26.1%; median age, 29 years; range, 16–82 years) with a median duration of 7 months (range, 1 to 12 months) after traumatic SCI.

Procedures

Data of patients were collected from patients' case files retrospectively. The study was approved by the local ethics committee. Data consisted of full medical history, physical and neurological examinations, and laboratory tests. All patients had the severity of their neurological states classified according to the American Spinal Injury

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Association (ASIA) classification. Patients' classifications were 102 (63.4%) ASIA A, 18 (11.2%) ASIA B, 18 (11.2%) ASIA C and 23 (14.3%) ASIA D. The level of injury ranged from C3 to L3 with 45 patients (27.9%) with tetraplegia and 116 patients (72%) with paraplegia.

The acute hepatitis B diagnosis was based on positive serum hepatitis B surface antigen (HBsAg), immunoglobulin M antibodies to the hepatitis B core antigen and negative immunoglobulin G antibodies to the hepatitis B core antigen together with elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase). Diagnosis of chronic HBV infection was based on HBsAg positivity and a previous history of known HBV infection for at least 12 months. Expert consultation from a gastroenterologist was obtained to confirm the diagnosis and commence treatment.

Statistical analyses

All analyses were conducted using software SPSS v11.5 (SPSS Turkey, Inc., Istanbul, Turkey). A Mann-Whitney test and a Fisher's exact tests were used to compare data, where applicable. Statistical significance was accepted at $P < 0.05$.

Results

In all, 28 patients had elevated liver enzymes (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase or γ -glutamyl transferase). Six of these patients were diagnosed with acute hepatitis B on the first hospitalization for rehabilitation. In all, 11 patients (4.2%) were HBsAg positive with a previously established diagnosis of HBV infection, 1 patient (0.4%) was anti-HCV positive. All of these 12 patients with chronic hepatitis infection had liver enzymes within normal limits either due to treatment or inactive disease. After a follow-up of 12 months, three of the acute hepatitis B patients recovered from the infection and became anti-hepatitis B surface antigen positive but three of them progressed into chronic hepatitis B stage (two inactive hepatitis B, one chronic active hepatitis B with persistently elevated liver enzymes).

Status of neurological deficits during initial hospitalization; patients with acute hepatitis B were similar to other patients without HBV in terms of age and ASIA score. The time-frame between the SCI and initiation of rehabilitation was longer in the acute hepatitis B patients than non-HBV patients (Table 1).

Among patients with acute hepatitis, two of them were operated for decubitus ulcers and two received hemopneumothorax surgery. Review of the patients medical files revealed that the main reason for delay in rehabilitation was extreme fatigue encountered during the course of acute hepatitis. The second reason was a withdrawal of all potentially hepatotoxic drugs, such as non-steroid anti inflammatory drugs, anti-spasticity medicine, neurogenic bladder drugs, which are required for better treatment consistence.

Discussion

Rehabilitation aims after SCI include maximizing physical independence and preventing secondary complications.² To achieve desired results, a rehabilitation program should be initiated as soon as possible after injury. Secondary complications after SCI may interrupt the rehabilitation program, such as pressure ulcers, nosocomial infections, venous thromboses, contractures, fractures and heterotopic ossification. Patients with SCI have increased risk of infection, which is associated with re-hospitalization and mortality in the post-acute phase following SCI.^{4,5} Hepatitis infections are usually overlooked among these obstacles, even in endemic countries.

Patients with SCI may exhibit disruption of immune functions at various levels of immune response. Decentralization of autonomic system to lymphoid organs including spleen may be an important factor in disruption of immune response.⁶ SCI patients may have muted neutrophil phagocytosis, natural killer cell cytotoxicity and T-lymphocyte activation compared with healthy controls.⁷ Furthermore, degree of reduced phagocytosis and impaired B-cell functions may be correlated with level of SCI injury.^{8,9}

The hepatitis B virus infection is a global public health problem. It is estimated that there are more than 350 million HBV carriers in the world, of whom roughly 1 million die annually from HBV-related liver disease.¹⁰

HBV is the most commonly transmitted blood-borne virus in healthcare settings.^{11,12} Acute hepatitis B infections in health care settings occur through using finger stick devices for glucose monitoring, blood transfusions; subdermal electrodes for electroencephalograms; and unsafe practices while using multiple-dose vials of medications, or from surgeons, even without evidence of inadequate infection control.^{13,14}

Table 1 Comparisons of patients with acute hepatitis B, chronic hepatitis B and non-HBV patients (median (range))

	Acute HBV patients (n = 6)	Chronic HBV patients (n = 11)	Non-HBV patients (n = 143)	P
Age	33.3 (27–39)	45 (25–67)	32.9 (16–82)	NS ^a
Male/female ratio	5/1	8/3	107/36	NS ^b
Spinal cord injury to hospitalization (months)	5 (1–10)	4 (2–11)	6.5 (1–12)	NS ^a
ASIA scores at baseline (A/B/C/D)	2/0/3/1	4/1/4/2	95/16/12/20	—
Duration of first hospitalization (days)	71 (40–4583)	38 (30–52)	38 (21–73)	$\leq 0.01^a$
Cost of hospitalization	4.583 (4.010–10.473)	4.139 (1.843–4.953)	4.538 (1.363–6.949)	NS ^a
History of operation (except surgery for vertebra)	4/6	0	20/143	0.003 ^b

Abbreviations: ASIA, American Spinal Injury Association; HBV, hepatitis B virus; NS, nonsignificant.

^aBoth for acute HBV versus chronic HBV and acute HBV versus non-HBV (Mann-Whitney *U*).

^bFisher's exact tests.

NS: $P > 0.05$.

The estimated prevalence of HBsAg positivity in Turkey is 4.57%. The prevalence of HBsAg positivity among patients who apply to hospitals ranges from 1.30 to 10.88%, depending on region.¹⁵ The setting in which we conducted the study is a tertiary referral center and accepts patients from all over the country. A total of 11 patients (6.8%) had a history of known HBsAg positivity in our study. The patients with acute HBV increase the HBsAg positivity seroprevalence significantly to 9.3% among patients with-in the first year of traumatic SCI. The rate of progression from acute to chronic hepatitis B is <5% for adult acquired infection.¹⁶ In our study, progression from acute to chronic hepatitis B was 50%. Held *et al.*¹⁷ reported that in mice, SCI is associated with the disruption of immune responses due to the interruption of neural pathways that regulate immune effectors functions required to control and eliminate the mouse hepatitis virus infection. These may be the cause of a high rate of progression to chronic HBV infection along with other mechanisms mentioned above.

The patients with acute hepatitis infection were hospitalized for a prolonged period of time. No patients had liver failure during the course of the infection but severe fatigue, loss of appetite, together with decreased caloric intake, deterioration of liver functions hindering initiation of required medications for rehabilitation and inability to exercise caused delays in affective treatment for neurological deficits.

Mass vaccination for HBV was suggested by the World Health Organization in 1997 and has been included in childhood vaccination programmes in the last decade.¹⁸ Most of the adult population in many countries is not safeguarded against HBV. A recent study by Toy *et al.*¹⁵ has revealed that HBsAg seroprevalence in hospital setting varies between 1.30 and 10.88%, depending on the region in Turkey. The establishment of screening and vaccination protocols in high risk adult patients who are not included in vaccination programmes may prevent the spread of hepatitis B, health-care and financial losses.

The retrospective collection of data was the main limitation of the study. Although unlikely, there may be undiagnosed cases with acute hepatitis B.

Conclusion

Patients with SCI are frequently hospitalized, which increases the risk of hepatitis B infection, especially in medium and high endemic countries such as Turkey, Russia, China, India and some population pockets in United States of America.^{19,20} This is the first report about increased risk of high chronicity of HBV in patients with SCI. Further studies are needed to determine cost effectivity and response to hepatitis B vaccination in SCI patients.

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Conflict of interest

The authors declare no conflict of interest.

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