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Falls in Patients With Liver Cirrhosis

ABSTRACT

Health-related quality of life (HRQOL) has become an important outcome for patients with liver cirrhosis as the number of transplantation candidates increases by the progression of treatment strategies. Falls and fall-related injuries are common in patients with liver cirrhosis and negatively affect HRQOL. Many factors increase the risk for falls such as minimal hepatic encephalopathy, psychoactive drugs, muscle strength, autonomic dysfunction, hyponatremia, and sleep problems. It is important to understand the underlying mechanisms for falls in cirrhotic patients to prevent severe injuries such as fractures, decrease healthcare costs, and improve HRQOL. Healthcare professionals, including physiotherapists and nurses, should be aware of the higher risk for falls in this population and therapeutic interventions must be designed for patients, especially those waiting on the transplant list.

Management of liver cirrhosis has changed considerably by progression of treatment strategies leading to significant improvements in patient survival (Gines, Cardenas, Arroyo, & Rodes, 2004). Increased survival rates raised the number of candidates waiting for liver transplantation. As a result, health-related quality of life (HRQOL) has remarkably gained importance for cirrhotic patients as well as those with other chronic diseases (Loria, Escheik, Gerber, & Younossi, 2013). It is regarded as an outcome for the efficiency of clinical interventions and a selection criterion for liver transplantation (Les et al., 2010).

Recent studies on patients with liver cirrhosis have focused on determinants of HRQOL including physical, psychological, and social aspects. In addition to many factors such as cognitive dysfunction, ascites, hypoalbuminemia, anemia, and psychiatric comorbidities (Les et al., 2010; Hauser, Holtmann, & Grandt, 2004), falls has also been reported as an independent factor for impaired HRQOL in patients with cirrhosis (Roman, Cordoba, Torrens, Guarner, & Soriano, 2012).

Falls in Patients With Liver Cirrhosis

Falls and fall-related injuries are common in chronic liver diseases (Frith et al., 2010, 2012). "Hepatic osteodystrophy" is extremely common in patients with chronic liver diseases and cirrhotic patients show an approximately twofold relative increase in the risk of fracture, regardless of the etiology of cirrhosis (Luxon, 2011). Frith et al. (2010) reported a fall history in 72% of the patients with primary biliary cirrhosis. Seventy percent of the patients who had fallen in that study were injured, including bone fractures and hospital admissions (Frith et al., 2010). Prevalence of fractures has been reported to be between 3% and 22% in cirrhotic patients, regardless of the etiology, leading to high morbidity and mortality rates (Tsai et al., 2013). Therefore, it is very important to clarify underlying mechanisms and prevent falls in patients with liver cirrhosis to improve patients' quality of life, preserve physical functions, and diminish healthcare costs.

The World Health Organization defines a *fall* as "an event which results in a person coming to rest inadvertently on the ground or floor or other lower level" (World Health Organization, 2012). Simply, falls occur as a result of inability to maintain posture. Previous

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studies showed a deterioration in postural control of cirrhotic patients, which was correlated to disease severity (Aref, Naguib, Hosni, & El-Basel, 2012; Schmid et al., 2009). Moreover, postural instability and gait impairments were reported as the early signs of "chronic Parkinsonism associated with liver cirrhosis," which was found in nearly 21% of patients in the study by Burkhard, Delavelle, Du Pasquier, and Spahr (2003). Similarly, Jover et al. (2005) evaluated 46 cirrhotic patients using the Unified Parkinson's Disease Rating Scale; 22 patients showed extrapyramidal signs.

Assessment of postural stability by either objective methods or clinical tools may help to detect fall risk. Frith et al. (2010) reported poor balance as a significant risk factor for falls in patients with primary biliary cirrhosis. However, very few studies focused on balance and postural control of patients with cirrhosis. Schmid et al. (2009) and Aref et al. (2012) used posturography (a gold standard method to assess postural stability) to detect disturbances in balance and postural control in patients with liver cirrhosis. Unfortunately, this computerized system is expensive and not available for every setting. Therefore, functional clinical tools such as the Berg Balance Scale, Timed Up & Go Test, Sit-To-Stand Test, or specific questionnaires for fall risk can also be used. Soriano et al. (2012) assessed cirrhotic patients with the Timed Up & Go Test and recorded longer test durations for patients categorized as "fallers" with cognitive dysfunction in comparison to "nonfallers."

Risk Factors for Falls in Patients With Liver Cirrhosis

Minimal Hepatic Encephalopathy

Minimal hepatic encephalopathy (MHE), clinically manifested as "cognitive dysfunction," is one of the most investigated parameters related to fall risk in patients with cirrhosis. Soriano et al. (2012) reported a 40.4% fall incidence in cirrhotic patients with cognitive dysfunction whereas it was only 6.2% in patients without cognitive dysfunction. In another retrospective study, incidence of falls in patients with MHE was reported as 40%. According to the same study, primary healthcare services were required in 8.8% of the cases and 6.6% of the patients needed hospitalization because of falls (Roman, Cordoba, Torrens, Guarner, & Soriano, 2011).

The effect of cognitive dysfunction on fall risk was also studied using posturographic analyses. Aref et al. (2012) assessed patients with dynamic posturography and found a deterioration in balance control in relation to the degree of hepatic encephalopathy. Similarly, Schmid et al. (2009) indicated a worse postural control in patients with hepatic encephalopathy, which was correlated with disease progression.

Minimal hepatic encephalopathy impairs attention, coordination, and orientation, and affects daily activities, work performance, and motor functions such as driving (Bajaj et al., 2008). Falls probably occur as a result of similar mechanisms in patients with MHE mainly because of increased reaction times and motor slowing.

Psychoactive Drugs

In relation to MHE, patients on psychoactive medication showed higher fall incidence. The association between MHE and falls was stronger in patients on psychoactive drugs (Roman et al., 2011). Soriano et al. (2012) found higher frequency of falls in patients taking psychoactive drugs, which was also related to abnormal psychometric hepatic encephalopathy scores.

Cirrhotic patients use various psychoactive medications for depression, fatigue, neuropsychiatric symptoms of hepatic encephalopathy, and sleep disorders (Bianchi et al., 2005). Therefore, the possible effects of psychoactive drugs on falls should be addressed in further studies as they have side effects such as postural dizziness, hypotension, somnolence, motor slowing, attention deficits, and cognitive dysfunction, which may independently increase the risk for falls.

Muscle Strength

Loss of skeletal muscle mass is one of the most common complications of liver cirrhosis. It affects HRQOL, outcomes after liver transplantation, and even survival. The term "hepatic cachexia" refers to a loss of muscle mass or loss of fat mass or a combination (Dasarathy, 2012). The multifactorial mechanism for muscle loss in liver cirrhosis has not yet been clearly defined; but, it is known that whole body protein turnover is altered in cirrhosis. Poor dietary intake, malabsorption, increased intestinal protein loss, decreased hepatic protein synthesis, abnormal substrate utilization, and hypermetabolism lead to "protein-energy malnutrition" in cirrhosis (Peng et al., 2007). Energy demand is supplied by muscle proteins and fats because of the dysfunctions in gluconeogenesis and glucose storage.

Additional effects of muscle mass loss and mitochondrial dysfunction decrease muscle strength and endurance in cirrhotic patients. A reduced number of mitochondria and decreased mitochondrial oxidative capacity results in mitochondrial dysfunction, which is thought to be one of the reasons for "peripheral fatigue" (Hollingsworth et al., 2008; Jacobsen, Hamberg, Quistorff, & Ott, 2001).

The other mechanism for muscle strength loss may be hemodynamic alterations due to autonomic dysfunction specifically in some etiologies of cirrhosis. Blood pressure changes, especially relative hypotension, may result in hypoperfusion in peripheral muscles,

leading to decreased muscle endurance and peripheral fatigue (Newton, Pairman, Wilton, Jones, & Day, 2009). Because muscle performance is sensitive to alterations in perfusion pressure between physiological limits during low workloads, the ability of a muscle to generate force may decline as the perfusion pressure decreases (Wright, McCloskey, & Fitzpatrick, 2000).

Previous studies found significant decreases in hand-grip, lower extremity, and respiratory muscle strength in cirrhotic patients (Galant, Forgiarini, Dias, & Marroni, 2012; Jones, Coombes, & MacDonald, 2012). Frith et al. (2010) and Soriano et al. (2012) showed a relationship between fall risk and lower extremity muscle strength in patients with cirrhosis. Further studies are required to assess the possible effects of muscle loss on fall risk and postural stability in liver diseases.

Autonomic Dysfunction

"Autonomic dysfunction" is frequent in primary biliary cirrhosis and nonalcoholic fatty liver disease. Decreased baroreceptor sensitivity and altered blood pressure responses result in orthostatic symptoms (Lhuillier et al., 2006). Changes in electrolyte homeostasis, alterations in responses to vasoconstrictors and dilators, and disorders in arteriovenous circulation contribute to autonomic dysfunction in chronic liver diseases clinically manifested as postural dizziness, syncope, diminished cognition, fatigue, falls, urinary incontinence, and sexual dysfunctions (Frith & Newton, 2009). Even though it is not possible to generalize the results for all etiologies of cirrhosis, autonomic dysfunction has been reported as an independent risk factor for falls in patients with primary biliary cirrhosis and in elderly cirrhotic patients (Frith et al., 2010, 2012).

Hyponatremia

An abnormal regulation of body fluid homeostasis in patients with cirrhosis results in "hyponatremia." It is defined as a reduction of serum sodium less than 130 mmol/L for liver diseases, whereas normal serum sodium level is 135–145 mmol/L. The prevalence of hyponatremia in cirrhosis defined as serum sodium level lower than 130 mmol/L is 21.6%, whereas it increases up to 49.4% if the cutoff level of 135 mmol/L is used (Gines & Guevara, 2008).

Two types of hyponatremia develop in patients with cirrhosis (Angeli, Wong, Watson, & Gines, 2006). "Hypovolemic hyponatremia" occurs because of extracellular fluid loss from the kidneys and gastrointestinal system. In this type, low serum sodium is associated with plasma volume contraction, signs of dehydration, and prerenal azotemia. Encephalopathy frequently occurs in this type, whereas edema and ascites are absent. In "hypervolemic or dilutional hyponatremia," extracellular fluid volume and plasma volume increase causing edema and ascites to occur (Gines & Guevara, 2008). Although the direct relation between hyponatremia and fall risk in cirrhosis has not been studied yet, fall incidence was reported higher in hyponatremic cirrhotic patients in comparison with patients with normal level of serum sodium in addition to lower scores in physical and mental domains of HRQOL (Sola et al., 2012). Similarly, in healthy adults and especially in the elderly, low serum sodium level is associated with falls and fall-related fractures as a consequence of attention deficits and balance and gait abnormalities (Renneboog, Musch, Vandemergel, Manto, & Decaux, 2006). Therefore, future studies should be designed to explore the possible effects of hyponatremia on fall incidence in patients with cirrhosis.

Sleep Problems

Patients with liver diseases suffer from a wide range of sleep disorders (De Cruz, Espiritu, Zeidler, & Wang, 2012). Studies showed lower sleep quality and "daytime somnolence" in cirrhotic patients (Montagnese, Middleton, Mani, Skene, & Morgan, 2009). Sleep problems mainly arise from hepatic encephalopathy and fatigue. However, the exact mechanism has not been clarified. One of the two existing hypotheses suggests "central mechanisms," such as decreased cerebral sensitivity to darkness and brightness due to circadian rhythm abnormalities. The other hypothesis, "peripheral mechanism," considers the effect of decreased melatonin clearance (Montagnese, Middleton, Mani, Skene, & Morgan, 2010).

The effect of sleep problems on fall risk in patients with liver cirrhosis has also not been investigated. However, Newton and Jones (2012) reported a relationship between sleep disorders and functional impairments in patients with primary biliary cirrhosis and nonalcoholic fatty liver diseases. Effect of excessive daytime sleepiness on attention and steadiness is already known. Studies of patients with Parkinson's disease and the community-dwelling elderly suggest the same hypothesis for patients with cirrhosis (Spindler et al., 2013; Stone et al., 2014).

Summary

Falls are multifactorial for patients with liver cirrhosis (Figure 1). Prevention of falls is very important for cirrhotic patients as they result in a wide range of injuries from contusion to fractures. Falls and fall-related injuries create economic and social burden not only to patients but also to their families by delayed recovery process and increased healthcare costs.

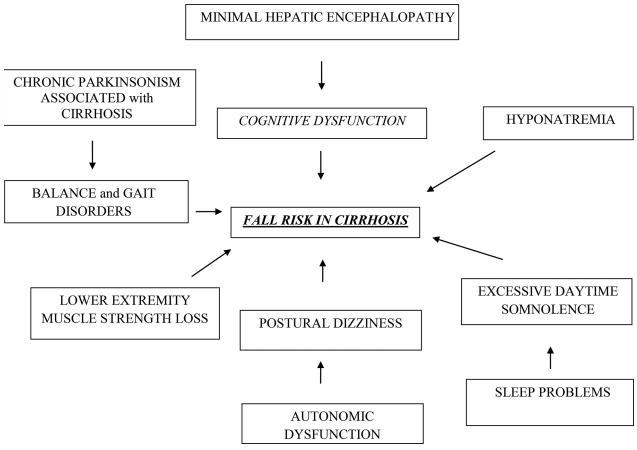

FIGURE 1. Possible risk factors for falls in patients with liver cirrhosis.

All healthcare professionals, including physiotherapists and nurses, should be aware of the higher fall risk in cirrhotic patients, whether during their hospital stays or daily life. Exercise programs, therapeutic interventions, and patient/caregiver education should be designed to prevent falls and fall-related injuries, especially for patients waiting on the transplantation list. ✪

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