Prevalence and Treatment of Neuropathic Pain in Kidney and Liver Transplant Recipients

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Abstract

Objectives: Neurologic complications are common after kidney and liver transplant. Neurologic complications affect mortality and morbidity in transplant recipients, and neuropathic pain is an important symptom affecting a patient’s quality of life. The aim of the present study was to provide readers with our experience regarding causes and treatment of neuropathic pain in patients undergoing kidney and liver transplant at our transplantation center.

Materials and Methods: The medical data of 553 kidney transplant recipients and 258 liver transplant recipients who received transplant procedures at the Başkent University Transplantation Center between 2008 and May 2016 were retrospectively reviewed. Fifty-one patients who were examined by an expert neurologist and diagnosed with neuropathic pain on the basis of clinical, neurologic examination, and laboratory findings were included for analyses.

Results: Among 811 transplant recipients, 51 patients (6.2%) were diagnosed with neuropathic pain. Of these, 22 were female and 38 were male patients, and 42 were kidney transplant recipients and 9 were liver transplant recipients. Causes of neuropathic pain included uremia, diabetes mellitus, ischemic peripheral arterial disease, inflammatory neuropathy, vasculitis, discopathy, postherpetic neuralgia, carpal tunnel syndrome, and multiple myeloma. Patients with symptoms too mild to affect daily life activities were treated conservatively. Plasmapheresis, gabapentin, pregabalin, alpha-lipoic acid, and duloxetine were administered as treatment modalities and medications.

Conclusions: Neuropathic pain was lower in our transplant recipients than in the general population. Treatment medications were effective for transplant recipients at lower doses for the management of neuropathic pain impairing quality of life than doses for the general population.

Key words: Liver failure, Neuropathy, Renal failure, Solid-organ recipients

Introduction

Neurologic complications are an important cause of mortality and morbidity in solid-organ recipients.1 A lesion or a disease of the somatosensorial system may cause neuropathic pain, which has a prevalence of 7% to 8% in the general population.2 The causes of neuropathic pain in transplant recipients include uremia, diabetes, inflammatory disorders, conditions secondary to immunosuppressive agents, zona zoster infections, cancer, and central disorders such as stroke and spinal cord injuries.3-6

Materials and Methods

Laboratory and electrophysiological findings, neurologic examination findings, diagnostic properties, and treatment modalities of 553 kidney transplant recipients and 258 liver transplant recipients who underwent transplant procedures at Başkent University Transplantation Center between 2008 and May 2016 were retrospectively reviewed. Patients diagnosed with neuropathy by a neurology expert were included in our analyses.

Statistical analyses

Statistical analyses were performed with SPSS software (version 16.0 for Windows, SPSS, Inc, Chicago, IL, USA). Data are expressed as percentages for categorical variables.

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Among 811 transplant recipients 51 (6.2%) were diagnosed with neuropathic pain. Of these, 22 were female and 29 were male patients (Table 1). Of 51 patients, 42 (82.3%) had kidney transplant and 9 (17.7%) had liver transplant procedures (Table 2).

Causes of neuropathic pain included uremia, diabetes mellitus, ischemic peripheral arterial disease, inflammatory neuropathy, vasculitis (Sjögren syndrome), discopathy, postherpetic neuralgia, carpal tunnel syndrome, and multiple myeloma (Table 3).

As expected, uremia and diabetes mellitus were the most common causes of neuropathic pain in kidney transplant recipients. Two patients developed peripheral ischemic injury secondary to diabetes and had severe neuropathic pain. Postherpetic pain secondary to zona zoster infection was considered to have occurred secondary to immunosuppressive agent use. A patient was diagnosed with vasculitic neuropathic pain secondary to Sjögren syndrome. Two patients had neuropathic pain secondary to discopathy; 4 patients had neuropathic pain associated with carpal tunnel syndrome, 1 patient had multiple myeloma as cause, 5 patients had neuropathic pain secondary to immunosuppressive medication use, and 2 patients had demyelinated neuropathy and associated neuropathic pain (Table 3).

Three liver transplant recipients had neuropathic pain secondary to diabetes, 1 secondary to postherpetic neuralgia, 1 secondary to lumbar discopathy, and 3 secondary to immunosuppressive agents (Table 3).

Treatment agents included α-lipoic acid, duloxetine, gabapentin, pregabalin, and plasmapheresis (Table 4). Tests of solid-organ function showed no adverse associations with medication use during follow-up. Gabapentin and pregabalin were monitored using renal function tests, and duloxetine and alpha-lipoic acid were monitored using liver function tests.

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Thirteen kidney transplant recipients received nonpharmacologic conservative therapy (hand-wrist splints, exercise, corset, vigorous blood glucose monitoring and control). Two patients were treated with duloxetine at 30 mg/day. Five patients were administered pregabalin at 25 mg, with 3 patients having doses increased to 75 mg/day. Twelve patients were started on gabapentin at 100 mg/day, with 6 of these patients subsequently needing a dose as high as 300 mg/day. Eight patients with diabetic neuropathy were given alpha-lipoic acid. Two patients (one had quadriplegia and the other had paraparesis) were diagnosed to have developed acute inflammatory demyelinating neuropathy, which occurred after episodes of diarrhea. Both patients had plasmapheresis followed by physical rehabilitation, after which patients showed nearly total recovery from neurologic deficits. All liver transplant recipients received medical treatment for neuropathic pain. Seven patients received gabapentin 100 mg/day, which had to be increased to 300 mg/day for 2 recipients and to 600 mg/day in another recipient. Other patients were started on pregabalin 75 mg/day, which had to be increased to 150 mg/day in 2 recipients (Table 4).

Discussion

Past work has shown the prevalence of neuropathic pain after transplant to be 1% to 2%. Fernandez-
Ramos and associates reported a neuropathic pain prevalence of 1.4% among 140 solid-organ transplant recipients.\(^1\) Derle and colleagues found a prevalence of peripheral neuropathy of 1.7% after liver transplant.\(^6\) We found a neuropathic pain prevalence of 6.2%. This was brought about by a greater number of patients with diabetes and the longer follow-up (as long as 8 years among transplant recipients). No consensus has been reached yet as to how neuropathic pain should be treated in transplant recipients. In transplant recipients, preservation of the transplanted organ is a priority. In these patients, it is also more common for medications to reach toxic levels due to the use of multiple medications and limited organ function.\(^2\) We preferred to use conservative treatment (ie, no medications) for neuropathic pain that was not severe enough to affect daily life.

Mour and associates reported that medications used after transplant procedures and newly developed infections increase the rate of neurologic complications.\(^3\) Ce and colleagues reported that neurologic complications occurred at a rate of 16% in transplant recipients and found that immunosuppressive-associated herpes zoster was the most common cause of neurologic complications.\(^5\) Potluri and associates reported that multiple medications, impaired cellular immunity, accelerated atherosclerosis, and frequent metabolic abnormalities increase the prevalence of neurologic complications.\(^4\)

In our patients, medication-induced neuropathy was the result of postherpetic neuralgia, whereas inflammatory neuropathy was related to immunosuppressive agent use.

No consensus exists for the treatment of neuropathic pain in solid-organ transplant recipients.\(^2\) In these patients, it is of great importance to preserve the transplanted organs; hence, we administered and maintained the lowest possible doses of medications against neuropathic pain and followed liver and kidney functions closely.

The efficacy of gabapentin and pregabalin for pain relief was comparable. Because these have a high level of evidence against neuropathic pain,\(^7\) we used these agents for most of our patients. Former studies have reported that gabapentin and pregabalin were more efficacious at doses of 600 mg/day and 150 mg/day; however, we observed pain relief at lower doses.\(^7\) In some of our patients, borderline organ functions may have increased plasma concentrations of these medications. Duloxetine was found particularly efficacious in diabetic patients,\(^8\) although hepatotoxicity has been associated with its use.\(^9\) We therefore avoided using this agent in liver transplant patients. We administered duloxetine in 2 diabetic kidney transplant recipients and obtained analgesic effects at a dose of 30 mg/day.

Alpha-lipoic acid is mainly used for diabetic neuropathy because of its antioxidant properties. Some studies have confirmed its role in the prevention of disease progression and as a neuroprotective agent.\(^10\) A recent study demonstrated that alpha-lipoic acid may protect against ischemia-reperfusion injury in patients undergoing kidney and pancreatic transplant.\(^11\) We also used alpha-lipoic acid and observed no adverse effects in 8 patients who had undergone renal transplant.

In conclusion, we found the prevalence of neuropathic pain to be lower in our transplant recipients than in the general population. Patients with neuropathic pain responded to low-dose medications.

References