Retrospective review of the safety of Hizentra in neuromuscular patients with renal failure

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Introduction

Patients with a variety of neuromuscular diseases require immune globulin as part of their treatment regimen. All forms of immune globulin, however, contain a black box warning for the potential for renal failure. This risk is increased in patients with pre-existing renal disease and often makes it impossible to treat these patients with intravenous immune globulin. Treatment options then have to include corticosteroids or other immunosuppressive medications which may be contraindicated in patients with other comorbid diseases. To date there is no data on the safety of subcutaneous immune globulin in patients with renal disease.

Methods

Three patients with neuromuscular diseases who had renal failure were treated with Hizentra. Patients were monitored with labs to evaluate electrolytes and glomerular filtration rate as an estimation of their ongoing renal function. Patient also received neurologic exams to determine if the Hizentra was adequately managing their neuromuscular diseases.

Case1. A 56 year old male who was status post renal transplant and graft versus host disease developed progressive motor and sensory deficits over 4 months to the point that he was wheelchair bound. Nerve conduction studies showed a severe demyelinating neuropathy consistent with CIDP. The patient was on Tacrolimus, cyclosporine, and prednisone as well as other medications. He had significant chronic renal disease with a GFR of 37 (normal >60). He responded initially to 5 cycles of plasmaphresis but did not want ongoing plasmaphresis as he had been on dialysis in the past. His transplant team did not want to add additional immunosuppressive medication and his nephrologist was concerned about the risks of intravenous immune globulin. He was started on Hizentra 5 grams twice a week for three months and had continued improvement in his strength to the point that he was able to walk with a walker. He has continued on Hizentra for over 1 year and has had a return to normal strength in all muscle groups except for his distal legs which remained weak at 2-3/5. His renal function has improved with a recent GFR of 47. He has had no ~~other~~ significant side effects from the Hizentra.

Case 2. A 65 year old woman developed ptosis, diplopia, and proximal muscle weakness. She was diagnosed with myasthenia gravis and evaluation revealed a stage IV thymoma. She underwent thymectomy and was started on prednisone, mestinon, and chemotherapy. She did well for approximately two years but then had recurrence of her thymoma requiring more aggressive chemotherapy. This led to a worsening of her myasthenia symptoms with increased weakness to the point that she was unable to ambulate independently and needed a walker. She had mycophenylate added to her prednisone and mestinon and she was started on 2 grams/kg/month of IVIG and had a marked improvement in her myasthenia. However during the first six months of therapy she developed progressive renal dysfunction. Her GFR fell from 67 to 29 and the IVIG was stopped. She then developed increased muscle weakness and she was started on Hizentra 10 grams twice a week. She has continued on this dose for six months and her GFR has stabilized at 30. Her MG symptoms are well treated now and she has been able to taper off of the prednisone.

Case 3. A 37 year old male with diabetes developed progressive weakness and numbness. Nerve conduction studies revealed that he had CIDP and he was started on IVIG 2 grams/kg/month. He had an excellent recovery in his strength over the next six months and the IVIG was tapered down to 1 gram/kg/month. He continued on this dose for 14 months. However he developed progressive renal failure with a GFR that declined from 70 to 47. He was switched to Hizentra 10 grams twice a week with excellent management of his symptoms. His GFR remained stable at 49 and he had no side effects from the Hizentra.

Figure 1.

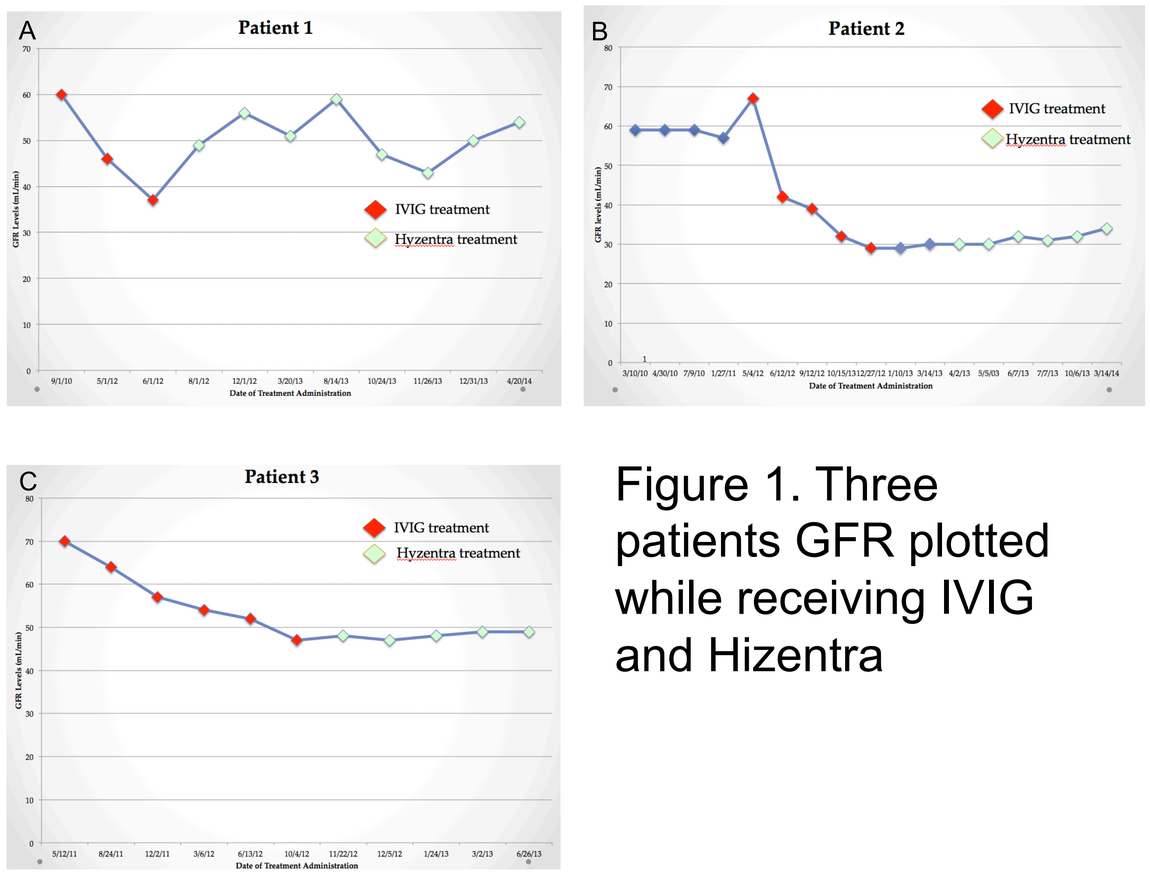

Figure 1. Three patients GFR plotted while receiving IVIG and Hizentra

Conclusions

All forms of immune globulin contain the same warning concerning the risk of renal failure particularly in patients with pre existing renal disease. This risk is believed to be higher in patients who receive products that contain sucrose. Therefore patients with pre-existing renal disease or patients who develop renal dysfunction while on intravenous immune globulin present a difficult therapeutic dilemma.

One theory concerning the development of renal dysfunction in patients receiving IVIG has to do with the osmotic load that the renal tubules are exposed to when receiving intravenous immune globulin. The estimates are that renal dysfunction may occur in as many as 6.7% of patients receiving IVIG (1) Therefore it is recommended that renal function be monitored in any patient receiving immune globulin.

We present three patient who had significant renal dysfunction while receiving IVIG who we chose to treat with Hizentra subcutaneously. These patients had Myasthenia Gravis or CIDP and had a good clinical response to Hizentra with stabilization of their renal function.

Although further and larger studies are needed we believe that delivering Hizentra subcutaneously may be able to be used in patients with renal dysfunction. However close observation for progressive renal decline is mandatory.

Bibliography

1. **Levy, JB; Pusey CD. Nephrotoxicity of Intravenous Immunoglobulin. QJM 2000 Nov;93(11) 751-55.**