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Short Communication
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Treatment of Painful Peripheral Neuropathy with Erenumab - An Observational Study

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Abstract

Introduction: Painful peripheral neuropathy is usually an acquired condition with significant morbidity and inadequate treatment. In this study, we aimed to determine if blocking CGRP receptors present at the Dorsal Root Ganglion (DRG) with erenumab would benefit patients.

Methods: We treated 15 subjects, mostly diabetic and idiopathic etiologies of painful neuropathy with erenumab 140 mg subcutaneously on a monthly schedule for 3 months. A washout period of 1 month of previous failed conventional therapies prior to our study was required. Using a 2 tailed paired t test, we analyzed the reduction in numeric pain score from baseline. Adverse effects were recorded.

Results: The overall reduction in baseline neuropathic pain over 3 months in 13 subjects was 69.8%, ($p<0.05$). Two patients were non-responders. One patient had transient injection site pain.

Conclusion: Compared to previous conventional therapies, erenumab was associated with a faster and more effective reduction in neuropathic pain with almost no adverse effects. These findings underscore the need for a large placebo-controlled study to determine if erenumab should be the preferred treatment of painful peripheral neuropathy.

Keywords: Erenumab; Cgrp; Painful neuropathy

Introduction

Calcitonin Gene-Related Peptide (CGRP) is a neuropeptide that exists in Trigeminal Ganglia (TG) and mediates neurogenic inflammation and the transmission of trigeminovascular nociceptive signal from intracranial vessels to the central nervous system. Erenumab is a CRRP- receptor monoclonal antibody which is Food and Drug Administration (FDA) approved for the preventative treatment of migraine. It has an excellent safety profile, impressive efficacy data, and can be effective as quickly as one week, and has virtually no adverse effects except for very low incidence of injection site reactions (5%) and constipation 1% to 3%. The risk of hypertension is 0.14/100 patient years [1].

CGRP and its receptor are also widely expressed in sensory nerves with cell bodies in the Dorsal Root Ganglion (DRG), somatosensory and autonomic peripheral nerves, and in A delta and C-fiber peripheral nerves [2]. Therefore, in patients with painful distal small or large fiber sensory neuropathy, reduction in pain could be expected by blocking CGRP ligand or its receptor at these sites. Kang et al. had recently demonstrated that patients who were treated with erenumab for migraine who had concomitant painful peripheral neuropathy, had significant reduction in neuropathic pain [3]. After obtaining IRB approval from our institution, we treated and assessed the efficacy of erenumab in reducing pain from peripheral neuropathy who did not have migraine.

Methods

Fifteen patients with painful neuropathy were treated with erenumab 140 mg subcutaneously after a 4-week washout period of previous failed analgesic medications. Of the 15 patients, etiology of the painful peripheral neuropathy was idiopathic in 7 (46%), diabetes in 7 (46%), and long COVID in 1 (8%). The average age was 48, (age range 44 to 85). Diagnosis was established by history, examination, laboratory testing, and electrodiagnostic testing. Baseline Numeric Pain Scale (NPS) measurements and vital signs were taken. Patients were excluded if they were pregnant, attempting conception, or under 18 years. Patients returned for follow-up in one month. If they had a significant response, erenumab dosing was continued for 2 additional monthly doses. We monitored injection site reactions, elevations in blood pressure, and any other adverse effects. The statistical significance of the changes in NPS from baseline to the end of 3 months was analyzed with a 2-tailed paired *t* test.

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Table 1: NPS scores at 3 months of monthly treatment (P<0.05).

Age/Sex (n=15)	Etiology of Painful Neuropathy	Baseline NPS1-10	NPS 30 days post 1st erenumab 140 mg sq dose	NPS 30 days post 2nd erenumab 140 mg sq dose	NPS 30 days post 3rd erenumab 140 mg sq dose	Adverse Reactions
54 F	CAN-idiopathic	8	0	0	0	Transient injection site pain
48 M	SFN-diabetes	8	3	3	0	None
85 F	CAN-idiopathic	9	3	3	3	None
62 F	SFN-idiopathic	10	10			
44 F	SM Neuropathy-Diabetes	10	6	4	4	None
50 F	SM Neuropathy-Diabetes	9	4	3	2	None
46 F	SM Neuropathy-Diabetes	9	2	2	2	None
65 F	SM Neuropathy- Diabetes	9	3	3	3	None
64 M	CAN-Idiopathic	7	2	2	2	None
65 F	CAN-idiopathic	9	9			
72 M	SM Neuropathy-Diabetes	9	6	3	3	None
66 M	SFN- Idiopathic	9	7	7	6	None
37 M	Long Covid SFN	7	3	2	2	None
75 F	SM Neuropathy-Diabetes	9	9			
59 F	CAN-Idiopathic	8	4	4	4	None

CAN: Chronic Axonal Neuropathy; SM: Sensor-Motor; SFN: Small Fiber Neuropathy

Results

With treatment of erenumab, 13 patients reported a 69.8% decrease in NPS scores at 3 months of monthly treatment (P<0.05). All 13 responders responded to the first dose of erenumab after one month and maintained the response by month 3. Two patients had no response to erenumab. Except for transient injection site pain in one patient, no other adverse effects were reported see Table 1.

Discussion

This study provides strong evidence that an important physiologic function of CGRP seems to be its association with pain transmission and modulation. It is found in high concentrations in nociceptive A delta and C-fiber DRG and TG neurons and in their terminals in the outer laminae of the spinal cord dorsal horn. Erenumab impressively reduced neuropathic pain without any adverse effects in most of our patients. The rapid response within a month and sustained after 3 months mirrors the efficacy seen in patients with migraine. Erenumab works by blocking the CGRP receptor and has no independent analgesic activity.

Limitations of our study is inherent on the small sample size without a placebo-controlled cohort. However, erenumab was already extensively studied with a placebo-controlled cohort and was FDA approved for the treatment of episodic and chronic migraine. Other etiologies of painful neuropathy such as alcohol, or autoimmune states were not included. But most of our cases were diabetes and idiopathic which is the most prevalent cause of peripheral neuropathy. The 3-month duration was modeled after the sustained effect with peak efficacy in the first week seen in the migraine studies. Patients were given the option of continuing erenumab after the 3-month study period ended.

Despite several available therapies, treatment of neuropathic pain is inadequate. Meta-analyses, indicate that only a minority of patients with painful neuropathy have an adequate response to pharmacological treatment and that most drugs have intolerable side effects [4]. All of our patients were debilitated by painful neuropathy. They all attempted conventional therapies such as Gabapentin, Pregabalin, Duloxetine and Tricyclic antidepressants. The results were either unsuccessful reduction in neuropathic pain, or intolerable adverse effects such as sedation, weight gain, or cognitive dysfunction. Erenumab was far more effective, worked within 4 weeks (in most cases within 1 week), and had virtually no adverse effects. A large placebo-controlled study is warranted to determine if erenumab should be the preferred drug for the treatment of painful neuropathy.

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