

Role of Pregablin in Neuropathic Pain

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ABSTRACT

Objective: To evaluate the role of pregablin in neuropathic pain

Study Design: Prospective descriptive study

Place and Duration of Study: This study was conducted in the department of medicine of Al-Tibri Medical College & Hospital from Jan. 2011 to Jan 2012.

Materials and Methods: A prospective study conducted in a private hospital of Karachi from Jan 2011 to Jan 2012. A total 107 cases were enrolled. All patients are adult above 18 years of age. The neuropathic pain was analyzed by Leeds Assessment of Neuropathic symptoms & sign (LANSS). The pain was assessed by numeric pain rating scale. The data was recorded on a preset performa. Primary disease was also controlled and all the patients were given pregablin 50-150mg/day for two-six weeks. The symptoms were re assess by numeric pain scale. The SPSS 16 used to analysed.

Results: Total number of patients were 107. Male were 52 while female were 55. The patients were grouped according to pathology. The most common pathology was Diabetes in 49 cases (45.79%) followed by hypertension in 35 cases (32.71%) and herpes zoster in 27 cases (25.23%). The age ranges from 42-72 years with mean age is 56.66 ± 16 . The dose ranges from 50-150 mg per day and the duration of treatment were two- six weeks. The pregablin was superior in relieving pain and sleep in patient with diabetic neuropathy and post herpetic neuralgias. The adverse effects noted were somnolence, lethargy and ataxia. Two of the cases were stopped treatment due to somnolence.

Conclusion: The result of adding pregablin in the treatment of a patient with neuropathic pain was very successful and it is improving the quality of life and sleep.

Key Words: Neuropathic pain, pregablin, neuropathy

INTRODUCTION

The chronic disease like diabetes mellitus and hypertension really detoriate the life of a patient inspite of good control. The acute disease like Herpes Zoster, trauma and prolapsed intervertebral disc really hamper the ease of a person and lead to very painful situation. Lesions of the peripheral¹ or central nervous pathways for pain typically result in a loss or impairment of the pain sensation but if somehow, damage or dysfunction occurs to these pathway it will lead to a pain call “Neuropathic Pain”.² Damage to peripheral nerves as occur in Diabetic neuropathy or to the primary afferents as in herpes zoster.

Neuropathic pain³ typically have an unusual burning, tingling or electric shock like quality and may be triggered by very light touch. They may have sensory deficit or hyperpathia. A variety of mechanism contribute to neuropathic pain. The increased sensitivity and spontaneous activity is due to increased sodium channels which sensitized the primary afferent nociceptors and damaged primary afferents. Damage primary afferents may also develop sensitivity to norepinephrine.

Patients will peripheral nerve injury can develop a severe burning pain in the region innervated by the nerve. The pain typically begins after a delay of hours

to days or even weeks. The ideal treatment for any pain is to remove the cause. Sometimes treating the underlying condition does not immediately relieve pain. Some conditions are so painful that rapid and effective analgesia is essential. Analgesics are the first line of treatment like NSAIDs but they have their own side effects in longer use. Sometimes opioiods are also used as potent pain relieving drugs. Opioids produce analgesia by actions in the central nervous system. They activate pain inhibitory neurons and directly inhibit pain transmission neurons⁴.

Pregablin^{5 6 7} is a structural derivative of the inhibitory neurotransmitter gama aminobutyric acid (GABA). Pregablin is structurally related to gabapentin is structurally related to gabapentin and has a similar pharmacological profile and anticonvulsant and analgesia activity. The predominant mechanism of action is thought to be through its presynaptic binding to the $\alpha 2 \delta$ ^{8 9} subunit of voltage gated calcium channels which in turn leads to reduced release of neurotransmitters e.g. glutamate and substance P. The oral bioavailability^{10 11} is 90 % and dose independent. It does not bind to plasma protein and this readily penetrates the blood brain barrier. Over 98% of pregablin is not metabolized in the liver. It is well tolerated with slight G.I. upsets, ataxia and somnolence are the only side effects.

Among treatment non opioids medication have been found effective, pregablin¹² beside tricyclic antidepressant (TCA) are considered first line therapy for neuropathic pain and it is preferred over TCA if patient has a history of congestive cardiac failure or arrhythmias or if there is risk of suicide.

METHODS & MATERIALS

A prospective study conducted in a private hospital a 300 bedded hospital Al Tibri Medical Hospital affiliated with Al Tibri Medical College in the vicinity of district Malir Karachi. Duration of the study was one year from Jan.2011 to Jan. 2012. A total of 107 cases were enrolled. All patients were adults. Patients attended OPDs were taken only. The patients were having other primary pathologies that were specifically managed. We included and excluded neuropathic pain according to history, examination, routine test like blood complete picture, renal profile, liver profile, and special tests like RBC folate, serum B 12 level, NCV, EMG, MRI Screening spine. The neuropathic pain was assessed by Leeds Assessment of neuropathic symptoms & sign (LANSS). The pain was assessed by Numeric pain rating scale. The patients were followed for a period of six weeks.

Damage or dysfunction of peripheral or central neurons pathways can produce neuropathic pain. For example damage to peripheral nerves as occur in diabetes neuropathy or to primary afferents as in herpes zoster in the peripheral; nerves system while in central nerves system pain may be produced by damage to spinothalamic pathways or thalamus as in stroke, multiple sclerosis and spinal cord injury.

All patients were seen by one of the author at hospital. For primary disease associated examination and detailed neurological examination besides detailed medical history was taken and blood test were done. All data were recorded manually and management plan was established and weekly follow ups were advised which were thoroughly followed for six weeks. Except two cases were stop treatment because of somnolence.

The data was collected on a preset performa and analyzed by one of the author using SPSS version 16.

RESULTS

During the study medical data of 107 patients were analyzed. Male were 52(48.5%) while females were 55(51.5%). Mean age was 56.66 ± 16 , (range 42-72years). The patients were divided into groups according to their primary pathologies. As the diseases were chronic so longer the disease more will be the complications. Basic data was given in Table No.1

Among 107 patients, there were eight big groups of diseases i.e. diabetes mellitus, hypertension, and herpes zoster comprised of more than 60% of the cases. The dose was range 50-150mg/day. The dose was once or

twice daily. The duration of the treatment was from two to six weeks. Most of the patients had been benefited from the first week of the pregablin was added.

The diabetes neuropathy were in 49 cases(45.79%), hypertension were in 35 cases(32.71%), herpes zoster were in 27 cases(25.23%), trauma was in 17 cases(15.88%), joint diseases were in 15 cases(14.01%) and prolapsed intervertebral disc in 19 cases (17.75%) shown in Table No.2. The pain according to the numeric pain scale was divided into three groups A i.e. mild type had 37 cases(34.5%), in group B the moderate type had maximum number of cases i.e. 43 cases (40.18%) and in group C the cases were 27(25.23%) as given in Table No.3

The dose of pregablin was also divide into three groups, i.e in group I 50mg /day was benefited in 41 of cases(38.31%), in group II 100mg/day was given and it was helpful in 39 cases (36.44%) and in group III the dose was 150mg/day and the 27 cases(25.23%) were treated as shown in Table No. 4 The dose was kept optimum for the relief of the symptoms and then continued it for four weeks. In 67 cases (62.61 %) of cases the symptoms were controlled in the first week of the treatment but the treatment was continued for four weeks. In 24 cases (22.08%) the treatment was continued for more than four weeks.

Patient with herpes zoster may need the treatment for longer duration and more than half were diabetic and hypertensive, so their pain threshold was very low and they need treatment for longer period.

Table No. 1: Basic Characteristic

Indicators/Variables	N(%)
Gender	
Male	52(48.59%)
Female	55(51.40%)
n	107
Year to be enrolled in the study	93(86.91%)
2011	14(13.08%)
2012	107
n	
Marital status	
Single	09(8.41%)
Married	98(91.58%)
n	107
Smoking behavior	
Yes	37(34.57%)
No	70(65.42%)
n	107
Age	
Range	41-72 years
Mean	56.66 ± 16
n	107

Among the patients prolapsed intervertebral disc and joint diseases the use of pregablin was successful and patient were benefited in terms of pain and sleep

disturbances who either not fit for surgery or they did not opt surgery initially. The cases from acute trauma usually settle with short course of pregablin while of chronic would need the drug for longer period.

Table No. 2: Diseases group

Diseases	Male	Female	Total
Diabetes mellitus	23	26	49(45.79%)
Herpes zoster	15	12	27(25.23%)
Hypertension	23	12	35(32.71%)
Prolapse intervertebral disc	11	08	19(17.75%)
Trauma	09	08	17(15.88%)
Joint diseases	06	09	15((14.01%)

Table No. 3: Pain scale

Grade Of Pain	No. Of Patients
Grade A (1-5)	37 (34.5%)
Grade B (6-8)	43 (40.18%)
Grade C (9-10)	27 (25.23 %)

Table No. 4: Pregablin

Dose of Pregablin		Duration of Treatment	
Dose	No Of Patients	Duration of Treatment	No. of Patients
50 mg	41 (38.31%)	1-2 Weeks	67 (62.61%)
100 mg	39 (36.44%)	3-4 Weeks	16 (14.95%)
150 mg	27 (25.23%)	>4 Weeks	24 (22.42%)

DISCUSSION

The population in this study was in their adulthood. The age of patients were ranging between 42-72 years with mean age of 56.66 ± 16 years. The disease like diabetes mellitus, hypertension, herpes zoster, joint diseases prolapsed inter vertebral disc were common in late life usually. The primary diseases would remain progressive beside its good control. The chronic diseases with their worse complications were not managed with simple medicine. In this study these chronic diseases would lead to the neurological damage or dysfunction that ends up with the painful situation called neuropathic pain. This pain lead to the miserable situation and decreased the quality of life. For the pain management different classes of analgesic were used some time they were benefited but not completely or their dose schedule was also painful to controlled and their chronic use lead to their side effects, i.e. gastrointestinal upsets, somnolence, fluid over load. This is the time to add a nerve stabilized^{13 14} in the regime to alter the symptoms and change the mood of the patients. The drug with less side effects, negligible interaction good efficacy and easy dosing. So in this study pregablin was added in a low dose with easy dosing and two to six weeks and the results was seen that the patients were benefited in terms of quality and sleep.

Frampton JE¹⁵ Lesser H. Sharma¹⁶ and Richter RW 2005 and Quilici S et al¹⁷ showed similar results in painful diabetic neuropathy. The diabetes mellitus and hypertension were chronic diseases and they need first optimum control of the primary illness and all were control according the latest guide lines. Chiechio S et al¹⁸ and Toth C¹⁹ showed the use of pregablin in lower dose would be benefited for patients with diabetic neuropathy.

Among the diseases included in this study the herpes zoster^{20 21 22} was the most notorious in causing neuropathic pain, not only in intensity but duration as well. They all need a higher dose and longer duration for the proper control of the pain. Ven Seventer et al²³ showed similar results in terms of pain relief and sleep disturbances in patient with post herpetic neuralgias.

The group with trauma²⁴, joint diseases and prolapsed intervertebral disc²⁵ responded very well with the pregablin in low doses and for short duration. The joint disease except the acute trauma were chronic and may need slight prolongation of the drug if the patients either not afford the replacement option or their comorbid did not allowed besides this pregablin physiotherapy was also helpful in some cases.

The other studies^{11 12 21 23 24 26} had showed that these latest drugs are of benefit for the patients in neuropathic pain. Finnerup showed that pregablin had more favorable dosing and linear kinetics, better efficacy, safety and less drug inter-action. The dose of less than 100mg/day was benefited in 80% of patients. The dose should be adjusted in patient with renal impairment and need more studies for its long term efficacy and tolerability.

CONCLUSION

The novel drug pregablin is a good choice for neuropathic pain, that improving the pain feeling and well being of a patient in much lower dose without major side effects. It is recommended that other studies be required to prove its efficacy.

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