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(REVIEW ARTICLE)

A review on comparative study of effectiveness of pregabalin and carbamazepine in painful diabetic peripheral neuropathy using mc gill's pain questionnaire

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Abstract

Diabetic neuropathy is a unique degenerative disorder of the peripheral nervous system that preferentially targets sensory axons and autonomic axons. The loss of sensory function that begins distally in the lower extremities is known as Diabetic neuropathy. It is characterized by burning pain, paresthesias and numbness in stocking glove pattern that progress proximally from the feet and hands. Diabetic neuropathy is a highly prevalent condition that substantially affects patients by increasing falls causing pain and reducing quality of life. The major risk factors for diabetic neuropathy is hyperglycemia. In addition to poor glycemic control, more-severe symptoms of diabetic neuropathy are associated with advanced age, hypertension, the duration of diabetes, dyslipidemia, smoking and heavy alcohol intake. Diabetic neuropathy is a major cause for disability of feet and hands globally. Anti-convulsants like pregabalin and carbamazepine are the medications used in the treatment of painful diabetic neuropathy.

Keywords: Peripheral neuropathy; Diabetes Mellitus; Pregabalin; Carbamazepine; Mc Gill pain questionnaire.

1. Introduction

"The pain caused by a lesion or disease of somatosensory nervous system is the definition for neuropathic pain given by International Association for the Study of Pain (IASP)." [1]

Diabetes is a complex metabolic disorder which is characterized by high blood glucose levels, due to inadequate insulin secretion by pancreas. Inability of target cells to reuptake glucose from blood [2].

Diabetic neuropathy is one of the most frequent complications ad affects between 28% & 49% of patients [3].

Initial inciting event is a "dying back" axonopathy principally affecting sensory neurons.

This can be used to test a range of sensory function. Patients often present with varying degrees of numbness, tingling or burning in extremities [4].

Early assessment of symptoms helps avoid neuropathic foot ulcers to combat potential morbidity and mortality.

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Resulting from the pathophysiology poor wound healing potential, can lead to limb compromise, local to systemic infection [5].

Exact cause of diabetic peripheral neuropathy is not known. Diabetes affects 382 million people worldwide, and its prevalence will be increasing to 59w million by the year 2035 [6].

In the severe cases, patients lose their appetite and experience significant weight loss, which is reported in the literature as “Diabetic neuropathic cachexia.”

1.1. Causes

The exact cause of diabetic neuropathy is not known. But it includes, causes such as:

Alcohol use disorder, Nutritional deficiencies (low B12, high B6), Guillain-Barre syndrome, Toxins overdose, Hereditary or genetic conditions, Infections (HIV), Malignancy and Hypothyroidism [7].

1.2. Signs & Symptoms [8]

- Pain in the legs and arms
- Sansation of numbness of the limbs.
- Causeless heat on the palms and feet.
- Rapid fatigue.
- Muscle weaknes
- Tingling
- Burning pains
- Cramps
- Distal weakness of limbs
- Altered sweating

1.3. Mc Gill's Pain Questionnaire

SHORT-FORM McGILL PAIN QUESTIONNAIRE

RONALD MELZACK

PATIENT'S NAME: _____ DATE: _____

	NONE	MILD	MODERATE	SEVERE
THROBBING	0)	1)	2)	3)
SHOOTING	0)	1)	2)	3)
STABBING	0)	1)	2)	3)
SHARP	0)	1)	2)	3)
CRAMPING	0)	1)	2)	3)
GNAWING	0)	1)	2)	3)
HOT-BURNING	0)	1)	2)	3)
ACHING	0)	1)	2)	3)
HEAVY	0)	1)	2)	3)
TENDER	0)	1)	2)	3)
SPLITTING	0)	1)	2)	3)
TIRING-EXHAUSTING	0)	1)	2)	3)
SICKENING	0)	1)	2)	3)
FEARFUL	0)	1)	2)	3)
PUNISHING-CRUEL	0)	1)	2)	3)

Figure 1 Mc Gill's Pain Questionnaire [9]

The Mc Gill pain questionnaire, also known as Mc Gill pain index, is a scale of rating pain developed at Mc Gill University by Mel Zack in 1975. The objective is to evaluate MPQ as a multi-dimensional measure of pain in people with diabetic neuropathy [10]. Review of the 100 studies demonstrated that pain intensity (n=99 studies) and pain quality (n=97) were measured more frequently than pain location, pattern and behaviour parameters, demonstrated that pain intensity (n=99 studies) and pain quality (n=97) were measured more frequently than pain location, pattern and behaviour parameters [11].

1.4. Diagnosis [12]

- Clinical findings
- Nerve Conduction Studies
- Toronto Clinical Neuropathy Score
- Michigan Diabetic Neuropathy Score
- Skin Punch Biopsy
- Pin Prick Sensation
- Vibration Perception

1.5. Skin Punch Biopsy [13]

A skin biopsy is a process used to take samples of a patient's skin cells for laboratory testing. The most common use of a skin biopsy is for skin problem diagnosis. Procedures for skin biopsies include:

- Trim the biopsies
- Perform punch biopsy
- Surgical biopsy

1.6. Pin Prick Sensation

A painful tingling or prickling feeling that is typically felt in the hands, feet, arms, or legs is known as pins and needles. Compression of nerves resulting from pressure on a particular area of the arm or leg is a common cause [14].

1.7. Nerve Conduction Studies

In order to detect nerve injury, electromyography, or EMG, involves monitoring and recording the electrical activity in your muscles. To assess the electrical activity of a muscle contraction, a tiny needle, or electrode, is placed into the muscle. The skin is covered with flat electrodes, and the nerves are stimulated by a small electric current. Medical personnel will document the nerves' reaction to the electric current [15].

1.8. Pharmacological Treatment

Table 1 Pharmacological Treatment [16]

	Pregabalin	**Carbamazepine**
Brand Name	Lyrica, Pregabalin	Zeptol, Tegrital
Class	Cyclic GABA Analogues	Iminostilbene
Dose	75-150mg BD	Adults- 200 to 400mg/day Child – 15 to 30mg/kg/day
MOA	It binds to alpha-2-delta subunits of voltage gated Ca2+ influx at the nerve terminals. Which inhibits excitatory neurotransmitter release including glutamate, norepinephrine, serotonin, and dopamine.	Carbamazepine depress activity in the nucleus ventralis of the thalamus or decreases synaptic transmission which leads to neural discharge by limiting the influx of Na+ ions across the cell membrane.
Pharmacokinetics	Absorption-oral Bioavailability-90% Distribution- Throughout the body Metabolism- liver	Absorption – Orally Bioavailability- 75 to 85% Distribution- Metabolism- Liver

	Elimination- Renal 98% - urine. Half-life – 6.3 hrs.	Elimination- Half-life - 12-17hrs. Primary through urine
ADR's	Dizziness Headache Blurred vision Weight gain Peripheral edema Nausea Constipation	Hyponatremia Agranulocytosis Teratogenic Dizziness Headache Ataxia Vertigo

2. Conclusion

Results of the study suggests that treatment with pregabalin is associated with faster and better improvement in diabetic neuropathy. The alpha lipoic acid is found to be as effective as pregabalin. However, carbamazepine appears to be inferior to the other two drugs. Therefor pregabalin is used as First line therapy in diabetic neuropathy. The occurrence of peripheral diabetic neuropathy was more among the individuals with high FBS levels which indicates the necessity of controlled glycemic levels in the prevention of complications associated with diabetes furthermore, clinical trials on large scales with comparative analysis among already existing drugs and novel drugs need to be done to develop a localized and more potent treatment option with minimal side effects.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that this study has no conflict of interest.

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