Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2016, 8(7):540-543

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Evaluation of adverse drug reactions of gabapentin to pregabalin in patients of painful diabetic peripheral neuropathy

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ABSTRACT

Gabapentin and pregabalin are widely used therapeutic agents in patients with diabetic neuropathic pain. Their use has also brought about a wide number of adverse drug reactions. The aim of the study is to evaluate serious and/or unexpected adverse drug reactions associated with gabapentin and pregabalin in patients with painful diabetic peripheralneuropathy. In this study the adverse drug reactions were assessed and graded according to WHO Causality scale(Naranjo Causality scale),Severity(Modified Hartwig and Siegel scale),Preventability(Schumock and Thornton scale).Patients who were 18-75 years of age with pain attributing to diabetic neuropathy were included in the analysis. Data regarding demographic details, medicalhistory, allergichistory, details of diabetic peripheral neuropathy were documented. All the adverse drug reactions occurred was documented in Central Drugs Standard Control Organization (CDSCO) ADR form and reported to Pharmacovigilance committee at Department of Pharmacology in Sree Balaji Medical College. In a total of 100 patients with painful diabetic peripheral neuropathy, 42 were observed with Adverse Drug Reactions out of which patients treated with pregabalin has reported less ADRs when compared to patients treated with gabapentin. These ADRs were observed and graded according to WHO Causality, Severity and Preventability scale.

Keywords: Adverse drug reactions, Pharmacovigilance, WHO assessment scales.

INTRODUCTION

World Health Organization(WHO) defines an Adverse Drug Reaction(ADR) is “a response to a drug, which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy for a disease and for the modification of function excluding failure to accomplish the intended purpose”[1].An adverse drug reaction is an expression that describes harm associated with the use of given medications at a normal dose(s)[2].Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects, or any other medicine related problem[3]. Pharmacovigilance is an integral part of the drug therapy but still not practiced widely in many Indian hospitals [4].Diabetic Neuropathy is a nerve damaging disorder which is one of the most common microvascular complications of diabetes mellitus. Symptoms of Diabetic neuropathy range from mild dysestesias to severe unremitting pain that can profoundly affect the quality of life. Neuropathic pain in diabetes is defined as pain initiated or caused by a primary dysfunction in the nervous system and occurs in up to 26% of all the patients with diabetes. Apart from glycemic control, current guidelines recommend the use of anticonvulsants in the treatment of diabetic peripheral neuropathy. GABA analogs like Gabapentin and pregabalin, a newer generation anticonvulsants, are licensed for the treatment of neuropathic pain and their use has also brought a wide number of ADRs.Both Gabapentin and Pregabalin are structural analogues of gamma-aminobutyricacid (GABA) which was initially introduced as an antiepileptic drug. It binds to α2-δ protein

subunit of voltage-gated calcium channels widely distributed in the central and peripheral system. This inhibits calcium influx and reduces excitatory neurotransmitter release in pain pathways [5].This study was done to evaluate serious and/or unexpected adverse drug reactions associated with gabapentin and pregabalin in patients with painful diabetic peripheral neuropathy.

EXPERIMENTAL SECTION

The aim of the study is to evaluate serious and/or unexpected adverse drug reactions associated with gabapentin andpregabalin in patients with painful diabetic peripheral neuropathy. The study was a open, longitudinal interventional carried out over a period of three months conducted in Department of General Medicine in Diabetic clinic, Sree Balaji Medical College and Hospital. Patients who were 18-75 years of age with pain attributing to diabetic neuropathy were included in the analysis. Data regarding demographic details, medical history, allergic history, details of diabetic peripheral neuropathy were documented.

The study was divided into two arms and study strength was limited to 100 patients, out of which 50 patients receiving gabapentin and 50 patients receiving pregabalin were included in the study. Patient's voluntary informed written consent was obtained after explaining the risks and benefits. Adverse Drug Reactions were assessed according to WHO Assessment Scale: Certain, probable, possible, un-assessable/unclassifiable, unlikely, conditional/unclassified[6] and graded according to WHO Causality scale(Naranjo Causality scale)[7], Severity(Modified Hartwig and Siegel scale)[8],Preventability(Schumock and Thornton scale)[9].All the adverse drug reactions occurred were documented in Central Drugs Standard Control Organization(CDSCO) ADR form and reported to Pharmacovigilance committee on Department of Pharmacology in Sree Balaji Medical College and Hospital.

RESULTS AND DISCUSSION

Adverse drug reactions have to be considered as one of the major causes of iatrogenic disease and they can have a detrimental effect on a patient's well being and the overall health care system. In general no drug is absolutely safe and an ADR can occur when it is administrated alone or in combination. A continuously ongoing ADR program in a hospital can help to improve organizational risk management activities, assess the safety of drug therapies, measure ADR incidence rates over time and educate health care professionals on drug effects and increase their level of awareness regarding ADRs[10].The accuracy of this information to the health care professionals helps in promoting drug safety and better patient care[11].Among the 100 patients, a total of 42 adverse events were reported and confirmed as ADRs. Out of which 30 adverse events was reported in patients receiving Gabapentin and 12 adverse events were reported in patients receiving pregabalin (Figure.1)

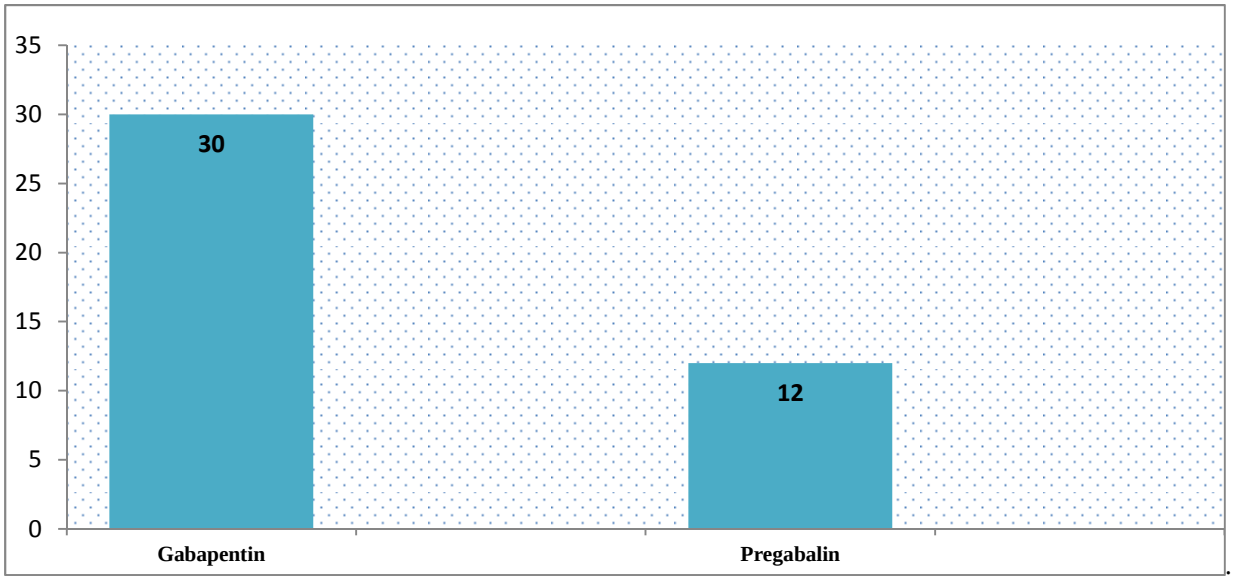

Figure 1.Distribution of adverse effects of Gabapentin and Pregabalin treatment among study population

The distribution of individual adverse effects of Gabapentin and Pregabalinamong the study population was categorized accordingly in Figure 2 and Figure 3.

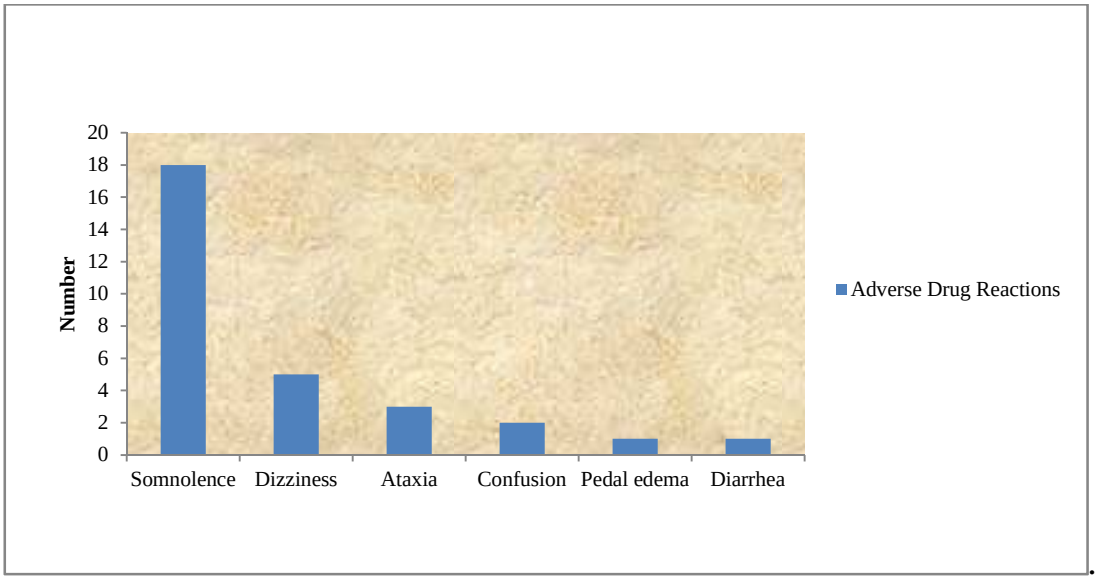

Figure.2: Distribution of individual adverse effects of Gabapentin

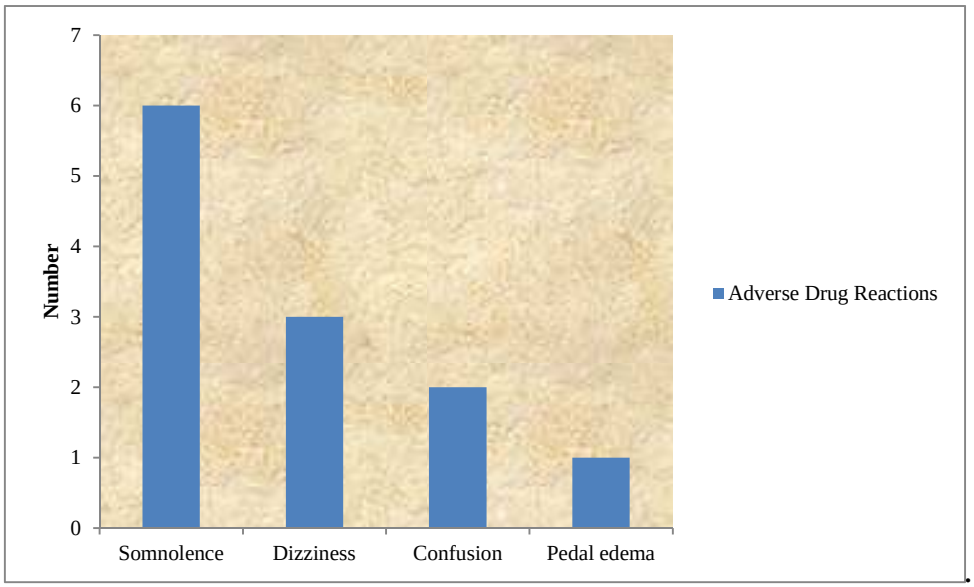

Figure.3: Distribution of individual adverse effects of Pregabalin

Causality Assessment:

To strengthen the validity of the findings of the study, causality assessment was done for individual cases in both the groups by using Naranjo'salgorithm Table1. The details of the causality assessment.

Table 1:Causality assessment using the Naranjos Algorithm Probability Scale

Types	Number of ADRs	Percentage
Possible	10	22.0
Probable	32	78.0
Definite	0	0
Total	42	100.0

Severity assessment

On evaluation of the severity of ADRs by Hartwiget.al, scale it was evident that most of the ADR reported in the study were of moderate severity. Details of the severity assessment are given in Table 2.

Table 2: Severity of ADRs according to Modified Hartwig and Siegel Scale

Types	Number of ADRs	Percentage
Mild	18	41.5
Moderate	24	58.5
Severe	0	0
Total	42	100.0

Preventability Assessment:

On evaluation of the chances of preventability of ADRs using modified Schumock and Thornton scale, it was evident that most of them were not preventable. Details of the preventability assessment are given in Table 3.

Table 3: Preventability of ADRs according to modified Schumock and Thornton scale

Types	Number of ADRs	Percentage
Definitely preventable	5	12.2
Not preventable	37	87.8
Total	42	100.0

Statistical Analysis:

The divided 2 groups are analyzed according to the severity level of the reaction using SPSS 22.0 (Statistical Package for Social Sciences Inc., USA) by Chi-Square test. Since the p value is < 0.001 it rejects null hypothesis (H_0), hence there is significant association in occurrence of increased Adverse effects with Gabapentin treatment as compared to Pregabalin.

Drugs	Adverse effects present(%)	Adverse effects absent(%)	Total(%)
Gabapentin	30(60)	20(40)	50(100)
Pregabalin	12(24)	38(76)	50(100)

In this prospective study we have found that the incidence of adverse effects were more in Gabapentin group when compared to pregabalin group.The pharmacological and pharmacokinetic profiles of pregabalin provide a predictable basis for its use in clinical practice.

CONCLUSION

This study provides information on Adverse Drug Reactions prevalent with the use of gabapentin and pregabalin. The number of Adverse Drug Reaction events were less common and less severe in patients treated with pregabalin when compared to gabapentin.

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