

Adverse Drug Reactions Of Pregabalin And Nortriptyline In Patients With Chronic Low Backache With Radiculopathy - A Prospective Observational Study

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Abstract

Background and Objectives: - The safety of Pregabalin and Nortriptyline have been proved individually in chronic low backache with radiculopathy. However, there are limited number of studies comparing the tolerability of Pregabalin and Nortriptyline in chronic low backache with radiculopathy. Hence the present study is designed to determine the tolerability of Pregabalin versus Nortriptyline. It is an prospective observational study.

Methods: - Patients with chronic low backache with radiculopathy 15–60 years of age without specific cause and significant neurological deficit were included. Patients were followed up at 2 and 4 weeks and their side effect were noted.

Results: - There was no statistical difference between pregabalin and nortriptyline groups in terms of visual analogue scale for pain score, from baseline to 2 weeks and from baseline to week 4. The incidence of side effects were statistically less in the nortriptyline group compared to pregabalin group.

From the results of the present study it can be concluded that both pregabalin and nortriptyline are effective in the treatment of chronic low backache with radiculopathy with radicular pain but incidence of adverse events are more with the pregabalin compared to nortriptyline.

Conclusion: - Anticonvulsants and TCAs are very effective in moderate to severe pain while the other drugs like NSAIDs and opioids are more effective in mild to moderate pain.

Key words : Low back pain; NSAIDs; Opioids; pregabalin; nortriptyline; Efficacy;

INTRODUCTION

World Health Organization (WHO) defined as Adverse Drug Reaction (ADR) is “a response to a drug, which is noxious, 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. Pharmacovigilance has been defined by the WHO as the ‘science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems.’². Pharmacovigilance is an integral part of the drug therapy but still not practiced extensively in many Indian hospitals. There are limited number of studies available for the same topic, hence this study was taken.

Objectives: - To compare the tolerability of pregabalin versus nortriptyline in the treatment of patients with the chronic low backache with radiculopathy

Methodology: - The study was conducted from November 2014 to December 2015 in patients attending the Orthopaedic and Spine outpatient department at M.S.Ramaiah Medical College & Teaching Hospital. The study was approved by the institutional ethics committee.

Method of collection of data:- Patients who were diagnosed to have chronic low backache with radiculopathy at the Orthopaedic and Spine outpatient department at M.S.Ramaiah Medical College & Teaching Hospital and who fulfilled the following inclusion and exclusion criteria, were included in the study.

INCLUSION CRITERIA-

1. Patients aged between 18 -60 years having the chronic low backache with radiculopathy
2. Lumbar radicular symptoms existing for more than 3 months.
3. Symptoms involving one or both lower limbs or buttocks.

EXCLUSION CRITERIA:

1. Medical co- morbidities such as unstable angina disease, advanced diabetes, hypertension and cancer.
2. Pregnancy or lactation.
3. History of depression requiring treatment with antidepressants within the 6 months preceding study participation
4. Patients with Cervical or Thoracic myelopathy.
5. Fibromyalgia.

SAMPLE SIZE CALCULATION.

The sample size was calculated from the study by J.Kalita³ et al in comparison with two independent samples.

In the current study expecting analogous result and to get a precision of 95% confidence interval and considering 18% difference between the two drugs as clinically significant difference, the study needs a minimum of 57 subjects in each arm .

It was 4 weeks, prospective comparative study. Patients who are clinically diagnosed as a chronic low backache with radiculopathy and fulfilled the inclusion criteria and willing for follow up were recruited in the study. Informed consent was obtained before the enrolment.

In one arm, 57 patients received tablet Pregabalin 75mg orally and the other arm 57 patients received tablet Nortriptyline 25mg each tablet once daily after food at bedtime.

Tolerability of the study drugs was assessed based on the side effects reported by the patients during their visit or by telephonic interview. Patients were asked to note down the side effects, if any, in a diary on a daily basis so that the frequency of the side effects could be assessed.

Safety was assessed based on the number of patients experiencing side effects after 2 weeks and after 4 weeks of treatment.

RESULTS

Table no-1.

Side effects	Treatment groups			
	Pregabalin		Nortriptyline	
	After 2 weeks (n=57)	After 4 weeks (n=57)	After 2 weeks (n=57)	After 4 weeks (n=57)
Sedation	21	21	2	2
Vertigo	18	3	4	4
Dry mouth	6	6	22	17
Restlessness	12	12	1	1
Postural hypotension	0	0	17	8
Urinary retention	0	0	10	5

Table no- 2

After 4 weeks of treatment	Pregabalin	Nortriptyline
Side effects present	55	55
Side effects absent	2	2
After 2 weeks of treatment		
Side effects present	53	40
Side effects absent	4	17

There is a statistical difference with a $p = 0.0030$ between the 2 groups after 4 weeks of treatment.

DISCUSSION

The present study was carried out to compare the tolerability of pregabalin and nortriptyline in chronic low backache with radiculopathy during the study period of 1 month.

The most common side effects of TCAs include sedation, anticholinergic effects (e.g., dry mouth, constipation, and urinary retention) and orthostatic hypotension. Secondary amine TCAs (nortriptyline and desipramine) are preferred

because they are better tolerated than tertiary amine TCAs (amitriptyline and imipramine) but have comparable analgesic efficacy⁴.

Common side effects for nortriptyline include xerostomia, xerophthalmia, constipation, weight gain, postural hypotension, and sedation^{5,6,7,8}.

Previous studies have showed that nortriptyline was associated with sinus tachycardia and increased ventricular ectopy in an RCT where the patients had a history of depression and ischemic heart disease⁹. Fuzier R et al study has showed haematological ADRs associated with pregabalin¹⁰.

CONCLUSION

From the results of the present study, it can be concluded that incidence of adverse events are more with the pregabalin compared to nortriptyline.

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Ethical Approval: This study was approved by the Institutional Ethics Committee

REFERENCES

1. International drug monitoring: The role of hospital. Geneva, Switzerland: World Health Organization; 1969 (technical report series No.425). (Cited on 11-11-2020) available on http://apps.who.int/iris/bitstream/10665/40747/1/WHO_TRS_425.pdf
2. Tripathi, K., 2021. Essentials of medical pharmacology. 8th ed. JP, p.93.
3. Kalita J, Kohat AK, Misra UK, Bhoi SK. An open labeled randomized controlled trial of pregabalin versus amitriptyline in chronic low backache. *J Neurol Sci.* 2014;342(1–2):127–32
4. Watson CPN, Vernich L, Chipman M, Reed K. Nortriptyline versus amitriptyline in postherpetic neuralgia: a randomized trial. *Neurology* 1998;51:1166–71.
5. G. Dieckmann, S. Goyal, P. Hamrah Neuropathic corneal pain: approaches for management *Ophthalmology*, 124 (11S) (2017), pp. S34-S47
6. 4.L. Colloca, T. Ludman, D. Bouhassira, et al. Neuropathic pain *Nat Rev Dis Primers*, 3 (2017), p. 17002
7. S. Derry, P.J. Wiffen, D. Aldington, R.A. Moore Nortriptyline for neuropathic pain in adults *Cochrane Database Syst Rev*, 1 (2015), p. CD011209
8. F.T. Fraunfelder, J.J. Sciubba, W.D. Mathers The role of medications in causing dry eye *Journal of ophthalmology*, 2012 (2012), p. 285851
9. Roose SP, Laghrissi-Thode F, Kennedy JS, Nelson JC, Bigger JT, Pollock BG, et al. Comparison of paroxetine and nortriptyline in depressed patients with ischemic heart disease. *JAMA* 1998;279:287–91
10. Fuzier R, Serres I, Guitton E, Lapeyre-Mestre M, Montastruc JL; French Network of Pharmacovigilance Centres. Adverse drug reactions to gabapentin and pregabalin: a review of the French pharmacovigilance database. *Drug Saf.* 2013 Jan;36(1):55-62. doi:10.1007/s40264-012-0006-6. PMID: 23315296.