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Case Series

Adverse drug reactions due to gabapentin-nortriptyline in patients with neuropathic pain in a tertiary care teaching hospital

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ABSTRACT

Gabapentin and Nortriptyline are used to treat neuropathic pain. Gabapentin belongs to a group of drugs called anti-convulsant and Nortriptyline belongs to tricyclic antidepressant. Gabapentin acts by binding to the specific site on voltage-gated calcium channels. This helps in relieving nerve pain and lowers the risk of seizure. Nortriptyline works by preventing the released chemical messengers in brain (serotonin and norepinephrine) from being reabsorbed back into the nerve cells. As a result, it prolongs the effect of serotonin and norepinephrine in the brain and over time, this helps to relieve depression and lighten the mood. We are reporting a case series including 3 patients having neuropathic pain and taking tablet gabapentin-nortriptyline in department of neurology, Patna medical college and hospital, Patna developed some adverse drug reactions. Causality assessment was done in each case by Naranjo scale. Each case was filled properly in ADR (adverse drug reaction) reporting form and was sent to nearby adverse drug reaction monitoring centre (AMC). During the posting for pharmacovigilance in neurology department of Patna medical college and hospital, Patna from 01/07/2022 to 30/09/2022 we got three adverse drug reactions due to gabapentin-nortriptyline. Two of them were due to Gabapentin and one was due to nortriptyline. Gabapentin-nortriptyline is one of the most commonly used drugs in neurology department. It causes some frequent as well as some rare adverse drug reactions which are required to be assessed and finally reported to the nearby AMC.

Keywords: Gabapentin, Nortriptyline, Neuropathic pain, Adverse drug reaction

INTRODUCTION

Neuropathic pain due to radiculopathy, diabetes, herpes zoster or other causes is a major concern in neurology department. Gabapentin-nortriptyline combination is most frequently used nowadays to treat the neuropathic pain. It is very effective in treating neuropathic pain.

Gabapentin is an analogue of the neurotransmitter γ -aminobutyric acid with anticonvulsant and analgesic properties, and is widely used to treat neuropathic pain.¹ The exact mechanism of action is unknown, but the therapeutic action on neuropathic pain is thought to involve voltage-gated N-type calcium ion channels. Gabapentin is thought to bind to the $\alpha 2\delta$ (alpha-2-delta)

subunit of the voltage-dependent calcium channel in the central nervous system.² Gabapentin is efficacious against various pain syndromes such as neuropathic pain, chronic pain, and postherpetic pain.³

The consensus is that Nortriptyline inhibits the reuptake of serotonin and norepinephrine by the presynaptic neuronal membrane, thereby increasing the concentration of those neurotransmitters in synapse. Additionally, Nortriptyline inhibits the activity of histamine, 5-hydroxytryptamine, and acetylcholine. Nortriptyline increases the pressor effect of norepinephrine but hinders the pressor response of phenethylamine. However, research has found additional receptor effects, including desensitization of adenylyl cyclase, down regulation of beta-adrenergic

receptors and down regulation of serotonin receptors. Proposed mechanism of nortriptyline in neuropathic pain is increase in norepinephrine levels acting within dorsal root ganglia on β_2 -adrenoceptors expressed by non-neuronal adrenoceptors satellite cells. This stimulation of β_2 -adrenoceptors reduces neuropathy-induced production of TNF α , resulting in relief of neuropathic pain.⁴

Due to being one of the most commonly used drugs in neurology department, it is also important to collect data about its safety by reporting the adverse drug reactions due to it. We are reporting adverse drug reactions due to gabapentin-nortriptyline in neurology department, Patna medical college and hospital, Patna in three months from 01/07/2022 to 30/09/2022 during posting for pharmacovigilance.

CASE SERIES

During our posting in neurology department of Patna medical college and hospital, Patna for pharmacovigilance we got three adverse drug reactions due to gabapentin-nortriptyline in three months. Causality assessment was done by Naranjo scale for each case. Each case was noted properly in ADR reporting form and was sent to nearby AMC.

Case 1



Figure 1: MRI of the spine showing large disc extrusion at L1-L2 and additional disc herniations at L2-L3.

A female patient of age 53 years having previously lower backache due to radiculopathy as shown in Figure 1 came to neurology department, Patna medical college and hospital, Patna on 23/08/2022 with complains of facial swelling. She was on the treatment for the neuropathic pain with tablet gabapentin-nortriptyline (200 mg and 10 mg) at bed time for 1 month. By neurologist dose of gabapentin and nortriptyline was reduced to half and renal function test was done. Renal function test was normal and the facial swelling subsided after reducing the dose of gabapentin. Causality assessment for facial swelling and

gabapentin was done by Naranjo scale with the result “probable”. Score as per Naranjo scale-6. Case was noted properly in ADR reporting form and was sent to nearby AMC.

Case 2

A 29 years old female patient came to neurology department, Patna medical college and hospital, Patna on 30/08/2022 with complains of ataxia. Previously she was on treatment for lower back pain due to radiculopathy as shown in Figure 2 with tablet gabapentin-nortriptyline (200 mg, 10 mg) at bed time for 15 days. The dose of gabapentin-nortriptyline reduced to half by neurologist and then the complains of ataxia diminished and finally relieved successfully. The causality assessment for ataxia and gabapentin was done by Naranjo scale with the result “probable”. Score as per Naranjo scale was 6. Case noted properly in ADR reporting form and was sent to nearby AMC.



Figure 2: MRI of LS spine showing disc herniation at L5-S1.

Case 3

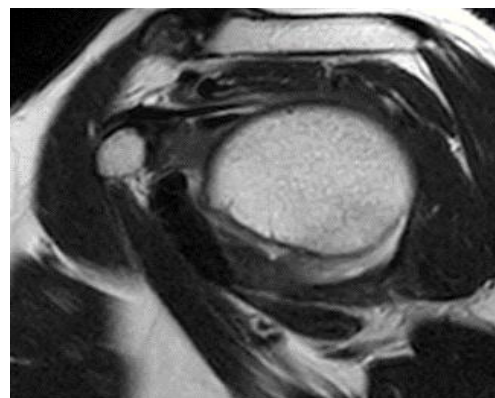


Figure 3: MRI of right shoulder showing adhesive capsulitis.

A 35 years old female patient came to neurology department, Patna medical college and hospital, Patna on

06/09/2022 with complains of constipation. Previously she was on treatment for pain due to right frozen shoulder as shown in Figure 3 with tablet gabapentin-nortriptyline (200 mg, 10 mg) at bedtime for 7 days. She was managed by starting tablet prucalopride, 1 mg, BD. Prucalopride is a 5-HT₄ receptor agonist and it normalises bowel

movement in case of constipation. Complains of constipation relieved after that. Causality assessment for constipation and nortriptyline done by Naranjo scale with the result “probable”. Score as per Naranjo scale-7. Case noted properly in ADR reporting form and sent to nearby AMC. Summary of the three cases is given in Table 1.

Table 1: Adverse drug reactions due to gabapentin-nortriptyline.

Cases	Adverse drug reaction	Causative drug	Score as per Naranjo scale	Causality assessment by Naranjo scale
Case 1	Facial swelling	Gabapentin	6	Probable
Case 2	Ataxia	Gabapentin	6	Probable
Case 3	Constipation	Nortriptyline	7	Probable

DISCUSSION

Combined gabapentin and nortriptyline seem to be more efficacious than either drug given alone for neuropathic pain, therefore it is recommended to use of this combination in patients who show a partial response to either drug given alone and seek additional pain relief.⁵

Drowsiness, dizziness, loss of co-ordination, tiredness, blurred or double vision, unusual eye movements, or tremor are common side-effects of gabapentin. A small number of people may experience depression, suicidal thoughts or attempts, or other mental or mood problems. Older adults may be more sensitive to the side-effects of Gabapentin, especially swelling of the hands/ face/ ankles/ feet, slow or shallow breathing, dizziness, or loss of co-ordination. Nortriptyline has anticholinergic side-effects like: drowsiness, dry mouth, blurred vision, constipation, weight gain, or trouble urination. It has also other side-effects like increased appetite and tinnitus. An occasional side-effect is a rapid or irregular heartbeat.

CONCLUSION

Gabapentin-nortriptyline is indicated in treatment of severe neuropathic pain, refractory neuropathic pain and postherpetic neuralgia. It is used to treat long lasting (chronic) pain caused by nerve damage due to diabetes, shingles or spinal cord injury. It reduces pain and it's associated symptoms such as mood changes, sleep problems, and tiredness. Its side-effects are also common and frequently observed. Being one of the most commonly used drugs in neurology department, it is important to report adverse drug reactions due to it for its better safety.

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