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ABSTRACT

Neuropathic pain presents significant clinical challenges due to its complex pathophysiology and varied patient response to treatment. While multiple pharmacologic options are available, healthcare provider's preferences and prescribing behaviors can influence treatment outcomes and patient adherence. This study aimed to evaluate the preferences of healthcare providers in India and their current prescription trends in the management of neuropathic pain. A cross-sectional survey was conducted among 755 practicing healthcare professionals across India, comprising 376 orthopedic specialists and 379 physicians. A structured questionnaire was used to assess preferred drug molecule from tricyclic antidepressant class, factors affecting drug selection (e.g., perceived efficacy, patient tolerability, cost), preferred combination and prescribing trends of Nortriptyline, Pregabalin and Mecobalamin (NPM) combination. Descriptive statistics were used to analyze the responses. Nortriptyline was the most preferred tricyclic antidepressant for neuropathic pain (40.98%), followed by amitriptyline (33.26%) and protriptyline (15.66%). Efficacy was the primary determinant in drug selection (45.92%), followed by tolerability (32.29%), compliance (18.88%), and cost (7.61%). The NPM combination was frequently prescribed, especially for diabetic neuropathy, though concerns about cost and safety influence its adoption. Healthcare providers (HCPs) generally prescribe this combination for 1-3 months, but adherence was a challenge, with only 13.30% of patients showing adherence rate of over 75%. The 40-60 years age group was the primary demographic for NPM prescriptions. Cost and size of the tablet/capsule were pivotal factors in brand selection. Nortriptyline was the preferred tricyclic antidepressant for neuropathic pain among Indian healthcare providers, with efficacy, tolerability, and compliance being key factors in drug selection. The NPM combination was commonly prescribed, especially in diabetic neuropathy, despite concerns regarding cost and safety. Patient adherence to this regimen was relatively low, highlighting the need for strategies to improve long-term compliance.

Keywords: Neuropathic pain, nortriptyline, pregabalin, mecobalamin, combination.

INTRODUCTION

Neuropathic pain (NP) is a complex, chronic pain condition resulting from damage or disease

affecting the somatosensory nervous system. It is estimated to affect up to 10% of the global population and is frequently associated with

conditions such as diabetic neuropathy, postherpetic neuralgia, spinal cord injuries, and chemotherapy-induced peripheral neuropathy [1,2]. Unlike nociceptive pain, neuropathic pain is often resistant to conventional analgesics, necessitating the use of adjuvant therapies such as antidepressants, anticonvulsants, and combination regimens [3].

Tricyclic antidepressants (TCAs), particularly amitriptyline and nortriptyline, have long been used as first-line agents in NP management due to their dual action on noradrenergic and serotonergic pathways, which modulate pain perception [4]. Pregabalin, a gabapentinoid, is also widely prescribed owing to its efficacy in reducing neuronal excitability by modulating calcium channels [5]. Furthermore, mecobalamin (methylcobalamin), neurologically active form of vitamin B12, is frequently included in treatment combinations due to its role in nerve regeneration and myelin repair [6].

Despite the range of therapeutic options available, the clinical management of pain is often neuropathic hindered heterogeneous treatment responses, adverse effect profiles, patient non-adherence, and costrelated barriers. In this context, the prescribing behavior and preferences of healthcare providers (HCPs) play a critical role in optimizing treatment outcomes. Factors such as perceived efficacy, side-effect profile, tolerability, and drug accessibility can significantly influence drug selection and treatment duration [7,8]. India

presents a unique landscape in neuropathic pain management due to its diverse patient population, varying socioeconomic conditions, and evolving healthcare infrastructure. However, limited data exist on how HCPs in India approach the pharmacologic management of NP, particularly with respect to preferred agents within the TCA class, the use of fixed-dose combinations like Nortriptyline, Pregabalin, and Mecobalamin (NPM), and the practical considerations that guide these decisions.

This study aimed to address this gap by conducting a cross-sectional survey among physicians and orthopedic specialists across India to identify current prescription trends, drug preferences, and influencing factors in the management of neuropathic pain. Understanding these patterns is essential for informing future guidelines, improving adherence strategies, and tailoring interventions that align with real-world clinical practices.

METHODOLOGY

Study Design and Setting:

This was a cross-sectional, questionnaire-based survey conducted among practicing orthopedics and consulting physicians involved in the diagnosis and management of neuropathic pain across India. Participation was voluntary, and confidentiality of responses was assured. The goal was to gather real-world insights on current prescription trends, preferred combination and prescribing trends of Nortriptyline, Pregabalin

and Mecobalamin (NPM) combination in neuropathic pain management. The study was approved by the Altezza Institutional Ethics Committee (IEC) having Protocol Number: 2024/MPL/O/01.

Survey Participants:

The participants included orthopedics and consulting physicians who routinely manage patients with neuropathic pain. A total of 755 participants responded to the questionnaire. Inclusion criteria (1) Licensed healthcare providers. (2) Actively involved in prescribing neuropathic pain medications. (3) Willing to provide informed consent for participation. All data were collected prospectively, and all participants responded to a uniform 10-item questionnaire. Participants voluntarily

completed the questionnaire after being informed about the research objectives, providing full consent to participate. The study involved no patient contact or clinical intervention.

Application of Questionnaire:

A structured 10-item questionnaire developed to assess orthopedics and consulting physician's preferences and perceptions regarding neuropathic pain management, particularly focusing on tricyclic antidepressants and nortriptyline, pregabalin and mecobalamin combination (Table 1). The survey questionnaire was proposed by the author of the study and is not a validated tool in neuropathic pain management.

No.	Questions	Options
1	Preferred Molecule Among Tricyclic Antidepressants	Nortriptyline
		Amitriptyline
		Protriptyline
		Other
2	Reason for Molecule Preference	Efficacy
		Safety Profile
		Compliance
		Cost
		Any Other
3	Common Indication for Nortriptyline, Pregabalin, and Mecobalamin (NPM)Combination	Diabetic Neuropathy
		Chronic Pain
		Spinal Cord Injury
		Post-Herpetic Neuralgia
		Low Back Pain
4	Frequency of Prescribing NPM Combination	25-50% of cases

		10-25% of cases
		<10% of cases
		>50% of cases
5	Major Concerns for Not Prescribing NPM Combination	Cost
		Safety
		Compliance
		Efficacy
ĵ	Duration of NPM Prescription	1 month
		2-3 months
		15 days
		>3 months
7	Patient Adherence to NPM Prescription	25-50% adherence
		50-75% adherence
		<25% adherence
		>75% adherence
8	Most Preferred Molecule/Combination	Nortriptyline + Pregabalin
		+ Mecobalamin
		Nortriptyline + Pregabalin
		Plain Nortriptyline
		Any Other
9	Common Age Group f or NPM Prescription	40-60 years
		60-75 years
		25-40 years
		>75 years
10	Important Brand Features f or NPM Combination	Cost
		Size of Tablet/Capsule
		Availability
		Onset of
		Action/Technology
		Frequency of Reminders

Data Collection:

The questionnaire was administered through interviews over a 3-months period. Respondents were encouraged to answer all items honestly based on their current clinical practices and beliefs. No identifying personal or institutional information was collected to maintain confidentiality.

Statistical Analysis:

Data from the completed questionnaires were entered into Microsoft Excel and analyzed using descriptive statistics. Categorical variables were expressed in percentages and frequencies. No inferential statistics were applied, as the

objective was to assess trends and opinions rather than test hypotheses.

RESULTS

A cross-sectional survey of 755 healthcare professionals, including 376 orthopedic specialists and 379 physicians, revealed key insights into prescribing trends and preferences in the management of neuropathic pain in India. Among tricyclic antidepressants, nortriptyline was the most preferred molecule (40.98%), followed by amitriptyline (33.26%) and protriptyline (15.66%). Efficacy was the leading factor influencing molecule selection (45.92%). followed by safety (32.29%), compliance (18.88%), and cost (7.61%). The fixed-dose combination of nortriptyline, pregabalin, and mecobalamin was most commonly prescribed for diabetic neuropathy (43.88%), with other indications including chronic pain (29.72%), spinal cord injury (19.00%), low back pain (15.00%), and post-herpetic neuralgia (11.37%). In terms of prescribing frequency, nearly half of the respondents (47.96%) reported using the NPM combination in 25–50% of NP cases, while 22.74% used it in 10-25%, and 12.12% in more than 50% of cases. The most cited barriers to prescribing NPM included high cost (34.12%), safety concerns (27.46%), compliance issues (24.67%), and perceived efficacy (22.42%). Most providers prescribed the NPM combination for a duration of 1 month (38.30%) or 2-3 months (33.04%). However, patient adherence to therapy remained suboptimal, with only

13.30% of clinicians reporting adherence rates above 75%, and the majority indicating 25–50% adherence (39.05%). Regarding formulation preferences, nortriptyline + pregabalin + mecobalamin was favored by 39.27% of 36.26% respondents. while preferred nortriptyline + pregabalin, and 17.16% prescribed nortriptyline alone. The most common age group receiving NPM prescriptions was 40-60 years (53.32%), followed by 60-75 years (23.28%) and 25-40 years (19.20%). Key brand selection criteria included cost (36.00%), tablet/capsule (26.18%), size availability (24.57%), onset of action or formulation technology (19.00%), and reminder frequency (11.48%). These findings underscore both the clinical rationale behind prescribing behaviors and the practical challenges faced in optimizing neuropathic pain management.

Both healthcare professional groups showed a clear preference for nortriptyline and amitriptyline with orthopedics favoring nortriptyline more prominently. Efficacy drives molecule preference across both groups, with orthopedics placing slightly more emphasis on safety, while consulting physicians consider compliance and cost marginally more. Both groups identified diabetic neuropathy as the leading indication, with orthopedics slightly more focused on chronic pain and low back pain. Both prescribed NPM combination groups moderate frequencies. while consulting physicians used it slightly more in 25-50% of cases. Cost remained the primary barrier for

both groups; consulting physicians expressed slightly more concern about safety and Orthopedics favored compliance. shorter durations (1 month), while consulting physicians were more likely to prescribe for 2-3 months. Both groups faced significant adherence challenges, with adherence rates between 25-75% being most common. Both healthcare professional groups favored the combination and predominantly prescribed it for patients aged 40-60 years. Cost was the top priority for both groups, with minor differences in preferences for other features.

DISCUSSION

The findings from this cross-sectional survey of 755 healthcare professionals in India provide valuable insights into the prescribing patterns, preferences and challenges associated with the management of neuropathic pain, particularly with the use of the nortriptyline, pregabalin, and mecobalamin fixed-dose combination. The preference for nortriptyline (40.98%) over amitriptyline (33.26%)and protriptyline (15.66%) among tricyclic antidepressants aligns with global trends favouring nortriptyline due to its favourable side-effect profile compared to amitriptyline. For instance, a systematic review by Finnerup et al. [3] highlighted nortriptyline's efficacy in NP management with fewer anticholinergic side effects, making it a preferred choice for conditions like diabetic neuropathy and post-herpetic neuralgia. This preference was particularly pronounced among orthopaedic

specialists (46.27%) in our study, likely due to their focus on safety, which corroborates findings from a European study by Gray et al. [9], where safety concerns significantly influenced TCA prescribing decisions.

Efficacy emerged as the primary driver for molecule selection (45.92%), consistent with guideline recommendations from the International Association for the Study of Pain (IASP), which emphasize evidence-based efficacy for TCAs and anticonvulsants like pregabalin in NP management [10]. The frequent use of the NPM combination for diabetic neuropathy (43.88%) reflects established role in addressing this prevalent condition in India, where diabetes affects over 77 million individuals [11]. The combination of nortriptyline, pregabalin, and mecobalamin likely offers synergistic effects, with pregabalin targeting neuropathic pain through calcium channel modulation and mecobalamin supporting nerve repair, as supported by clinical studies [12]. However, the use of this combination for other indications, such as chronic pain (29.72%) and low back pain (15.00%), suggests a broader application, potentially driven by clinical experience rather than robust evidence, as these indications lack strong guideline support as per latest evidencebased recommendations from Attal et al., [13]. The moderate prescribing frequency of the NPM combination (47.96% in 25-50% of NP cases) indicates cautious adoption, possibly due to barriers such as high cost (34.12%), safety

concerns (27.46%), and suboptimal patient adherence (39.05% reporting 25-50% adherence). Cost as a primary barrier is particularly relevant in the Indian context, where out-of-pocket healthcare expenditure remains high as reflected by a study from Garg & Karan et al., [14]. This finding echoes studies from lowand middle-income countries, where cost significantly limits access to NP medications [15]. The slightly higher emphasis on safety orthopedic specialists and compliance among consulting physicians may reflect their differing patient populations and clinical priorities. Orthopedists, often managing musculoskeletal-related NP, may prioritize safety to minimize adverse effects in patients with comorbidities, while physicians, dealing with diverse NP etiologies, may focus on compliance to ensure therapeutic continuity. Patient adherence remains a critical challenge, with only 13.30% of clinicians reporting adherence rates above 75%. This aligns with literature highlighting poor adherence to NP medications due to side effects, complex regimen, and socioeconomic factors [16]. The

preference for shorter treatment durations (1

compared to 2-3 months among physicians

suggests differing approaches to balancing

efficacy and adherence, potentially influenced

by patient follow-up patterns. The predominance

of NPM prescriptions in the 40-60 age group

(53.32%) reflects the high burden of diabetic

chronic

pain

in

this

and

38.30%) among orthopedics

month by

neuropathy

demographic, consistent with epidemiological data from India [17].

Formulation preferences, with 39.27% favoring the NPM combination and 36.26% opting for nortriptyline + pregabalin, suggest a tailored approach to NP management. The inclusion of mecobalamin in the NPM combination may be driven by its perceived neuroprotective benefits, though evidence remains mixed [6]. Brand selection criteria, led by cost (36.00%) and tablet/capsule size (26.18%), underscore practical considerations prescribing in decisions, particularly in resource-constrained settings. These findings align with studies indicating that formulation characteristics, such as ease of administration, influence prescribing behavior in chronic conditions [18].

The differences between orthopedic specialists and consulting physicians, while subtle, highlight the need for tailored educational interventions to optimize NP management. Orthopedics preference for shorter durations and greater focus on safety may reflect their surgical orientation and shorter patient interaction times, whereas physicians' emphasis on compliance and longer durations may stem from managing chronic conditions in outpatient settings. Future research should explore these differences through qualitative studies to better understand decision-making processes.

Limitations of the study:

This study has limitations, including its crosssectional design, which limits causal inferences, and its reliance on self-reported data, which may introduce bias. Additionally, the survey did not capture patient perspectives, which are critical for understanding adherence challenges. Future studies should incorporate longitudinal designs and patient-reported outcomes to validate these findings and assess the real-world effectiveness of the NPM combination. Moreover, cost-effectiveness analyses could guide policy interventions to improve access to NP medications in India.

CONCLUSION

In conclusion, the survey highlights the prominence of nortriptyline-based regimens, particularly the NPM combination, in managing neuropathic pain in India, driven by efficacy and tempered by cost and adherence challenges. These insights underscore the need for strategies to enhance affordability, improve patient adherence, and align prescribing practices with evidence-based guidelines to optimize NP management.

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