

## Original Research Article

# Clinician's Perspectives and Prescription Practice of sodium valproate in the Management of migraine, bipolar disorder, and seizures in Indian Healthcare settings

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## 1 ABSTRACT

**Objective:** To gather clinicians' perspectives on the management of neurological disorders such as migraine, bipolar disorder (BPD), and seizures, as well as the prescription practice of sodium valproate in Indian settings.

**Methodology:** This cross-sectional, multi-response survey was conducted among clinicians specialized in migraine, BPD, and seizure management. The selected participants completed a 29-question questionnaire distributed via email or online platforms. The survey explored prescription practices, clinical observations, and preferences regarding sodium valproate and neurological disorder management. Data analysis involved descriptive statistics, with responses presented as frequencies and percentages.

**Results:** The survey involved 340 participants, and nearly half (45.88%) of them indicated that sodium valproate was their preferred choice for managing migraine, seizures, and BPD. Around 45% of the respondents noted that women are most frequently affected by migraine. Approximately 55% of the clinicians identified anxiety as the most common comorbid condition associated with migraine. About 47% of the participants preferred sodium valproate for migraine prophylaxis, while the majority (76.76%) of the clinicians chose it as the preferred treatment for BPD. Roughly 40% of the respondents reported that a daily dose of 300 mg of sodium valproate was commonly used for migraine. Approximately 54% of participants found that sodium valproate was most often prescribed to individuals in the 18-45 years age group. Additionally, 65% of the participants reported headaches or dizziness as common adverse effects of sodium valproate.

**Conclusion:** This study revealed that sodium valproate was a widely preferred treatment for migraine, seizures, and BPD among Indian clinicians, particularly for women and individuals aged 18-45 years. The findings highlighted the prevalent use of 300 mg daily dose for migraine and the common association of anxiety with migraine.

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2  
3 **Keywords:** *Migraine, BPD, seizures, sodium valproate, comorbid conditions, adverse effects*

## 4 1. INTRODUCTION

5  
6 The burden of migraine, bipolar disorder, and seizures is significant, affecting millions  
7 worldwide. These conditions not only impair individuals' quality of life but also contribute to  
8 broader societal challenges, including economic costs and healthcare demands [1-  
9 3]. Migraine accounts for 4.9% of global ill health measured in years lived with disability

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10 (YLDs), impacting over 1 billion people, with India reporting the highest prevalence in 2019  
11 at approximately 213,890,208 cases [4,5]. Globally, around 70 million people live with  
12 epilepsy, with nearly 12 million in India [6]. The World Mental Health survey estimates a  
13 global prevalence of BPD at 0.8%, with the incidence among adolescents and young adults  
14 increasing from 79.21 per 100,000 in 1990 to 84.97 per 100,000 in 2019 [7,8]. In India, a  
15 population-based study found current and lifetime prevalence rates of BPAD at 0.3% and  
16 0.5%, respectively [8].

17 Sodium valproate (valproic acid), which belongs to the class of drugs known as  
18 anticonvulsants or antiepileptics, was approved by the Food and Drug Administration (FDA)  
19 for treating complex partial seizures, simple and complex absence seizures, and as an  
20 adjunctive therapy for multiple seizure types in both adults and pediatric patients. Sodium  
21 valproate inhibits voltage-gated sodium channels to reduce neuronal excitability and seizure  
22 activity. It also inhibits gamma-aminobutyric acid (GABA) transaminase, thereby boosting  
23 GABA levels and enhancing inhibitory effects. Additionally, sodium valproate promotes  
24 GABA synthesis by increasing glutamic acid decarboxylase activity and inhibits histone  
25 deacetylases (HDACs), influencing gene expression. Furthermore, sodium valproate  
26 modulates calcium channels, impacting neuronal signaling and pain pathways [9].

27 Understanding the prescription practice of sodium valproate was crucial for optimizing its  
28 use, improving patient outcomes, and enhancing neuronal health management. The present  
29 survey aims to collect expert opinions on the clinical application of sodium valproate  
30 maintenance therapy for migraine, seizures, and BPD within Indian healthcare settings.

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## 31 2. MATERIALS AND METHODS

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32 We carried out a cross-sectional, multiple-response questionnaire-based study involving  
33 clinicians with expertise in managing migraine, seizures, and BPD in the major Indian cities  
34 from June 2023 to December 2023. The study was conducted after getting approval from  
35 Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian  
36 Regulatory Authority, Drug Controller General of India.

### 39 2.1 Questionnaire

40 The questionnaire booklet named SCORE (Sodium Valproate Efficacy & Tolerability Profile)  
41 study was sent to the clinicians who were interested in participating in this study. The  
42 SCORE study questionnaire included 29 questions focusing on current prescription practices,  
43 clinical observations, and preferences related to sodium valproate, as well as experiences  
44 with migraine, seizures, and BPD in routine practice.

### 46 2.2 Participants

47 An invitation was sent to leading clinicians in treating migraine, seizures, and BPD in March  
48 2023 for participation in this Indian survey. About 340 doctors from major cities of all Indian  
49 states representing the geographical distribution shared their willingness to participate and  
50 provided necessary data. Participants were asked to complete the questionnaire without  
51 discussing it with their peers. A written informed consent was obtained from each physician  
52 before initiation of the study.

### 55 2.3 Statistical Methods

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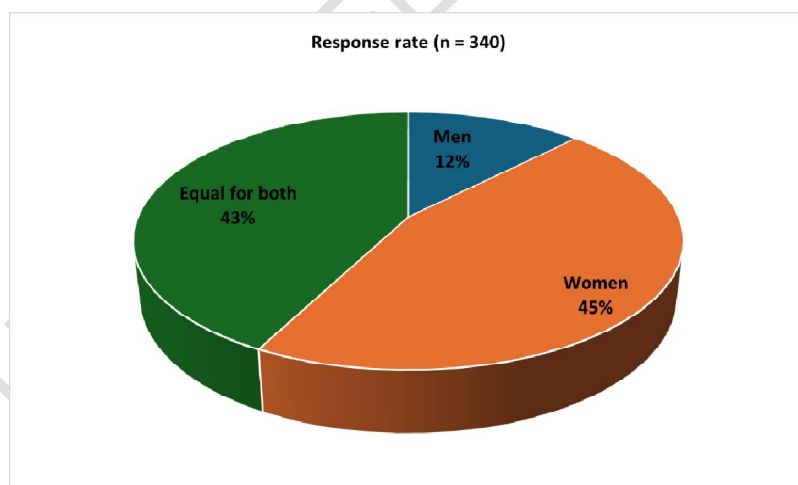
57 Descriptive statistics were employed for data analysis with categorical variables presented  
 58 as percentages. The frequency of each variable and its corresponding percentage was  
 59 calculated to illustrate its distribution. Graphs and pie charts were created using Microsoft  
 60 Excel 2013 (version 16.0.13901.20400) to visually depict the distribution of categorical  
 61 variables.

### 62 3. RESULTS

63  
 64 Out of 340 clinicians surveyed, nearly half (45.88%) of the respondents reported that sodium  
 65 valproate was the preferred choice for migraine prophylaxis, seizures, and BPD (Table 1).  
 66 Over half (52.65%) of the participants indicated that an average of 6-10 patients present with  
 67 migraine headaches per day. Approximately 47% of the clinicians noted that fewer than 5  
 68 patients present with a history of seizures daily, and about 58% of the participants reported  
 69 that fewer than 5 patients present daily with BPD. Approximately 45% of participants noted  
 70 that women were most affected by migraine, while 43% of the clinicians observed that both  
 71 genders equally experience migraine (Fig. 1) and about 55% of the participants identified  
 72 anxiety as the most common comorbid condition in patients with migraine (Table 2).  
 73

74 **Table 1: Distribution of response to the preferred use of sodium valproate in clinical**  
 75 **disorders**

Preference	Response rate (n = 340)
Migraine prophylaxis	9.41%
Seizures	19.71%
BPD	15.88%
All of the above	45.88%



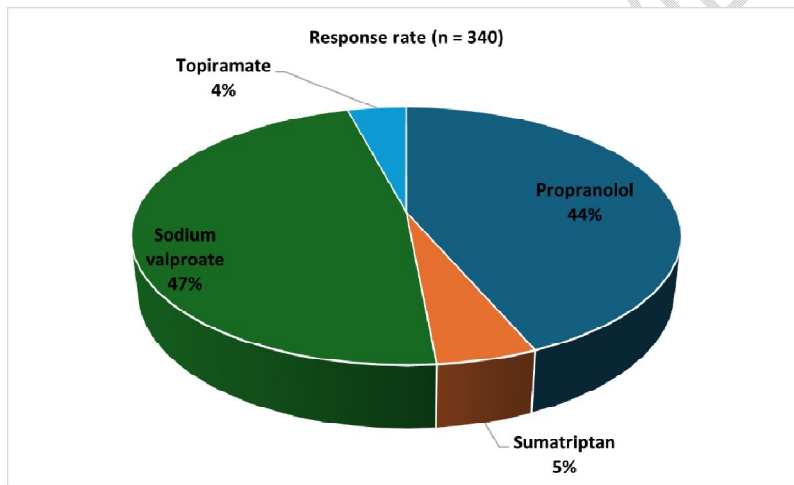
77  
 78 **Fig. 1: Distribution of response to the predominant gender presenting with migraine**  
 79 **headaches in clinical settings**

80  
 81 **Table 2: Distribution of response to most common comorbid condition noted in**  
 82 **patients diagnosed with migraine**

Common comorbid condition	Response rate (n = 340)
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Anxiety	55.29%
Panic disorder	14.71%
Hypertension	10%
Diabetes	0.88%
Depression	11.76%
All of the above	7.35%

83 Approximately 27% of clinicians noted that men were most affected by BPD, while about  
84 61% of respondents stated that the 18-35 age group was most affected by migraine. About  
85 49% of participants indicated that the 36-50 age group was most affected by BPD. About  
86 47% of experts preferred sodium valproate for migraine prevention, while 44% of participants  
87 preferred propranolol for the same purpose (Fig. 2), while nearly 77% selected it as the  
88 preferred treatment for BPD (Table 3).



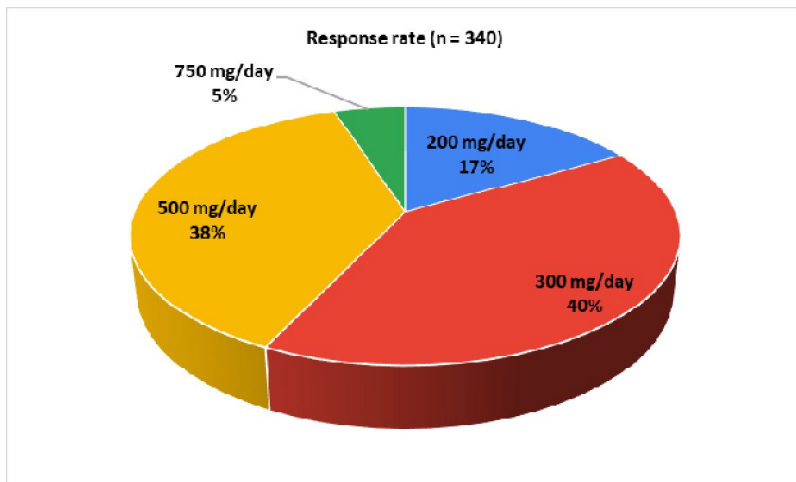
89  
90 **Fig. 2: Distribution of response to preferred drug choice for patients with migraine**  
91 **prophylaxis**

92  
93 **Table 3: Distribution of response to preferred drug choice for patients with BPD**

Preference	Response rate (n = 340)
Olanzapine	7.94%
Quetiapine	4.41%
Sodium valproate	76.76%
Lithium	9.12%
No preference	1.76%

94  
95 Approximately 54% of participants reported that levetiracetam was the most effective  
96 antiepileptic based on its efficacy in seizures. Almost half (48.82%) of the respondents noted  
97 that 20-40% of patients were treated with sodium valproate for migraine prophylaxis, and

98 about 43% reported the same proportion of patients receiving the drug as treatment for BPD.  
 99 Nearly half (50.88%) of the clinicians indicated that 20-40% of patients were treated with  
 100 sodium valproate for seizures. Approximately 40% of participants indicated that a daily dose  
 101 of 300 mg of sodium valproate was commonly used for migraine, while 38% reported that  
 102 the daily dose was 500 mg (Fig. 3). Approximately 48% of the clinicians stated that a daily  
 103 dose of 500 mg was commonly used for BPD, and 56% recommended the same dosage for  
 104 seizures. Nearly 54% of the participants found that the 18-45 age group was most  
 105 prescribed with sodium valproate (Table 4).



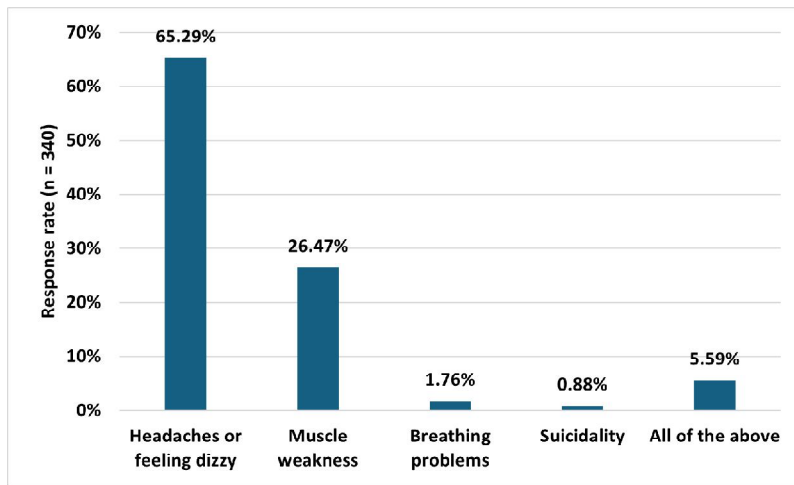
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107 **Fig. 3: Distribution of response to the daily dose of sodium valproate commonly used**  
 108 **for migraine**

109 **Table 4: Distribution of response to common age group prescribed with sodium**  
 110 **valproate**

Age (years)	Response rate (n = 340)
<12	2.06%
12-18	11.76%
18- 45	54.12%
45-60	10.59%
>60	0.29%
All age groups	21.18%

111 Around 65% of the participants reported that fewer than 5% of patients experience  
 112 osteoporosis (OP) or osteopenia as side effects of sodium valproate, with 31% observing  
 113 these effects in patients aged 46-60 years. About 39% of the clinicians noted that OP or  
 114 osteopenia typically develops after 12-24 months of treatment. Additionally, 65% of the  
 115 participants reported headaches or dizziness as common adverse effects of sodium  
 116 valproate (Fig. 4).



117

118 **Fig. 4: Distribution of response to adverse effects reported with the use of sodium**  
 119 **valproate**

120

121 About 62% of the clinicians stated that brivaracetam has the advantage of lesser behavioral  
 122 disturbances compared to sodium valproate, and more than half (58.24%) of the participants  
 123 considered the flavor of sodium valproate syrup important for pediatric patients.  
 124 Approximately 53% of the respondents found levetiracetam to be the most effective  
 125 antiepileptic syrup based on its efficacy in seizures, and around 68% of the participants  
 126 reported that levetiracetam injection was most effective for generalized tonic-clonic seizures.  
 127 About 35% of the respondents indicated that 16-40% of individuals show improved  
 128 outcomes with sodium valproate therapy for migraine, and 47% of the participants preferred  
 129 dose escalation as the strategy for patients failing to respond to the initial sodium valproate  
 130 treatment for migraine.

131

#### 132 4. DISCUSSION

133

134 The survey indicated that sodium valproate was a widely preferred treatment for migraine,  
 135 seizures, and BPD among clinicians in India, reflecting its established role in neurological  
 136 disorder management. Vatzaki et al. highlighted that sodium valproate was widely used for  
 137 migraine prophylaxis and was included in primary European guidelines [10]. Similarly,  
 138 Silberstein et al. found that the drug was effective for migraine prevention, helping to reduce  
 139 the frequency and severity of attacks [11]. In the realm of epilepsy, Marques et al. identified  
 140 sodium valproate as the most effective antiepileptic drug for genetic generalized epilepsies  
 141 [12]. Furthermore, Balagura et al. highlighted its broad spectrum of activity and diverse  
 142 mechanisms of action, which have made it a first-line treatment for most seizure types in  
 143 children for the past fifty years [13]. In the context of BPD, Roosen and Sienaert provided  
 144 evidence supporting the use of sodium valproate for rapid cycling, while Charles L. Bowden  
 145 affirmed its value as an effective treatment for BPD [14].

146 Many survey participants observed that women were more severely affected by migraine.  
 147 Nappi et al. reported that migraine was more prevalent in women, with 17% of women  
 148 meeting the diagnostic criteria for the condition. They also found that migraine frequency in  
 149 women varies with the menstrual cycle and pregnancy, and that combined hormonal

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150 contraception (CHC) or hormone replacement therapy (HRT) can either trigger or modify  
151 migraine [15]. Similarly, Kalkman et al. noted that migraine prevalence was two to three  
152 times higher in women compared to men [16]. Singh et al. described migraine as a common  
153 neurological disorder with a higher prevalence in women, marked by painful and debilitating  
154 headaches [17]. Kumar and Kadian found that the overall prevalence of migraine was  
155 estimated at 16%, with a sex prevalence ratio of 3:1, indicating a significantly higher  
156 frequency in women [18].

157 Most survey respondents identified anxiety as the most prevalent comorbid condition in  
158 patients with migraine. Cuciureanu et al. emphasized that anxiety was a frequent  
159 comorbidity associated with migraine, influencing disease prognosis, treatment, and clinical  
160 outcomes [19]. Senaratne et al. observed that symptoms of anxiety disorder were  
161 significantly more common in patients with migraine than those without [20]. Additionally,  
162 Jeyagurunathan et al. reported that anxiety and mood disorders were approximately two to  
163 ten times more prevalent among individuals with chronic migraine compared to the general  
164 population [21].

165 Many of the participants in the survey preferred sodium valproate for migraine prophylaxis,  
166 Kumar and Kadian noted that sodium valproate was used for migraine prophylaxis and was  
167 considered one of the first-line agents for migraine prevention [18]. Similarly, Vatzaki et al.  
168 reported that sodium valproate was commonly used to treat pre-chronic and chronic  
169 migraine [10].

170 The majority of the survey respondents identified sodium valproate as the preferred  
171 treatment for BPD. Chen et al. confirmed that sodium valproate was a commonly preferred  
172 medication for maintaining BPD [22]. Smith et al. concluded that sodium valproate effectively  
173 reduces depressive symptoms in acute bipolar depression and is well-tolerated [23].  
174 Additionally, Zheng et al. highlighted that sodium valproate was widely used as an  
175 anticonvulsant for the maintenance treatment of BPD [24].

176 Many of the survey participants reported that a 300 mg daily dose of sodium valproate was  
177 commonly used for migraine. In line with this finding, Rahman et al. noted that the initial  
178 dosage of sodium valproate for migraine prophylaxis typically ranges from 250 to 500 mg,  
179 administered twice daily for one week [25]. Diener et al. reported that intravenous  
180 administration of sodium valproate, at doses of either 300 mg or 800 mg, was effective in  
181 treating acute migraine attacks [26]. Pascual et al. reported that the maintenance dose of  
182 sodium valproate typically ranges from 300 to 1000 mg daily [27].

183 Many of the participants stated that the 18-45 age group was most prescribed sodium  
184 valproate. In a study by Evans et al. conducted in England and Wales, it was reported that  
185 87.7 out of every 1,000 individuals prescribed valproate were women or girls aged 14 to 45  
186 years [28].

187 Most of the participants identified headaches and dizziness as common adverse effects of  
188 sodium valproate. Rahman et al. confirmed that dizziness and headaches were frequently  
189 associated with the drug [25]. Montalbano et al. reported additional common side effects  
190 including nausea, vomiting, constipation, increased appetite, weight gain, somnolence, and  
191 tremor [29]. Philip B. Bradley also noted that sodium valproate can cause dizziness, mild  
192 hypotension, and mild thrombocytopenia in some patients [30].

193 The major strengths of the survey include its large sample size and input from neurological  
194 disorder specialists regarding the effectiveness of sodium valproate. However, the results  
195 may be subject to bias due to reliance on expert opinion, and varying perspectives among

196 clinicians could affect the findings. Additionally, the survey might not fully incorporate  
197 emerging evidence or evolving trends in the management of neurological disorders such as  
198 migraine, seizures, and BPD. It is crucial to acknowledge these limitations when interpreting  
199 the results and to recognize the need for further research to confirm the findings of the  
200 survey. Future studies could investigate the long-term effects of sodium valproate and  
201 explore strategies for improving patient education.

## 202 5. CONCLUSION

203  
204 This study's findings highlight sodium valproate as the preferred treatment for managing  
205 neurological disorders such as migraine, BPD, and seizures, aligning with earlier studies that  
206 recognize its effectiveness and its status as a first-line treatment. The data indicate its  
207 prevalent use across various age groups, particularly in the 18-45 age range, with dosage  
208 preferences ranging from 300 mg to 500 mg daily.

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