

# Gabapentin and pregabalin in dermatology

Asit Mittal, Chesta Agarwal, Manisha Balai, Ayush Taneja

## Introduction

The anticonvulsants gabapentin and pregabalin are of interest to dermatologists. The drugs have found uses in conditions that are frequently of interest to dermatologists and often primarily present to a dermatologist. These drugs are likely to find greater use in dermatology practice in future. This review is intended to familiarize dermatologists with these drugs.

## History

Pregabalin was synthesized in 1990 as an anticonvulsant. It was invented by Richard Bruce Silverman at Northwestern University in Chicago, Illinois. The drug was approved in the European Union in 2004. The US received Food and Drug Administration approval for use in treating epilepsy, diabetic neuropathic pain and postherpetic neuralgia in December 2004. Gabapentin was originally approved by the U.S. Food and Drug Administration in December 1993 for use as an adjuvant medication to control partial seizures in adults; that indication was extended to children in 2000. In 2004, its use for treating postherpetic neuralgia (neuropathic pain following shingles) was approved.

## Mechanism of Action

Gabapentin consists of a gamma amino butyric acid molecule covalently bound to a lipophilic cyclohexane ring (C<sub>9</sub>H<sub>17</sub>NO<sub>2</sub>) [Figure 1]. It is a centrally active gamma amino butyric acid agonist, with its high lipid solubility aimed at facilitating its transfer across the blood–brain barrier. Despite their design as gamma amino butyric acid agonists, neither gabapentin nor pregabalin mimics gamma amino butyric acid when

iontophoretically applied to neurons in primary culture.<sup>1</sup> These compounds bind with a high affinity to a protein in cortical membrane with amino acid sequence identical to that of calcium channel subunit  $\alpha 2\delta$ -1.<sup>2</sup> It has been speculated that the anticonvulsant effect of gabapentin is mediated by  $\alpha 2\delta$ -1 protein, but whether and how binding of gabapentin to this protein regulate neuronal activity remains unclear.<sup>1</sup> Pregabalin binding is reduced but not eliminated in mice carrying a mutation in  $\alpha 2\delta$ -1 protein.<sup>3</sup> It is unclear whether the anticonvulsant and analgesic effect of gabapentin and pregabalin are mediated by affecting calcium currents, and if so how.

## Pharmacokinetics

Gabapentin is not metabolized. It is eliminated via renal mechanism and is excreted unchanged. It does not induce hepatic enzymes. Absorption is nonlinear and dose-dependent at very high doses, but the elimination kinetics is linear. The drug is not bound to plasma protein. Drug–drug interactions are negligible. The half-life is relatively short ranging from 5.0 to 8.0 hours, hence, it is administered two or three times per day.<sup>4</sup> It requires gradual adjustment of the dose. In contrast to gabapentin, pregabalin has linear and dose proportion absorption in therapeutic dose range (150 to 600 mg/d). It also has rapid onset of action and more limited dose range.<sup>4</sup> Similar to gabapentin, it is also not metabolized and is almost entirely excreted unchanged in the urine. It is not bound to plasma proteins and has virtually no drug–drug interaction, again resembling the characteristics of gabapentin. Similarly, other drugs do not affect the pharmacokinetics of pregabalin. The half-life of pregabalin ranges from approximately 4.5 hour to 7.0 hours, thus, requiring more than once daily dosing in most patients.<sup>4</sup>

## Dosing

The initial dosage of gabapentin is 300 mg/d and can be increased up to 1200 mg three times a day.<sup>5,6</sup> It can be started

Department of Dermatology, Venereology and Leprology, R. N. T. Medical College, Udaipur, Rajasthan, India

**Correspondence:** Dr. Asit Mittal,  
Department of Dermatology, Venereology and Leprology,  
R. N. T. Medical College, Udaipur - 313 001, Rajasthan, India.  
E-mail: asitmittal62@gmail.com

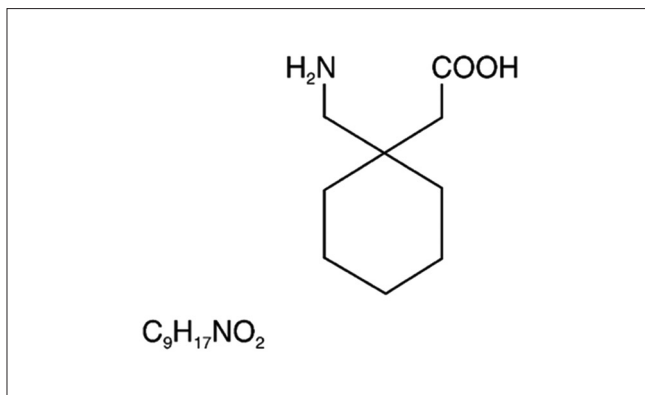
Access this article online	
Quick Response Code:	Website: www.ijdv.com
	DOI: 10.4103/ijdv.IJDVL_480_17

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** reprints@medknow.com

**How to cite this article:** Mittal A, Agarwal C, Balai M, Taneja A. Gabapentin and pregabalin in dermatology. Indian J Dermatol Venereol Leprol 2018;84:634-40.

**Received:** June, 2017. **Accepted:** December, 2017.



**Figure 1:** Chemical structure of gabapentin

at its effective dose rather than gradually titrated upwards in dosage.<sup>7</sup> It should not be discontinued abruptly, but rather tapered gradually, because it can lead to withdrawal-related side-effects.<sup>8</sup> It has a high toxicity ratio, minimizing the chance of adverse effects with even very high overdoses,<sup>9</sup> hence, routine monitoring of clinical laboratory parameters is not required.<sup>5</sup> Pregabalin is started at an initial dose of 150 mg/d and can be increased up to 600 mg/d.<sup>10</sup>

## Clinical Uses

### Postherpetic neuralgia and other similar neuropathies

Approximately 10–15% of herpes zoster patients will develop postherpetic neuralgia, which can persist for many years. Dermatologists are often the primary care providers for postherpetic neuralgia patients. Several trials conducted previously reported statistically significant reduction in average daily pain after gabapentin and pregabalin.<sup>11–17</sup> Gabapentin is the first oral medication approved in the USA for this condition.<sup>5</sup> Reviews of controlled studies showed that patients suffering from postherpetic neuralgia experienced a statistically significant reduction in average daily pain after treatment with gabapentin. The study also showed that those receiving gabapentin experienced improvement in sleep and overall quality of life.<sup>11</sup> Gabapentin is useful in the treatment of neuralgia in all areas of the body [Table 1]. Its positive effect on neuralgia includes trigeminal neuralgia,<sup>18</sup> glossopharyngeal neuralgia refractory to the usual medical treatments<sup>19</sup> and facial neuritis.<sup>20</sup> It is also useful in treating inflammatory pain.<sup>21</sup> Gabapentin is also effective in the treatment of human immunodeficiency virus (HIV) neuropathy,<sup>22</sup> painful diabetic neuropathy<sup>23</sup> and diabetic neuropathic pain.<sup>24</sup> Of particular interest to dermatologist is the probable usefulness of this drug in decreasing the trophic ulcerations that results from neuropathy in diseases such as HIV, leprosy and diabetes that are prone to such ulcers.<sup>5</sup> Pregabalin is found to be efficacious in treating Red scrotum syndrome (poorly understood, chronic dysesthetic erythema primarily involving the anterior scrotum).<sup>25</sup>

### Pruritus

Generalized pruritus is a distressing symptom that can occur in several dermatologic and systemic disorders. Strong

**Table 1: Various uses of gabapentin in dermatology**

Neuropathic pain
Postherpetic neuralgia
HIV neuropathy
Diabetic neuropathic pain
Neuralgia
Glossopharyngeal neuralgia
Trigeminal neuralgia
Facial neuritis
Skin hypersensitivity
Allodynia
Buccofacial allodynia
Mechanical allodynia
Reflex sympathetic dystrophy
Dynia
Glossodynia
Carotidynia
Vulvodynia
Orchidynia
Prostatodynia
Coccygodynia
Proctodynia
Scalp dysesthesia
Hot flashes
Temperature-sensitive dermatosis
Dysesthetic pain after reconstruction surgery
Pruritus
Brachioradial pruritus
Uremic pruritus
Pruritus of unknown origin
Seizure due to AIP
Self-injurious behavior in Lesh-Nyhan syndrome
Steroid induced mania
Piloileiomyoma-related pain
Pain of vasolabile conditions
Erythromelalgia

HIV: Human immunodeficiency virus, AIP: Acute intermittent porphyria

similarities exist between neural induction, transmission and processing of pruritus and pain. While itch is transmitted by a functionally distinct subset of neurons, overlap exists between the mediators and receptors involved in the pathogenesis of these sensations.<sup>26</sup> In addition, it is now clear that chronic itch is influenced by a phenomenon of neural hypersensitization in a process that parallels what has been observed in chronic pain.<sup>27</sup> In the wake of these discoveries, agents that target the neural system have emerged as effective antipruritic therapies.<sup>28</sup> Gabapentin has been reported to be an effective antipruritic agent in uremic pruritus,<sup>29–36</sup> brachioradial pruritus,<sup>9,37–40</sup> pruritus associated with wound healing in burns<sup>41</sup> and notalgia paresthetica<sup>42</sup> and pruritus of unknown origin.<sup>6,43</sup> Its effect in pruritus can be central and peripheral. It inhibits voltage-dependent calcium ion channels located in the spinal cord (with particular high density in the superficial laminae of the dorsal horn), inhibiting the release of excitatory

neurotransmitters. Other mechanisms involved are increase in the synthesis of  $\gamma$ -aminobutyric acid from glutamate by altering the activity of glutamic acid decarboxylase in neurological tissue,<sup>44</sup> inhibition of the release of calcitonin gene-related peptide, a neuropeptide, described as an itch mediator.<sup>45</sup> Gabapentin also increases the threshold to experience nociception.<sup>46</sup> Related drug Pregabalin, a gamma amino butyric acid analogue of gabapentin, has been used in the treatment of uremic pruritus,<sup>47-50</sup> brachioradial pruritus,<sup>51,52</sup> pruritus in prurigo nodularis<sup>53</sup> and polycythemia vera-associated aquagenic pruritus.<sup>54</sup> It was hypothesized that the beneficial effect of Pregabalin in chronic pruritus may result from counteracting the effects on the central sensitizing processes involved in the generation of chronic itch.<sup>55</sup> It has also been reported to improve interleukin 2<sup>56</sup> and cetuximab-related<sup>57</sup> pruritus in cancer patients. However, at present there are insufficient data to conclude that these anticonvulsants can be an effective therapeutic alternative in the management of pruritus.

#### Gabapentin in various dynias

The “dynias” are a group of chronic, focal pain syndromes with a predilection for the orocervical and urogenital regions. They include glossodynia, carotidynia, scalp dysesthesia, vulvodinia, orchidynia, prostatodynia, coccygodynia and proctodynia [Table 1].<sup>5</sup> In some cases, the dynia occur secondarily, but more often, despite an exhaustive evaluation, no etiology is found, and in these cases the cause of pain

remains enigmatic. Sometimes, these patients initially present to dermatologist. These dynias are found responsive to gabapentin. Allodynia is a sensation of pain to slight touch. It is another complication of postherpetic neuralgia. It can be effectively treated by gabapentin which can block both the static and dynamic components of mechanical allodynia.<sup>58</sup> It also relieves cutaneous hyperalgesia after skin has been sensitized to pain.<sup>58</sup> Reflex sympathetic dystrophy is a condition involving persistent pain that results from nerve injury. It has a variety of cutaneous manifestations, including atrophy, edema, erythema, bullae, and ulcers.<sup>59</sup> Gabapentin has a role in the control of reflex sympathetic dystrophy-related pain in children<sup>60</sup> and adults.<sup>61</sup>

#### Other uses

Gabapentin has shown benefit in pain related to leiomyomas<sup>5</sup> in patients with painful sclerodermatous changes that have affected nerve conduction,<sup>62</sup> pain of the vasolabile condition and erythromelalgia.<sup>63,64</sup> Gabapentin has also shown benefits in various conditions associated with neurologic problems and skin. It is useful in the treatment of dysesthetic pain after reconstructive surgery,<sup>65</sup> seizures due to acute intermittent porphyria,<sup>66</sup> self-injurious behavior in Lesch-Nyhan syndrome<sup>67</sup> and as a prophylaxis against steroid-induced mania.<sup>68</sup> Finally, gabapentin improves pain control during wound dressing of cancer patients,<sup>69</sup> suggesting that it might have a role in toxic epidermal necrolysis patients who complain of “painful skin.”<sup>70</sup> In a recent article, gabapentin was also found to be effective for

**Table 2: Summary of studies showing effect of gabapentin and pregabalin in various dermatological conditions**

Use	Studies	Year	Study design	Level of evidence
Postherpetic neuralgia	Zhang <i>et al.</i> A randomized, double blind placebo-controlled trial to assess the efficacy and safety of gabapentin enacarbil in patients with neuropathic pain associated with postherpetic neuralgia. <i>J Pain</i>	2013	RCT	Level I
	Wallace <i>et al.</i> Gabapentin extended-release tablets for the treatment of patients with postherpetic neuralgia: A randomized, double-blind, placebo-controlled, multicentre study. <i>Clin Drug Investig</i>	2010	RCT	Level I
	Gilron <i>et al.</i> Nortriptyline and gabapentin, alone and in combination for neuropathic pain: A double-blind, randomized controlled crossover trial. <i>Lancet</i>	2009	RCT	Level I
	Jensen <i>et al.</i> Assessment of pain quality in a clinical trial of gabapentin extended release for postherpetic neuralgia. <i>Clin J Pain</i>	2009	RCT	Level I
	Rice and Maton S. Gabapentin in postherpetic neuralgia: A randomized, double-blind, placebo-controlled study. <i>Pain</i>	2001	RCT	Level I
	Rowbotham <i>et al.</i> Gabapentin for the treatment of postherpetic neuralgia: A randomized controlled trial. <i>J Am Med Assoc</i>	1998	RCT	Level I
	Liu <i>et al.</i> A randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of pregabalin for postherpetic neuralgia in a population of Chinese patients. <i>Pain Pract</i>	2017	RCT	Level I
	Achar <i>et al.</i> Comparative study of clinical efficacy of amitriptyline and pregabalin in postherpetic neuralgia. <i>Acta Dermatovenol Croat</i>	2012	RCT	Level I
	Guan <i>et al.</i> Efficacy of pregabalin for peripheral neuropathic pain: Results of an 8-week, flexible-dose, double-blind, placebo-controlled study conducted in China. <i>Clin Ther</i>	2011	RCT	Level I
	Zin <i>et al.</i> A randomized, controlled trial of oxycodone versus placebo in patients with postherpetic neuralgia and painful diabetic neuropathy treated with pregabalin. <i>J Pain</i>	2010	RCT	Level I
Dworkin <i>et al.</i> Pregabalin for the treatment of postherpetic neuralgia: A randomized, placebo-controlled trial. <i>Neurology</i>	2003	RCT	Level I	

Contd...

Table 2: Contd...

Use	Studies	Year	Study design	Level of evidence	
Neuralgias	Pandey <i>et al.</i> Gabapentin for refractory idiopathic trigeminal neuralgia. <i>J Indian Med Assoc</i>	2008	Case report	Level III	
	Marelti <i>et al.</i> Gabapentin treatment of glossopharyngeal neuralgia: A follow up of 4 year of a single case. <i>Eur J Pain</i>	2002	Case report	Level III	
	Carlsen <i>et al.</i> Gabapentin treatment of glossopharyngeal neuralgia with cardiac syncope. <i>Ugeskr laeger</i>	2002	Case report	Level III	
	Garcia Callejo <i>et al.</i> Use of gabapentin in glossopharyngeal neuralgia. <i>Acta Otorrinolaringol Esp</i>	1999	Case report	Level III	
	Sist <i>et al.</i> Gabapentin for idiopathic trigeminal neuralgia: Report of two cases. <i>Neurology</i>	1997	Case report	Level III	
	Lucier and Franm L. Use of gabapentin in a case of facial neuritis. <i>Anesth Analg</i>	1997	Case report	Level III	
	Garcia Callejo <i>et al.</i> Clinical response of gabapentin for glossopharyngeal neuralgia. <i>Rev Neurol</i>	1994	Case report	Level III	
	Uremic pruritus	Foroutan <i>et al.</i> Comparison of pregabalin with doxepin in the management of uremic pruritus: A randomized, single-blind clinical trial. <i>Hemodial Int</i>	2017	RCT	Level I
Nofal <i>et al.</i> Gabapentin: A promising therapy for uremic pruritus in hemodialysis patients: A randomized-controlled trial and review of literature. <i>J Dermatolog Treat</i>		2016	RCT	Level I	
Hassan <i>et al.</i> Efficacy and safety of gabapentin for uremic pruritus and restless leg syndrome in conservatively managed patients with chronic kidney disease. <i>J Pain Symptom Manage</i>		2015	Cohort study	Level II	
Yong <i>et al.</i> Uremic pruritus is improved by gabapentin. <i>Int J Dermatol</i>		2014	Case report	Level III	
Shavit <i>et al.</i> Use of pregabalin in the management of chronic pruritus. <i>J Pain Symptom Manage</i>		2013	Clinical trial	Level II	
Solak <i>et al.</i> Pregabalin versus gabapentin in the treatment of neuropathic pruritus in maintenance haemodialysis patients: A prospective, crossover study. <i>Nephrology</i>		2012	RCT	Level I	
Rayner <i>et al.</i> Uraemic pruritus: Relief of itching by gabapentin and pregabalin. <i>Nephron clin pract</i>		2012	Clinical trial	Level II	
Marquez <i>et al.</i> Uremic pruritus in hemodialysis patients: Treatment with desloratidine versus gabapentin. <i>J Bras Nefrol</i>		2012	Clinical trial	Level II	
Razeghi <i>et al.</i> Gabapentin and uremic pruritus in hemodialysis patients. <i>Ren Fail</i>		2009	Clinical trial	Level II	
Naini <i>et al.</i> Gabapentin: A promising drug for the treatment of uremic pruritus. <i>Saudi J Kidney Dis Transpl</i>		2007	RCT	Level I	
Manenti L <i>et al.</i> Gabapentin in the treatment of uraemic itch: An index case and a pilot evaluation. <i>J Nephrol</i>		2005	Clinical trial	Level II	
Gunal <i>et al.</i> Gabapentin therapy for pruritus in haemodialysis patients: A randomized, placebo-controlled, double-blind trial. <i>Nephrol Dial Transplant</i>		2004	RCT	Level I	
Brachioradial pruritus		Atış and Bilir Kaya B. Pregabalin treatment of three cases with brachioradial pruritus. <i>Dermatol Ther</i>	2017	Case report	Level III
		Vestita <i>et al.</i> Brachioradial pruritus in a 47-year-old woman treated with pregabalin. <i>G Ital Dermatol Venereol</i>	2016	Case report	Level III
	Carvalho <i>et al.</i> Brachioradial pruritus in a patient with cervical disc herniation and Parsonage - Turner syndrome. <i>An Bras Dermatol</i>	2015	Case report	Level III	
	Uldall pallesen <i>et al.</i> Brachioradial pruritus effectively treated with gabapentin. <i>Ugeskr Laeger</i>	2012	Case report	Level III	
	Yilmaz <i>et al.</i> brachioradial pruritus successfully treated with gabapentin. <i>J Dermatol</i>	2010	Case report	Level III	
	Kanitakis. Brachioradial pruritus: Report of a new case responding to gabapentin. <i>Eur J Dermatol</i>	2006	Case report	Level III	
	Winhoven <i>et al.</i> Brachioradial pruritus: Response to treatment with gabapentin. <i>Br J Dermatol</i>	2004	Case report	Level III	
	Dynias	Dubey <i>et al.</i> Gabapentin therapy for glossodynia due to an unusual case. <i>Anesth Analg</i>	2008	Case report	Level III
Meiss <i>et al.</i> Gabapentin - a promising treatment in glossodynias. <i>Clin Exp Dermatol</i>		2002	Case report	Level III	
Ben David <i>et al.</i> Gabapentin therapy for vulvodynias. <i>Anesth Analg</i>		1994	Case report	Level III	
Sclerodermatous changes	Fischhoff and Sirois D. Painful trigeminal neuropathy caused by severe mandibular resorption and nerve compression in a patient with systemic sclerosis: Case report and literature review. <i>Oral Surg Oral Med Oral Pathol Oral Radiol Endod</i>	2000	Case report	Level III	

Contd...

Table 2: Contd...

Use	Studies	Year	Study design	Level of evidence
Erythromelalgia	McGraw and Kosek P. Erythromelalgia pain managed with gabapentin. <i>Anesthesiology</i>	1997	Case report	Level III
	Ceyhan et al. A case of erythromelalgia: Good response to treatment with gabapentin. <i>J Drugs Dermatol</i> 2010	2010	Case report	Level III
Dysesthetic pain after reconstructive surgery	Otley. Gabapentin for the treatment of dysesthetic pain after reconstructive surgery. <i>Dermatol Surg</i>	1999	Case report	Level III
Acute intermittent porphyria	Arora and Mahajan V. Gabapentin in seizures due to AIP. <i>Neurol India</i>	2000	Case report	Level III
Lesch-Nyhan syndrome	McManaman and Tam DA. Gabapentin for self-injurious behavior in Lesch-Nyhan syndrome. <i>Pediatr Neurol</i>	1999	Case report	Level III
Steroid-induced mania	Ginsberg and Sussman N. Gabapentin as prophylaxis against steroid-induced mania. <i>Can J Psychiatr</i>	2001	Case report	Level III
Wound dressing care	Devulder et al. Gabapentin for pain control in cancer patients' wound dressing care. <i>J Pain Symptom Manage</i>	2001	Case report	Level III
Toxic epidermal necrolysis	Moshfeghi and Mandler HD. Ciprofloxacin-induced toxic epidermal necrolysis. <i>Ann Pharmacother</i>	1993	Case report	Level III
Notalgia paresthetica	Maciel et al. Efficacy of gabapentin in the improvement of pruritus and quality of life of patients with notalgia paresthetica. <i>An Bras Dermatol</i>	2014	Clinical trial	Level II
	Loosemore et al. Gabapentin treatment for notalgia paresthetica, a common isolated peripheral sensory neuropathy. <i>J Eur Acad Dermatol Venereol</i>	2007	Case report	Level III

RCT: Randomized controlled trial. Level I: RCT, Level II: Case series, Level III: Case Report

Table 3: Side effects

Most common
Drowsiness/sedation
Malaise/lassitude
Cutaneous
Ulcers in mouth due to pancytopenia
Easy bruising
Fluid retention (leg)
Weight gain
Allergic eruptions
Stevens-Johnsons syndrome
Other side effects
Cholestasis
Hepatotoxicity
Anorgasmia
Dyskinesia
Reversible acute renal allograft dysfunction

Vismodegib-induced muscle cramps.<sup>71</sup> Pregabalin was also used for the treatment of painful hand-foot skin reaction associated with darafenib.<sup>72</sup> Studies showing effect of gabapentin and pregabalin in various dermatological conditions have been described briefly in Table 2.

### Adverse Effects

These drugs are relatively safe with very few serious adverse effects [Table 3]. The most frequently reported adverse event is drowsiness/sedation. This is seen during the first month of treatment.<sup>5</sup> This is also one of the most common cause for discontinuation of the drug.<sup>6</sup> Others causes include dizziness, malaise/lassitude and ataxia.

Rarely, they can cause pancytopenia, causing fever, sore throat and ulcers in the mouth, or unusual bleeding and easy bruising, fluid retention in the legs and weight gain.<sup>5,6</sup> A few cases of allergic eruptions<sup>73</sup> and Stevens–Johnson's syndrome<sup>74</sup> have also been reported.

Very rarely gabapentin has induced cholestasis<sup>75</sup> and hepatotoxicity.<sup>76</sup> Studies conducted for its efficacy in pregnancy showed no congenital anomalies among the infants. However, the crude mortality rate was up to five times higher than in the general population.<sup>77</sup> There are a few isolated reports about anorgasmia in women taking gabapentin.<sup>78</sup>

### Conclusion

Gabapentin and pregabalin are very promising medications in the treatment of painful conditions that often are domain of dermatologists such as postherpetic neuralgia, painful tumors, neuropathic ulcers or pain during dressing changes in conditions such as toxic epidermal necrolysis. Of great interest to a dermatologist is its use in chronic itch unresponsive to other medication. However, at present, there is insufficient data to suggest that these anticonvulsants can be an effective alternative to treat various types of skin sensitivities and pruritus. Future large randomized controlled studies are required that use behavioral methodology rather than subjective methodology. The chances of placebo effects are quite high with subjective methodologies.

### Financial support and sponsorship

Nil.



**Conflicts of interest**

There are no conflicts of interest.

**References**

- MacNamara JO. Pharmacotherapy of the epileptics. In: Brunton LL, editor. Goodman & Gilman's the Pharmacological Basis of Therapeutics. 12<sup>th</sup> ed. China: McGraw-Hill Companies; 2011. p. 583-607.
- Gee NS, Brown JP, Dissanayake VU, Offord J, Thurlow R, Woodruff GN, *et al.* The novel anticonvulsant drug, gabapentin (Neurontin), binds to the alpha2delta subunit of a calcium channel. *J Biol Chem* 1996;271:5768-76.
- Field MJ, Cox PJ, Stott E, Melrose H, Offord J, Su TZ, *et al.* Identification of the alpha2-delta-1 subunit of voltage-dependent calcium channels as a molecular target for pain mediating the analgesic actions of pregabalin. *Proc Natl Acad Sci U S A* 2006;103:17537-42.
- Porter RJ, Meldrum BS. Antiepileptic drug gabapentin and pregabalin. In: Katzung BG, Masters SB, Trevor AJ, editors. Basic and Clinical Pharmacology. 12<sup>th</sup> ed. New Delhi: Tata McGraw-Hill; 2012. p. 403-27.
- Scheinfeld N. The role of gabapentin in treating diseases with cutaneous manifestations and pain. *Int J Dermatol* 2003;42:491-5.
- Yesudian PD, Wilson NJ. Efficacy of gabapentin in the management of pruritus of unknown origin. *Arch Dermatol* 2005;141:1507-9.
- Ferrendelli JA. Concerns with antiepileptic drug initiation: Safety, tolerability, and efficacy. *Epilepsia* 2001;42 Suppl 4:28-30.
- Norton JW. Gabapentin withdrawal syndrome. *Clin Neuropharmacol* 2001;24:245-6.
- Winhoven SM, Coulson IH, Bottomley WW. Brachioradial pruritus: Response to treatment with gabapentin. *Br J Dermatol* 2004;150:786-7.
- US Food and Drug Administration. Lyrica (Pregabalin) full Prescribing Information.
- Rowbotham M, Harden N, Stacey B, Bernstein P, Magnus-Miller L. Gabapentin for the treatment of postherpetic neuralgia: A randomized controlled trial. *JAMA* 1998;280:1837-42.
- Rice AS, Maton S; Postherpetic Neuralgia Study Group. Gabapentin in postherpetic neuralgia: A randomised, double blind, placebo controlled study. *Pain* 2001;94:215-24.
- Dworkin RH, Corbin AE, Young JP Jr, Sharma U, LaMoreaux L, Bockbrader H, *et al.* Pregabalin for the treatment of postherpetic neuralgia: A randomized, placebo-controlled trial. *Neurology* 2003;60:1274-83.
- Zin CS, Nissen LM, O'Callaghan JP, Duffull SB, Smith MT, Moore BJ, *et al.* A randomized, controlled trial of oxycodone versus placebo in patients with postherpetic neuralgia and painful diabetic neuropathy treated with pregabalin. *J Pain* 2010;11:462-71.
- Guan Y, Ding X, Cheng Y, Fan D, Tan L, Wang Y, *et al.* Efficacy of pregabalin for peripheral neuropathic pain: Results of an 8-week, flexible-dose, double-blind, placebo-controlled study conducted in China. *Clin Ther* 2011;33:159-66.
- Athanasakis K, Petrakis I, Karampli E, Vitsou E, Lyras L, Kyriopoulos J, *et al.* Pregabalin versus gabapentin in the management of peripheral neuropathic pain associated with post-herpetic neuralgia and diabetic neuropathy: A cost effectiveness analysis for the Greek healthcare setting. *BMC Neurol* 2013;13:56.
- Liu Q, Chen H, Xi L, Hong Z, He L, Fu Y, *et al.* A randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of pregabalin for postherpetic neuralgia in a population of Chinese patients. *Pain Pract* 2017;17:62-9.
- Sist T, Filadora V, Miner M, Lema M. Gabapentin for idiopathic trigeminal neuralgia: Report of two cases. *Neurology* 1997;48:1467.
- García Callejo FJ, Marco Algarra J, Talamantes Escrivá F, Martínez Beneyto MP, Esparcia Navarro M, Morant Ventura A, *et al.* Use of gabapentin in glossopharyngeal neuralgia. *Acta Otorrinolaringol Esp* 1999;50:175-7.
- Lucier E, Franm L. Use of gabapentin in a case of facial neuritis. *Anesth Analg* 1997;85:1410.
- Werner MU, Perkins FM, Holte K, Pedersen JL, Kehlet H. Effects of gabapentin in acute inflammatory pain in humans. *Reg Anesth Pain Med* 2001;26:322-8.
- Newshan G. HIV neuropathy treated with gabapentin. *AIDS* 1998;12:219-21.
- Porta-Etessam J, García-Morales I, Martínez-Salio A, Berbel A, Benito-León J. Gabapentin in acute painful diabetic neuropathy. *Eur J Neurol* 2000;7:365.
- Pérez HE, Sánchez GF. Gabapentin therapy for diabetic neuropathic pain. *Am J Med* 2000;108:689.
- Miller J, Leicht S. Pregabalin in the treatment of red scrotum syndrome: A report of two cases. *Dermatol Ther* 2016;29:244-8.
- Roberson DP, Gudes S, Sprague JM, Patoski HA, Robson VK, Blasl F, *et al.* Activity-dependent silencing reveals functionally distinct itch-generating sensory neurons. *Nat Neurosci* 2013;16:910-8.
- Ikoma A, Steinhoff M, Ständer S, Yosipovitch G, Schmelz M. The neurobiology of itch. *Nat Rev Neurosci* 2006;7:535-47.
- Vinik AI. Clinical practice. Diabetic sensory and motor neuropathy. *N Engl J Med* 2016;374:1455-64.
- Gunal AI, Ozalp G, Yoldas TK, Gunal SY, Kirciman E, Celiker H, *et al.* Gabapentin therapy for pruritus in haemodialysis patients: A randomized, placebo-controlled, double-blind trial. *Nephrol Dial Transplant* 2004;19:3137-9.
- Manenti L, Vaglio A, Costantino E, Danisi D, Oliva B, Pini S, *et al.* Gabapentin in the treatment of uremic itch: An index case and a pilot evaluation. *J Nephrol* 2005;18:86-91.
- Naini AE, Harandi AA, Khanbabapour S, Shahidi S, Seirafiyani S, Mohseni M, *et al.* Gabapentin: A promising drug for the treatment of uremic pruritus. *Saudi J Kidney Dis Transpl* 2007;18:378-81.
- Razeghi E, Eskandari D, Ganji MR, Meysamie AP, Togha M, Khashayar P, *et al.* Gabapentin and uremic pruritus in hemodialysis patients. *Ren Fail* 2009;31:85-90.
- Marquez D, Ramonda C, Lauxmann JE, Romero CA, Vukelic VL, Martinatto C, *et al.* Uremic pruritus in hemodialysis patients: Treatment with desloratidine versus gabapentin. *J Bras Nefrol* 2012;34:148-52.
- Yong AS, Lee KY. Uremic pruritus is improved by gabapentin. *Int J Dermatol* 2014;53:e404-5.
- Cheikh Hassan HI, Brennan F, Collett G, Josland EA, Brown MA. Efficacy and safety of gabapentin for uremic pruritus and restless legs syndrome in conservatively managed patients with chronic kidney disease. *J Pain Symptom Manage* 2015;49:782-9.
- Nofal E, Farag F, Nofal A, Eldesouky F, Alkot R, Abdelkhalik Z, *et al.* Gabapentin: A promising therapy for uremic pruritus in hemodialysis patients: A randomized-controlled trial and review of literature. *J Dermatolog Treat* 2016;27:515-9.
- Kanitakis J. Brachioradial pruritus: Report of a new case responding to gabapentin. *Eur J Dermatol* 2006;16:311-2.
- Yilmaz S, Ceyhan AM, Baysal Akkaya V. Brachioradial pruritus successfully treated with gabapentin. *J Dermatol* 2010;37:662-5.
- Uldall Pallesen KA, Bygum A. Brachioradial pruritus effectively treated with gabapentin. *Ugeskr Laeger* 2012;174:1830-1.
- Carvalho S, Sanches M, Alves R, Selores M. Brachioradial pruritus in a patient with cervical disc herniation and parsonage-turner syndrome. *An Bras Dermatol* 2015;90:401-2.
- Mendham JE. Gabapentin for the treatment of itching produced by burns and wound healing in children: A pilot study. *Burns* 2004;30:851-3.
- Maciel AA, Cunha PR, Laraia IO, Trevisan F. Efficacy of gabapentin in the improvement of pruritus and quality of life of patients with notalgia paresthetica. *An Bras Dermatol* 2014;89:570-5.
- Park JM, Jwa SW, Song M, Kim HS, Ko HC, Kim MB, *et al.* Efficacy and safety of pregabalin for the treatment of chronic pruritus in Korea. *J Dermatol* 2012;39:790-1.
- Bennett MI, Simpson KH. Gabapentin in the treatment of neuropathic pain. *Palliat Med* 2004;18:5-11.
- Fehrenbacher JC, Taylor CP, Vasko MR. Pregabalin and gabapentin reduce release of substance P and CGRP from rat spinal tissues only after inflammation or activation of protein kinase C. *Pain* 2003;105:133-41.
- Gustafsson H, Flood K, Berge OG, Brodin E, Olgart L, Stiller CO, *et al.* Gabapentin reverses mechanical allodynia induced by sciatic nerve ischemia and formalin-induced nociception in mice. *Exp Neurol* 2003;182:427-34.
- Solak Y, Biyik Z, Atalay H, Gaipov A, Guney F, Turk S, *et al.*

- Pregabalin versus gabapentin in the treatment of neuropathic pruritus in maintenance haemodialysis patients: A prospective, crossover study. *Nephrology (Carlton)* 2012;17:710-7.
48. Shavit L, Grenader T, Lifschitz M, Slotki I. Use of pregabalin in the management of chronic uremic pruritus. *J Pain Symptom Manage* 2013;45:776-81.
  49. Foroutan N, Etrman A, Nikvarz N, Shojai Shahrokh Abadi M. Comparison of pregabalin with doxepin in the management of uremic pruritus: A randomized single blind clinical trial. *Hemodial Int* 2017;21:63-71.
  50. Vestita M, Cerbone L, Calista D. Brachioradial pruritus in a 47-year-old woman treated with pregabalin. *G Ital Dermatol Venereol* 2016;151:727-8.
  51. Atış G, Bilir Kaya B. Pregabalin treatment of three cases with brachioradial pruritus. *Dermatol Ther* 2017;30:e12459.
  52. Yue J, Jiao S, Xiao Y, Ren W, Zhao T, Meng J, *et al.* Comparison of pregabalin with ondansetron in treatment of uraemic pruritus in dialysis patients: A prospective, randomized, double-blind study. *Int Urol Nephrol* 2015;47:161-7.
  53. Mazza M, Guerriero G, Marano G, Janiri L, Bria P, Mazza S, *et al.* Treatment of prurigo nodularis with pregabalin. *J Clin Pharm Ther* 2013;38:16-8.
  54. Ehrchen J, Ständer S. Pregabalin in the treatment of chronic pruritus. *J Am Acad Dermatol* 2008;58:S36-7.
  55. Ehrchen J, Ständer S. Pregabalin: A new neuropathic disorder. *Clin Neurol Neurosurg* 2006;108:803-5.
  56. Lee SH, Baig M, Rusciano V, Dutcher JP. Novel management of pruritus in patients treated with IL-2 for metastatic renal cell carcinoma and malignant melanoma. *J Immunother* 2010;33:1010-3.
  57. Porzio G, Aielli F, Verna L, Porto C, Tudini M, Cannita K, *et al.* Efficacy of pregabalin in the management of cetuximab-related itch. *J Pain Symptom Manage* 2006;32:397-8.
  58. Dirks J, Petersen KL, Rowbotham MC, Dahl JB. Gabapentin suppresses cutaneous hyperalgesia following heat-capsaicin sensitization. *Anesthesiology* 2002;97:102-7.
  59. Sundaram S, Webster GF. Vascular diseases are the most common cutaneous manifestations of reflex sympathetic dystrophy. *J Am Acad Dermatol* 2001;44:1050-1.
  60. Tong HC, Nelson VS. Recurrent and migratory reflex sympathetic dystrophy in children. *Pediatr Rehabil* 2000;4:87-9.
  61. Mellick GA, Mellick LB. Reflex sympathetic dystrophy treated with gabapentin. *Arch Phys Med Rehabil* 1997;78:98-105.
  62. Fischhoff DK, Sirois D. Painful trigeminal neuropathy caused by severe mandibular resorption and nerve compression in a patient with systemic sclerosis: Case report and literature review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;90:456-9.
  63. McGraw T, Kosek P. Erythromelalgia pain managed with gabapentin. *Anesthesiology* 1997;86:988-90.
  64. Ceyhan AM, Gurses I, Yildirim M, Akkaya VB. A case of erythromelalgia: Good response to treatment with gabapentin. *J Drugs Dermatol* 2010;9:565-7.
  65. Otley CC. Gabapentin for the treatment of dysesthetic pain after reconstructive surgery. *Dermatol Surg* 1999;25:487-8.
  66. Arora A, Mahajan V. Gabapentin in seizures due to acute intermittent porphyria. *Neurol India* 2000;48:194-5.
  67. McManaman J, Tam DA. Gabapentin for self-injurious behavior in Lesch-Nyhan syndrome. *Pediatr Neurol* 1999;20:381-2.
  68. Ginsberg DL, Sussman N. Gabapentin as prophylaxis against steroid-induced mania. *Can J Psychiatry* 2001;46:455-6.
  69. Devulder J, Lambert J, Naeyaert JM. Gabapentin for pain control in cancer patients' wound dressing care. *J Pain Symptom Manage* 2001;22:622-6.
  70. Moshfeghi M, Mandler HD. Ciprofloxacin-induced toxic epidermal necrolysis. *Ann Pharmacother* 1993;27:1467-9.
  71. Caliskan E, Taşçı İ, Bek S. Gabapentin for the management of vismodegib-induced muscle cramps. *Indian J Dermatol Venereol Leprol* 2017;83:505-6.
  72. Lilly E, Burke M, Kluger H, Choi J. Pregabalin for the treatment of painful hand-foot skin reaction associated with dabrafenib. *JAMA Dermatol* 2015;151:102-3.
  73. Available from: <http://www.med.umich.edu/1libr/prescrpt/epil12.htm#side>. [Last accessed on 2002 Oct 13].
  74. DeToledo JC, Minagar A, Lowe MR, Ramsay RE. Skin eruption with gabapentin in a patient with repeated AED-induced Stevens-Johnson's syndrome. *Ther Drug Monit* 1999;21:137-8.
  75. Richardson CE, Williams DW, Kingham JG. Gabapentin induced cholestasis. *BMJ* 2002;325:635.
  76. Lasso-de-la-Vega MC, Zapater P, Such J, Pérez-Mateo M, Horga JF. Gabapentin-associated hepatotoxicity. *Am J Gastroenterol* 2001;96:3460-2.
  77. Wilton LV, Shakir S. A postmarketing surveillance study of gabapentin as add-on therapy for 3,100 patients in England. *Epilepsia* 2002;43:983-92.
  78. Grant AC, Oh H. Gabapentin-induced anorgasmia in women. *Am J Psychiatry* 2002;159:1247.