REVIEW ARTICLE

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A Comparison of the Pharmacokinetics and Pharmacodynamics of Pregabalin and Gabapentin

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Abstract

Pregabalin and gabapentin share a similar mechanism of action, inhibiting calcium influx and subsequent release of excitatory neurotransmitters; however, the compounds differ in their pharmacokinetic and pharmacodynamic characteristics. Gabapentin is absorbed slowly after oral administration, with maximum plasma concentrations attained within 3–4 hours. Orally administered gabapentin exhibits saturable absorption – a nonlinear (zero-order) process – making its pharmacokinetics less predictable. Plasma concentrations of gabapentin do not increase proportionally with increasing dose. In contrast, orally administered pregabalin is absorbed more rapidly, with maximum plasma concentrations attained within 1 hour. Absorption is linear (first order), with plasma concentrations increasing proportionately with increasing dose. The absolute bioavailability of gabapentin drops from 60% to 33% as the dosage increases from 900 to 3600 mg/day, while the absolute bioavailability of pregabalin remains at ≥90% irrespective of the dosage. Both drugs can be given without regard to meals. Neither drug binds to plasma proteins. Neither drug is metabolized by nor inhibits hepatic enzymes that are responsible for the metabolism of other drugs. Both drugs are excreted renally, with elimination half-lives of approximately 6 hours.

Pregabalin and gabapentin both show dose-response relationships in the treatment of postherpetic neuralgia and partial seizures. For neuropathic pain, a pregabalin dosage of 450 mg/day appears to reduce pain comparably to the predicted maximum effect of gabapentin. As an antiepileptic, pregabalin may be more effective than gabapentin, on the basis of the magnitude of the reduction in the seizure frequency. In conclusion, pregabalin appears to have some distinct pharmacokinetic advantages over gabapentin that may translate into an improved pharmacodynamic effect.

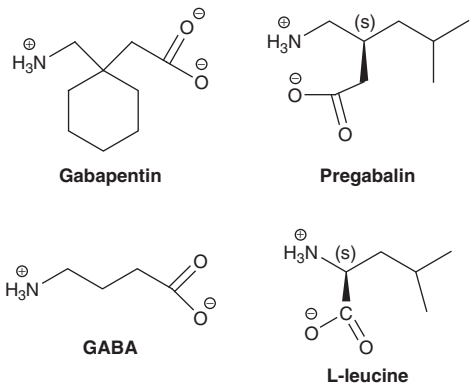

Fig. 1. Chemical structures of gabapentin, pregabalin, γ-aminobutyric acid (GABA) and L-leucine.

Pregabalin and gabapentin are members of a unique class of compounds characterized by their high-affinity binding to the $\alpha_2\delta$ protein, an auxiliary subunit of voltage-gated calcium channels in central nervous system neuronal tissues.[1] Both drugs reduce the release of neurotransmitters from brain tissues. Although the mechanism of action of pregabalin and gabapentin is not fully understood, studies with these compounds in genetically modified mice (modified to alter the binding affinity of these ligands to the $\alpha_2\delta$ subunit) have indicated that selective binding to the $\alpha_2\delta$ subunit is necessary for both pregabalin and gabapentin and their associated antinociceptive, anticonvulsant and anxiolytic-like effects.[2-4] Structure-activity studies of a variety of compounds that are structurally related to gabapentin and pregabalin have supported the premise that both high-affinity binding and transport of the compounds into the brain compartment are required for pharmacological action.[5]

Pregabalin and gabapentin are non-natural, branched-chain amino acids (figure 1). Both are chemical analogues of γ-aminobutyric acid (GABA); however, neither drug has activity in GABAergic neuronal systems.[6-8] Functionally, they are similar to the essential, metabolizable, branched-chain amino acid, leucine, with regard to competitive binding to $\alpha_2\delta$ subunit types 1 and 2[9] and facilitated movement across cellular membranes by system-L transporters.[5] Each of these characteristics is a necessary, but individually insufficient, requirement for the pharmacological activity of this class of compounds.[5]

Gabapentin was originally approved in the UK in 1993 and is currently marketed in more than 100 countries for treatment of epilepsy and neuropathic pain disorders. Gabapentin is approved in the US for adjunctive treatment of partial seizures and for treatment of postherpetic neuralgia. Pregabalin was approved in 2004 by the European Agency for the Evaluation of Medicinal Products (now known as the European Medicines Agency) for treatment of adults with peripheral neuropathic pain and as adjunctive therapy for adults with partial seizures, with or without secondary generalization. Subsequent approvals in the EU were granted for neuropathic pain (peripheral or central) and for generalized anxiety disorder. In the US, the FDA approved pregabalin in 2005 for the management of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia in adults, and as adjunctive therapy for adults with partial-onset seizures. In June 2007, pregabalin was also approved by the FDA for management of fibromyalgia.

This review explores some differences in the pharmacokinetics and pharmacodynamics of pregabalin and gabapentin, which might render one medication advantageous over the other in some clinical settings. The medical literature was searched through MEDLINE, using the drug names as search terms, with research in humans receiving preference to animal or *in vitro* research. We used information from published abstracts and clinical study protocols to complement peer-reviewed articles as required to more fully explain a topic. Additionally, we developed a dose-response model for pregabalin and gabapentin in the treatment of postherpetic neuralgia, using a pooled analysis of four studies of pregabalin and two studies of gabapentin, and a dose-response model in the treatment of epilepsy, using three studies of pregabalin and six studies of gabapentin.

1. Pharmacokinetics

Pregabalin and gabapentin have undergone extensive research to determine their absorption, distribution, metabolism and elimination properties.

1.1 Absorption

Pregabalin and gabapentin immediate-release formulations readily disintegrate; the drugs are highly soluble in aqueous media (table I). Doses of the capsule (pregabalin and gabapentin) and tablet (gabapentin) formulations are bioequivalent to solution doses. There are significant differences in the absorption properties of these two drugs. The system-L transporter family facilitates large, neutral, amino acid transport (LAT), including phenylalanine, leucine, isoleucine and valine,[11] as well as intestinal absorption of both gabapentin and pregabalin. Preclinical studies have suggested that gabapentin is transported solely by the LAT1 transporter,[12] resulting in dose-limited absorption, presumably because of saturation of the facilitated transport process.[11,13,14] Pregabalin absorption seems to be mediated by an additional pathway, thus allowing for near-complete, non-saturable absorption into the blood-

stream.[15] *In vitro* studies have suggested that pregabalin and gabapentin have different capacities and rates of uptake by the L-type transport system in Caco-2 cells.[16]

The maximum rate of absorption of pregabalin is approximately 3-fold greater than that of gabapentin. In healthy subjects, pregabalin is rapidly absorbed, with peak blood concentrations attained within 1 hour.[17] The rate of gabapentin absorption is relatively slow, with peak plasma concentrations occurring around 3 hours postdose.[14] The rate and extent of absorption are influenced by the absence or presence of the transporter(s) along the gastrointestinal tract, which facilitates the passage of each of these compounds from the intestinal lumen to the systemic circulation. Colonic intubation studies[18] have indicated that systemic absorption of gabapentin occurs primarily in the small intestine, with minimal absorption in the colon, which limits gabapentin absorption. In contrast, systemic absorption of pregabalin occurs over a longer segment of the gastrointestinal tract. In addition to absorption in the small intestine, colonic intubation studies have indicated that pregabalin absorption extends into the ascending portion of the colon.[19]

In 33 healthy subjects, pregabalin displayed linear pharmacokinetics over its recommended dose range of 75 to 900 mg/day (figure 2), as reflected in dose proportionality observed for the plasma concentration and the area under the plasma concentration-time curve (AUC). Gabapentin, in contrast, displays saturable absorption, which decreases with increasing dose, as tested in 96 healthy subjects.[14,20] Mean gabapentin steady-state minimum plasma concentration ($C_{min,ss}$) values increase with increasing dose, but the increase is not dose proportional. This observation is consistent with the *in vitro* Caco-2 experiments, which predicted a nonlinear absorption profile for gabapentin and a more linear relationship for pregabalin.[16]

Table I. Summary of the physical chemistry properties of gabapentin and pregabalin[10]

Property	Gabapentin	Pregabalin
Molecular weight (g/mol)	171.24	159.22
pKa	3.7	4.2
pKb	10.7	10.6
Aqueous solubility (mg/mL)	>100	32.1
Log P[a]	–1.25	–1.35
Intestinal transport	System-L amino acid transporter 1	System-L amino acid transporter(s)

a pH 7.4 phosphate buffer.

pKa = acid dissociation constant; **pKb** = base dissociation constant.

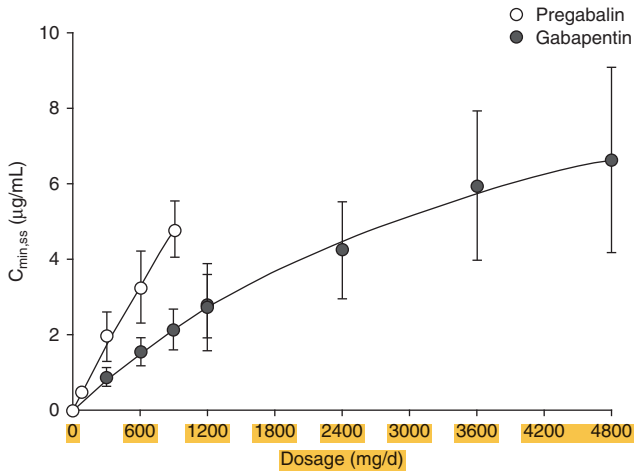

Fig. 2. Mean (± SD) steady-state minimum plasma drug concentration ($C_{min,ss}$) values in healthy subjects given pregabalin or gabapentin every 8 h.[14,20]

1.2 Bioavailability

With regard to the fraction of the dose absorbed, the lowest gabapentin dose studied (100 mg every 8 hours) is associated with absolute bioavailability of approximately 80%. This value was shown to decrease with increasing dose to an average of 27% absolute bioavailability for a 1600 mg dose every 8 hours.[11,21] In contrast, oral bioavailability of pregabalin averaged ≥90% across the full dose range of 75 to 900 mg/day studied.[22] The maximum plasma drug concentration (C_{max}) and AUC – both measures of exposure – increase linearly with dosages ranging from 75 to 900 mg/day. This range includes and exceeds the efficacious dosage range (150–600 mg/day) studied in phase III pregabalin trials. The variability (coefficient of variation) in the pregabalin C_{max} and AUC values is generally 10–15%,[20] whereas the variability in the estimates for gabapentin is generally 20–30%. The saturable absorption process and the interindividual variability in this process contribute significantly to the higher variability observed with gabapentin.[23] For gabapentin, the time to reach the C_{max} following drug administration (t_{max}) is a function of the dose administered, with low doses of 100 mg having a t_{max} of ≈1.7 hours, and the t_{max} increases to 3–4 hours following higher single doses. In contrast, the t_{max} of pregabalin is considerably shorter – generally averaging ≤1 hour following single-dose administration of 1–300 mg.[24,25]

Both gabapentin and pregabalin can be administered without regard to food, but differences in absorption during the fed and fasting states distinguish the two drugs (table II). For gabapentin, a standard meal and a high-fat meal both result in an approximate 10% increase in the C_{max} and AUC, with no signi-

Table II. Gabapentin and pregabalin pharmacokinetic parameter values following administration to fasting subjects and subjects fed a standard or high-fat breakfast. (Adapted from Bockbrader et al.,[20] with permission. Copyright © 2010 by Sage Publications. Reprinted by Permission of SAGE Publications.)

Parameter	Fed (test)[a]	Fasting (reference)[a]	Ratio (%) [90% CI][b]
Gabapentin			
Standard breakfast (n = 12)			
C_{max} (μg/mL)	3.78	3.49	108.0 [88.9, 131.0]
t_{max} (h)	3.3	3.5	94.3 [NA]
AUC_{∞} (μg • h/mL)	39.6	36.7	108.0 [91.8, 126.0]
High-fat breakfast (n = 12)			
C_{max} (μg/mL)	3.06	2.82	108.0 [97.8, 120.0]
t_{max} (h)	3.6	3.3	109.0 [NA]
AUC_{∞} (μg • h/mL)	29.9	27.2	110.0 [98.6, 123.0]
Pregabalin			
Standard breakfast (n = 11)			
C_{max} (μg/mL)	2.59	3.78	68.6 [64.0, 73.6]
t_{max} (h)	3.17	0.615	515.0 [NA]
AUC_{∞} (μg • h/mL)	25.4	26.7	94.9 [92.0, 98.0]
High-fat breakfast (n = 14)			
C_{max} (μg/mL)	2.60	3.47	74.8 [68.0, 82.2]
t_{max} (h)	2.29	1.25	183.0 [NA]
AUC_{∞} (μg • h/mL)	25.5	27.3	93.3 [91.4, 95.2]

a Mean values.

b Ratio of fed/fasting.

AUC_{∞} = area under the plasma concentration-time curve from time zero to infinity; **C_{max}** = maximum plasma drug concentration; **NA** = not applicable; **t_{max}** = time to reach the C_{max}.

ficant change in the t_{max}. These increases are not of clinical significance, and no dose adjustment is required when gabapentin is administered with food.[26] Although both standard and high-fat meals decrease the rate of pregabalin absorption, neither has a significant effect on the extent of absorption. Administration of pregabalin with food reduces the mean C_{max} values by 25–31% and prolongs the absorption process. The mean t_{max} values increase by ≈1 hour, ranging from 2.3 hours in the fasted state to 3.2 hours in the fed state. However, because only the rate and not the extent of pregabalin bioavailability is affected by food, pregabalin can be given without regard to the timing of meals.[20]

1.3 Distribution

According to findings from whole-body autoradiography studies in mice, rats and monkeys, the distribution characteristics of gabapentin and pregabalin are quite similar.[10,27] Likewise, the brain : whole-blood ratio is similar for the two drugs. In humans, both plasma gabapentin and plasma pregabalin concentrations are similar to the whole-blood concentrations, indicating that both drugs penetrate red blood cells. Neither gabapentin nor pregabalin is bound to plasma proteins; thus drug-drug interactions with any highly protein-bound agent are not anticipated. The disposition of gabapentin[14,28] and pregabalin[29] in the cerebrospinal fluid (CSF) following oral administration is similar. Sparse sampling following single-dose gabapentin administration indicated that gabapentin concentrations in the CSF were approximately 9–14% of the corresponding plasma concentrations. The percentage of the gabapentin concentration (CSF/plasma) increased with time after drug administration and following multiple-dose administration.

Following single-dose administration of pregabalin, serial CSF and plasma samples were obtained at 2, 4, 6, 8 and 24 hours. The percentage of the pregabalin concentration in the CSF ranged from approximately 1% to 30%. The mean plasma pregabalin concentrations in the human study peaked at 2 hours (the first sampling time in the study) and decreased by an apparent first-order process. The mean CSF pregabalin

concentrations peaked much later (at least 8 hours post-dose) and then decreased at a slower rate relative to that observed for plasma. Gabapentin and pregabalin steady-state CSF exposure would be expected to have an attenuated peak-to-trough fluctuation relative to that of plasma.[14,28,29]

Gabapentin and pregabalin are secreted into milk by lactating rodents, and gabapentin has been found in human breast milk at concentrations similar to those in plasma. Although use of pregabalin in lactating women has not been studied, secretion of pregabalin into human breast milk would be expected.[30,31]

A slight difference in the apparent volume of distribution (V_d) values of pregabalin and gabapentin has been observed in humans. The V_d estimates (independent of drug bioavailability) based on population pharmacokinetic analyses of gabapentin and pregabalin are 0.8 and 0.5 L/kg, respectively.[10] For both drugs, the V_d is relatively small and similar to that of total body water. This observation is consistent with their high aqueous solubility, low lipophilicity and lack of significant tissue binding, as observed in whole-body autoradiography studies.

1.4 Metabolism

The metabolic profiles of gabapentin and pregabalin are similar. In dogs, both are metabolized to the corresponding *N*-methyl metabolite.[18] Both compounds undergo negligible metabolism in mice and rats; in humans, metabolites account for <1% of the dose.[22,27] An effect of liver disease on the pharmacokinetics of gabapentin and pregabalin has not been studied. However, since both compounds undergo negligible metabolism, their pharmacokinetics are not expected to be different from those observed in healthy subjects.

1.5 Excretion

With minor exceptions, renal excretion of gabapentin and pregabalin is similar and is essentially the only pathway for systemic elimination of the drugs. Gabapentin and pregabalin plasma clearances are highly correlated with renal function, and dosage adjustments are necessary for both drugs in patients with impaired renal function. Studies in patients undergoing haemodialysis have indicated that a 4-hour treatment lowers the plasma concentrations of gabapentin and pregabalin by approximately 50%.[32,33]

Slight differences between gabapentin and pregabalin in the relationship between plasma drug clearance and renal function have been observed. In population pharmacokinetic analyses in subjects with creatinine clearance (CL_{CR}) of 100 mL/minute, plasma gabapentin clearance was approximately 125 mL/minute, whereas plasma pregabalin clearance was approximately 70 mL/minute.[10] For gabapentin, the renal clearance value is similar to or slightly greater than the CL_{CR} value. It is not known if gabapentin renal elimination is dependent on a reabsorption process; however, cimetidine (a known inhibitor of renal tubular secretion) reduces gabapentin renal clearance by approximately 12%.[18] Therefore, renal tubular secretion is involved in the renal elimination of gabapentin. For pregabalin, the renal clearance value is less than the glomerular filtration rate, which indicates that a tubular reabsorption process is involved in renal clearance. Whether renal secretion is also involved is not known. Elimination half-life parameter estimates for the two drugs are similar. The reported gabapentin elimination half-life estimates range from 5.0 to 7.0 hours and those for pregabalin average 6.3 hours, indicating that both drugs achieve steady state within 24–48 hours.[23,24]

1.6 Drug Interactions

Approximately 50–75% of gabapentin doses, ranging from 1800 to 4800 mg/day, are not absorbed.[34] Any agent that prolongs the transit time of gabapentin in the small intestine could potentially enhance the bioavailability of gabapentin. Eckhardt et al.[35] demonstrated that the bioavailability of gabapentin increased by 50% when a 600 mg dose was co-administered with oral morphine. Other agents that decrease small-bowel motility could have a similar effect on the extent of gabapentin absorption, although this has not been confirmed clinically. Pregabalin has systemic absorption of ≥90% and would not be significantly affected by agents that reduce gastrointestinal motility.

Neither gabapentin nor pregabalin, at concentrations equal to or greater than those observed at efficacious dosages, inhibits the major cytochrome P450 (CYP) enzymes (CYP1A2, CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4) that mediate xenobiotic metabolism in humans. In addition, pregabalin has been shown to not induce expression of the CYP enzymes CYP3A4 and CYP1A2 *in vitro* at concentrations equal to or greater than those observed at efficacious dosages.[36] Therefore, drug-drug interactions due to inhibition of the metabolism of other agents by gabapentin or pregabalin, or due to induction of the metabolism of other agents by pregabalin, are unlikely. In addition, the pharmacokinetics of these compounds are not expected to vary as a function of genetic polymorphisms of metabolizing enzymes.[37]

Table III. Summary of phase III postherpetic neuralgia trials conducted with either gabapentin or pregabalin

Drug	Subjects (n)	Dosage (mg/d)	Regimen	Duration (wk)	Reference
Gabapentin	229	3600	TID	8	41
Gabapentin	334	1800, 2400	TID	7	40
Pregabalin	252	75, 150	TID	5	38
Pregabalin	238	150, 300	TID	8	42
Pregabalin	173	300/600[a]	TID	8	39
Pregabalin	368	150, 300, 300/600[a]	BID	13	43

a In this study, patients with CL_{CR} between 30 and 60 mL/min received a dosage of 300 mg/d, and patients with CL_{CR} >60 mL/min received a dosage of 600 mg/d.

BID = twice daily; **CL_{CR}** = creatinine clearance; **TID** = three times daily.

2. Pharmacodynamics

2.1 Neuropathic Pain

Gabapentin and pregabalin both show dose-response relationships in the treatment of postherpetic neuralgia and partial seizures. For both drugs, efficacy increases with increasing dose; however, differences do exist. Using data from six phase III studies,[38-43] a population pharmacokinetic-pharmacodynamic model was developed to describe the relationship between daily gabapentin or pregabalin administration and reduction in the pain score of patients experiencing pain associated with postherpetic neuralgia (table III). The dosages administered in the two gabapentin studies were 1800, 2400 and 3600 mg/day, given three times daily, with a 3- to 4-week dose-titration phase. The dosages administered in the four pregabalin studies were 75, 150, 300 and 600 mg/day, given three times daily or twice daily, with a 1-week dose-titration phase. Since daily pain scores were measured as integral, ordinal values on an 11-point numeric rating scale,[44] the pregabalin and gabapentin dose-response models were developed to treat the daily pain score as an ordered categorical response. For both pregabalin and gabapentin, the observed treatment effects in the mean pain score reductions and model-predicted values were in good agreement (figure 3).

The treatment effect in the placebo group varied from study to study, such that three of the six studies showed an approximate 0.5-point reduction in the pain score, while the remaining three studies showed a greater than 1.0-point reduction. Variability in the placebo effect was comparable between the gabapentin and pregabalin studies. The pain score reduction with pregabalin was greater and was achieved at a lower daily dose than with gabapentin. While there was a plateau in the maximal effect of gabapentin at the doses studied, the pain reduction with pregabalin tended to increase as the dosage increased to 600 mg/day. Model predictions suggested that a pregabalin dosage of 450 mg/day would produce a pain score reduction comparable to the predicted maximum effect of gabapentin. The treatment effects of the pregabalin 600 mg/day twice-daily regimen were similar to those observed with the three-times-daily regimen. As confirmed by exposure-response modelling, the exposure-response relationship for the twice-daily regimen was not statistically different from that for the three-times-daily regimen.[45]

2.2 Epilepsy

Using seven phase III studies (table IV),[46-51] a population pharmacokinetic-pharmacodynamic model was developed to describe the relationship between the daily dosage of gabapentin

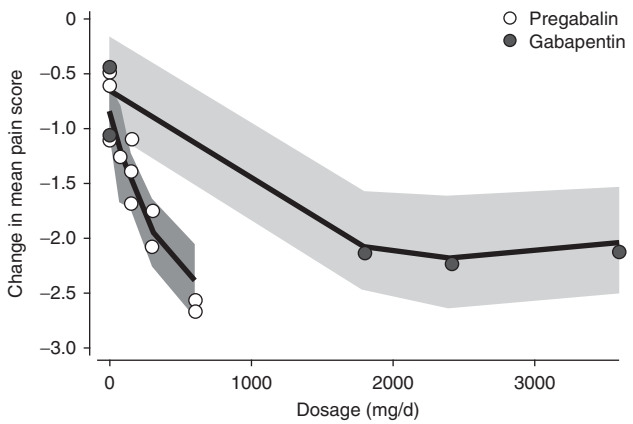

Fig. 3. Observed and model-predicted treatment effects of mean pain reduction in six trials (two gabapentin and four pregabalin trials, as detailed in table III) involving patients with postherpetic neuralgia. Each datapoint represents the mean pain score reduction in a treatment group (the 0 mg dose represents placebo) in a single study. Each shaded area corresponds to 95% of the predicted interval for the mean pain score reduction with the drug, and the thick black lines represent the 50th percentile of the predicted mean pain score reduction.[38-44]

Table IV. Summary of phase III epilepsy trials conducted with either gabapentin or pregabalin

Drug	Subjects (n)	Dosage (mg/d)	Regimen	Duration (wk)	Reference
Gabapentin	127	1200	TID	12	46
Gabapentin	306	600, 1200, 1800	TID	12	47
Gabapentin	272	900, 1200	TID	12	48
Gabapentin	87	900, 1200	TID	12	48
Pregabalin	312	600	BID, TID	12	49
Pregabalin	287	150, 600	TID	12	50
Pregabalin	453	50, 150, 300, 600	BID	12	51

BID = twice daily; **TID** = three times daily.

or pregabalin and the reduction in the seizure frequency in refractory patients with partial seizures. The dosages administered in the four gabapentin studies were 600, 900, 1200 and 1800 mg/day, given three times daily; the dosages administered in the three pregabalin studies were 50, 150, 300 and 600 mg/day, given three times daily or twice daily. The observed median percentage changes in the seizure frequency from baseline for gabapentin and pregabalin are shown in figure 4. Comparison of the dose-response relationships for both drugs revealed two important distinctions: (i) pregabalin was 2.5 times more potent than gabapentin, as measured by the dosage that reduced the seizure frequency by ≥50%; and (ii) pregabalin was more effective than gabapentin on the basis of the magnitude of the reduction in the seizure frequency. The curve describing the dose-response relationship for gabapentin was relatively flat, partly because of the saturable absorption process described above. As the daily dosage increases, the fraction that is absorbed decreases. Accordingly, the slope of the dose-response relationship at dosages greater than 1800 mg/day (the highest dose studied in phase III trials) is expected to remain shallow. Unlike gabapentin, pregabalin shows a steep dose-response relationship, which is, in part, due to its greater potency and linear pharmacokinetics.

2.3 Adverse Effects

Pregabalin and gabapentin are generally well tolerated. Dizziness is the most commonly reported adverse effect of pregabalin, followed by somnolence, which is the most frequent reason for treatment discontinuation (4%). Other adverse effects include dry mouth, oedema and blurred vision. Dizziness and somnolence are the most commonly reported adverse effects of gabapentin, occurring in >20% of patients. Confusion and peripheral oedema have also been reported. The adverse effects of both drugs are dose dependent and reversible.[52]

3. Discussion and Conclusions

Comparison of the pharmacokinetic and pharmacodynamic properties of gabapentin and pregabalin indicates several similarities in negligible protein binding, no adjustment required for dosing with food, negligible metabolism in humans, a strong correlation between plasma clearance and renal function, similar elimination half-life estimates with attainment of steady state within 24–48 hours, and no inhibition of enzyme systems that are responsible for drug metabolism in humans.

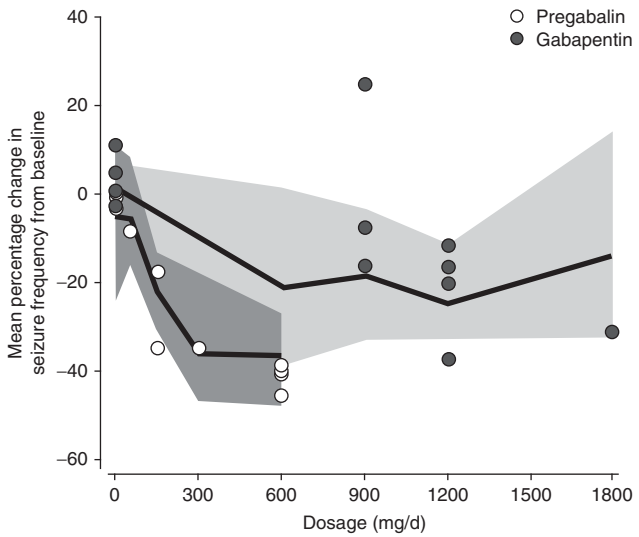

Fig. 4. Observed and model-predicted seizure frequency (mean percentage change from baseline) vs dose (gabapentin: 0–1800 mg/d, pregabalin: 0–600 mg/d) in patients with refractory partial seizures, as detailed in table IV. Pregabalin (50–600 mg/d) and gabapentin (600–1800 mg/d) showed a dose-related decrease in the seizure frequency in patients with refractory partial seizures. Each datapoint represents the mean percentage change in the seizure frequency from a treatment group (the 0 mg dose represents placebo) in a single study. Each shaded area corresponds to 95% of the predicted interval for the reduction in the seizure frequency with the drug – that is, the model-predicted 10th–90th percentiles for the median percentage change in the seizure frequency from baseline for gabapentin and pregabalin. The thick black lines represent the 50th percentile of each predicted reduction.[46-51]

Small differences in the chemical structure of the first- and second-generation $\alpha_2\delta$-binding anticonvulsant compounds are clearly important and differentiate the pharmacokinetic and pharmacodynamic properties of pregabalin from those of gabapentin. First, pregabalin has the distinct advantage of non-saturable absorption at clinically relevant dosages, resulting in linear pharmacokinetics. Next, pregabalin has a steeper dose-response relationship than gabapentin. Finally, pregabalin seems to achieve a greater treatment effect in postherpetic neuralgia and epilepsy than gabapentin. The differences in potency assessed here, in combination with the distinctive pharmacokinetic and pharmacodynamic properties of each drug, provide information that clinicians may find useful when considering treatment with gabapentin or pregabalin.

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