Respiratory depression reports with gabapentin versus pregabalin in the FDA Adverse Event Reporting System, 2024

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Abstract

Background. Gabapentin and pregabalin are often used alongside opioids, and the FDA has warned of serious breathing problems with both drugs.

Objective. To compare reporting of respiratory depression for gabapentin versus pregabalin in the FDA Adverse Event Reporting System (FAERS), and to examine whether this differs when an opioid is also reported.

Methods. Disproportionality analysis of FAERS reports from the four quarters of 2024 (1,480,549 reports after removing deleted cases and keeping the latest version of each case). Respiratory depression was defined as any of five MedDRA preferred terms. We calculated the proportional reporting ratio (PRR) and reporting odds ratio (ROR) with 95% confidence intervals, comparing each drug with reports listing neither drug and gabapentin directly with pregabalin, in all reports and by opioid status. A sensitivity analysis used a stricter three-term outcome.

Results. Respiratory depression was reported in 123 of 5,268 gabapentin-only reports (2.3%), 85 of 6,516 pregabalin-only reports (1.3%) and 7,306 of 1,468,374 reports listing neither drug (0.50%). Compared with reports listing neither drug, the ROR was 4.78 (95% CI 3.99 to 5.73) for gabapentin and 2.64 (2.13 to 3.28) for pregabalin. For gabapentin versus pregabalin the ROR was 1.81 (1.37 to 2.39) in all reports, 2.10 (1.50 to 2.95) with an opioid reported and 2.00 (1.21 to 3.31) without. The sensitivity analysis gave 1.82 (1.35 to 2.46) in all reports.

Conclusions. In 2024 FAERS reports, respiratory depression was reported disproportionately more often with gabapentin than with pregabalin. Estimates were similar with and without an opioid reported, with wider intervals in the no-opioid group. FAERS data cannot show causation or incidence.

Keywords: gabapentin; pregabalin; respiratory depression; pharmacovigilance; FAERS; disproportionality analysis

Introduction

Gabapentin and pregabalin are gabapentinoids whose use has grown. In a national survey of US adults, the share using a gabapentinoid rose from 4.0% in 2015 to 4.7% in 2021 [2].

In December 2019, the US Food and Drug Administration warned that serious breathing difficulties may occur with gabapentin and pregabalin in patients with respiratory risk factors. These include the use of opioid pain medicines or other drugs that depress the central nervous system, conditions that reduce lung function such as chronic obstructive pulmonary disease, and older age. The FDA required new warnings about respiratory depression for these drugs [1].

Observational studies have examined gabapentinoids together with opioids. In a nested case-control study of older women with breast cancer and neuropathic pain in SEER-Medicare, combined opioid and gabapentin use was associated with higher odds of respiratory depression than opioid monotherapy (adjusted odds ratio 1.513) and than neither drug class (adjusted odds ratio 1.595) [3]. In a propensity-matched cohort of 133,720 US Medicare beneficiaries with spine-related diagnoses, a composite respiratory outcome (including respiratory failure, pneumonia and mechanical ventilation) occurred in 5.2% of those treated with gabapentin plus opioids and 4.2% of those treated with a tricyclic antidepressant or duloxetine plus opioids (adjusted hazard ratio 1.19, 95% CI 1.13 to 1.25) [4].

Spontaneous reporting databases have also been used. In the Japanese Adverse Drug Event Report database (2004 to 2023), respiratory depression showed a disproportionality signal for pregabalin (information component 1.28, 95% CI 0.83 to 1.73) but not for mirogabalin, and opioid use was associated with higher odds of somnolence reports with pregabalin [5]. That study did not include gabapentin. Earlier FAERS studies of gabapentin and pregabalin examined abuse and misuse [7,8], delirium [9] and psychiatric events [10], including a comparison of the two drugs [10]. A study in the World Health Organization pharmacovigilance database compared the safety of pregabalin and gabapentin [11]. A commentary on respiratory concerns with gabapentinoids summarised the FDA's own review of FAERS cases but reported no new analysis [12]. In a PubMed search on 26 October 2026 ("gabapentinoids FAERS", "pregabalin FAERS" and "gabapentin pharmacovigilance"), we did not find a FAERS study that compared respiratory depression reporting for gabapentin with pregabalin by opioid status.

We therefore used the FDA Adverse Event Reporting System (FAERS) to compare reporting of respiratory depression for gabapentin versus pregabalin, and to examine whether this differed when an opioid was also reported on the same report.

Methods

Data source

We used the FDA Adverse Event Reporting System (FAERS), a public database of spontaneous adverse event reports. We downloaded the quarterly ASCII data files for January to December 2024 (2024 Q1 to Q4) from the FDA website [6] on 22 and 24 October 2026. Three tables were used: DEMO (report and case identifiers), DRUG (drugs listed on each report, with their role) and REAC (reactions, coded as MedDRA preferred terms).

Case selection

The four quarters were combined. Cases listed in the FDA deleted-case files for the four quarters were removed. Where a case appeared in more than one version, only the latest

version was kept. This reduced 1,619,665 reports to 1,480,549 reports. Reports listing both gabapentin and pregabalin (n = 391) were excluded from all comparisons.

Exposure

Gabapentin and pregabalin were identified from the active ingredient field. When that field was blank, the drug name was used (gabapentin or Neurontin; pregabalin or Lyrica). A drug was counted as an exposure only when its role on the report was primary suspect or secondary suspect. Exact matching on the active ingredient excluded related products such as gabapentin enacarbil and compounded creams.

Outcome

The outcome was respiratory depression, defined as a report listing at least one of five MedDRA preferred terms: respiratory depression, respiratory failure, acute respiratory failure, respiratory arrest and hypoventilation. In a sensitivity analysis, the outcome was restricted to three terms (respiratory depression, respiratory arrest and hypoventilation) to test whether the results depended on the broader term respiratory failure.

Opioid co-reporting

A report was classified as having an opioid when the active ingredient field of any drug on the report, in any role, contained the name of one of 11 opioids (oxycodone, hydrocodone, morphine, fentanyl, tramadol, codeine, methadone, buprenorphine, hydromorphone, oxymorphone, tapentadol). Combination products containing these ingredients were therefore included.

Statistical analysis

We used disproportionality analysis. For each comparison, a two-by-two table was built from the numbers of reports with and without the outcome among exposed and comparison reports. We calculated the proportional reporting ratio (PRR) and the reporting odds ratio (ROR), with a 95% confidence interval for the ROR based on the standard error of its logarithm. Three comparisons were made: gabapentin versus reports listing neither drug, pregabalin versus reports listing neither drug, and gabapentin directly versus pregabalin. Each comparison was made in all reports, in reports with an opioid, and in reports without an opioid. Results are hypothesis-generating; disproportionality in spontaneous reports does not establish a causal relationship or an incidence.

Quality checks

The main counts were checked with a second implementation, written separately from the analysis code using Python's standard csv module. It recomputed the number of cases kept after cleaning, the number of gabapentin-only and pregabalin-only reports, and the number of reports with the main outcome, and these matched the main analysis. The reporting odds ratio formula was checked on a worked example, and the full analysis was re-run to confirm that it produced an identical results file.

Software and code availability

Analyses were performed in Python 3.14.8 using pandas 3.1.0. The code, results tables and instructions to reproduce the analysis are available at https://github.com/rxilucifer/faers-gabapentin-pregabalin.

Ethics

This study used publicly available, de-identified data and did not require ethics committee approval.

Results

Study population

After cleaning, 1,480,549 reports from 2024 were analysed. Gabapentin was listed as a primary or secondary suspect in 5,659 reports and pregabalin in 6,907 reports. Of these, 391 reports listed both drugs and were excluded from the comparisons, leaving 5,268 gabapentin-only reports, 6,516 pregabalin-only reports and 1,468,374 reports listing neither drug. In total, 7,515 reports listed at least one of the five respiratory terms, and 62,798 reports listed an opioid.

Main analysis

Respiratory depression was reported in 123 of 5,268 gabapentin-only reports (2.3%), 85 of 6,516 pregabalin-only reports (1.3%) and 7,306 of 1,468,374 reports listing neither drug (0.50%). Compared with reports listing neither drug, the reporting odds ratio (ROR) was 4.78 (95% CI 3.99 to 5.73) for gabapentin and 2.64 (2.13 to 3.28) for pregabalin. In the direct comparison, the ROR for gabapentin versus pregabalin was 1.81 (1.37 to 2.39) (Table 1).

Reports with and without an opioid

Among reports listing an opioid, respiratory depression was reported in 77 of 1,930 gabapentin-only reports (4.0%), 62 of 3,198 pregabalin-only reports (1.9%) and 1,058 of 57,483 reports listing neither drug (1.8%). The ROR for gabapentin versus pregabalin was 2.10 (1.50 to 2.95). Pregabalin showed no disproportionality compared with reports listing neither drug (ROR 1.05, 0.81 to 1.37), whereas gabapentin did (ROR 2.22, 1.75 to 2.81).

Among reports without an opioid, respiratory depression was reported in 46 of 3,338 gabapentin-only reports (1.4%), 23 of 3,318 pregabalin-only reports (0.7%) and 6,248 of 1,410,891 reports listing neither drug (0.44%). The ROR for gabapentin versus pregabalin was 2.00 (1.21 to 3.31).

The confidence intervals for the direct comparison overlapped between the opioid and no-opioid groups. We did not test formally for a difference between the groups.

Sensitivity analysis

When the outcome was restricted to respiratory depression, respiratory arrest and hypoventilation, the ROR for gabapentin versus pregabalin was 1.82 (1.35 to 2.46) in all reports, 2.38 (1.66 to 3.41) in reports with an opioid and 1.60 (0.91 to 2.80) in reports without an opioid (Table 2). The result for all reports was almost the same as in the main analysis.

Tables

Table 1. Reports of respiratory depression (five terms), PRR and ROR with 95% CI. Counts are reports with / without the outcome.

Reports	Comparison	Exposed	Comparison group	PRR	ROR (95% CI)
All	Gabapentin vs neither	123 / 5,145	7,306 / 1,461,068	4.69	4.78 (3.99 to 5.73)
All	Pregabalin vs neither	85 / 6,431	7,306 / 1,461,068	2.62	2.64 (2.13 to 3.28)
All	Gabapentin vs pregabalin	123 / 5,145	85 / 6,431	1.79	1.81 (1.37 to 2.39)
Opioid	Gabapentin vs neither	77 / 1,853	1,058 / 56,425	2.17	2.22 (1.75 to 2.81)
Opioid	Pregabalin vs neither	62 / 3,136	1,058 / 56,425	1.05	1.05 (0.81 to 1.37)
Opioid	Gabapentin vs pregabalin	77 / 1,853	62 / 3,136	2.06	2.10 (1.50 to 2.95)
No opioid	Gabapentin vs neither	46 / 3,292	6,248 / 1,404,643	3.11	3.14 (2.35 to 4.21)
No opioid	Pregabalin vs neither	23 / 3,295	6,248 / 1,404,643	1.57	1.57 (1.04 to 2.37)
No opioid	Gabapentin vs pregabalin	46 / 3,292	23 / 3,295	1.99	2.00 (1.21 to 3.31)

Table 2. Sensitivity analysis: gabapentin vs pregabalin with the stricter outcome (respiratory depression, respiratory arrest, hypoventilation). Counts are reports with / without the outcome.

Reports	Gabapentin	Pregabalin	PRR	ROR (95% CI)
All	105 / 5,163	72 / 6,444	1.80	1.82 (1.35 to 2.46)
Opioid	73 / 1,857	52 / 3,146	2.33	2.38 (1.66 to 3.41)

Reports	Gabapentin	Pregabalin	PRR	ROR (95% CI)
No opioid	32 / 3,306	20 / 3,298	1.59	1.60 (0.91 to 2.80)

Discussion

In this analysis of 2024 FAERS reports, respiratory depression was reported disproportionately more often with gabapentin than with pregabalin (ROR 1.81, 95% CI 1.37 to 2.39). The estimates were similar in reports with an opioid (2.10, 1.50 to 2.95) and without one (2.00, 1.21 to 3.31), and a sensitivity analysis with a stricter outcome gave a similar overall result (1.82, 1.35 to 2.46).

Earlier observational studies in Medicare populations reported higher odds or risk of respiratory events with gabapentin combined with opioids [3,4]. Those studies compared gabapentin plus opioids with opioids alone, with neither drug class, or with other drug classes, and did not compare gabapentin with pregabalin. A pharmacovigilance study in Japan reported a respiratory depression signal for pregabalin [5]. Our study adds a comparison of gabapentin and pregabalin in the same database. Because the designs, populations and outcomes differ, the results cannot be compared directly.

Disproportionality measures describe reporting patterns. They are influenced by who receives each drug, how long each drug has been marketed and what prompts a report, so our results do not show that one drug is more likely than the other to cause respiratory depression.

The result for pregabalin in reports with an opioid (ROR 1.05, 95% CI 0.81 to 1.37, compared with reports listing neither drug) should not be read as pregabalin being safe in that setting. The comparison reports also contain opioids, which can themselves cause respiratory depression, so the background rate is higher in that group. The confidence intervals for gabapentin versus pregabalin overlapped between the opioid and no-opioid groups, and we did not test formally for a difference between them.

Strengths of this study are the use of public data for a full year, the removal of deleted and duplicate case versions, a sensitivity analysis, and public code that reproduces the results. Its limitations are those of spontaneous reports: they show association, not causation or incidence, and reporting depends on media attention and time on the market. Respiratory failure has many causes. We did not adjust for age, sex, dose or other illnesses, we used one year only, cases reported twice under different case IDs cannot be detected, and the groups without an opioid are small.

In conclusion, respiratory depression was reported disproportionately more often with gabapentin than with pregabalin in 2024 FAERS reports. These findings generate hypotheses. Further work could add more years and adjust for age and sex.

Declarations

- **Funding:** This research received no specific funding.

- **Conflicts of interest:** The author declares no conflicts of interest. The author has no financial relationship with any manufacturer of gabapentin, pregabalin or opioids, and received no payment for this work.
- **Use of AI assistance:** Generative AI (Claude, Anthropic) was used to help draft and edit the text and to help write and debug the analysis code. The author ran the analysis, checked the results against the code output, checked the key figures taken from the cited sources, and takes full responsibility for the content.
- **Reporting guideline:** This study was reported following the STROBE guideline for cross-sectional studies, where applicable to spontaneous-report data. Patient characteristics such as age and sex, and missing data, were not analysed.
- **Data availability:** The FAERS quarterly data are public and available from the FDA. The analysis code and results tables are available at https://github.com/rxilucifer/faers-gabapentin-pregabalin.

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