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ORIGINAL RESEARCH ARTICLE

Adverse Drug Reactions to Gabapentin and Pregabalin

A Review of the French Pharmacovigilance Database

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Abstract

Background Gabapentin and pregabalin are widely used as antineuropathic pain drugs. Their use is also associated with the development of adverse drug reactions (ADRs), mainly neuropsychiatric.

Objective The aim of this work was to study 'serious' and/or 'unexpected' adverse reactions associated with pregabalin and gabapentin.

Study Design We studied ADRs reported to the French Pharmacovigilance System occurring between 1995 and 2009.

Main Outcome Measure For each ADR associated with gabapentin or pregabalin, we noted year, patient age and sex, type of adverse reaction, as well as the imputability score. Reporting rate of serious ADRs for gabapentin and pregabalin was estimated with regard to data of use (obtained from the French National Health Insurance Fund) using the defined daily dose. A global and descriptive analysis of the adverse reactions for each drug is presented. Secondly, details of deaths and ADRs with an imputability score of at least 'probable' or 'likely' were presented.

Results Overall, 1333 cases were recorded (725 related to gabapentin, 608 related to pregabalin), mainly neuropsychiatric ADRs. Among the 22 deaths recorded, 8 were related to gabapentin in obstetrical situations. Other less well-documented ADRs were identified, such as hepatitis associated with gabapentin and haematological ADRs associated with pregabalin.

Conclusion This study confirmed the prevalence of neuropsychiatric ADRs associated with gabapentin or pregabalin. A high rate of death occurred with gabapentin in an obstetrical context. New adverse reactions have been noted, such as haematological or hepatic adverse reactions associated with pregabalin and gabapentin, respectively.

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1 Background

Gabapentin and pregabalin are widely used as antiepileptic and antineuropathic pain drugs. The main site of action appears to be on the α2-δ subunit of presynaptic, voltage-dependent calcium channels that are widely distributed throughout the peripheral and central nervous system [1, 2]. Both drugs undergo negligible metabolism and are excreted unchanged in the urine. This implies that pharmacokinetic interactions with other drugs are unlikely to occur [3].

Pregabalin has been approved for neuropathic pain, as an adjunctive drug for partial seizures in patients with epilepsy, and for generalized anxiety disorder [1]; it was labelled in France in 2004. Gabapentin, labelled in France in 1994, is also marketed for the treatment of partial seizures and in the treatment of neuropathic pain. When prescribed during the postoperative period, both drugs decreased pain scores and opioid consumption, but their use was also associated with the development of adverse drug reactions (ADRs) [4, 5].

In general use, both gabapentin and pregabalin are associated with dose-dependent ADRs, mainly mild-to-moderate and transient in nature. Many recent meta-analyses have focused on the ADRs induced by these two drugs. They mainly concern the central nervous system. Dizziness, somnolence, headache, diarrhoea, confusion and nausea are the more frequent ADRs reported with gabapentin [6–8], and dizziness and somnolence with pregabalin [9], followed by dry mouth, peripheral oedema, blurred vision and weight gain [1, 10].

Most previously published studies have focused on specific complications occurring in selected populations [11, 12]. Assessment of spontaneous reports of ADRs from a national pharmacovigilance system database is an alternative method validated by the WHO. In the latter method, data is gathered and analysed in fundamentally different ways. Analysis of spontaneous reports is the main method that allows for the early recognition of new drugs involved in ADRs as well as new ADRs [13, 14].

The aim of the present study was to detect early reports of ADRs to gabapentin and pregabalin, to characterize them, and to focus particularly on those ADRs poorly studied and described in the literature, using the French Pharmacovigilance Database system.

2 Methods

We studied ADRs reported between 1 January 1995 and 31 December 2009 to the French Network of Pharmacovigilance Centres and recorded into the French Pharmacovigilance Database. By law, every prescriber (physician, dentist or midwife) must report 'serious' or 'unexpected' ADRs to their French Regional Pharmacovigilance Centre. We previously investigated the profile of ADRs of several drugs used for pain relief, such as nefopam [15], local anaesthetics [16] or mild opiate analgesics (tramadol, dextropropoxyphen, codeine) [17]. Among the ADRs reported, we selected those in which gabapentin or pregabalin was considered as 'suspect'. For each ADR we noted year, patient age and sex, type of ADR (clinical symptoms, 'seriousness' and outcome) as well as the imputability score [13, 18]. A 'serious' ADR is defined as an adverse effect that is fatal or life threatening, that causes hospitalization or prolongation of hospitalization, or permanent or significant disability (recommendations of the International Committee on Harmonization from the WHO Collaborating Centres for International Drug Monitoring [19]). The imputability score is the assessment of the causality of a drug in the development of an undesirable effect. Intrinsic imputability score is classified into five levels: 'unlikely', 'possible', 'probable', 'likely' and 'very likely' [18]. Only reports with an imputability score of at least 'possible' were analysed.

First, details of all ADRs associated with gabapentin or pregabalin reported in the database were presented. Deaths were particularly highlighted. In the second part, we focused on some poorly-studied ADRs reported with the two drugs. Only ADRs with an imputability score for gabapentin or pregabalin of at least 'probable' were presented. Concomitant drugs that may be involved in the occurrence of the ADR were also reported. The risk for each drug to develop such ADRs was analysed based on the Summary of Product Characteristics (SPC) found on the website of the French Agency for the Safety of Health Products (http://www.ansm.sante.fr) and the literature.

Using a method applied elsewhere [17], consumption of gabapentin and pregabalin in France for the same period (from 2006 to 2009) was obtained from the French National Health Insurance System (Caisse Nationale d'Assurance Maladie). Annual consumption of gabapentin and pregabalin was available from 2006. This was divided by the defined daily dose (DDD) of gabapentin (Anatomical Therapeutic Chemical [ATC] code N03AX12, DDD = 1800 mg) and pregabalin (ATC code N03AX16, DDD = 300 mg) according to the WHO [20], and expressed in the number of patients treated per year. The reporting rate of 'serious' ADRs was presented according to their consumption expressed in person-years.

3 Results

Among the 282,304 ADRs registered between 1995 and 2009 into the French Pharmacovigilance Database, we identified 1333 reports (0.47 % of the total) in which gabapentin ($n = 725$; 54 %) and pregabalin ($n = 608$; 46 %) were suspected as the cause of 2415 ADRs in total (1244 and 1171, for gabapentin and pregabalin, respectively). We observed an increase in reports involving gabapentin between 1995 and 2002, followed by a steady annual number of 60–80 reports every year (Fig. 1). For pregabalin, around 180 reports were observed every year, from 2007. Figure 1 also presented the increased consumption of pregabalin from 2006, whereas gabapentin consumption remained steady.

Demographic data are presented in Table 1. ADRs occurred more frequently in women and older patients in the pregabalin group than in the gabapentin group. Thirty-eight patients (29 receiving gabapentin and 9 receiving pregabalin) were children aged < 18 years.

Pregabalin was most frequently the only drug involved in the ADRs (45.6 %), whereas gabapentin was more frequently involved with co-suspected drugs (the only drug involved in 29.4 % of cases [Table 1]). In more than 25 % of cases, four or more suspected drugs involved in the ADRs were associated with gabapentin. More than 40 % of

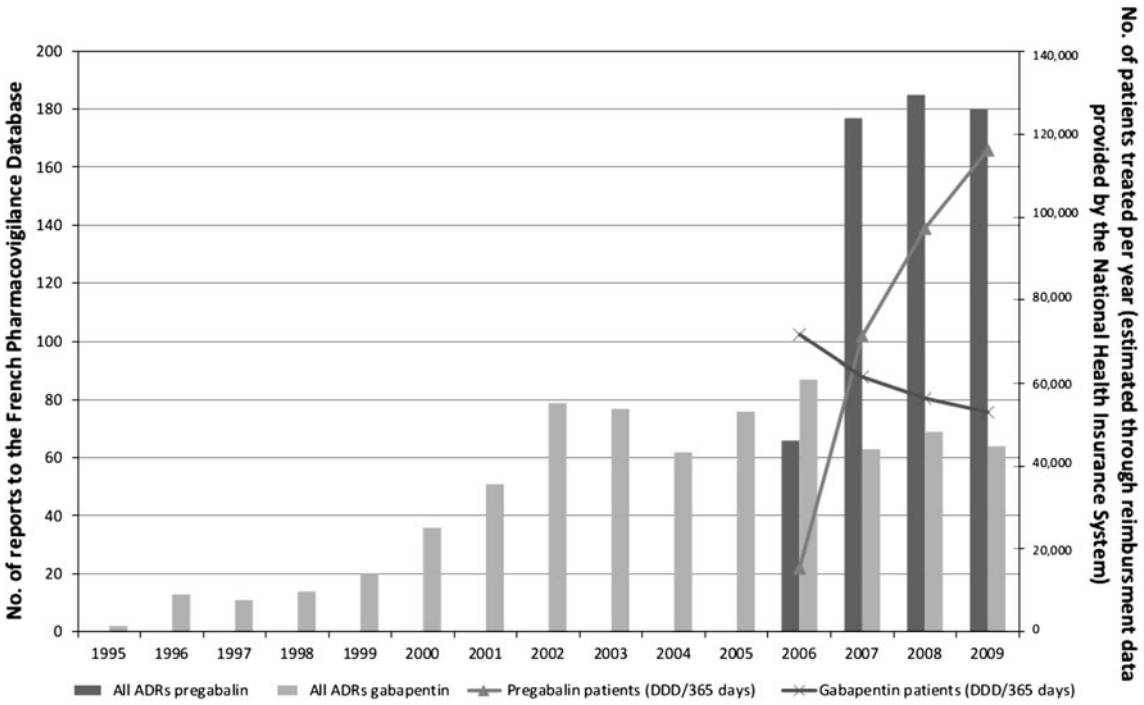

Fig. 1 Number of adverse drug reactions with gabapentin and pregabalin from 1995 to 2009, and number of patients treated by year, from 2006 to 2009. *ADRs* adverse drug reactions, *DDD* defined daily dose

these ADRs were 'serious'. Twenty-two deaths with an imputability score of at least 'possible' were reported during the study period (5 with pregabalin and 17 with gabapentin; $p < 0.05$). Nine of the 17 deaths in the gabapentin group occurred during pregnancy or delivery (Table 2). Polymalformation syndrome was reported in at least six cases. An antiepileptic drug was concomitant in three cases. The remaining deaths were cardiovascular (three cases), haematological (two cases: agranulocytosis and immunological thrombocytopenia), allergic (one case), hepatic (one fulminate hepatitis) and neurological (one case) complications. The five deaths in the pregabalin group were hepatic (two acute hepatitis), cardiovascular (two sudden death) and haematological (one agranulocytosis) complications.

For the two drugs, the most frequently reported ADRs were neuropsychiatric (35.2 % vs. 29.1% for the pregabalin and gabapentin groups, respectively [Tables 3 and 4]). As expected, somnolence, confusion and dizziness were the most frequently occurring neuropsychiatric ADRs reported for the two drugs. Interestingly, some other poorly studied neuropsychiatric ADRs,such as hallucination, agitation or aggressiveness, have been highlighted.

Haematological adverse effects were the second most commonly reported ADRs in the pregabalin group ($n = 42$; 6.9 % [Table 3]). These ADRs concerned male and female (sex ratio = 1.1), with a mean age of 66 ± 20 years. They were 'serious' in 67 % of cases. A recovery with no sequela was noted in 79 % of cases, even though one death was reported. Neutropenia, thrombocytopenia and leukopenia were the most frequently occurring ADRs reported for pregabalin (29.1 %, 23.6 % and 20 %, respectively). Table 5 lists the haematological ADRs reported with pregabalin with an imputability score of 'probable' (16.6 %) or 'likely' (4.8 %), along with concomitant drugs.

Hepatic ADRs ranked second in the gabapentin group ($n = 90$; 12.4 % [Table 3]). Overall, 37 out of 90 hepatic ADRs were hepatitis, as registered by the specialized pharmacovigilance centre in the database (mean age 57 ± 18 years, sex ratio = 1:1.6). The 37 hepatitis ADRs were considered as 'serious' in 57 % of cases. A recovery with no sequela was noted in 48.7 % of cases. One related death was reported. Gabapentin was the only drug involved in 27 % of cases. Table 6 lists the hepatitis cases reported with gabapentin with an imputability score of 'probable' or 'likely', along with concomitant drugs.

The reporting rate [95 % confidence interval] of 'serious' ADRs, presented according to drug consumption between 2006 and 2009, decreased for pregabalin (1684 [1037–2331], 1122 [876–1368], 770 [596–945] and 697 [545–849] million patient-years for 2006, 2007, 2008 and 2009, respectively). For gabapentin, we noted a steady reporting rate of 'serious' ADRs during the same period (530 [362–699], 552 [350–704], 620 [415–826] and 603 [394-812] million patient-years for 2006, 2007, 2008 and 2009, respectively).

Table 1 Main characteristics of reports for gabapentin and pregabalin

Characteristics of reports	Gabapentin ($n = 725$)	Pregabalin ($n = 608$)
Age (y)	58 ± 21	63 ± 18
Sex ratio (male:female)[a]	1:1.10	1:1.56
Number of drugs involved[b]		
1	213 (29.4)	276 (45.6)
2	118 (16.2)	85 (14.0)
3	102 (14.1)	76 (12.6)
4	103 (14.2)	51 (8.4)
≥5	189 (26.1)	117 (19.4)
Seriousness	351 (48.4)	262 (43.3)
Outcome[c]		
Recovery with no sequelae	423 (59.4)	412 (68.4)
Not yet recovered	155 (21.7)	94 (15.6)
Unknown	70 (9.8)	45 (7.5)
Related death	17 (2.4)	5 (0.8)
Other	48 (6.7)	46 (7.7)
Imputability score		
Possible	582 (80.3)	460 (75.7)
Probable	118 (16.3)	114 (18.7)
Likely	25 (3.4)	33 (5.4)
Very likely	0 (0)	1 (0.2)

Data are expressed as mean ± SD or n (%)

[a] Four sets of data were missing in each group

[b] Three sets of data were missing in the pregabalin group

[c] Twelve sets of data were missing with gabapentin and six with pregabalin

4 Discussion

Apart from the well-described neuropsychiatric ADRs that ranked first for the two drugs, this study highlighted poorly-studied ADRs, namely haematological ADRs associated with pregabalin and hepatic ADRs associated with gabapentin.

Haematological ADRs ranked second in the pregabalin group. Most of these effects were neutropenia (29 % of haematological cases with one death), whereas neutropenia is a rare event with pregabalin, i.e. only one case report found in the literature [21]. Thirteen cases (23.6 %) of thrombocytopenia possibly induced by pregabalin were noted in our study. A search of MEDLINE using the search terms 'thrombocytopenia' and 'pregabalin' yielded no published cases. One journal (not indexed) reported a case of possible thrombocytopenia induced by pregabalin in a 91-year-old woman [22]. The estimated minimum incidence of drug-induced thrombocytopenia is about 10 cases per million population per year [23]. Generally, the platelet count falls 7 days or more after starting a new drug and returns to normal in less than a week. Among the drugs commonly implicated as triggers of drug-induced thrombocytopenia, anticonvulsant agents (carbamazepine, phenytoin, valproic acid) are often listed [23]. Mechanism of such ADRs (immune-allergic or toxic) remains unclear to date. Further investigations are mandatory to better understand the mechanism leading to neutropenia or thrombocytopenia. Table 5 reports the ADRs with an imputability score for pregabalin of at least 'probable' or 'likely'. This strengthens the role of pregabalin as the cause of occurrence of these ADRs, particularly in the four cases where pregabalin was the sole drug. In the five remaining cases, concomitant drugs noted may have induced haematological ADRs. However, those ADRs are usually considered as rare in the SPC of the different drugs. The second surprising result of the study concerned hepatic ADRs, with 37 cases of gabapentin-related hepatitis, all considered as 'serious'. This ADR is rated as unspecified in the SPC. Few case reports described this effect with gabapentin in the literature [24, 25]. The occurrence of hepatic ADRs is difficult to explain from a pharmacological point of view. Indeed, gabapentin is not protein bound, does not induce hepatic enzymes, is not metabolized and is renally excreted [3]. Like pregabalin, no pharmacokinetic drug-drug interactions have been identified in formal interaction studies and, based on the pharmacokinetic profile, none would be expected [26]. Eight 'probable' or 'likely' hepatitis cases were reported with gabapentin (Table 6). In four cases, gabapentin was the sole drug involved and in the four remaining cases, different concomitant drugs were reported. Apart from paracetamol (acetaminophen) [two cases], the SPC of the concomitant drugs did not mention any hepatic adverse effects. An increase of the liver enzymes has been rarely reported with tramadol, fluoxetine and ibuprofen. This strengthens the role of gabapentin in the occurrence of hepatitis. This kind of ADR needs to be confirmed by further investigation.

More than four in ten ADRs associated with both gabapentin and pregabalin were considered 'serious', very close to the 44.8 % of cases usually considered as 'serious' in the French Pharmacovigilance Database [27]. Twenty-two deaths in which gabapentin or pregabalin was involved, were reported. Further clarification of the nine deaths in the gabapentin group occurring in an obstetrical context is given in Table 2. The published literature cites case reports only [28]. In a specific study aiming to assess maternal and fetal complication in a parturient female treated with gabapentin, Montouris concluded that gabapentin exposure during pregnancy did not lead to an increased risk of adverse maternal and fetal events [29]. In a recent Danish study, first-trimester exposure to an antiepileptic drug, including gabapentin, compared with no exposure, was not associated with an increased risk of

Table 2 Details of the nine obstetrical deaths reported with gabapentin during the study period

Year	Sex	Age	Concomitant drugs	ADRs	Death	Imputability score[a]
1997		NB	NA	Aortic coarctation, IVC	D3	Possible
1996	F	NB	Valproic acid	Polymalformation syndrome, multiple congenital disorders	D1	Possible
1998	F	IU	CarbamazepIne	Polymalformation syndrome, thoracic tumour	15 PW	Possible
2005	F	IU	Alprazolam, paracetamol (acetaminophen)-dextropropoxyphene, clonazepam, paroxetine	Polymalformation syndrome, oesophageal atresia, maxillary hypoplasia, facial dysmorphism	30 PW	Possible
2006	F	IU	Prazepam	Miscarriage	6–7 PW	Possible
2006	F	IU	NA	Omphalocele, cranial malformation, imperforate anus	12 PW	Possible
2008	F	IU	Topiramate	Intruterine fetal death	27 PW	Possible
2008	M	IU	Valproic acid	Diaphragmatic hernia, facial dysmorphism, club-foot, finger anomaly, major lung hypoplasia	21 PW	Possible
2007	M	IU	Levonorgestrel, short and long-acting insulin	Intruterine fetal death	33 PW	Possible

[a] Imputability is classified into five levels (I0–I4): 'unlikely', 'possible', 'probable', 'likely' and 'very likely'

ADR adverse drug reaction, *D* day of life, *F* female, *IU* intrauterine, *IVC* interventricular communication, *M* male, *NA* not applicable, *NB* newborn, *PW* pregnancy week

Table 3 Type of adverse drug reactions reported for gabapentin and pregabalin

Type of ADRs	Total ($n = 1333$)	Gabapentin ($n = 725$)	Pregabalin ($n = 608$)
Neuropsychiatric	425 (31.9)	211 (29.1)	214 (35.2)
Hepatic	122 (9.2)	90 (12.4)	32 (5.3)
Cutaneous	105 (7.9)	69 (9.5)	36 (5.9)
Haematological	99 (7.4)	57 (7.9)	42 (6.9)
Allergic	76 (5.7)	53 (7.3)	23 (3.8)
Digestive	53 (4.0)	26 (3.6)	27 (4.4)
Cardiorespiratory	61 (4.6)	25 (3.4)	36 (5.9)
Blurred vision	40 (3.0)	22 (3)	18 (3)
Related pregnancy	19 (1.4)	17 (2.4)	2 (0.3)
Oedema	55 (4.1)	17 (2.4)	38 (6.2)
Electrolytic	23 (1.7)	16 (2.2)	7 (1.2)
Renal	43 (3.2)	14 (1.9)	29 (4.8)
Muscular	27 (2.0)	9 (1.2)	18 (3)
Weight gain	33 (2.5)	8 (1.1)	25 (4.1)
Administration error	14 (1.1)	7 (1)	7 (1.2)
Sexual disorder	11 (0.8)	5 (0.7)	6 (1)
Other	127 (9.5)	79 (10.9)	48 (7.8)

Data are expressed as n (%)

major birth defects [30]. However, antiepileptic drugs increase the risk of major congenital malformations, particularly when containing valproate [31]. A recent case-control study confirmed that exposure to valproic acid during the first trimester was associated with significant increases in the risk of spina bifida, atrial septal defect, cleft palate, hypospadias, craniostenosis and polydactyly [32]. Valproic acid was involved in two of the nine obstetrical deaths reported in our study, with multiple malformations, such as facial dysmorphism or finger anomaly. Contrary to this, the same study did not mention an increased risk of diaphragmatic hernia or clubfoot with valproic acid exposure. Intrauterine exposure to carbamazepine also increases the risk of spina bifida, but does not seem to increase the incidence of other malformations compared with no exposure to antiepileptic drugs [33]. The case in which carbamazepine was a concomitant drug was related to polymalformation syndrome without spina bifida. Carbamazepine is less teratogenic than valproic acid [33]. The American Academy of Neurology recommends avoidance of valproic acid during pregnancy, if possible [34]. The use of other antiepileptic drugs during pregnancy should be considered on an individual basis. With the exception of valproic acid, all other concomitant drugs are not considered teratogenic. This strengthens the potential role of gabapentin in the occurrence of such ADRs. Further study is warranted to better understand the relationship between gabapentin and obstetrical deaths.

The difference in the frequency of 'serious' ADRs reported with pregabalin compared with gabapentin (Fig. 1) may be related to the Weber effect [35]. A higher peak in reports occurs during the first years after product

Table 4 Main characteristics of neuropsychiatric adverse drug reactions

Characteristics of neuropsychiatric ADRs	Gabapentin ($n = 211$)	Pregabalin ($n = 214$)
Age (y)	63 ± 20	65 ± 18
Sex ratio (male:female)	1:1.1	1:2.1
Seriousness	111 (53)	103 (49)
Outcome[a]		
Recovery with no sequelae	152 (73.4)	161 (76.3)
Not yet recovered	39 (18.8)	17 (8.1)
Unknown	7 (3.4)	17 (8.1)
Related death	1 (0.5)	0 (0)
Other	8 (3.9)	16 (7.5)
Imputability score		
Possible	146 (69.2)	150 (70.1)
Probable	58 (27.5)	46 (21.5)
Likely	7 (3.3)	17 (7.9)
Very likely	0 (0)	1 (0.5)
Type of ADRs (n)	391	511
Somnolence	41 (10.5)	49 (9.6)
Confusion	28 (7.2)	43 (8.4)
Dizziness	25 (6.4)	40 (7.8)
Falls	0 (0)	21 (4.1)
Trembling	0 (0)	19 (3.7)
Hallucination	16 (4.1)	0 (0)
Agitation	11 (2.8)	0 (0)
Aggressiveness	8 (2.0)	4 (0.8)
Other	262 (67.0)	335 (65.6)

Data are expressed as mean ± SD or n (%)

ADRs adverse drug reactions

[a] Four sets of data are missing in the gabapentin group and three in the pregabalin group

approval. With time, the difference between the two drugs decreased. This has been demonstrated for other drugs, for example NSAIDs [36].

The present study confirms the high prevalence of neuropsychiatric effects associated with gabapentin and pregabalin, which is well-described elsewhere [9, 10, 37]. Neuropsychiatric symptoms noted in the present study, such as somnolence, confusion or dizziness, are the same as those usually reported in literature. Interestingly, no case of overdose has been reported in our study. Gabapentin or pregabalin overdose or misuse was reported in the literature [38–42]. More recently, a Swedish study concluded that pregabalin is likely to be associated with the potential for patients to be abusive [43]. The finding of 12 cases of aggressiveness with both drugs need further investigation (Table 4). Recently, dopaminergic agonists, benzodiazepines and serotoninergic antidepressants have been considered as the main pharmacological classes able to induce aggressive behaviour [44]. In the same study, the putative role of other drugs involved in this ADR has been emphasized.

Finally, some other ADRs associated with pregabalin, such as blurred vision or weight gain, were less frequently reported in the present study. Blurred vision was only reported in 3 % of all ADRs associated with pregabalin in our study, whereas it was significantly noted in the recent meta-analysis on the pregabalin adverse event profile [10]. This may be explained by the fact that blurred vision is a well-known and not 'serious' adverse effect. Similar comments may be made for weight gain [10].

The main limit of the present study is related to the methodology used in the pharmacovigilance database analysis. This was described in a previous publication using the same methodology [16]. This main drawback

Table 5 Details of the nine cases of haematologic ADRs reported with pregabalin that occurred during the study period with an imputability score of 'probable' (I2) or 'likely' (I3)

Year	Sex	Age (y)	Seriousness	Concomitant drugs	ADR	Imputability score[a]
2008	F	70	Not serious	NA	Leukopenia	Probable
2008	F	49	Not serious	NA	Leukopenia, thrombocytopenia	Probable
2008	M	76	Serious	Furosemide, aspirin (acetylsalicylic acid)	Thrombocytopenia	Likely
2008	M	80	Serious	Azathioprine	Acute agranulocytosis, fever	Probable
2008	F	18	Not serious	Valproic acid, carbamazepine	Neutropenia	Probable
2006	F	85	Serious	NA	Leukopenia	Likely
2007	M	71	Serious	Paracetamol (acetaminophen)-tramadol	Agranulocytosis, thrombocytopenia	Probable
2008	M	57	Not serious	NA	Neutropenia	Probable
2008	M	48	Not serious	Amitryptyline, piperacillin/ tazobactam, ciprofloxacin	Leukopenia, neutropenia	Probable

[a] Imputability score is classified into five levels (I0–I4): 'unlikely', 'possible', 'probable', 'likely' and 'very likely'

ADR adverse drug reaction, *F* female, *M* male, *NA* not applicable

Table 6 Details of the eight cases of hepatitis reported with gabapentin that occurred during the study period with an imputability score of 'probable' (I2) or 'likely' (I3)

Year	Sex	Age (y)	Seriousness	Concomitant drugs	Imputability score[a]
2004	M	27	Not serious	NA	Probable
2005	M	70	Not serious	Tiapride, misoprostol, amiloride, meprobamate	Probable
2006	M	30	Serious	Caffeine, paracetamol (acetaminophen), immunoglobulin	Probable
2004	F	48	Serious	Tramadol	Probable
2004	F	67	Not serious	NA	Likely
2006	M	59	Serious	NA	Likely
2001	F	47	Serious	Fluoxetine, tetrazepam, hydroxychloroquine, paracetamol, opium, caffeine, ibuprofen	Probable
2002	M	60	Serious	NA	Probable

[a] Imputability score is classified into five levels (I0–I4): 'unlikely', 'possible', 'probable', 'likely' and 'very likely'

F female, *M* male, *NA* not applicable

concerns underreporting, which is a two-sided problem: it is generally substantial, but perhaps more complicating is its variability. However, one of the first goals of this system is to generate early signals [27]. By highlighting obstetrical, hepatic and haematological ADRs, this study confirmed such interests.

5 Conclusion

In this analysis of the French Pharmacovigilance Database, we observed that a high rate of death occurred with gabapentin in an obstetrical context. Apart from the well-described neuropsychiatric effects associated with pregabalin and gabapentin, other frequent ADRs have been noted, such as haematological or hepatic ADRs, considered as 'serious' in the majority of cases, associated with pregabalin and gabapentin, respectively. Further investigation is mandatory to better understand the safety profile of these two widely used drugs.

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