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Interactions between antiseizure medications and contraception: a study about the knowledge of patients and their specialist physicians

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HIGHLIGHTS

- Contraception can be challenging for women with epilepsy
- Women with epilepsy have limited knowledge concerning the interactions between contraception and antiseizure medications
- Neurologists also have limited knowledge concerning the type of anti-seizure medicine which can interact with contraception
- The possible decrease in efficacy of lamotrigine when associated with combined contraception is not well known by patients and neurologists
- These knowledge gaps may limit the effectiveness and compliance of contraceptive methods for women with epilepsy

ABSTRACT

Planning pregnancy is very important for women with epilepsy (WWE), because of the potential teratogenic effects and neurodevelopmental disorders of different antiseizure medications (ASMs). Nevertheless, contraception in WWE can be challenging due to the existence of drug interactions between ASMs and hormonal contraception. The aim of this study was to assess women's knowledge of potential interactions between their ASMs and contraceptive options. The second objective was to assess neurologist knowledge of the potential interactions between ASMs and contraceptive methods.

An anonymous online survey was proposed to reproductive-age WWE during consultation with their neurologist. Another online survey was proposed to neurologists. These surveys were performed through a French regional medical network.

A total of 79 patients agreed to respond to the survey. Forty-nine women used lamotrigine alone or in combination, 15 used an enzyme-inducing ASM alone or in combination, 13 used non-enzyme-inducing ASM and 2 used both lamotrigine and an enzyme-inducing ASM. Half of the WWE had mistaken beliefs about interactions between their ASM and contraception. Among them, 35% of the women treated with an enzyme-inducing ASM were unaware of a potential decreased efficacy of hormonal contraception. Moreover, 51% of the women who were taking lamotrigine did not know that combined hormonal contraception might decrease the efficacy of their ASM. On the other hand, 64.5% of WWE without an enzyme-inducing ASM wrongly thought that their ASM can decrease their hormonal contraceptive efficacy. A total of 20 neurologists answered the online survey. It revealed specific gaps concerning interactions between ASM and contraceptives; in fact, 35% of answers concerning the identification of specific enzyme-inducing ASMs were wrong.

This study therefore highlights the need for educational efforts for both WWE and their physicians regarding drug interactions between ASMs and hormonal contraceptives.

KEY WORDS: contraception, epilepsy, antiseizure medications, interactions, patient knowledge, WWE

1

2 **1. INTRODUCTION:**

3 More than 500,000 people in France have epilepsy [1], one third of whom are women of childbearing
4 age. For these women, pregnancy planning is critical since some antiseizure medications (ASMs)
5 carry a teratogenic risk. The French National Agency For Medicine Safety (ANSM) recently published
6 a summary of all the data in the literature concerning the safety of ASMs during pregnancy [2]. An
7 increase in the overall frequency of congenital malformations compared to the general population
8 has been found for carbamazepine and phenytoin with a risk ratio of about 2-3 [2,3], for topiramate,
9 phenobarbital and primidone with risk ratio of 3 [2,3] and for valproate with a risk ratio of
10 approximately 4-5 [4,5]. The teratogenic risk is even higher when several ASMs are combined or
11 when prescribed at high doses [6]. Moreover, studies have shown an association between *in utero*
12 exposure to different ASMs and the occurrence of neurodevelopmental disorders in children [7,8].

13 Finding a suitable, satisfying contraceptive method for women taking ASMs is therefore a major
14 issue. The first study that reported interactions between hormonal contraception and ASMs was
15 published in 1972 [9]. Most of the older-generation ASMs (phenobarbital, primidone, phenytoin,
16 carbamazepine) are known to have CYP3A4-inducing properties, increasing the metabolism of
17 hormonal contraception and thus reducing its efficacy. This applies to hormonal contraception,
18 including combined hormonal contraceptives (CHC) (oral, pill and vaginal ring) and progestogen-only
19 contraceptives (POCs) (pill, subdermal implant), regardless of the route of administration (oral,
20 subcutaneous or vaginal) [10,11]. This inducing effect was also shown for more recent drugs:
21 oxcarbazepine, eslicarbazepine as well as perampanel and topiramate when given in high doses (≥ 12
22 mg/day for perampanel and > 200 mg/day for topiramate). When women are taking an enzyme-
23 inducing ASM, the only highly effective contraceptive methods are thus the copper intrauterine
24 device (IUD) or the hormonal IUD, whose efficacy was confirmed in recent studies due to the local
25 progestin effect on the endometrium [12–14]. The depot medroxyprogesterone acetate (DMPA)
26 injection method is also an alternative for those patients, but its use may lead to several side effects
27 [15]. The World Health Organization has lately published revised recommendations about
28 contraceptive use for patient with epilepsy [16].

ASM: antiseizure medication

WWE: women with epilepsy

CHC: combined hormonal contraceptive

POC: progestin-only contraception

IUD: intrauterine device

29

30 Lamotrigine is widely used in WWE of childbearing age because epidemiological studies have shown
31 a low risk of major congenital malformation and neurodevelopmental problems after prenatal
32 exposure [2,3,17,18]. However, CHCs may induce variations in the circulating level of lamotrigine
33 [19–22] due to the impact of estrogens on the uridine diphosphate glucuronosyl transferase
34 (UGT1A4), which may thus require dose adjustment when introducing or stopping a CHC. Indeed, the
35 introduction of the CHCs can lead to a decrease in the efficacy of lamotrigine with an increased risk
36 of seizures, and the cessation of CHCs can lead to an increase in lamotrigine concentration with a risk
37 of side effects.

38 In any case, women's satisfaction and compliance with their contraception are always more
39 important when it is the woman herself who has chosen her method of contraception [23,24].
40 Moreover, for WWE, information on the potential interactions between ASMs and contraception are
41 particularly important to avoid unintended pregnancy. Several studies, particularly in the United
42 States [25–29], have reported insufficient knowledge among WWE about the impact of their
43 treatment on contraceptive use.

44 The aim of this study was thus to assess knowledge among French WWE of the impact of their ASMs
45 on contraceptive methods. The secondary objective was to determine whether the neurologists
46 involved in WWE management were aware of the interactions between ASMs and contraception.

47

48 **2. METHODS:**

49

50 **2.1. Population:**

51 This study was carried out in France within the Midi-Pyrénées regional network in peripheral
52 hospitals, private neurology practices and the neurology department at the University Hospital of
53 Toulouse. Among this network, 93 neurologists were invited to propose an online survey to their
54 epileptic female patients. Documents about the objectives of this study and the online survey's link
55 were made available to patients in the waiting room of the neurologists' offices. The survey could be
56 also directly proposed by the physician.

57 Eligible participants included WWE of reproductive age taking an ASM. We excluded women under
58 18 years of age and those over the age of 45.

59 All 93 neurologists were also invited to answer a physician survey about interactions between
60 contraception and ASM.

61

62 **2.2. Data collection:**

63 This study was performed over a 15-month period between June 2018 and September 2019.

64 The survey was anonymous and only included multiple choice questions. The only demographic data
65 which was collected was the age of the women. They were asked to list all their current medications
66 and provide the names and daily dosages of current ASMs. We categorized ASM treatment as
67 monotherapy or polytherapy. We grouped ASMs into three categories based on their effects on
68 enzymatic metabolism: (1) enzyme-inducing ASMs, which included phenobarbital, phenytoin,
69 carbamazepine, oxcarbazepine, perampanel ≥ 12 mg daily and topiramate > 200 mg daily; (2)
70 glucuronidated ASMs, which included only lamotrigine; (3) non-enzyme-inducing ASMs, which
71 included levetiracetam, zonisamide, gabapentin, topiramate in dosages ≤ 200 mg daily, perampanel $<$
72 12 mg daily, lacosamide, clobazam, pregabalin and tiagabine, as well as valproate (even if it has an
73 inhibitor effect, the more recent data show no significant interaction with contraception) [11]. To
74 assess awareness of ASM–contraception interactions, women were asked if the ASM they were
75 currently taken could reduce the birth control method’s efficacy and whether combined hormonal
76 contraception might reduce the efficacy of the ASM (the English translation of the survey used for
77 this study is presented in the appendix). Moreover, to sustain the comprehension of the survey and
78 whenever necessary, questions were reformulated. One part of the survey was devoted to their
79 satisfaction with the contraception they were taking at the time of the survey. They were also asked
80 whether they felt they were adequately informed about possible interactions between contraception
81 and ASMs or whether they would have liked to be better informed. Finally, they were asked if they
82 experienced an unintended pregnancy while taking an ASM.

83

84 We relied on the most recent data in the literature [10,28] regarding drug interactions as well as the
85 latest national and international recommendations [15,16,30]. It should be noted that recently,
86 World Health Association has classified etonorgestrel implant as “2” (a condition where the
87 advantages of using the method generally outweigh the theoretical or proven risks)[16]. However,
88 French recommendations [30] still advise against combining this type of contraception with enzyme-
89 inducing treatments due to a number of data [31] which is why we considered this combination to be
90 at risk of unplanned pregnancy in this study. If a patient had more than a single ASM, all interactions
91 with hormonal contraceptives were considered.

92 Concerning the neurologists' survey, questions related to their knowledge of the enzymatic
93 metabolism effects of the different ASMs and the interactions between all contraceptive methods
94 with either lamotrigine, enzyme-inducing ASM or non-enzyme-inducing ASM.

95 This study was approved by the ethical committee of the University Hospital of Toulouse (under
96 number 217296 Vo).

97

98 **2.3. Statistical analyses:**

99 Descriptive analyses, including indicators of central tendency and dispersion (mean and standard
100 deviation) for quantitative variables, were performed.

101

102

103 **3. RESULTS:**

104 **3.1. Patient survey**

105 A total of 83 WWE responded to the survey. Four women were excluded because of age over 45
106 years, which left 79 women for the final analysis.

107 The mean age of the 79 women was 28.6 years (18–44 years). Among them, 62% (n=49) received
108 lamotrigine alone or in combination with a non-enzyme-inducing ASM, 21.5% (n=17) received an
109 enzyme-inducing ASM alone or in combination and 16.4% (n=13) a non-enzyme-inducing ASM alone
110 or in combination (Table 1). Only 2 women were using a combination of lamotrigine and an enzyme-
111 inducing ASM.

112 There were 49 WWE (62%) using contraception. Intrauterine device (IUD) was the most widely used
113 contraceptive method (47%), with 17 women using the copper IUD and 6 women using the
114 levonorgestrel IUD. Another 38% of the women (n=19) were taking a combined hormonal
115 contraception (CHC) and 10.2% a progestin-only contraception (POC) (implant (n=3), pill (n=2)).
116 Finally, 4% (n=2) of the women reported using mechanical contraception. The distribution of
117 contraceptive methods according to the type of ASM is shown in Figure 1. It should be noted that
118 53% of WWE treated with an enzyme-inducing ASM have no contraceptive method (vs. 34.7% in the
119 lamotrigine group and 30.8% in the non-enzyme-inducing ASM group). Moreover, 3 women using
120 enzyme-inducing ASM therapy used a CHC or POC as contraception and were therefore at risk of
121 unplanned pregnancy.

122 The women's responses regarding potential interactions with their ASMs are presented in Table 2.
123 Among the WWE, 50% have false beliefs about this subject. Of the 51 patients treated with
124 lamotrigine alone or in association, 51% did not know about the possible reduction in the efficacy of
125 their ASM in association with CHC. As for the 17 patients with an enzyme-inducing ASM alone or in
126 association, 35% did not know that their ASM could reduce the efficacy of hormonal contraceptive.
127 Furthermore, 64.5% of patient without an enzyme-inducing ASM wrongly believed that their ASM
128 could also interfere with their contraceptive efficacy.

129 Among the 49 WWE with a contraceptive method, 78% were satisfied with their contraception.
130 However, 53% of them declared that they needed more information about the interactions between
131 ASM and contraception.

132 There were 16 (20.2%) WWE who had experienced an unintended pregnancy. Among them, there
133 was 50% of false beliefs versus 43.7% in the WWE without any unintended pregnancy. There was a
134 larger proportion of unintended pregnancy in women with lamotrigine or non-enzyme- inducing ASM
135 (24.4% and 23.1% respectively) than in women with enzyme-inducing ASM (5.9%).

136

137 **3.2. Neurologist survey**

138 Of the 93 neurologists who were asked to participate to the WWE survey, 20 responded to the
139 physician survey (21.5%). Mean age was 46.5 years old [27-62 yrs]. Nine neurologists were working in
140 a public practice and 9 were on private practice, 2 of them having a mixt activity. There was a total of
141 84.3% correct answers about the knowledge of which ASM could decrease the efficacy of hormonal
142 contraceptives. There were 33% wrong answers about some specific enzyme-inducing ASMs (Table
143 3). About 40% of the neurologists did not know about the possible reduction of lamotrigine
144 concentration when introducing a CHC.

145

146 **4. DISCUSSION:**

147

148 The results of our study show that WWE have limited knowledge about the interaction between their
149 ASMs and hormonal contraception. Of the 79 WWE who responded to this survey, half of them had
150 false beliefs about the interactions between their current ASM and contraceptive method. First,
151 35.3% of the WWE who received an enzyme-inducing ASM didn't know that it could reduce
152 effectiveness of hormonal contraception, 51% of WWE treated by lamotrigine didn't know that CHC

153 could reduce effectiveness of their ASM and finally 64.5% of women treated with a non-enzyme-
154 inducing ASM mistakenly believed that it decreased the efficacy of hormonal contraception. The
155 insufficient knowledge about the interactions between ASM and hormonal contraception is therefore
156 likely to limit the choice of contraceptive method.

157 This global insufficient knowledge has already been reported in the literature, most often to an even
158 greater extent. Pack et al. [25] surveyed 148 WWE, of whom only 32% of those treated with an
159 enzyme-inducing ASM were aware of interactions with an oral contraceptive. In this study, 26% of
160 the women taking a non-enzyme-inducing ASM also wrongly thought that there was an interaction
161 with CHC. In the SAFETY study, of the 85 WWE between the ages of 13 and 18 years who were asked
162 if “regular birth control pills work well with seizure medicine,” only 8.2% answered correctly [26]. In a
163 study designed to evaluate an interventional education program in 42 WWE, a preintervention test
164 score of 1/10 was obtained on questions concerning interactions between contraception and several
165 ASMs, among them, topiramate, carbamazepine and lamotrigine [27]. In Dierking study [29], where
166 179 German WWE were asked if the effect of oral contraceptive was influenced by ASM, only 55% of
167 them answered correctly. With the exception of the Pack study [24], all of these studies focused on
168 the overall knowledge of WWE about interactions between ASM and oral contraceptives
169 independently of their own current treatment. We were more interested in whether women were
170 aware of the effects of their own treatment on the different contraceptive methods in order to help
171 them in their choice. In addition, none of the previously published studies asked questions about the
172 interaction between lamotrigine and CHC. Given that it is currently the most widely used treatment
173 in women of childbearing age because of its low teratogenicity, we felt it was important to examine
174 the knowledge of possible variations in lamotrigine efficacy when oral contraception is introduced or
175 stopped. This is of particular concern because these interactions may be poorly known by
176 practitioners (40% of neurologist in our study didn’t know about this interaction), even though they
177 have a major role in informing and counseling women with epilepsy.

178 In our study, neurologist survey show limited knowledge about which ASM could decrease efficacy of
179 hormonal contraception (37% of wrong answer). Several studies have reported a lack of awareness
180 of the interactions between ASMs and hormonal contraception among general practitioners, but also
181 among neurologists and gynecologist [32–34]. The Epilepsy Foundation in the United States [32]
182 showed that only 5% of the 3,500 multidisciplinary practitioners who were asked about various
183 issues concerning WWE had at least 2 out of 3 correct answers, including interactions of
184 contraception with enzyme-inducing ASM. A prior American study reported that only 4% of the 160
185 neurologists who were questioned knew the interaction between CHC and the 6 most common ASMs
186 [33]. Also, a Brazilian study found that among 42 neurologists surveyed, 93% were aware of the

187 possibility of interactions between ASMs and contraceptives, but there was insufficient knowledge
188 about the types of interactions between ASMs and contraception. 81% of them thus recommended
189 the copper IUD regardless of the type of ASM used [34].

190 Regarding the use of contraception, it should be noted that only 62% of our population were using a
191 contraceptive method compared to 71% in the general French population [35]. A greater proportion
192 of the WWE were using the IUD contraception (47% vs. 25.6% in the general French population) [35].
193 The greatest proportion of women not using contraception was found in the enzyme-inducing ASM
194 group (55%). Nevertheless, most WWE were taking a contraceptive method that was appropriate for
195 their ASM. Among the 49 WWE who were using contraception, only 3 of them (6%) had an enzyme-
196 inducing ASM associated with hormonal contraception. These results are rather reassuring,
197 particularly with regard to the data reported in the international literature, in which between 27%
198 [36] and 43% [37] of patients with an enzyme-inducing ASM were taking hormonal contraceptives.

199 However, it must be noted that 16 (20%) WWE in our survey declared having already had an
200 unintended pregnancy which is higher than what is reported in the general French population (12%)
201 [38] but remain low in comparison with data in the literature: in the study by Davis et al [39], 141
202 epilepsy patients aged 18 to 44 years were interviewed. Of the 77 patients who had ever had
203 children, 61% reported having at least one unplanned pregnancy (consistent with rates in the general
204 US population). Similarly, the Johnson et al. study [28] found an unplanned pregnancy rate of 52%
205 compared to 48% for women without epilepsy (not significant after adjustment for other co-factors).
206 The American study by Herzog et al [36] found much more worrying results with 78.9% of their
207 patients reporting an unplanned pregnancy. These results probably reflect cultural differences
208 between France and the United States, with a lower rate of unplanned pregnancies in French general
209 population [38,40]. Moreover, the enzyme inducing ASM group in our study is surprisingly the one
210 with the lowest rate of unintended pregnancy. This could be explained by the small number of WWE
211 in this group (n=16) but also because enzyme-inducing ASM are often used for more difficult to treat
212 type of epilepsy and are also at teratogenic risks for most of them, so WWE could have been better
213 informed of pregnancy risk in this group.

214 This study has several strength and limits. To our knowledge, this is the first study to evaluate the
215 knowledge of French WWE about interactions between ASMs and contraception. Moreover, women
216 were asked about their knowledge about their current own ASM and the correct answers of our
217 survey were analyzed accordingly. This is also the first study to assess knowledge of interactions
218 between lamotrigine and combined contraception. The main limitation of this study is the small
219 number of WWE, since this sample of 79 patients may not be representative of the general

220 population of treated WWE. However, our results are comparable to what has already been reported
221 in different countries and confirm the limits of the knowledge of WWE on the interaction between
222 epilepsy treatment and contraception. A recruitment bias is possible due to the diffusion mode of
223 our survey via neurologists, some of whom are specialists in epilepsy. This may have overestimated
224 the results about knowledge of WWE and accordingly limited the use of an ineffective contraception
225 method in women treated with enzyme-inducing ASMs in our population. The axis of progress
226 certainly remains the education of neurologists and gynecologists as well as general practitioners via
227 continuous training to allow for a personalization of the information that should be given to the
228 women regarding contraception methods and their compatibility with their ASMs. In those cases of
229 relatively rare diseases, the woman could become an “expert-patient” for her pathology, treatment
230 and recommendations for pregnancy and contraception. This is why different therapeutic education
231 programs are being developed more and more often to allow these women to have the best possible
232 care. The knowledge of the exhaustive and wide choice of available efficient contraceptive methods
233 is thus likely to increase the adherence, compliance and satisfaction of WWE. This can only
234 contribute to reducing the number of unplanned pregnancies in WWE.

235

236 **5. CONCLUSION:**

237

238 Our study has confirmed the limited knowledge regarding the interactions between ASM and
239 contraceptive methods, regardless to the type of ASM use (lamotrigine, enzyme inducing ASM or not
240 enzyme inducing ASM) as previously highlighted in several reports concerning both women treated
241 for epilepsy but also their neurologists. It is therefore important to reinforce all information actions
242 for the WWE, whether through their physician or through therapeutic education programs and
243 information leaflets.

Table 1: Distribution of ASMs in our population

	N (%)
Monotherapy	51 (64.5%)
Bitherapy	24 (30.4%)
Tritherapy	4 (5.1%)
Total	79
Lamotrigine alone or in association with a non-enzyme-inducing ASM	49 (62%)
Lamotrigine associated with an enzyme-inducing ASM¹	2 (2.5%)
Enzyme-inducing ASM alone or in association with other enzyme-inducing ASMs or non-enzyme-inducing ASMs	15 (19%)
Non-enzyme-inducing ASM alone or in association with other non-enzyme-inducing ASMs	13 (16.5%)
Total	79
Enzyme-inducing ASMs	
Oxcarbazepine	7
Carbamazepine	6
Eslicarbazepine	4
Topiramate (> 200 mg/day)	1
Phenobarbital	1
Non-enzyme-inducing ASMs	
Levetiracetam	16
Zonisamide	7
Lacosamide	6
Perampanel (\leq 10 mg/day)	3
Pregabalin	1
Topiramate (\leq 200 mg/day)	1
Tiagabine	1

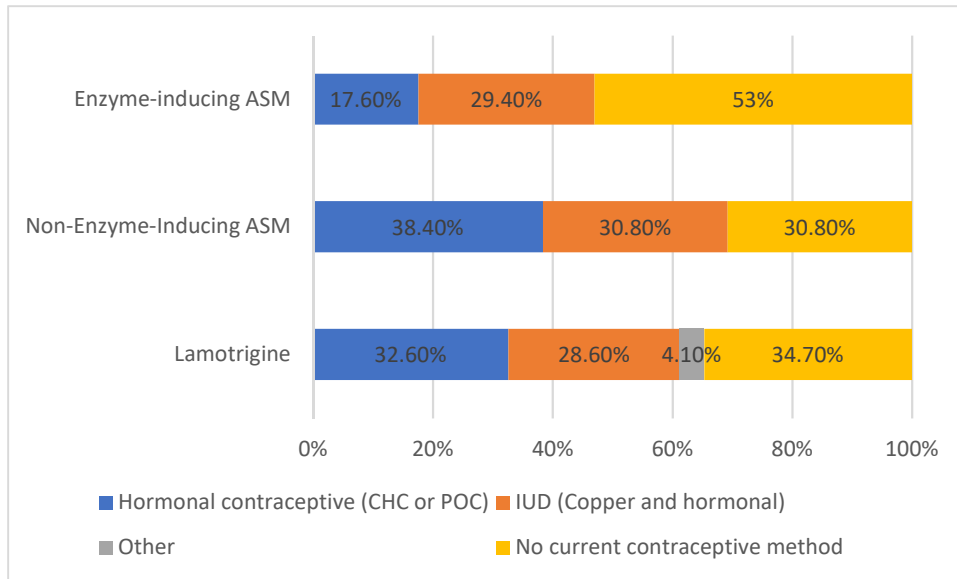
Table 2: Patients' answers about the interactions of their ASMs with contraception

	Patients with enzyme-inducing treatment* (n=17)	Patients without enzyme-inducing treatment (n=62)
Does your ASM decrease the efficacy of hormonal contraceptives?	Correct Answer: YES Yes: n=11 (65%) No: n=6 (35%)	Correct answer: NO No: n=22 (35.5%) Yes: n=40 (64.5%)
	Patients with lamotrigine treatment* (n=51)	Patients without lamotrigine treatment (n=28)
Do hormonal contraceptives decrease the efficacy of your ASM?	Correct answer: YES Yes: n=25 (49%) No: n=26 (51%)	Correct answer: NO No: n=21 (75%) Yes: n=7(25%)

* The 2 patients treated with both lamotrigine and an enzyme-inducing ASM were included in both groups.

Table 3: Neurologists' answers about which ASM could decrease the efficacy of hormonal contraceptives

	Correct answer N (%)	Wrong answer N (%)
Enzyme-inducing ASMs (correct answer: YES)	Yes: 67%	No: 37%
Carbamazepine	Yes: 17 (85%)	No: 3 (15%)
Phenytoin	Yes: 15 (75%)	No: 5 (25%)
Oxcarbazepine	Yes: 14 (70%)	No: 6 (30%)
Phenobarbital	Yes: 14 (70%)	No: 6 (30%)
Eslicarbazepine	Yes: 7 (35%)	No: 13 (65%)
Non-enzyme-inducing ASMs (correct answer: NO)	No: 94.3%	Yes: 5.7%
Valproate	No: 16 (80%)	Yes: 4 (20%)
Lacosamide	No: 19 (95%)	Yes: 1 (5%)
Zonisamide	No: 19 (95%)	Yes: 1 (5%)
Levetiracetam	No: 20 (100%)	Yes: 0 (0%)
Gabapentine	No: 20 (100%)	Yes: 0 (0%)
Pregabalin	No: 20 (100%)	Yes: 0 (0%)
Tiagabine	No: 20 (100%)	Yes: 0 (0%)
Lamotrigine	No: 17 (85%)	Yes 3 (15%)



ASM: antiseizure medication, CHC: combined hormonal contraceptive, POC: progestin-only contraception, IUD: internal uterine device

The two patients taking lamotrigine and an enzyme-inducing ASM were included in the enzyme-inducing treatment group.

Figure 1: Distribution of the types of contraception according to the type of ASM

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APPENDICES:

Patient survey

- 1) How old are you?
- 2) Which ASM are you currently taking?
- 3) Do you think that your current ASM could decrease the efficacy of your hormonal contraceptive method?
 - a. Yes
 - b. No
- 4) Do you think that the efficacy of your ASM could be decreased by combined hormonal contraceptives?
 - a. Yes
 - b. No
- 5) Do you use a contraceptive method?
 - a. Yes
 - b. No
- 6) If the answer is yes: which one?
- 7) Are you satisfied with your contraceptive method?
 - a. Yes
 - b. No
- 8) Do you need more information about the interactions between ASMs and contraception?
 - a. Yes
 - b. No
- 9) Have you ever had an unexpected or unintended pregnancy?

Neurologist survey

- 1) How old are you?
- 2) What is your current mode of practice?
 - a. Public
 - b. Private
 - c. Both
- 3) Which antiseizure medication do you believe may require the adaptation or modification of the type of contraception used in your patient because of the risk of contraceptive inefficacy?
 - a. Carbamazepine
 - b. Phenytoin
 - c. Oxcarbazepine
 - d. Phenobarbital
 - e. Eslicarbazepine

- f. Valproate
- g. Lacosamide
- h. Zonisamide
- i. Levetiracetam
- j. Gabapentine
- k. Pregabaline
- l. Tiagabine
- m. Lamotrigine
- n. All ASMs

4) Which ASMs do you think need to be adapted (doses) when introducing or stopping CHC?

- a. Carbamazepine
- b. Phenytoin
- c. Oxcarbazepine
- d. Phenobarbital
- e. Eslicarbazepine
- f. Valproate
- g. Lacosamide
- h. Zonisamide
- i. Levetiracetam
- j. Gabapentine
- k. Pregabaline
- l. Tiagabine
- m. Lamotrigine
- n. All ASMs