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Review Article

Epilepsy and Grossesse: Context and Care

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Abstract

Epilepsy is not the contraindication of pregnancy, but pregnancy in women with epilepsy is still classified as at risk even if the majority is uneventful. Epilepsy could alter the course of pregnancy and pregnancy could destabilize epilepsy. Pregnancy-associated epilepsy may interfere with the increase in the frequency of their seizures such as a decrease in plasma concentration of antiepileptic drugs. Added to this are the teratogenic effects of antiepileptic drugs. Pregnancy programming is essential in the epileptic patient, it optimizes antiepileptic treatment and improves management during pregnancy. Management consists of first stabilizing epilepsy before conception. The absence of seizures during the nine months prior to pregnancy is associated with a high probability that the pregnancy will proceed without any seizures. In the case of unplanned pregnancy, itis essential to work closely with neurologists, obstetricians, anaesthetists and paediatricians.

Keywords: *Epilepsy; Pregnancy; Management*

Introduction

Epilepsy is a set of syndromes and diseases characterized by a predisposition of the brain to develop seizures and the neurobiological consequences (cognitive, psychological and social) that result. Epileptic seizures are the expression of an excessive, hypersynchronous electrical discharge of neurons in cortical areas. It is a chronic condition whose management lasts on average 4 to 5 years in the absence of a recurrence of a crisis or even for life in certain clinical forms [1,2]. Epilepsy complicates a woman's reproductive life [3]. The occurrence of pregnancy in an epileptic woman is not uncommon, it is not a contraindication of either. In fact, about 0.5% of pregnant women are epileptic [4]. The combination of pregnancy and epilepsy is a major concern of patients, the patient's family, medical and allied practitioners. Pregnancy could destabilize epilepsy and even epilepsy could hinder the development of pregnancy. This article aims to describe the state of affairs and management of the association of pregnancy and epilepsy for the well-being of the child.

Effects of pregnancy on epilepsy

Pregnancy is a generic term that refers to all phenomena that range from conception to childbirth. It lasts between 37 and 41 weeks of amenorrhea. Pregnancy is divided into two periods, embryonic and fetal, corresponding to morphologically defined stages. The embryonic period covers the first 60 days of development and is characterized by organogenesis and external modeling of the individual

(morphogenesis). The fetal period ranges from the beginning of the ninth week of development to birth and corresponds to the period of fetal growth and maturation of tissues and functions [5]. During pregnancy, an increased trend in the frequency of seizures is observed in about 35% of women. Several factors may play a role in the resurgence of crises. This is the case with hormonal changes, including hyperestrogenia, metabolic changes, sleep disturbances, poor adherence to antiepileptic treatment for fear of teratogenicity, changes in plasma levels of antiepileptic drugs secondary to gravidic vomiting, drug interactions, expansion of plasma volume, increased cardiac output with increased liver and renal blood flow that accelerates the elimination of antiepileptic drugs [6,7].

To better manage, it is necessary to schedule pregnancy in epileptics ideally two years in advance. It consists of first stabilizing epilepsy before conception. The absence of seizures during the nine months prior to pregnancy is associated with a high probability that the pregnancy will proceed without any seizures. When a pregnancy is expected, the neurologist should optimize the medication as soon as possible. The goal should in principle be a treatment with a single drug (monotherapy) as low-dosed as possible. It is crucial that the treating neurologist knows before pregnancy the blood concentration of medication allowing the mother-to-be to avoid side effects and especially seizures. In the case of unplanned pregnancy, apart from antenatal consultations, a specialized neurology consultation should be routinely completed by quarter with an electroencephalographic examination and blood test of antiepileptic drugs [8,9].

Effects of epilepsy on pregnancy

Epilepsy itself may not have adverse effects on the proper course of pregnancy. Comparison of women with epilepsy who were not treated with antiepileptic and non-epileptic women showed no significant difference in the risk of fetal malformations [7]. The role of epilepsy in the occurrence of birth defects is probably secondary. Indeed, some studies show that there is no relationship between the occurrence of malformations and the existence of untreated epilepsy [6]. The role of seizures in the first trimester of pregnancy on the risk of congenital malformation was discussed but not confirmed thereafter. There is no relationship between the type of seizure or severity of epilepsy and the occurrence of malformations, except for the condition of epileptic pain that remains associated with high mortality [9]. Generalized tonic-clonic seizures can lead to lactic acidosis and decreased placental blood flow that can be harmful to the fetus. To date, neither the existence of epilepsy nor its type nor its severity are major risk factors for fetal malformation. There is no significant influence of epilepsy on the course of pregnancy and childbirth in relation to the general population. The repetition of the crisis is always harmful to pregnancy. Isolated maternal seizures usually do not affect the child [10].

Taking antiepileptic drugs

Several antiepileptic drugs are available, which are ancient molecules such as Phenobarbital, Valproate sodium, Carbamazepine, Clobazam, Clonazepam, Diazepam, Phenytoin, Phosphophenytoin, Felbamate and new molecules lamotrigine, levetiracetam, Topiramate, Gabapentin and Pregabalin. The choice depends on the type of epilepsy, the spectrum of efficacy of antiepileptic drugs and the physiological state of the patient.

In case of pregnancy or desire to pregnancy, it is necessary to stabilize epilepsy preferably in monotherapy with the old molecule if not the minimum number of antiepileptics. Stable epilepsy under treatment is generally more reassuring. The duration of treatment does not change in pregnant women and other patients. According to current recommendations, lamotrigine and levetiracetam are the two first-line antiepileptic drugs prescribed in pregnancy [4]. The recommended dose is individual depending on the patient's clinical and biological context, usually less than 200 mg/d for lamotrigine and less than 1 g/d for levetiracetam.

All conventional antiepileptic drugs cross the placental barrier and increase the risk of birth defects. In monotherapy, the percentage of birth defects is similar for all drugs, averaging 8%:

- 9% for valproic acid;
- 8% for carbamazepine;
- 6% for phenytoin;
- 8,5% for phenobarbital.

In addition, all ancient antiepileptics phenobarbital, primidone, carbamazepine, phenytoin and valproic acid behave as folic acid antagonists [9,11]. The prescription of folic acid (5 mg/d one month before conception and 2 months after) is warranted for antiepileptics because of their enzyme inducing properties that interfere with folate metabolism. A deficiency of folic acid, which may also be due to antiepileptics, increases the risk of malformations. This is why early intake of folic acid in high doses 5 mg before pregnancy and during the first trimester is recommended. Up to 50% of pregnancies are unplanned, the decisive stage of nervous system development takes place between the 21st and 26th days of the embryo, often before the expectant mother knows that she is pregnant. Preventive folic acid supplementation is therefore recommended for all women of childbearing age as soon as epilepsy is diagnosed. Some folic acid preparation information reports warn against seizures, but this "side effect" is very rare and only concerns epileptic absences. Folic acid supplementation has no impact on intellectual function. Indeed, the comparison between children born to women with epilepsy exposed to antiepileptic drugs who received folic acid supplementation prior to conception and those born to women with epilepsy who did not receive folic acid supplementation, does not show a significant difference in IQ between the two groups [11-13].

Other antiepileptic drugs are more reassuring because the risk of malformation does not exceed 2% of pregnant women on treatment, which are Oxcarbazepine, gabapentin, zonisamide [9].

With regard to teratogenicity, combination therapy increases the risk of fetal malformations significantly, especially in combination with Sodium Valproate or Topiramate. Sodium valproate appears to have the greatest teratogenic potential in monotherapy but also in combination therapy. This teratogen risk is dose-dependent, rising from 25% beyond 1500 mg/d and reproducible in all pregnancies. Aside from teratogenic risks, the use of Sodium Valproate during pregnancy is also associated with the child's neurodevelopmental risk and autistic disorder. Other drugs appear to have teratogenic potential that discourage their use during pregnancy. By these effects, Sodium Valproate, Phenobarbital, Phenytoin, Topiramate, carbamazepine during pregnancy [14,15] are not recommended.

There are other significant risks. The risk of bleeding for the child after birth. To reduce the risk of bleeding, infants receive drops of vitamin K or injectable 50 mg from birth. This is especially important for mothers' children whose enzyme inducers are treated with enzyme inducers, which can cause vitamin K deficiency [6].

The risk of chromosomal abnormalities is no higher than in the general population. In epileptic mothers on treatment, the frequency of birth defects is 6 to 8%, or 2 to 3 times that of the general population. These birth defects develop during the first trimester of pregnancy. The most serious are the heart, the skeleton, the digestive system, the kidney and urinary tract, the nervous system. Others are less severe like cleft labiopalatin. These malformations are mainly related to the use of antiepileptic drugs that pass from the blood of the mother to the fetus and which can, under certain conditions, disrupt the division of the cells that gradually build the future baby [6,9].

Birth of an epileptic woman

A vaginal birth is possible in most cases. As with all other pregnancies, a caesarean section is only indicated if the child's position requires it and the mother expressly requests it. More rarely, it should also be considered in the event of very frequent seizures, large and repeated seizures during childbirth or seizures preventing the parturient from participating in labor. The expectant mother should definitely continue to take her antiepileptics in the delivery room [10,15].

Other support and monitoring

As with the first prescription of any antiepileptic drugs, clinical tolerance (rash, daytime drowsiness, vomiting), biological (hemogram, Transaminases) during the trimesters, therapeutic education of the patient (epilepsy, adherence treatment, lifestyle) and evaluation of therapeutic response (socio-familial behavior and crisis interval) should be evaluated. Plasma drug monitoring and EEG examination are recommended during pregnancy, especially in patients with repeat seizures. You always have to educate the patient and the family. Ensuring the stability of the crisis, the reality in the face of discrimination of epileptics, many women with epilepsy have difficulty finding a couple. Therefore, it is necessary to reassure a couple and the family about the association of pregnancy and epilepsy, as well as the possible risks. Recommend the patient on a healthy, balanced, high-calorie diet avoiding toxics (alcohol, tobacco...) and moderate sports activity [1,5,8].

Conclusion

Pregnancy in women with epilepsy is said to be "at risk" even if most of them go well. The optimal management of pregnancy for these epileptic patients is based on close interdisciplinary collaboration between neurologists gynaecologists, obstetricians, anaesthetists and pediatricians. It all starts with information from the couple, the patient and/or the family about the association of pregnancy and epilepsy. Obstetricians and paediatricians will be notified of maternal treatment to guide the reception of the newborn. Pregnancy programming is essential in the epileptic patient, it optimizes antiepileptic treatment and improves management during pregnancy.

Conflicts of Interest

The authors do not declare any conflict of interest.

Authors' Contributions

Glorien Jemissair Lemahafaka and Julien Razafimahefa: Bibliographical research, writing.

Sonia Maminirina Fenomanana: Reading and correcting the gynecology and obstetrics side.

Alain Djacoba Tehindrazanarivelo: Reading and correcting the neurology side.

All authors have read and approved the final version of the manuscript.

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