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SLEEP MEDICINE PEARLS

Conception, Pregnancy, Delivery, and Breastfeeding in a Narcoleptic Patient with Cataplexy

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A 25-year-old woman presented with a history of episodes of sleepiness while sitting quietly, watching television, talking to others, and while driving; and partial cataplexy triggered mostly by laughter, manifested as slight knee buckling and subtle arm weakness at a frequency of one event every few weeks. She underwent a diagnostic all-night polysomnogram (PSG) with a total sleep time of 480 minutes, an apnea-hypopnea index of 0, and no periodic leg movements in sleep. The next morning the patient underwent a multiple sleep latency test (MSLT) that showed an average sleep onset of 3 minutes. Two of 4 naps had sleep onset REM (SOREM) episodes. She takes modafinil 200 mg in the morning and another dose in the afternoon as needed. Given the subtle nature of her cataplexy, other medications, such as selegeline, sodium oxybate, protriptyline, and fluoxetine, were not initiated. Modafinil resulted in dramatic functional improvement, including an ability to work full time and limited need for others to drive her. On follow-up she is doing well on modafinil but is planning on becoming pregnant for the first time. She asks about treatment of her narcolepsy during conception, pregnancy, delivery, and breastfeeding.

Question: What advice do you give this patient?

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Answer: Discontinue stimulant administration during attempts at conception and for the duration of pregnancy and breastfeeding unless, after careful discussion with the patient, the risks of narcolepsy outweigh the risks of treatment. Because of the risk of labor-induced cataplexy, the patient and her obstetrician should consider elective cesarean delivery.

The potential teratogenicity of modafinil is unknown (Table 1),[1] therefore the most cautious advice would be to discontinue the medication during conception and pregnancy. General advice in initiating modafinil treatment in a woman of childbearing age is that modafinil, a concentration-related inducer of cytochrome P450 enzymes, has been shown to cause a decrease in maximum plasma concentrations of ethinyl estradiol—the estrogen component in almost all combined oral contraceptive pills (OCPs).[2] As a result, the efficacy of OCPs may be decreased with concomitant modafinil use. As always, risks and benefits have to be assessed in each patient. Our patient was married, and her husband was the breadwinner of the family. As a result, she was not now required to work outside the home for financial solvency, and she was willing to abstain from driving. If a patient is required to drive, pemoline and sodium oxybate are the only two medications with less than category C rating indicated for treatment of excessive daytime sleepiness (EDS) in narcolepsy.[1,3,4] Due to a rare, potentially lethal liver toxicity, pemoline has not been available in the United States since 2005. As a result, the 2007 American Academy of Sleep Medicine (AASM) Standards of Practice Committee no longer recommends pemoline in the treatment of narcolepsy.[3] Sodium oxybate can be used but has a complicated dosing schedule and is a controlled substance distributed through a single central pharmacy.

After delivery, the patient may decide to restart her medications after her delivery and use formula to feed the baby; however, the immunological benefits of breastfeeding for infants have been well documented. Therefore, breastfeeding is most likely of benefit for the child, and the patient may decide to stay off medication to breastfeed. Even though methylphenidate has been shown in a single patient case report not to be present in breast milk, there is not enough evidence to recommend the use of this medication in breastfeeding narcoleptic women.[5] Presence of medication in breast milk can relate to the formulation used, elimination half-life of the medication, and the timing of the dose and feeding. Because of the difficulty controlling all of these variables, it is probably safest to advise against using these medications if the patient decides to breastfeed. Also, the effects of these medications on infant development are unknown.

Regardless of the presence or absence of narcolepsy, sleep is often altered during pregnancy, with increased number of awakenings, fatigue, leg cramps, and shortness of breath.[6] Women are also more likely to go to bed earlier and nap frequently during the day to compensate for nighttime disruption of sleep. Progesterone-sensitive upper airway mucosal edema[7] and abdominal girth associated changes in respiratory mechanics can lead to sleep disordered breathing in pregnant women. Pregnant women are also at increased risk of developing restless legs syndrome, associated with low serum ferritin and folate levels.[8] All these factors can exacerbate the EDS already experienced by the pregnant patient with narcolepsy.

Currently there are two reports in the literature of pregnant narcoleptics with cataplexy undergoing cesarean delivery. Ping et al. reported a woman who attempted a vaginal delivery and experienced cataplectic attacks consisting of limb weakness and lack of verbal responsiveness for a few minutes following each

Table 1—Medical Treatments of Narcolepsy and their Effects in Pregnancy

Medication (United States commercial trade name)	Indication in narcolepsy	Pregnancy category	Presence in breast milk
Modafinil (Provigil)	EDS	Unknown	Yes
Amphetamine, methamphetamine, dextroamphetamine	EDS	C*	Yes
Methylphenidate (Ritalin)	EDS	Unknown	No, in one case report [5]
Selegiline (Eldepryl)	EDS and cataplexy	C*	Unknown
Sodium oxybate, aka GHB(Xyrem)	EDS, cataplexy, disrupted sleep	B**	Unknown
Pemoline (Cylert)	None. Removed from the United States market in 2005 due to potential lethal hepatic toxicity.	B**	Unknown
Protriptyline (Vivactil)	Cataplexy, sleep paralysis, hypnagogic/hypnopompic hallucinations	Unknown	Unknown
Fluoxetine (Prozac)	Cataplexy, sleep paralysis, hypnagogic/hypnopompic hallucinations	C*	Yes

EDS: excessive daytime sleepiness. *pregnancy class C means that animals studies have shown teratogenic or embyrocidal effects, and there are no controlled human studies. **pregnancy class B means that animal studies indicate no fetal risk, but there are no controlled human studies.

Table 2—Instructions for Narcoleptic Women During Conception, Pregnancy, and Breastfeeding, During Periods Off Medication or Major Medication Changes

- Make arrangements to have others drive you
- Take showers instead of baths to decrease risk of drowning
- No swimming for the time being
- Avoid heights or other situations where having a sleep attack or cataplectic attack could be particularly hazardous
- Take naps during the day to help reduce the likelihood of sleep attacks
- Advice regarding handling your baby:
  - Wash the baby on a mat with a bowl of water so that should you have a sleep attack or cataplectic attack the baby will come to no harm
  - Do not wash the baby in an adult or baby bath
  - Breastfeed in a lying position to reduce the risk of injury to the baby should you have a sleep attack or cataplectic attack
  - Use a wheeled baby carriage to transport the baby around the house to help reduce risk

These instructions were written by Romy Hoque, M.D. as modified from instructions given to epilepsy patients. These recommendations are available at the Sleep Disorders Center of Louisiana State University School of Medicine in Shreveport to women of childbearing age who are considering becoming pregnant and modified based on level of cataplexy and home environment.

uterine contraction. The patient had difficulty proceeding with a vaginal delivery, and a cesarean delivery was performed.[9] Williams et al. reported a woman with narcolepsy, cataplexy, and glutaric aciduria type II with increasingly frequent cataplectic attacks as she approached 37 weeks' gestation. The clinical manifestations of this patient's cataplexy were not described; the patient underwent elective cesarean delivery.[10] In narcoleptic patients with clinically significant cataplexy, given the risk of labor induced cataplexy and difficulty progressing through a vaginal delivery, elective cesarean delivery should be carefully considered by the patient in consultation with both her sleep physician and her obstetrician.

After delivery, the physical demands and sleep deprivation of child care can also exacerbate EDS in the narcoleptic. Patients may express reluctance to discontinue medications because of concern about excessive sleepiness. If excessively sleepy off of their medications, they may revert to taking naps, resuming pharmacological treatment, or both. If the mother is at home with the baby during the day, she could nap when the baby does. If she works during the day, she should try to arrange a flexible schedule with reserved blocks of time to nap during work. Of course, the ability to arrange such a schedule depends upon the nature of the patient's work, the understanding of her employer, and the willingness of a sleep physician to act as her advocate to the employer.

Reluctance to be sleepy off of medical therapy has to be weighed against potential risks to the newborn. In the end, it is the patient's choice using current pharmacological information to make an informed decision. If the patient decides against use of medication, safety advice should be provided to the patient (Table 2).

Our patient chose to withdraw modafinil, stay at home, and not drive. She also planned to withhold modafinil during breastfeeding.

CLINICAL PEARLS

1. No stimulant for the treatment of narcolepsy has been proved to be safe during pregnancy. The pregnancy safety category for modafinil and methylphenidate is undefined; amphetamine is class C, and sodium oxybate is class B.
2. The decision to continue or withhold medications for narcolepsy should be made by an informed patient, weighing the risks and benefits outlined.
3. Because of the risk of labor-induced cataplexy, a pregnant woman with narcolepsy and clinically significant cataplexy should discuss the option of elective cesarean delivery with her sleep physician and obstetrician.
4. If medication is not used during pregnancy, safety precautions during pregnancy and after delivery are indicated to enhance safety for the mother/fetus and newborn.

DISCLOSURE STATEMENT

The authors have indicated no financial conflicts of interest.

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