

# ETHICAL PERSPECTIVES IN NEUROLOGY

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The practice of neurology presents a series of ethical challenges for the clinician. These rarely have simple or straightforward solutions, but require careful consideration by the neurologist. This section of *CONTINUUM*, written by colleagues with particular interest in the area of bioethics, provides a case vignette that raises one or more ethical questions related to the subject area of this issue. The discussion that follows should help the reader understand and resolve the ethical dilemma.

**NOTE:** The following scenario is hypothetical.

A 27-year-old woman has been treated by her neurologist for the past 5 years for migraine with aura. She has experienced migraine with aura since age 15. Prior to seeing the neurologist, she had six to eight migraines per month, each lasting 12 to 48 hours with visual aura, nausea, vomiting, photophobia, and phonophobia. They were disabling, as she missed many days of school and work. Her neurologist prescribed several prophylactic therapies, which were all discontinued due to either unfavorable side effects or lack of efficacy. However, divalproex sodium extended-release 1500 mg every night has been effective. Her migraine frequency has been 2 to 3 times per month for 2 years. She has had no side effects except for a very mild tremor, which she tolerates. She uses sumatriptan 20 mg nasal spray, which aborts her headaches if she takes it at onset of the aura.

At a routine visit with her neurologist, the patient discloses that she and her husband want to start a family. Her neurologist counsels her to stop the divalproex before attempting pregnancy because of the known risk of developmental anomalies with divalproex. Once she is pregnant, he will prescribe antiemetics and low-potency narcotics for the migraines instead of sumatriptan. She agrees to this plan but returns in 2 months because her migraine frequency has increased significantly and she is missing work again. She wants to restart the divalproex because she is at risk of losing her job (and thus her medical insurance). She also discloses that she is 6 weeks pregnant and intends to carry her fetus to term. She says she is willing to accept the risks associated with the divalproex in order to reduce her migraine frequency. The neurologist feels uncomfortable with her choice because of the risk of fetal malformations, but he is also sympathetic to her plight.

Moreover, the neurologist is troubled by the following ethical quandaries:

- (1) Should he concern himself only with the well-being of his pregnant patient, or should he consider that her fetus is also his patient?
- (2) How should he counsel her about the use of a potentially teratogenic medication during pregnancy? Is it ethical for him to express his opinion that he thinks her choice is wrong?
- (3) How should he balance the benefits of the treatment to a pregnant patient against the potential risks to the fetus?

**THE ETHICAL PRINCIPLES IN THE BALANCE**

- The principle of beneficence grounds the physician's obligation to protect and promote health-related interests over harms. The principle of respect for autonomy means that physicians ought to abide by the decisions of patients, even if the physician considers the decision unwise. In making their decisions, patients may, and often do, take into account factors other than medical considerations, such as religious beliefs, socioeconomic exigencies, and perspectives on reproductive choice. Respect for patient autonomy, as operationalized through the informed-consent process, obligates physicians to present patients with the existing range of valid therapeutic options and to implement the patient's ultimate choice.

**BENEFACTENCE, AUTONOMY, AND PREGNANCY**

- Although conflicts may arise between a physician's view of beneficence and a patient's autonomous choice, the fact of a pregnancy complicates this conflict. Ethical discussions about medical decisions affecting a pregnant woman and her fetus are often entangled in the discussion about the timing of "fetal personhood" and the abortion debate. Chervenak and McCullough (1997) have written extensively on this issue and have created a paradigm for discussing ethical conflicts during pregnancy that obviates a discussion about fetal personhood and the divisive concept of a "right to life."

As is the case with infants and children, a fetus is not neurodevelopmentally advanced enough to express opinions and beliefs. Physicians therefore have no autonomy-based obligations to the fetus. However, just as physicians have an ethical obligation to consider the health-related interests of the pregnant woman, so too do they have an ethical obligation to consider the health-related interests of the fetus. These obligations are based on beneficence and nonmaleficence. In a pre-viable pregnancy being taken to viability and on to term, the fetus is a patient as a result of the pregnant woman's decision to continue her pregnancy and present herself for ongoing care. Thus a beneficence-based obligation exists to prevent risk of exposure to the fetus. When it is ethically justified to risk such exposure, the standards of informed consent apply, which include explaining the clinical judgment about the risk-benefit balancing and ensuring that the pregnant woman understands and accepts the risk to the fetus. Since a fetus deserves the same beneficence considerations as the pregnant woman, the risks and benefits to both the pregnant patient and the fetal patient must be explained. Application of this framework to neurologic therapeutic interventions during pregnancy will fall into one of the following three risk-benefit paradigms.

- (1) The therapy is clearly beneficial to the woman and poses no real danger to the fetus. In this low-risk scenario, the effect of the treatment on the fetus is irrelevant because the risk of treatment to the fetus is negligible. Thus, in the migraine case presented, using low-potency narcotics and sedating antiemetics for migraine attacks would be acceptable without ethical quandary (Fox et al, 2005; Goadsby et al, 2008; Loder, 2007; Silberstein, 2005).
- (2) The treatment is clearly beneficial to the woman but may cause harm to the fetus. Under this circumstance, the nature of the mother's illness is critical to defining the relative benefits and risks of treatment. Chemotherapy for cancer or for a rapidly progressive and potentially fatal autoimmune condition such as primary angiitis of the CNS are clear examples in which high-toxicity agents

may be required to treat the mother, although the fetus could be harmed. The United States Food and Drug Administration classifies these high-toxicity agents as Category D Pregnancy. These agents have evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (eg, if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective). A scenario familiar to most neurologists is the pregnant patient with epilepsy. Seizures are potentially harmful to both mother and fetus, and the harm of uncontrolled seizures must be weighed against the potential toxicity and teratogenicity of the medications used to control the seizures.

- (3) The treatment is clearly beneficial to the woman; the disease is not associated with high morbidity or mortality risk to the woman, but treatment may cause harm to the fetus. Migraines are usually not thought to accrue the same degree of risk of harm to the mother as seizures and are usually of little detriment to the fetus. Use of divalproex sodium during pregnancy for migraine prophylaxis, especially during neural tube development in the first trimester, would seem particularly problematic from a nonmaleficence-based perspective. However, as in the case presented, migraine can cause chronic disability, which must be taken into account in the risk-benefit analysis.

Thus, the neurologist should take into account the impact of migraine on the woman's quality of life. If she has occasional migraines that can be managed nonpharmacologically or with low-risk medications, then there is a favorable benefit-to-risk ratio and no ethical dilemma. However, if the migraines are incapacitating and put her at risk of complications such as dehydration, then the beneficence balance shifts and greater risk may be ethically accepted in order to attain benefit. Additionally, Category D medications that normally are not used during pregnancy may be considered as reasonable alternatives.

Respect for the pregnant woman's autonomy dictates that she be allowed to make informed decisions about her health care even when her physician believes that she is making a "bad" choice for herself and her fetus. The neurologist is obligated to counsel the pregnant woman about the risks to the fetus in any informed-consent discussion and document the discussion in detail in the chart. Furthermore, the neurologist should consult with the patient's obstetrician, who is more likely to have experience handling therapeutic dilemmas of this type in pregnancy.

What then is the ethically permissible course of action in this hypothetical case?

- (1) If the neurologist believes the risk of teratogenicity to the fetus from divalproex is too great, he may strongly recommend that the divalproex not be used at all, or, since the risk of neural tube defects is highest in the first trimester, that the use of divalproex be delayed until the second trimester or later. Safer alternatives to divalproex should be offered, such as opioids, simple analgesics, and sedating antiemetics (Fox et al, 2005; Goadsby et al, 2008; Loder, 2007; Silberstein, 2005).
- (2) The natural history of migraine is that its frequency diminishes significantly during the second and third trimesters (Fox et al, 2005; Goadsby et al, 2008; Loder, 2007; Silberstein, 2005). Therefore, one could suggest to the patient to defer prophylactic treatment and try to tolerate the migraines for the first trimester while hoping that they will diminish subsequently.
- (3) If prophylaxis is still warranted, then a medication with a lower teratogenicity risk, such as propranolol, should be considered (Fox et al, 2005; Loder, 2007).

There is no obligation to eliminate risk to the fetus, as lack of risk cannot be guaranteed; however, the risk to the fetus should be minimized, and the benefit to the pregnant patient should be significant. Thus, if divalproex is the only option that allows the pregnant woman to continue her pregnancy in good health, the beneficence calculus shifts considerably.

A final important consideration is the legal implications of using a high-risk medication for migraine prophylaxis during pregnancy. The informed-consent process must be explicit and well documented. The neurologist must take extra care to use language the patient can understand and should explain, for example, the nature of a neural tube defect and its implications for the child and parents alike. A good method for demonstrating understanding is the teach-back method, in which the patient is asked to explain her understanding in her own words. All reasonable options with their attendant risks and benefits must be described and charted appropriately. If the patient's medical situation is grave enough that an effective medication that carries fetal risk is warranted, and if the patient accepts the risks after a detailed, well-documented, informed-consent process, the physicians have taken appropriate risk management steps.

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## REFERENCES AND SUGGESTED READINGS

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