

HIV AND THE OBSTETRIC PATIENT: ANESETHETIC CONSIDERATIONS

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Abstract

INTRODUCTION

The acquired immunodeficiency syndrome (AIDS) was first described in the United States in 1981 (1). This first reported description in 1981 went virtually unnoticed by most physicians but was in fact the herald for what is possibly the greatest health crisis of the late twentieth and early twenty first century. Worldwide over 40 million people were living with HIV/AIDS by the end of 2003 (2,3). Women now represent fifty percent of all adults living with HIV/AIDS worldwide, and this population has been steadily increasing over time (4). In the United States women have also represented and increasing proportion of AIDS cases, accounting for 26% of adult cases in 2001 (5).

With the increasing numbers of HIV- infected women, 80% of whom are of childbearing age, pregnancy in the setting of HIV infection has been a focus of much interest, research and often discrimination. With these facts in mind, it must be recognized that many anesthesiologists are now seeing these patients in their practice, or will be, and must address the questions these patients present with confidence. In order to do this the anesthesiologist must be familiar with both the obstetric and anesthetic management of this unique subset of parturients. This review will attempt to better acquaint the anesthesiologist with the effects of this disease and the drugs used in its' treatment on the mother and the developing fetus. Treatment options available to the anesthesiologist will be reviewed with a focus on neuro-axial techniques.

HIV INFECTION

HIV-1 is a retrovirus and a single stranded RNA virus. After it enters the cell the virus is copied by a reverse transcriptase, which enables the virus to produce double stranded DNA, this double stranded DNA is then integrated into the host's cells. The HIV-2 virus is a similar virus that

also produces the AIDS syndrome. HIV-2 is common in western Africa but is rarely seen in the U.S. The most common mode of infection is sexual transmission through the genital mucosa (17). The virus can be detected in the internal lymph nodes within 2 days, and within 5 days can be cultured from the plasma. At this point there is a rapid rise in plasma viremia that spreads to the lymphoid organs and the brain (18). Early in the course of the disease the CD4 T lymphocytes are infected, the decline in the CD4 cell count marks HIV progression. The plasma viral load is initially extremely high, and then declines in the clinical latency period. As the patient begins to experience constitutional symptoms and opportunistic infections occur viral load again increases.

Acute HIV infection is a transient, symptomatic illness with symptoms often including fever, fatigue, rash, headache, lymphadenopathy, pharyngitis, myalgia, nausea, vomiting and diarrhea. In two studies 87% of newly infected patients had symptoms and 95% sought medical attention (18,19). The virus may remain seemingly dormant for 10 years, however ultimately a rising viral count, extreme compromise of the immune system and a CD4 count of fewer than 200/mm³ heralds the final stages of the disease.

IDENTIFYING THE PREGNANT PATIENT WITH HIV/AIDS

The identification of the pregnant patient with HIV/AIDS should be of significant importance to the anesthesiologist (6). However somewhat shockingly it has been reported that only 20% of physicians inquire about substance abuse, and presumably an even smaller percentage inquire about the possibility of HIV infection (7). Testing of women before or during pregnancy is typically conducted according to the standard protocol for detection of antibody to HIV (8). The recommended HIV testing algorithm consists of an initial

screening with an FDA-licensed enzyme immunoassay (EIA) followed by confirmatory testing of repeatedly reactive EIAs with an FDA-licensed supplemental test (Western Blot). An HIV test should only be considered positive after screening and confirmatory tests are reactive.

Incorrect HIV test results occur primarily because of specimen-handling errors, laboratory errors, or failure to follow the recommended testing algorithm (9). Unfortunately, patients may report incorrect test results because they misunderstood previous test results (10). Though these occurrences are rare, further testing of pregnant women will result in additional indeterminate, false-positive, and incorrect results as nonspecific reactions producing indeterminate results have occurred more frequently among pregnant or parous women than among other persons (11). In these situations it will be especially important for the physician to consider not only additional testing, but also the woman's clinical condition.

For some women the labor and delivery setting is the first opportunity for HIV testing. Although results of conventional EIAs and Western Blots are typically not available for 1-2 weeks, rapid tests for detecting antibody to HIV can produce results in 10-68 minutes (12). This test can provide definitive negative and preliminary positive results at the time of testing and identify women who might need antiretroviral treatment and whose infants might benefit from chemoprophylaxis. The predictive value of a reactive rapid test is higher among persons with risk for HIV infection, especially in areas with high HIV prevalence (13).

A diagnosis of HIV infection in pregnancy frequently raises questions about the safety of regional anesthesia and analgesia in these patients. The origin of this controversy stems from the idea that induction of a spinal needle was likely to increase the patient's risk for the development of neurological sequelae of this disease (14). However, it has now been well established that HIV infection does not contraindicate the administration of neuroaxial anesthesia (15). HIV is a neurotropic virus, and the central nervous system is infected early in the course of the disease process (15,16).

CLINICAL MANIFESTATIONS

HIV disease is an extremely complex medical disorder with extensive systemic effects resulting in multi-organ disease (See Table 1). Staging systems for HIV disease facilitate clinical evaluation, therapeutic intervention, level of infirmity and gives prognostic information. In industrialized

countries the most widely used system for classifying HIV infection and AIDS was published by the United States Centers for Disease Control and Prevention in 1992 (20). Based on this system each stage of illness is based on two types of information: peripheral blood CD4 counts and clinical manifestations. CD4 cell counts are placed in three strata, ranging from relatively normal ($>500/\text{mm}^3$) to severe CD4 depletion ($<200/\text{mm}^3$). The clinical manifestations of HIV are also placed in three strata, generally in accordance with the level of immunologic dysfunction. Category A includes those who have minimal clinical findings, clinical findings that do not indicate immune injury, generalized lymphadenopathy, or resolved acute HIV infection. Category B includes conditions that indicate the presence of a defect in cell mediated immunity or conditions that appear to be worsened by HIV infection. Category C includes conditions that are considered AIDS defining, even in the absence of a CD4 cell count of $<200/\text{mm}^3$ (20).

The neurological, pulmonary, cardiovascular, and hematological changes and abnormalities associated with this disease should be of particular concern to the anesthesiologist.

The initial neurological involvement begins within days of the initial infection (18). Conditions reported with acute infection include: myelopathy, peripheral neuropathy, brachial neuritis, cauda equine syndrome, and Guillain-Barre syndrome (21). Anesthesia using neuraxial techniques in patients with preexisting central nervous system disorders has traditionally been met with some apprehension. The view in this regard has been that spinal anesthesia can lead to exacerbation of neurologic symptoms and should be avoided, while the use of intrathecal narcotics and epidural anesthesia are generally less likely to lead to exacerbations. However, it has been demonstrated that the risks commonly associated with neuraxial anesthesia in patients with preexisting central nervous system disorders may not be as frequent as were once thought (43). Hebl et al, performed a retrospective review of all patients at the Mayo Clinic from the period of 1988 to 2000 with a history of a CNS disorder who subsequently received a neuraxial anesthetic including parturients with MS, their review revealed that there were no new or worsening in preexisting neurologic deficits in the postoperative period (43). With this in mind it would seem that neuro-axial techniques in this patient population is safe, especially given the heightened risk associated with parturients and general anesthesia.

The later stages of the disease leads to severe immunologic

compromise and a variety of infectious or opportunistic infections. Cryptococcal infection is a unique but common source of meningitis, however tuberculosis and syphilitic meningitis are also a possibility (22).

Pulmonary complications associated with HIV disease are largely related to infectious agents. Those organisms most frequently indicated as leading to pulmonary complications include *Pneumocystis carinii*, tuberculosis, and aspergillosis (23).

Cardiovascular involvement is multi-factorial and includes chronic viral infection, co-infection, drug therapy and immunosuppression all of which work to affect the heart (24,25). Further AIDS is an increasingly recognized cause of, or strongly linked to cardiomyopathy, pulmonary hypertension, right ventricular dysfunction, myocarditis, pericardial effusion, and coronary artery disease (26).

Hematologic abnormalities occur with acute HIV infection and are in fact a hallmark of the disease. This is seen with the development of HIV -thrombocytopenia as the disease progresses secondary to a number of causes, including retroviral infection of megakaryocytes, or drug induced thrombocytopenia. (27). Patients are also subject to anemia of chronic disease and leukopenia (27).

Figure 1

Clinical Manifestations of AIDS/HIV

Nervous System

- Aseptic meningitis
- Myelopathy
- HIV Encephalopathy
- Dementia complex
- Peripheral neuropathy
- Autonomic neuropathy

Pulmonary System

- Opportunistic Infections
 - Pneumocystis carinii*, *mycobacterium tuberculosis*, *mycobacterium avium*

Cardiovascular System

- Pericardial effusion
- Myocarditis
- Dilated cardiomyopathy
- Endocarditis
- Pulmonary hypertension
- Myocardial infarction

Gastrointestinal System

- Oropharyngeal candidiasis
- Aphthous ulcers
- Leukoplakia
- Esophagitis
- Diarrhea

Renal System

- Focal and segmental glomerulosclerosis

Hematological System

- Thrombocytopenia
- Neutropenia
- Normocytic normochromic anemia
- Coagulation abnormalities

Endocrine System

- Adrenal insufficiency
- Hypothyroidism
- SIADH

Immunological

- Decreased immune function

DRUG THERAPY

The specific combination of antiretroviral therapy for a given patient takes many factors into account. These include, but are not limited to the specific side effects, dosing schedules, drug-drug interactions, and history of antiretroviral therapy. The drugs in use currently fall into four categories: nucleoside analogue reverse transcription inhibitors (NRTIs), non-nucleoside reverse transcription inhibitors (NNRTIs), protease inhibitors (PIs), and fusion inhibitors.

Although there are special considerations when using

antiretroviral drugs during pregnancy, the basic principle is that therapies of known or possible benefit to the woman should not be withheld during pregnancy unless there are known adverse effects for mother, fetus, or infant that outweigh the potential benefits (28).

The number of side effects seen with the antiretroviral drugs are numerous, and drug interactions significant (Table 2). Of special note are the protease inhibitors which have proven quite effective as a part of the treatment regime for HIV. They also have a wide range of side effects. The most important of which for the purpose of our discussion being, the inhibition of cytochrome P450 enzymes, with the greatest effect on drugs metabolized by the CYP3A4 enzyme (29). It has been demonstrated that ritonavir, one of the protease inhibitors, significantly inhibits the metabolism of fentanyl among volunteers receiving a brief course of ritonavir (30). The results of this study suggested a strong interaction between ritonavir and fentanyl metabolism seemingly indicating the need to modify the dosing of fentanyl in these patients.

Figure 2

Common Antiretroviral Agents and Their Side Effects

Nucleoside analogue reverse transcription inhibitors

Zidovudine (AZT/ZDV)	Oral/IV	Neutropenia, GI upset, Headache
Didanosine (DDI)	Oral	Peripheral Neuropathy, Pancreatitis
Zalcitabine (DDC)	Oral	Peripheral Neuropathy, Pancreatitis
Stavudine (D4T)	Oral	Peripheral Neuropathy
Lamivudine (3TC)	Oral	Anemia, GI Upset
Abacavir	Oral	GI Upset

Non-nucleoside reverse transcription inhibitors

Nevirapine	Oral	Rash, Hepatitis
Delavirdine	Oral	Rash
Efavirenz	Oral	Dizziness, Rash, Dysphoria

Protease Inhibitors

Saquinavir	Oral	Diarrhea, Hyperlipidemia
Indinavir	Oral	Nephrolithiasis, Hyperlipidemia
Ritonavir	Oral	GI upset, Circumoral numbness
Nelfinavir	Oral	Diarrhea, Hyperlipidemia

ANESTHETIC MANAGEMENT

When faced with the anesthetic management of a patient with HIV or AIDS the first step is to carefully review the status of the patient's disease and current treatment course. With this in mind it is essential that the patient's treatment begin with a careful history and physical. This should include a review of the patient's current medications, along with basic laboratory evaluations including a CD4 count. Important to note is that many patients with high CD4 counts ($> 500\text{--}700/\text{mm}^3$) are less likely to present unusual concerns as they are generally not treated with antiretrovirals and are less likely to present with opportunistic infections as those with more advanced disease. Contrastingly, in those with more advanced disease (CD4 count $<200/\text{mm}^3$) a more extensive laboratory evaluation is warranted. Helpful labs in

this group include, but are not limited to: blood count, clotting functions, liver panel, renal panel, viral load, ECG, chest radiograph, and echocardiography.

Importantly, despite theoretical concerns over the possibility of immune suppression with general anesthesia, there has not been any clear link to adverse outcomes (31,32). When considering a general anesthetic in this population the presence of underlying pulmonary or cardiac disease is more likely to be of significance.

The idea of regional anesthesia in the HIV patient has been a more controversial area (33). The early apprehension around regional anesthesia in this patient population focused on whether performing spinal or epidural anesthesia in this patient population would hasten the involvement of the CNS. It has however long been established that the CNS is involved in the progression of the disease in its earliest phases (33). This previous apprehension would be seemingly unfounded, as the failure to culture HIV from the CNS was more likely secondary to sampling error than to lack of a viral presence (34). The use of regional anesthesia has now been clearly demonstrated to be without the potential for unique adverse sequelae in this patient population (35).

Furthermore there is no clear evidence to suggest that there are any unique risks associated with an epidural blood patch in an HIV patient (36). However there exists a long list of potential complication arising from the failure to treat a post dural puncture headache (37).

The mode of delivery in the HIV patient is also of significance.

Especially in the patient with more advanced disease and higher viral load. It must be remembered that in our role as the anesthesiologist caring for the mother, we are also charged with protecting the fetus and preventing vertical transmission of the disease to the infant. It has been clearly demonstrated that cesarean section performed before the onset of labor and/or membrane rupture has been associated with clear decreases in mother to infant transmission ranging from 55-80% in the absence of antiretroviral prophylaxis and with ZDV alone (38,39). When making decisions about the mode of delivery it must also be remembered that the risk of maternal morbidity and mortality are increased with cesarean section over vaginal delivery (40). However, complication rates in most studies of HIV infected women were generally within the range reported among HIV uninfected women and were not of sufficient frequency to

outweigh the potential benefit in selected cases where scheduled cesarean section may further decrease the risk of vertical transmission (41). With this in mind the American College of Obstetricians and Gynecologists has stated that HIV infected women should be offered a scheduled cesarean delivery to further reduce the risk of vertical transmission beyond that of drug prophylaxis alone (42).

SUMMARY

The HIV/AIDS epidemic is on the verge of its third decade since originally being reported in 1981, and is one of the most devastating to have touched mankind. Though ongoing research continues to make strides towards improving the quality of life for these patients there is still no cure in sight. With this in mind we as anesthesiologists must be prepared to deal with this disease and the wide and often times complex problems it presents in order to provide our patient population with the quality of medical care which they deserve.

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