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REVIEW ARTICLE

AIDS:THREATS-CHALLENGES AND CONSIDERATIONS IN ANAESTHESIA-WHAT FUTURE BEHOLDS

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ABSTRACT

Acquired immunodeficiency syndrome (AIDS) has become a pandemic with ever looming danger of its transmission in health professionals. As such anesthesiologists and intensivists are exposed to potential risk of disease transmission on a daily basis. A continuous need is felt in this arena to prevent the catastrophic consequences of AIDS in our medical fraternity while treating such patients in operation theatres and critical care units Prioritization of safety measures should be mandatory for any health care provider. It requires a lot of attitudinal and behavioural modification and bridging of gaps in current preventive and precautionary measures, support from hospital authorities and an active role of governmental or regulating agencies to fill these gaps with appropriate global evidences is desirable and the need of the hour.

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INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) has become a pandemic with ever looming danger of its transmission in health professionals. The number of AIDS patients has increased tremendously over the last two decades, who present for surgical procedures as well as who get admitted in intensive care unit for their critical condition. As such anesthesiologists and intensivists are exposed to potential risk of disease transmission on a daily basis[1]. The guidelines and protocols formulated in the western world regarding prevention of disease transmission cannot be applied uniformly in the developing nations, such as India due to various factors and limitations. Hence a continuous need felt in this arena to prevent the catastrophic consequences of AIDS in our medical fraternity while treating such patients in operation theatres and critical care units

Epidemiology of hiv –Burden of the disease

Over the last decade we have seen tremendousadvancements in understanding and management of disease and the number of AIDS.17 million people were accessing antiretroviral therapy, 36.7 million [34.0 million–39.8 million] people globally were living with HIV, 2.1 million [1.8 million–2.4 million] people became newly infected with HIV,78 million [69.5 million–87.6 million] people have become infected with HIV since the start of the epidemic[10]. Related deaths are on a decline resulting in larger lifespans of HIV infected patients. Approximately 25% of them will require surgery during the time of their illness

The culprit virus

HIV is a spherical enveloped virus Retrovirus, (lentivirus)with ssRNA , 90-120nm in diameter with Icosahedral symmetry The virus is covered by a lipid bilayer that contains the envelope proteins gp120 and gp41,outer shell nucleocapsid (p17), Core of nucleocapsid (p24) and Polymerase antigen p31 p51 p66. Diploid RNA with several copies of reverse transcriptase, protease, integrase are also present.

Pathophysiology HIV VIRUS shows marked tropism for CD4+ helper T cells, due to the CD4 molecule's high affinity receptor for the viral gp120 glycoprotein[2]. After insertion into the host cell's genome, HIV viral mRNA is transcribed using the host's own RNA polymerase. This viral mRNA is then translated into many large polyproteins, which are further cleaved by a combination of viral and host cell proteases. These polyproteins are packaged into *immature virions* in the cytoplasm of the cell along with viral protease. These

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immature virions bud from the cell's membrane forming the mature HIV particle.

Modes of HIV/AIDS Transmission Sexual transmission (60-70%), Mother to child transmission (20-30%), Contaminated blood, blood productsand organ donations (2-5%), Contaminated needles (2-3%). Several high risk groups identified are: Promiscuous hetero and homosexuals, patients with other STDs, IV drug users, hemophiliacs ,patients from endemic areas.

Course of HIV infection: During the initial infection with HIV, the plasma viral load is extremely high. This initial period is referred to as the *acute stage*, and usually begins 2 to 4 weeks after infection. The cell-mediated arm of the immune system helps control the infection, and thus the viral load declines. This period of decreased HIV viral load is known as the *latency period*, and the patient is asymptomatic during this time. The *late stage* of HIV infection is known *as acquired immunodeficiency syndrome (AIDS)*, and has an average course of about 10 years. Due to the high viral loads, patients in the acute stage and late stage are the most infectious.

Diagnosis is based on detection of anti HIV Ig G antibodies by ELISA or the western blot test. In acute phase of seroconversion (2-12 weeks) the tests may be negative but these patients are infective. This is called the window period when HIV RNA test and p 24 antigen assays are helpful. Due to high viral loads, patients in the acute stages and the late stage are the most infectious.

Clinical presentation HIV is an extremely complex disease with multiorgan manifestations[6]

	Stage	Associated symptoms
1.	Asymptomatic	No symptoms Persistent generalised lymphadenopathy
2.	Mild Symptoms	Moderate weight loss (<10% body weight) Recurrent upper respiratory tract infections Viral or fungal skin infection Oral or skin lesion
3.	Advanced Symptoms	Severe weight loss (>10% body weight) Chronic diarrhea Persistent fever Oral lesions or candidiasis Pulmonary tuberculosis Severe bacterial infections Anemia, neutropenia, thrombocytopenia
4.	Severe symptoms AIDS	Wasting Syndrome (wt loss >10% body wt with wasting or body mass index< 18.5) Chronic Diarrhoea Persistent fever Encephalopathy, nephropathy, cardiomyopathy Recurrent bacterial infections Opportunistic Infections Malignancy

(Update in Anaesthesia: Samantha Wilson)

Treatment of HIV: Nutritious Diet, Psychological Counselling, Avoidance of smoking and alcohol, Anti Retroviral DrugsandTreatment of Opportunist Infections

Antiretroviral therapy

What is ARV? The use of a combination ARVs or highly active antiretroviral therapy (HAART) has been a major advance in the treatment of HIV infection. These drugs are classified into four classes according to the mechanisms of inhibition of viralreplication: reverse transcriptase enzyme inhibitors, protease enzyme inhibitors, integrase inhibitors and entry inhibitors. Adherence to antiretroviral therapy is of paramount importance, with adherence levels of below 95% being associated with increases in viral load and drug resistance. This naturally has implications for interruption of ARV therapy due to perioperative fasting. Fasting times should be kept to an absolute minimum.

HAART (Highly Active Antiretroviral Therapy) typical therapeutic regime is NRTI (nucleoside reverse transcriptase inhibitors)+PI(protease inhibitors)/NNRTI(non nucleoside reverse transcriptase inhibitors).

Aim of HAARTis to achieve an undetectable viral load and to improve quality and duration of life

Initiation of ARV – Treatment should begin if

Patient indications	Treatment options
History of AIDS defining illness or severe symptoms of HIV infection regardless of CD4+ T cell count	Initiate Treatment
CD4+ T cell count of 201-350 cells/mm3	Offer treatment to patient
CD4+ T cell count >350 cells/mm3 and plasma HIV RNA >100,000 copies/ml	Clinician's discretion
CD4+ T cell count >350 cells/mm3 and plasma HIV RNA <100,000copies/ml	Defer therapy

Current perioperative management of the patient with HIV[4]

ADVERSE EFFECTS Many side effects associated with ARVs should be looked for during pre-operative assessment.

- *Mitochondrial dysfunction*: lactic acidosis, hepatic toxicity, pancreatitis, peripheral neuropathy, myopathy, lipodystrophy (most commonly seen with NRTI)
- *Metabolic abnormalities*: fat maldistribution and change in body habitus, dyslipidaemia, hyperglycaemia and insulin resistance, bone disorders e.g. osteopaenia, osteoporosis and osteonecrosis
- *Bone marrow suppression*: anaemia, neutropenia and thrombocytopenia
- *Allergic reactions*: skin rashes and hypersensitivity responses.

Anaesthetic considerations A multisystem and multidisciplinary approach is recommended when faced with anaesthetic management plan of a HIV patient or AIDS. The first step is to carefully review the status of patient's disease and the current treatment course[3].

Preoperative evaluation of the patient should include

- History and risk factors, Physical examination, Laboratory tests, Assess organ involvement
- Accurate CD4+ T cell count → <200cells/mm3 – less viral load, less patients on ARV → >500-700/mm3– more viral load, more patients on ARV
- Drug History – Side Effects,interactions, Substance Abuse

Investigations

1. Routine laboratory evaluation like CBC, platelet count, clotting function evaluation, electrolytes, blood

grouping and tests for renal and hepatic function should be done.
2. Electrocardiogram, Echo heart, PFTs and ABG.
3. X-Ray chest and CT chest if warranted.MRI spine or brain if demyelination is suspected.

Multisystem involvement-To enable a thorough preoperative assessment it is important to be aware which organ systems can be involved in the HIV infected patient both as a direct consequence of chronic infection, due to opportunist infection or as a side effect ofARV drugs[7].

1. Cardiovascularsystem may be involved in a no of ways with most common –

- Dilated cardiomyopathy (DCM) (30-40%), Pericardial effusions, Endocarditis and valvular lesions especially in drug abusers
- Acute coronary syndrome, CAD
- Vasculitis, myocarditis- ranges in severity from asymptomatic to CHF, Pulmonary hypertension. [PHTN]

2. Respiratory system Both the upper and lower airway can be involved in HIV

Airway- Examine airway for HIV oropharyngeal involvement, Oral lesions can make airway challenging. These lesions can cause pain, abscess or edema that may make for a difficult airway/regurgitation/aspiration & obstruct the view of vocal cords. Painful oral lesions may lead to malnutrition and hypoalbuminemia as patient may refuse to eat.Candida (OPC), Kaposi's Sarcoma (OKS), Oral hairy leukoplakia (OHL), Recurrent apthous ulceration (RAU), HSV, VZV, HPV (warts)

Lungs-Subtle or overt lung pathology may need increased FiO2 intraoperatively. Routine placement of filters provide adequate protection against cross infection.These infections have the potential for impairing oxygenation. Care must be taken when placing tracheal tubes, to avoid risk of introducing an opportunistic infection. AIDS patients may be transported with masks if the mask were to decrease the likelihood of contracting an opportunistic infection. Disposable anesthetic delivery circuits with bacterial filters should be considered.Use of masks during transport and disposable anesthetic circuits have been used in institutions.

3.Gastrointestinal system Difficulty or pain on swallowing, Increased gastric emptying times Bleeding tendency on airway instrumentation/nasogastric tubeinsertion, Diarrhoea& dehydration, Hepatobiliary impairment, Pancreatitis.

4.Renal system Acute and chronic renal disease can be associated with HIV and thecauses of renal impairment can be multifactorial: These potential complications necessitate the avoidance ofnephrotoxic drugs, dose adjustment of renally excreted drugs. Need for adequate hydration to prevent further deterioration ofrenal function

5.Neurological system HIV can involve the neurological system by direct infection, inflammation, demyelination or a degenerative process. It can also be secondary to opportunistic infections, neoplasms or immunedeficiency. Full neurological examination pre-operatively with appropriatedocumentation is essential especially if regional anaesthesia is being considered.

6.Hematological system The following are commonly seen during HIV infection: Anaemia/pancytopenia (due to bone marrow suppression)/Neutropenia/Thrombocytopenia Persistent generalised lymphadenopathy, Haematological malignancies & Coagulation abnormalities. (increased chance of embolic episodes)

7.Endocrine & Metabolic system Common side effects of ARVs include:

- Lipodystrophy (truncal obesity, buffalo hump, peripheralwasting), hyperglycemia, hyperlipidemia/ dyslipidemia, CADs.
- Metabolic syndrome (raised plasma triglycerides, cholesterol, glucose)
- Disorders of the hypothalamic–pituitary–adrenal axis (HPA) includingCushing's syndrome and Addison's disease
- Hyponatraemia due to syndrome of inappropriate antidiuretic hormone or adrenal failure
- Hypo-or abuse disorders are more prevalent in HIV, Lactic acidosis

8.Active alcohol and substance abuse

Alcohol and substance is hence important to obtain a detailed history of substance use and screen them by urine toxicology. For elective surgery an appropriate period of abstinence with the use of substitutes such as methadone, BZD.

9.Drug allergies HIV infection is associated with higher incidence of medication allergies so a meticulous historytaking is a must.

Summary of perioperative considerations

- Surgery should not be withheld on the basis of HIV status alone. Neither CD4 cell count nor HIV viral load should be used as sole determinants of a given patient's surgical risk. Strict asepsis to be exercised as HIV patients are susceptible toinfections due to immunosuppression. Perioperative continuation of ART is recommended due to increasing problems of drug resistance in HIV treatment.Some ARVs are available in liquid form (Zidovudine, Enfuvirtide) enabling administration via feeding tube or gastrostomy. Consider drug interactions of ARV[3].
- ASA class is more important than HIV status in possibility of administering perioperative critical care to the patient. Anaesthetic plan should be tailored to individual patient and type of surgery. Proper posture is important as they suffer from neuropathy/myelopathy/ coagulopathy.

Postoperative period

Criterion for management of patients with communicable disease is followed in PACU. Nurses incharge of taking care of these patients should not concurrently take care of other patients in the hospital.

Strict monitoring is needed as there is increased incidence of wound dehiscence, wound infection, SIADH should be kept in mind in postoperative period.

Regional anaesthesia vs General anaesthesia

The type of anesthesia used in HIV patients is debatable.

The presence of HIV is not an absolute contraindication to regional anaesthesia and there is no evidence that HIV progression is increased by CNB.Concerns of regional anaesthesia are centered on the safety of spinal and epidural procedures with fear of extension of HIV infection in CNS. Hughes *et al* have furthermore demonstrated the safety and efficacy of regional anaesthesia.

Advantages of Regional Anaesthesia

- The stress of surgery and anaesthesia decrease CMI with less pronounced effects with regional anesthesia.
- Requirement of parental opioid is decreased and thus the untoward drug interactions can be skipped.
- No difference in hemodynamics, HIV viral load, blood loss and postoperative complications was found.

Contraindications posed by HIV that decrease appeal of Regional Anaesthesia are:

- Myopathy (secondary to ARV),Neoplasm (vertebral or spinal), CNS infection,Coagulopathy
- Sepsis, Bloody tap (fear of seeding HIV to CNS)

It is essential to thus conduct a full preoperative neurological assessment and to document any neurological deficits.It is safe to use epidural blood patch (EBP) to treat post dural puncture headache (PDPH.Prolonged epidural catheterisation may be contraindicated in severely compromised patients.

General anesthesia is safe??

Despite theoretical concerns, general anesthesia is not associated with any significant undesirable outcomes.Some transient immunological changes are noted but are clinically insignificant

Pharmacodynamic interactions can be managed by avoidinganaesthetic agents such as halothane or methoxyflurane that cause hepatic or renal dysfunction. Propofol and NRTIs may bothpotentially promote mitochondrial toxicity and lactic acidosis and itmay be wise to avoid propofol infusions in patients receiving ARVs.

Pharmacokinetic interactions are more complicated and are primarilydue to liver enzyme induction or inhibition, particularly the CYP4503A4 enzyme[4]. Protease inhibitors (PIs) and NNRTIs are the mostcommonly implicated group of ARVs in drug interactions.

- Opioids. The effects of fentanyl may be enhanced by ritonavirdue to liver enzymeinhibition and this enzyme inhibition reduces fentanyl clearance.
- Benzodiazepines. Saquinavirmay inhibit midazolam metabolism.
- Calcium channel blockers may have enhanced hypotensive effectsdue to enzyme inhibition.
- Local anaesthetics such as lignocainemay have increased plasmalevels due to enzyme inhibition.
- Neuromuscular blockereffects may be prolonged, even a singledose of vecuronium for instance.
- Atracurium, Etomidate, Remifentanyl, Desfluraneare preffered as independent of cytochrome P450 metabolism.
- Succinylcholine should be used with caution in renal dysfunction and myopathies.
- CMV adrenalitis may affect haemodynamics and patients need intraoperative steroids.

Infection control: **Universal Precautions**

APPLY to: blood andbody fluids (blood, semen, vaginal secretions, tissues, CSF, pleural, pericardial, peritonealand amniotic fluids) DO NOT apply to -: faeces / urine, Sputum/ vomitus, Sweat, Tearsunless they contain blood[9].

1. **Washing Hands** - One of the most important requirements and the one that is most commonly ignored is washing hands, before and after seeing a patient
2. **Wearing Gloves** - A pair of disposable plastic gloves have to be worn whenever the potential for a contact with the patient's body fluid exists. At surgery, where there is a risk of injury from sharp objects, double gloving with good quality latex gloves is recommendedexpensive.
3. **Eye Glasses/Cap/Mask** - The eyes are to be protected from split secretions by wearing goggles
4. **Foot Wear** - The feet are notorious for little cuts and abrasions that may be contaminated by body fluids.
5. **Impervious Gown** - While disposable impervious gowns are available, the cost may not be justifiable
6. **Needles and Sharps** - Manipulation of needles like bending and re-sheathing should be avoided. The used needles are to be deposited in thick walled puncture resistant containers for later incineration
7. **Surgical technique** - Risk from needle prick injuries are greatest when working in depths like pelvis, thediaphragmatic hiatus or the chest.
8. **Soiled linen** - Soaking soiled linen for 30 minutes in1:100 bleach solution (hypochlorite solution) kills theHIV virus completely. These can then be processednormally with washing and autoclaving as usual.
9. **Metal Instruments** - Metal instruments are washedwith soap and water. They are then soaked in 2%Glutaraldehyde solution for 30 minutes to kill thevirus. The sharp instruments are transferred to anothercontainer with fresh glutaraldehyde and soaked for afurther six hours. The other instruments are autoclaved.
10. **Plastic tubings** - The anaesthetic tubings, tubings usedfor suction and those used in rotary pumps are all soaked in 2% Glutaraldehyde for six hours after cleaning with soap and water or ethylene oxide sterilization.

HIV and Pain: Drugs which have been used with variable success are: Acetaminophen, Codeine, Morphine, topical capsaicin, viscous xylocaine, Amitryptiline, Carbamazepine. Mexiletine, Prednisolone. Pain is common in advanced HIV disease and can be very difficult to treat. The etiology of this pain can be multifactorial, including opportunistic infections such as herpes simplex, HIV related arthralgia, peripheral neuropathy and drug related pain.

HIV and critical care: Acute respiratory failure is the commonest cause of ICU admissions in HIV patients. Pneumocystis is the responsible pathogen in 25-50% cases. Pneumatocoele and pneumothorax may manifest. Non invasive ventilation techniques may be associated with less incidence of pneumothorax.

Blood transfusion: There is evidence that allogeneic blood transfusion in the HIV infected patient can lead to transfusion-related immunomodulation (TRIM) and can result in an increase in HIV viral load. Blood should therefore only be transfused where unavoidable to maintain patient safety.

The child with HIV: More than 80% of HIV-infections in children are due to transplacentalexposure to maternal HIV during the perinatal period. 13% of HIVinfectedchildren are exposed during blood transfusions and 5% from blood products for treatment of coagulation disorders

Obstetrics and HIV: 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

Post Exposure Prophylaxis (PEP) Evaluation should start within hours of exposure, Assess the nature of injury, patient's uremic status (HIV+, -, unknown), The side effects of PEP medications should be weighed against the likely risk of exposure. Immediately following an exposure[4]:

- Injuries should be washed with soap and water, Eyes should be irrigated with clean water
- Baseline testing for HIV, HBsAg & HCV
- Date and Time, Detail of procedure,Type of body fluid and amount
- Determine the nature of inoculum (percutaneous or mucosal splash, large/ small blood volume, hollow/closed needle injury.

Prompt reporting is essential because in some cases, HIV PEP should be started as soon as possible (preferably within 2 hrs) with a maximum of 4 weeks, Post exposure counselling done by experts and patient's permission to treat to be obtained. The HIV antibody test should be carried out if exposure is <2 hours and test should be repeated at 6-12 weeks and thereafter at 6 months as source patient can be in the window period.

Basic 2 drug regime = Zidovudine (600mg/day) + Lamivudine (150 mg BD)

Expanded 3 drug regime = Basic 2 drug regime + one of the following; Indinavir (800mg TDS on empty stomach), Nelfinavir (750mg TDS with meals), Efavirenz (600mg OD at bedtime), Abacavir (300 mg BD)

 # Nevirapine should never be used for PEP as the risk of fatal hepatotoxicity outweighs the risk of HIV infection.

FOLLOW UP: 6weeks, 12weeks, 6monthsIf source is tested HIV negative PEP should be discontinued.

HIV Vaccine

The International AIDS Vaccine Initiative (IAVI) has partnered with the ministry of health and family welfare in India through the National AIDS Control Organisation (NACO) and the Indian Council ofMedical Research (ICMR) since 2002 to implement the AIDS vaccine research and development programme[11].

Conclusion

The number of HIV infection are increasing across the globe although modern medical care and current therapies prolong the life of patients, the disease itself has no cure. It thus becomes necessary to review the current treatment modalities and pharmacological strategies evolving with the disease process. Prioritization of safety measures should be mandatory for nay health care provider[12]. It requires a lot of attitudinal and behavioural modification and bridging of gaps in current preventive and precautionary measures, support from hospital authorities and an active role of governmental or regulating agencies to fill these gaps with appropriate global evidences is desirable and the need of the hour.

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