PROLONGED MUSCLE WEAKNESS FOLLOWING GENERAL ANESTHESIA IN A PARTURIENT ON COMBINED ANTIRETROVIRAL THERAPY

- A case Report -

JOTISH MATHEW*, MADAN MOHAN MADDALI** AND JUTTA FAHR***

Abstract

We report a case of an otherwise healthy; ambulatory 32 year old parturient on combined antiretroviral therapy that developed prolonged muscle weakness needing postoperative artificial ventilation. Despite no preoperative indication of muscle weakness, she developed respiratory insufficiency following general anesthesia with drugs that are deemed safe for her condition. After ruling out all the likely causes for her respiratory insufficiency that needed 12 hrs of artificial ventilation, we address the issue of undiagnosed preoperative muscle weakness as a likely cause for her problem. The role of a preoperative neurological evaluation to caution the anesthesiologist of the likelihood of a possible need for prolonged artificial ventilation following general anesthesia in this subgroup of patients, emphasized.

Key words: Anesthesia; Cesarean section, HIV infection; Complications.

From Department of Anesthesia, Royal Hospital, Muscat, Sultanate Oman.
* MD, Specialist in Anesthesia.
** MD, Senior Consultant in Anesthesia.
*** AFA, Senior Consultant in Anesthesia.
Correspondence: Dr. Madan Mohan Maddali, Senior Consultant in Anesthesia, Royal Hospital, P.B. No: 1331, P.C: 111, Seeb, Muscat, Oman. E-mail: madan@omantel.net.com. Tele/Fax: 00 968 24590192.

Introduction

Overt or concealed muscle weakness may be present in Human Immunodeficiency Virus [HIV] infected patients who are on antiretroviral therapy. This may have profound implications if the patient has to undergo general anesthesia with muscle relaxants.

We report a rare case of an HIV infected parturient on combined antiretroviral therapy with no obvious preoperative muscle weakness and had a planned Lower Segment Cesarean Section [LSCS] under general anesthesia with drugs that are recommended to be safe in this category of patients. She developed protracted muscle weakness needing postoperative artificial ventilation. The aim of this report is to warn that such a possibility of undiagnosed sub clinical muscle weakness exists which might need a better preoperative neurological evaluation.

Case report

A 32 yrs old (ASA I) primigravida whose preoperative physical examination was unremarkable and all investigation were normal [Table 1]. She reported no limitation of physical activity and had no signs of muscle weakness or muscle wasting. Therefore no preoperative neurological consultation was advised. She acquired HIV infection following an open heart surgery during her childhood for an atrial septal defect closure. She was on oral antiretroviral drugs lamivudine [300 mg bid], stavudine [40 mg bid] and kaletra (lopinavir [400 mg] and ritonavir [100 mg] combination bid) for more than 10 years.

As patient refused a regional block, general anesthesia with customary rapid sequence induction was administered under standard monitoring care [ECG, non-invasive blood pressure, pulse oxymetry, $EtCO_2$, temperature and a peripheral nerve stimulator]. Following the delivery of a male baby [Apgar score: 10], intravenous zidovudine infusion that was started 2 hours before operation was discontinued. Further anesthesia was maintained with infusions of propofol [4-6 mg/kg/hr] and remifentani1 [0.07-1 μg kg^{-1} min^{-1}]. Intravenous

cisatracurium was the non-depolarising agent used for muscle relaxation after the initial intubating dose of intravenous succinylcholine. Towards end of operation diclofenac, a nonsteroidal anti-inflammatory drug [NSAID]; [75 mg IM] was administered. The total duration of surgery was about 60 min.

Table 1

Preoperative investigations

Total Hb [10.4-16 gms%]	10.6
Platelet count [10^3/mm^3]	386000
CD_4^+ T count [Cells/mm^3]	879*
CD8 count [Cells/mm^3]	>2000
C4: C8 ratio	1: 0.34
Viral load [RNA copies/m1]	Undetectable**
S. Bilirubin levels [3-17 umol/L]	16
Urea [Normal-2.5-6.5 umol/L] Creatinine [Normal-40-70 umol]	3.8 35.25
Bl. sugar [umol/L]	6.0

* By definition HIV positive patient meets the criteria for AIDS when the CD_4^+ T cell counts drop below 200 mm^{-3}. Regardless of surgical procedure, there is a mortality rate of 13.3% 6 months postoperatively when the CD_4^+ T count is <50 mm^{-3} and a mortality of 0.8% when CD_4^+ T count is >200 mm^{-3}.

** A successful anti HIV therapy means viral load suppression to an undetectable blood level.

At the conclusion of operation, propofol and remifentani1 infusions were stopped and the patient was allowed to awake. A peripheral nerve stimulator confirmed neuromuscular recovery with good efforts of spontaneous breathing. Intravenous neostigmine 2.5 mg and atropine 1.2 mg were further used to offset any residual non-depolarising muscle relaxant activity.

Following extubation she was hemodynamically stable with good oxygen saturations for about 10 min. after this she became tachypneic with weak respiratory efforts. Even at this juncture, the nerve stimulator confirmed good neuromuscular activity. Patient remained conscious throughout and obeyed command. As she was getting tired she was reintubated and was shifted to the intensive care unit [ICU] where she was extubated after 12 hrs of artificial ventilation.

All investigations sent from the ICU were normal. Chest X-ray was clear, serum creatinine kinase, lactate and lactic dehydrogenase were not deranged. Patient was conscious with no respiratory difficulty after extubation in the ICU and was discharged home on the third day.

Following up neurological evaluation after a month revealed no signs of muscle wasting or weakness.

Discussion

There are about 42 million individuals living with HIV/AIDS as of December 2002[1]. In future more parturients might present for cesarean section, as it is believed that antiretroviral therapy and an elective cesarean section before rupture of membranes can minimize vertical transmission of HIV.

Within this context the case presented is interesting as it serves as a warning for clinicians of the possibility of prolonged muscle weakness as a complication following general anesthesia. It highlights the importance of a proper preoperative neurological evaluation even in apparently normal patients with no restriction of physical activity.

The highly active antiretroviral therapy [HAART] regimen for the treatment of HIV infected patients include three drug protocols combining a protease inhibitor [Pi] or non-nucleoside reverse transcriptase inhibitor [NNRTI] with two nucleoside reverse transcriptase inhibitors [NNRTI] with two nucleoside reverse transcriptase inhibitors [NRTIs][2,3].

Our patient was on a 3-drug regimen of two NRTIs [oral lamivudine

and stavudine] and one Pi combination [oral kaletra]. Lamivudine is the least neurotoxic. However, stavudine and zidovudine cause peripheral neuropathy.

Oral kaletra, a combination of Protease inhibitors also inhibits cytochrome P_{450}, which impairs the metabolism of midazolam and fentanyl. Our patient's viral loads were undetectable and she had good CD_4^+ T cell counts indicating adequate retroviral therapy with a good prognosis.

It is generally considered that intravenous etomidate, atracurium, remifentanyl and inhalation anesthetic desflurane are the preferred drugs as they are not dependent an cytochrome P_{450} hepatic metabolism in this group of patients[2,3].

When our patient needed reintubation after an apparently complete recovery from general anesthesia, we were unsure of the causative factor. The patient was on a Protease inhibitor, which tends to prolong the activity of intravenous midazolam or fentanyl. Ritonavir is known to have a strong interaction with fentanyl and a respiratory depression over a long time of period after fentanyl administration could be expected. Is there an interaction between ritonavir and remifentanil which was used? This is a question that could be looked into. However, there was no noticeable abnormality in the pupil size nor was there a reduced respiratory rate. Intravenous propofol and remifentanil that were used have a short duration of action and were used following reintubation in the ICU as well.

Could the muscle weakness be due to the muscle relaxants administered, the HIV infection per se, the antiretroviral drugs she was on, or due to a sub clinical muscle weakness that was not picked up in the preoperative examination?

The role of intraoperative muscle relaxants as a causative factor could be ruled out as the peripheral nerve stimulator showed full recovery from muscle relaxant activity and in addition cisatracurium, that was used is considered to be safe in these patients.

As for HIV per se producing muscle weakness, it is know that some 30% of adults suffering from AIDS develop neurological disorders.

Approximately 35% of patient manifest clinically with peripheral neuropathy [polyneuropathy and myopathy] and is the most frequent neurological complication in HIV patients[2].

The possibility also exists that the antiretroviral drugs could have contributed to the problem.

Preoperative anesthetic examination did not reveal any neurological deficits in this patient and it is possible a neurologist could have picked up a deficit that we could not envisage.

That leaves the suggestion of an undiagnosed preoperative sub clinical muscle weakness as the causative factor. Since the patient recovered completely after a short duration of artificial ventilation the patient might not have had a major neuropathy. This element of sub clinical muscle weakness is the highlight in this case report.

In conclusion, it should be emphasized that all practicing anesthesiologists should be familiar with HIV disease and should use prenatal anesthesia consultations and a team approach to assure optimal treatment for HIV patients. Regional anesthesia is a good option. When administering general anesthesia with narcotics and muscle relaxants, it is important to be aware that the HIV infection inherently mighty be associated with various types of neuropathies and that the antiretroviral drugs compound the problem. The action of retroviral drugs on the various enzyme systems, which are also responsible for the degradation of the sedatives and narcotics, should be kept in mind. Proper selection of anesthetic drugs might make the task easier. The possibility of an undiagnosed preoperative muscle weakness exists which might result in problems following general anesthesia. A neurological consultation preoperative is highly recommended to avoid a similar problem.

References

1. HUGHES SC: Of plague and pestilence. *J Clin Anesth*; 15:166-169, 2003.
2. EVRON S, GLEZERMAN M, HAROW E, SADAN O, EZRI T: Human immunodeficiency virus: anesthetic and obstetric considerations. *Anesth Analg;* 98:503-511, 2004.
3. hUGHES SC: HIV and anesthesia. *Anesthesiol Clin North America*; 22:379-404, 2004.