Obstetric use of nitroglycerin: Anesthetic implications

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ABSTRACT
Nitroglycerin has been used in anesthetic practice for induced hypotension and managing perioperative hypertension and myocardial ischemia. Contrary to the continuous low dose infusions (5-20 mcg/min) used for the same, intravenous bolus dosages are sometimes administered at the behest of obstetricians for removal of retained placenta. Use of nitroglycerine in managing retained placenta is undertaken as a last resort when other measures fail to relax the uterine smooth muscles. Intravenous nitroglycerine relaxes smooth muscle cells by releasing nitric oxide thus causing prompt cervico-uterine relaxation. However, administration of nitroglycerine in this manner is not without risks which should be kept in mind while using it for obstetric purposes. We hereby report a case of 22-year-old female scheduled for manual removal of placenta where unpredictable and unexpected hypoxemia was observed following nitroglycerine administration.

Key words: Hypoxemia, nitroglycerine, obstetrics

INTRODUCTION
Nitroglycerin (NTG) is an organic nitrate (glyceryl trinitrate) that relaxes smooth muscles and produces a generalized vasodilatation.[1] Intravenous infusions of nitroglycerin (5-15 mcg/min) have been widely used in anesthetic practice for managing patients with acute decompensated heart failure, perioperative myocardial ischemia and for achieving hypotensive anesthesia.[2,3] Due to its ability to relax smooth muscle, nitroglycerine has also been used as a uterine relaxant for delivery of retained placenta when all other measures fail to achieve the same.[4]

It is estimated that retained placenta complicates 2-3.3% of all vaginal deliveries.[5] The most common cause implicated is failure of retroplacental myometrial contractions. Without immediate treatment, life-threatening hemorrhage can occur. When conventional treatment with oxytocin fails, sequential administration of oxytocin and nitroglycerine have been used by the obstetricians with success.[6] NTG is either administered through sublingual route (1 mg) or intravenous boluses (50-100 mcg) to achieve the desired effect. However the use of nitroglycerine is not without side effects. Hypotension, tachycardia, and headache are usual complications. Another potential complication is hypoxia, the possible mechanism of which is blunting of protective hypoxic pulmonary ventilation drive due to the potent vasodilatation caused by NTG.[7] Although hypoxia with nitroglycerine has been extensively described with continuous infusions (5-15 mcg), it has not been reported with bolus dosages that are frequently administered in obstetrics. We hereby describe a case where unexpected hypoxemia was encountered in a young 22-year-old female following administration of boluses of NTG to facilitate extraction of retained placenta.

CASE REPORT
The patient has consented for the clinical details of the case for publication in the journal for academic purpose.

A 22-year-old primigravida presented to obstetrics department with complaint of fever on sixth postpartum day after having undergone vaginal delivery elsewhere. Although the patient was febrile on presentation, the vital parameters were found to be normal. The per abdominal examination by the obstetrician revealed the uterine height of 24 weeks and abdominal ultrasonogram done showed placenta invading into the myometrium, short of serosa. The patient was scheduled to undergo manual removal of placenta. All the biochemical and hematological...
investigations were found to be normal. Airway was found to be normal. The patient was kept fasting and tablet ranitidine (150 mg) and alprozolam 0.25 mg was administered as premedication on the day of surgery.

An intravenous line was secured with 20 G cannula in the operating room. Standard noninvasive monitoring was done using anesthesia monitor (S/5™ critical care monitor, Datex Ohmeda, Helsinki, Finland). Induction was achieved with injection (inj.) fentanyl (100 µg), inj. propofol (100 mg) along with inj. atracurium (25 mg). Proseal laryngeal mask airway (PLMA) size 3 was inserted and the correct placement was confirmed by lube test and end tidal carbon dioxide tracing on monitor. Anesthesia was maintained with nitrous oxide –oxygen in 60:40 ratio and sevoflurane (1 MAC). Despite repeated attempts, the operating surgeon failed to gain access to the uterine cavity owing to the closed internal os. Therefore it was decided to administer NTG as a bolus in the dose of 50 µg to facilitate prompt cervico uterine relaxation. The desired relaxation and access to placenta was achieved in this manner. However a modest fall in arterial oxygen saturation (SpO₂ -94%) was noticed and N₂O was discontinued to ascertain the cause of fall in saturation. The circuit disconnection, leaks, and soda lime exhaustion were ruled out. Chest auscultation revealed normal bilateral equal breath sounds. The oxygen saturation returned to normal (99%) after sometime. In the meantime, boluses of 50 µg and 100 µg of NTG were again repeated at the request of operating surgeon. The administration of second bolus led to significant fall in saturation with SpO₂ falling to 89%. Along with, tachycardia was also witnessed with fall in both systolic and diastolic blood pressures. An arterial blood gas sample drawn during this time period revealed a PaO₂ of 56.4 mmHg and the difference from the baseline (ABG) arterial blood gas is shown in Table 1. However, this episode of desaturation too responded to volume resuscitation and discontinuation of nitrous oxide.

Placenta was completely removed following uterine relaxation achieved by the use of NTG without substantial hemorrhage. At the completion of procedure, inj. glycopyrrolate (0.5 mg) and inj. neostigmine (2.5 mg) was administered and PLMA removed with the assumption of spontaneous respiration and reflexes. The postoperative period was uneventful and the patient was subsequently discharged after 3 days.

**DISCUSSION**

Nitroglycerine’s action on vascular smooth muscles is mediated through release of nitric oxide that is produced by the reduction reactions on the surface of endothelial cells. In addition to cyclic guanosine monophosphate (cGMP)-mediated smooth muscle relaxation, nitric oxide also causes both arterial and venous vasodilatation.

In addition to its numerous uses in anesthetic practice, NTG has proved to be a boon for the obstetricians in managing procedures where adequate cervico uterine relaxation is required. Apart from the prompt uterine relaxation, this drug has an advantage of rapid onset of action (75-95 seconds) which is faster than the available tocolytics. Administration of small boluses is not associated with significant blood loss and has the advantage of rapid termination of action.

Headache, palpitations, tachycardia, and hypotension are the most common side effects observed following administration of NTG, although the magnitude is minimal with low dosages. Owing to its vasodilating property, NTG is known to inhibit hypoxic pulmonary vasoconstriction (HPV) particularly when it is given as infusion for considerable time period resulting in hypoxemia. This particular side effect may be of concern in patients who are intolerant to hypoxia and therefore caution is required in patients with underlying lung disease, parenchymal lung disease associated with right to left shunts, cardiac disease, and severe anemia. Although role of boluses of NTG has been established successfully for facilitating uterine relaxation, hypoxemia has not been discussed so far as a side effect with bolus dosages. In the present case, probably the vasodilating property along with inhibition of HPV was primarily responsible for the unexpected hypoxia that was out of proportion to the dosages usually causing the same.

Therefore it is imperative to remember that in spite of all the advantages, NTG has the potential to cause severe hypoxemia even when administered as a bolus and caution is advised while administering it in individuals susceptible to the same.

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