Clinical Reports

Obstetrical analgesia in a parturient with antithrombin III deficiency

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Antithrombin III (AT III) deficiency is a rare inherited disorder which predisposes patients to thrombotic complications. Anticoagulation is necessary to prevent recurrent thrombosis and high doses of heparin are often required. Anticoagulation complicates analgesia in parturients with the condition. We describe such a patient, in pre-term labour, who was successfully managed during labour with intravenous nalbuphine and inhaled nitrous oxide (N_2O)

La déficience en antithrombine est une maladie héréditaire rare qui prédispose aux complications thrombogènes. L'anticoagulation est nécessaire pour la prévention des thromboses récidivantes et requiert des doses élevées d'héparine. L'anticoagulation complique évidemment l'anesthésie de la parturiente. Nous rapportons un cas d'une patiente en travail avant terme, dont l'accouchement s'est déroulé sans complications sous nalbuphine et protoxyde d'azote.

Coagulopathy is generally considered an absolute contraindication to spinal and epidural anaesthesia for labour and delivery.[1] Epidural and spinal haematomas with serious neurological deficits are rare complications following regional anaesthesia. Case reports of haematoma after lumbar puncture are associated with haemostatic abnormalities, in particular anticoagulant therapy, in the majority of cases.[2] The obstetric anaesthetist should be prepared to offer the parturient an alternative method of analgesia in this situation. Ideally, particularly in preterm labour, drugs administered to the mother should cause minimal fetal respiratory depression. The following case report describes the successful use of intravenous nalbuphine and nitrous oxide for analgesia during labour and vaginal delivery in an anticoagulated patient with antithrombin (AT) III deficiency in pre-term labour.

Key words
ANAESTHESIA: obstetrical;
BLOOD: coagulation;
PREGNANCY: analgesia.

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Case study

A 34-yr-old Caucasian woman with known AT III deficiency presented to the obstetrical unit at 34 wk gestation in labour. Her first pregnancy was complicated by a deep venous thrombosis at eight weeks gestation, which progressed to multiple pulmonary emboli and a possible left lung infarction. The pregnancy was subsequently terminated under paracervical block at ten weeks gestation. A second pregnancy underwent a spontaneous abortion at 12 wk while she was treated with heparin 5000 IU *sc* bid.

Her present pregnancy was complicated by a deep venous thrombosis at eight weeks gestation while receiving *sc* heparin therapy for which she was treated in hospital with *iv* heparin for two weeks. Before discharge from hospital she had Doppler ultrasound evidence of regression of the thrombus and since then had been treated with heparin 22,500 IU *sc* bid. without evidence of recurrence. She was receiving no other medication and her past medical history was unremarkable. She reported an allergy to Coumadin which resulted in a rash. The physical examination revealed no abnormality apart from bruising at injection sites. The patient's weight and height were 62 kg and 160 cm respectively. Laboratory investigations: Hb 102 $g \cdot L^{-1}$, WBC 12.2, $\times 10^9 \cdot L^{-1}$, platelets 189, $\times 10^9 \cdot L^{-1}$, Pt 12 sec/control 11 sec, PTT 42 sec/control 34 sec. Upon consultation with her haematologist, the dose of heparin was decreased to 7 500 IU *sc* qid with plans to resume the former dosage two to four hours after delivery.

The patient requested analgesia once active labour commenced. Earlier in her pregnancy an anaesthesia consultation had been obtained where the analgesia options for labour were discussed. She had been informed of the contraindication to lumbar epidural analgesia on the basis of her anticoagulation. Informed consent was obtained for the use of *iv* nalbuphine and nitrous oxide. She was treated with *iv* nalbuphine at a dosage of 10 mg (in 2.5 mg increments over ten minutes), which was repeated every two to three hours during the first stage of labour. She received a total of 30 mg of nalbuphine with the last dose given two and one half hours before delivery. The maternal vital signs and mental status were monitored frequently and no change was noted after the administration of nalbuphine. The parturient's blood pressure was 110/60–130/80 with a heart rate of 80–100 and a respiratory rate of 18–20. She remained somewhat anxious but felt she received acceptable pain control. No nausea or vomiting was noted. Fetal heart rate monitoring revealed good beat-to-beat variability with no abnormal patterns. During the second stage of labour, one hour and 50 min after the last dose of nalbuphine, the parturient received 50% nitrous oxide in oxygen. This was self-administered with each contraction and supervised by an anaesthetist. It was administered from a standard anaesthetic machine equipped with scavenging apparatus. This provided adequate analgesia. The duration of first and second stage of labour was 10½ hr and 51 min respectively. There were no complications except some meconium staining of the amniotic fluid was noted prior to vaginal delivery. The fetal heart rate tracing revealed no evidence of fetal distress. A healthy infant was delivered by spontaneous vaginal birth with Apgar scores of 9 at one and five minutes. The infant weighed 2860 gm. The estimated blood loss was 400 ml.

The pre-term infant was transferred to the Neonatal ICU. Apart from one apnoeic episode, which was short and responded to stimulation, the neonatal course during follow-up was uneventful. The patient was interviewed 36 hr after delivery and she expressed satisfaction with the analgesia she obtained.

Discussion

Antithrombin III deficiency is one of a group of prothrombotic disorders which are inherited as autosomal dominant traits. As a group they account for less than ten percent of patients with recurrent thromboembolism.[3] The clinical presentation is that of recurrent episodes of venous thromboembolism in patients with strong family histories of thrombotic disease. Patients usually become symptomatic by their early twenties.

Antithrombin III complexes with all the serine protease procoagulant proteins and blocks their biological activity. The rate of this reaction is enhanced by heparin. Plasma AT III concentrations only slightly below normal increase the risk of thrombosis. The diagnosis of AT III deficiency is made by an immunoassay of AT III and heparin cofactor activity. Patients with this disorder may be treated with heparin during acute thrombosis or embolism, since there is usually sufficient normal AT III to act as heparin cofactor.

Chronic oral anticoagulation is recommended after the first clinical thrombotic episode.[3] Coumadin crosses the placenta[4] and because of risks of fetal bleeding as well as teratogenicity, heparin is the anticoagulant of choice in pregnancy.[2] Prophylactic anticoagulation should be instituted in asymptomatic individuals before medical or surgical procedures which are known to be associated with an increased risk of thrombosis.[3] This risk may be increased by the hypercoagulable state associated with pregnancy.[5]

Heparin therapy complicates epidural analgesia for labour due to the risk of epidural haematoma formation and possible spinal cord or nerve root compression.[1] One option for management in this situation is to discontinue heparin therapy and allow the PTT to normalize before institution of epidural anaesthesia. In view of the parturient's strong history of thrombotic complications and additional risk due to the hypercoagulable state of pregnancy it was felt that discontinuing anticoagulation during the peripartum period, and at a time of highest risk of thrombosis, would be unacceptable. As well, patients who stop their anticoagulation treatment during pregnancy may carry a higher risk than those who have never received anticoagulation.[2] The magnitude of the risk for thrombosis even with anticoagulation was deemed by the attending haematologist to be considerable. It may be justifiably argued that perhaps the risk of bleeding is quite low in a patient with such an increased risk for thrombosis. The literature does not provide any information to aid quantification of this risk. We considered the parturient's anticoagulant treatment with documented prolonged PTT a contraindication to lumbar epidural anaesthesia.[2]

Alternatives to lumbar epidural analgesia in labour include hypnosis, TENS (transcutaneous electrical nerve stimulation), psychoprophylaxis (Lamaze), inhalational agents (N_2O) and systemic narcotic administration using either intermittent narcotic injection or patient-controlled analgesia (PCA). Their various advantages and disadvantages have been described in a recent editorial.[6]

Systemic narcotics are widely used for pain relief in obstetrics. Their potential adverse effects on the parturient and fetus are well known, and include respiratory depression, obtundation of protective reflexes, postural hypotension, nausea and vomiting, decreased GI motility,

abnormal progression of labour and neonatal respiratory depression and change in neurobehavioural status.[7] In view of these potential adverse effects narcotics are used to reduce pain and not to eliminate it completely. Also, analgesia may be unsatisfactory due to sub-optimal dose and dosing schedules. This patient received small doses of nalbuphine titrated by an anaesthetist to effect which may approximate PCA (patient controlled analgesia)[8] and explains her satisfaction with the analgesia.

Nalbuphine with its reported ceiling effect on respiratory depression was chosen for labour analgesia to avoid the possible maternal and fetal respiratory depression attending morphine or meperidine analgesia during a potentially prolonged labour. Nalbuphine is one of the newer synthetic agonist-antagonist narcotic analgesics with primarily strong kappa and sigma agonist and weak mu antagonist effects.[7] Increasing the dose of nalbuphine does not result in increasing respiratory depression.[9] However, this potential advantage may not be clinically relevant because of a comparable ceiling effect on analgesia.[7] The main reported side effects are drowsiness and dizziness.[7] Nalbuphine has fewer psychomimetic effects than pentazocine.[7]

The pharmacokinetic behaviour of an *iv* bolus of nalbuphine in pregnancy appears to follow a two-compartment pharmacokinetic model with an initial distribution time of 4–20 min and a terminal elimination half-life of 2.4 ± 0.4 hr.[10] Like all narcotics, it readily crosses the placenta with fetal/maternal ratios of 0.3–0.6.

Narcotics may have effects on FHR patterns. The most frequently observed changes are decreases in short- and long-term variability. This effect has been attributed to depression of the fetal CNS and direct effects on the fetal myocardium. As well, a benign sinusoidal FHR pattern has been seen following narcotic administration of alphaprodine, butorphanol, meperidine,[11] and nalbuphine.[7] The sinusoidal pattern was originally described in Rh-sensitized or dying fetuses.[12] Despite its association with narcotic administration there has been no direct effect on fetal morbidity or mortality.[12] However, in view of the potential for abnormal FHR patterns, FHR monitoring is necessary. In this case continuous monitoring was deemed essential as the fetal depressant effects of narcotics may be accentuated in pre-term neonates. It is wise to institute constant maternal cardiorespiratory monitoring with the availability of a narcotic antagonist and facilities for resuscitation of mother and newborn.

Nitrous oxide (50%) in oxygen has a long record of safety in obstetrical analgesia.[6] Widespread use over many years suggests it is beneficial and safe. Its advantages include rapid pulmonary uptake and elimination and the ease of administration thus allowing the parturient more control of degree of analgesia.[13] It was introduced in this case, during the second stage, to avoid narcotic use in the two-three hours immediately preceding delivery and thus minimize neonatal respiratory depression. The use of N_2O as an analgesic during the second stage of labour has been reported to yield a high degree of patient satisfaction,[14] although complete analgesia requires supplementation with pudendal blocks for delivery[13] which was contraindicated in this case. Potential adverse effects include over-sedation and the loss of protective airway reflexes predisposing the patient to aspiration.[13] In our institution, nitrous oxide is not routinely administered during labour due to inadequate labour room ventilation and possible hazards of environmental pollution.[15] In this case the parturient was satisfied with the effectiveness of the analgesia she obtained and no adverse effects were noted on the patient or the neonate.

Antithrombin III deficiency presents many problems for the anaesthetist. We present a case of a patient with AT III deficiency receiving heparin therapy who received satisfactory analgesia for labour and delivery of a preterm infant using *iv* nalbuphine and nitrous oxide. No severe adverse maternal-fetal effects were noted. Appropriate maternal-fetal monitoring was instituted with facilities for neonatal resuscitation.

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