NEURAXIAL ANESTHESIA IN ANTICOAGULATED PARTURIENT- SHOULD WE CANCEL?

Magdy Abdelaziz Mansour, MD¹, Tarek Abdelzaher Karkor, MD².
¹Department of Anesthesiology, Medical Research Institute, Alexandria University.
²Department of Obstetrics and Gynecology, Faculty of Medicine, Alexandria University.

ABSTRACT

In this prospective study 16 parturients on chronic anticoagulant therapy for a history of life-threatening thromboembolic disease were scheduled for elective cesarean section under neuraxial block. They stopped taking warfarin 5 days prior to surgery and LMWH (1.5 mg.kg⁻¹) was given twice daily sc 3 days before the operation. Heparin was stopped 12 hours before surgery regarding INR < 1.4 and restarted in the first post operative day/ Warfarin was restarted together with LMWH after stabilization of the patients medical conditions. LMWH was discontinued when INR > 2. The results were compared to a control group comprised of 16 randomly selected non warfarin treated parturients who underwent elective CS during the same period. Mean perioperative decrease in hemoglobin was 1.3 ± 0.3 gm/dL and 1.4 ± 0.1 gm/dL in heparin and control group respectively. The need for blood transfusion did not significantly differ between the two groups. Average hospitalization period in heparin group was 4.3 ± 0.5 days compared to 2.2 ± 0.3 days in the control group (P < 0.01). No long term hemorrhage or thromboembolic complications were recorded 3 months postoperatively. Elective cesarean section under neuraxial block can be conducted safely in those high risk patients with regimen that allows a brief but controlled interruption to their full anticoagulation.

Key words: Anesthesia: Cesarean section; Anesthetic techniques: Regional: epidural; Blood, Anticoagulants: heparin, warfarin.

INTRODUCTION

Parturients on chronic oral anticoagulated therapy typically have a mechanical prosthetic heart valve, chronic atrial fibrillation or a history of recurrent venous thrombosis; conditions which predispose them to venous or atrial thromboembolism.(1) This present a major perioperative management problem due to the threat of significant hemorrhage associated with surgery(2) and the risk of thromboembolism associated with discontinuation of anticoagulants.(3) This study was designed to assess the safety of cesarean section under neuraxial anesthesia in parturients on long term anticoagulation therapy and efficacy of LMWH to maintain anticoagulation, avoiding major thromboembolic and hemorrhagic risks of surgery.

PATIENTS AND METHODS

The study was carried out during the period from May 2002 to Dec. 2005, sixteen parturients on chronic anticoagulant therapy (Warfarin 2-4mg) scheduled for elective cesarean section were included in this study.

The study protocol was reviewed and approved by the institutional ethics committee. All patients gave a written consent.

Warfarin therapy was required for prothetic heart values in 9 patients, chronic atrial fibrillation in 5 and recurrent deep venous thrombosis in 2 patients.

A protocol was followed whereby there was a short interruption to the perioperative anticoagulation. Parturients stopped taking warfarin 5 days prior to surgery and subcutaneous low molecular weight heparin (enoxparin, 1.5 mg, kg⁻¹ twice daily) was started 2 days later (3 days before surgery). International normalized ratio (INR) was assessed a day before surgery, if INR < 1.4, LMWH was stopped 12 hours before surgery, but if INR > 1.4 fresh frozen plasma was transfused to correct clotting factors at first before surgery.

Premedication consisted of ranitidine 150 mg po the evening before and again on the morning of surgery. After transfer to the operating theatre, sodium citrate 30 ml po was given. An iv cannula was inserted into a peripheral vein, infusion of saline 0.9% was commenced and a preload of 500 ml infused. Non invasive monitoring was instituted, consisting of ECG, non-invasive blood pressure measurement and oxygen saturation. Metoclopramide 10mg iv was given. With the patient in sitting position, an
epidural catheter was inserted at L₂-L₃ interspace, using loss of resistance to air to identify epidural space. A test dose of 2.5 ml hyperbaric bupivacaine 0.5% was given with no evidence of intrathecal injection. A 24 gauge spinal needle was used to administer an intrathecal dose of 2.5 ml hyperbaric bupivacaine 0.5% at L₃-L₄ interspace.

The patient was lowered to a lying position with 15° left lateral tilt on the operating table. Skin prick testing revealed a sensory block to T₄ bilaterally, and surgery was allowed to commence. Oxygen, 4L min⁻¹ was administered via a face mask. Following delivery, oxytocin 10 u iv was given, producing sustained uterine contraction. Heparin was restarted again in the first postoperative day. Postoperative pain relief was provided by epidural infusion of bupivacaine 0.1% at a rate of 10ml hr⁻¹. Postpartum hemorrhage was defined as an estimated loss of more than 1000 ml of blood, or drop of at least 2 gm% of hemoglobin or 10% in hematocrit 24 to 72 hr after giving birth. Oral anticoagulant (warfarin 2-4 mg po) was restarted together with heparin after stabilization of the patient’s medical condition (stable hemodynamics, absence of neurological deficits, absence of post partum hemorrhage). Clotting function was assessed and LMWH was discontinued when INR > 2, if INR < 2, LMWH was continued together with oral anticoagulants till INR was controlled. This interruption for such a short period was not felt to pose any serious risk of thromboembolism.

Hemoglobin level and INR were monitored before and after surgery. Follow up assessment included duration of vaginal bleeding, decrease in hemoglobin, need for blood transfusion (expressed by mean value of transfused blood units per patient) and hospital stay.

Subsequently, the patients were seen regularly in the outpatient clinic and followed carefully for the occurrence of thromboembolic events during the following 3 months postoperatively.

The results were compared with a control group comprised of 16 randomly selected non warfarin treated parturients underwent elective caesarean section during the same period. Data were expressed as mean ± SD and were analysed using student’s t-test and Chi-square test. P < 0.05 was considered to be statistically significant. Statistical analysis was performed using SPSS (version 9) computer software.

RESULTS

Data of maternal weight, height, parity and infant gestational age and weight are summarized in table 1.

Mean preoperative hemoglobin was 10.8 ± 1.6 gm % in heparin group compared to 11.2±1.3 in control group (P = 0.22) (table 2). Mean postoperative change in hemoglobin level was -1.3±0.3 gm% in heparin group compared to -1.4±0.1 gm% in the control group (P = 0.32) (table 2).

Need for intraoperative blood transfusion did not significantly differ between the 2 groups. It was required in 2 cases in heparin group compared to one case in the control group, each needing 1 unit of blood (P = 0.68). Post partum hemorrhage occurred in only one anticoagulated parturient requiring 2 units of blood. Accordingly, hospital stay was significantly prolonged in heparin group compared to that of the control group being 4.3±0.5 and 2.2±0.3 days respectively (< p = 0.001).

None of the infants born to LMWH-treated mothers has hemorrhagic complications. All parturients of the heparin group were discharged home after warfarin loading dose and heparin therapy was discontinued when INR > 2.0. During the next 3 months follow up, no patient had significant delayed bleeding or thromboembolic events.

DISCUSSION

The appropriate perioperative anticoagulant management of parturients scheduled for elective cesarean section, who receive chronic prophylactic oral anticoagulant therapy, remains controversial. These patients are considered to be particularly at high risk of thromboembolic complications due to discontinuation of anticoagulant therapy. On the other hand, neuraxial block in patient receiving anticoagulant therapy carry the risk of development of epidural hematoma due to
Table (1): Parturient data. No significant differences. Data are expressed as mean ± SD.

<table>
<thead>
<tr>
<th></th>
<th>Heparin (n = 16)</th>
<th>Control (n = 16)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>28.52±1.24</td>
<td>27.73±0.88</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78.7±2.14</td>
<td>79.6±2.12</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165.41±1.5</td>
<td>163.32±1.3</td>
<td></td>
</tr>
<tr>
<td>Parity - Nulliparous</td>
<td>5</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>- Multiparous</td>
<td>11</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>37.22±0.3</td>
<td>38.61±0.4</td>
<td></td>
</tr>
<tr>
<td>Infant weight (gm)</td>
<td>2860±50.2</td>
<td>3000±62.4</td>
<td></td>
</tr>
</tbody>
</table>

Table (2): Procedural characteristics. Data are expressed as mean ± SD.

<table>
<thead>
<tr>
<th></th>
<th>Heparin (n = 16)</th>
<th>Control (n = 16)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop. HG (gm%)</td>
<td>10.8±1.6</td>
<td>11.2±1.3</td>
<td>0.22</td>
</tr>
<tr>
<td>Postop. change in HG (gm%)</td>
<td>-1.3±0.3</td>
<td>-1.4±0.1</td>
<td>0.32</td>
</tr>
<tr>
<td>Intraop. blood transfusion</td>
<td>2 cases</td>
<td>1 case</td>
<td>0.68</td>
</tr>
<tr>
<td>Hospital stay (day)</td>
<td>4.3±0.5</td>
<td>2.2±0.3</td>
<td>*0.001</td>
</tr>
</tbody>
</table>

* Statistically significant, P < 0.05.

continued bleeding from epidural venous plexus. Extreme approaches involve either a 4 day perioperative withdrawal of anticoagulant treatment (2 days before and 2 days after) which has a definitive risk of thromboembolic complications or proceeding with uninterrupted anticoagulant therapy. Others have recommended merely omitting warfarin on the evening before surgery. These techniques increase the probability of hemorrhage.

Nevertheless, today the most widely used management strategy is reversal of oral anticoagulation with concurrent heparin anticoagulation. It implies that heparin is discontinued approximately 12 hours preoperatively, resumed as soon as possible postoperatively and continued until oral anticoagulant therapy can be safely resumed. This treatment modality, which interrupt full anticoagulation only for a few hours is considered effective and safe yet it is inconvenient, requiring longer perioperative hospitalization, repeated heparin dose titration and close monitoring with repeated blood tests to perform dose adjustment which is costly.

Use of heparin as a preoperative substitute for prophylactic oral anticoagulant was recommended by Spandorfer et al. LMWH preparations have been designed to improve the efficacy and safety ratio of unfractionated heparin which are more cost effective.

LMWH have less effect on measurable clotting time such as partial thromboplastin time, as well as less inhibitory action on platelet aggregation, with a lower incidence of bleeding complications and full preservation of the antithrombotic efficacy. They have been found to be at least as effective and safe as other anticoagulant agents such as unfractionated heparin or warfarin. Moreover, these agents have a predictable dose dependant anticoagulant effect, and therefore they do not require close laboratory monitoring. Also, the incidence of adverse effects associated with anticoagulation, such as bleeding, osteoporosis and heparin induced thrombocytopenia is lower with LMWH compared to unfractionated heparin.

This study clearly showed that LMWH therapy during cesarean section under neuraxial block did not result in higher risk of either hemorrhagic, thromboembolic or neurological complications compared to control group. In agreement with the results of the present study, Maslovitz et al found that discontinuation of LMWH 12 hr before epidural catheter placement and cesarean section did not result in any
hemorrhagic or neurological complications for either the mother or the infant.

Despite somewhat longer hospitalization time compared to the control group, this LMWH protocol is essentially more cost effective than alternative anticoagulation regimens in view of its overall safety and efficacy. Laboratory monitoring of the INR and partial thromboplastin time (PTT), and tedious titration associated with heparin loading and maintenance are avoided.

A combined spinal epidural technique was chosen in order to obtain optimum conditions for surgery and patient comfort. Epidural anesthesia alone provides a slower onset block with a reduced frequency and severity of maternal hypotension. The final sensory level can be titrated by the addition of local anesthetic. The epidural catheter can be left in place to provide postoperative pain relief. However, compared with spinal anesthesia, epidural anesthesia carries a greater likelihood of failure due to technical problems. Epidural anesthesia also requires larger doses of local anesthetic with a consequent increase in neonatal exposure and an increase in maternal shivering. Spinal anesthesia provides a faster onset, more reliable block than epidural anesthesia, using a much smaller dose of local anesthetic. However, disadvantages of spinal anesthesia include a greater risk of hypotension with attendant nausea and vomiting, the possibility of postdural puncture headache and a limited duration of action. By combining spinal with epidural anesthesia, it was hoped to obtain the best from each technique and minimize the side effects.

In summary, we found that it is possible to carry out elective cesarean section under neuraxial block with minimal surgical complications and without any neurological complications in this high risk group of patients. This is achieved at the cost of an extra day of hospital admission before surgery.

REFERENCES
14. Agnelli G, Sonaglia F. Low-molecular-weight-heparins: are they interchange-