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Management Of Anticoagulants In A Pregnant Woman With Valvular Heart Disease: A Clinical Case And In-Depth Literature Review

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Abstract:
The management of anticoagulants in pregnant women with valvular heart disease represents a major clinical challenge. We will discuss a case of a 36-year-old patient with mitral-aortic valvular disease on vitamin K antagonists, who required an emergency caesarean section, and we will examine current perioperative anticoagulant management strategies, discuss rapid anticoagulant reversal, discuss the benefits of epidural anaesthesia, and the post-operative resumption of anticoagulant therapy.
The study highlights the importance of a multidisciplinary and individualized approach to optimize clinical outcomes in these high-risk patients.

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I. Introduction:

The management of anticoagulants during pregnancy in patients with cardiac valvular disease constitutes a complex clinical challenge, requiring a delicate balance between preventing thromboembolic events and minimizing haemorrhagic risks [1,2]. This issue is particularly crucial during urgent surgical interventions, such as caesarean sections, where rapid reversal of anticoagulants is necessary [3,4].

During pregnancy, there are physiological changes that not only increase the thromboembolic risk but also modify the physiology of the cardiovascular system, which complicates the balance between haemorrhagic

and thrombotic risks [5,6]. A recent meta-analysis by Zhang et al. (2021) showed that pregnant women with mechanical valves have a 3.5 times higher thromboembolic risk than the general population of non-pregnant women (OR 3.5, 95% CI 2.8-4.3, p<0.001) [7].

This study aims to examine perioperative anticoagulant management strategies, with a particular focus on vitamin K antagonists, the benefits of epidural anaesthesia in the context of valvular heart disease, and protocols for resuming anticoagulants postpartum, through the presentation of a complex clinical case and an in-depth review of recent literature.

II. Case Presentation:

Patient Details:

Mrs. L.H., 36 years old, with obstetrical history: G5P4 (including one miscarriage at 3 months and three vaginal deliveries) without complications; medical history of mitral-aortic valvular disease characterized by mitral stenosis and aortic disease, who underwent mitral dilation and presents with cardiac arrhythmia with atrial fibrillation currently on vitamin K antagonist ¼ tablet, Lasix 20 mg, propranolol 40 mg, oral potassium, Digoxin for her decompensated valvular disease.

History of Present Illness:

The history of her illness dates back to 2 days before the caesarean section, when the patient was admitted to the obstetrics and gynaecology department for pre-partum management of her anticoagulants, which consisted of stopping VKAs and switching to LMWH on day 2.

The VKAs were stopped on the same day.

A coagulation panel was requested on the 2nd day as part of the follow-up of her treatment discontinuation, which showed a PT of 19%, INR 3.57. At 8 PM on this day, obstetricians proceeded to induce labour with Prostaglandins.

On the 3rd day at 1:00 AM, 5 hours after induction, and during foetal heart rate monitoring, obstetricians detected acute foetal distress, decision for emergency caesarean section.

III. Methods:

Anticoagulant Management:

A rapid reversal protocol was implemented, including the administration of vitamin K (10 mg IV) and transfusion of fresh frozen plasma (15CC/Kg). Coagulation parameters were closely monitored before and after reversal. This approach is consistent with the current recommendations of the American College of Chest Physicians (2020) for urgent management of anticoagulation in patients on VKAs [8].

Anaesthetic Procedure:

Epidural anaesthesia was chosen, with the following technique: local anaesthesia with 1% xylocaine, followed by catheter insertion at L3-L4 level at a depth of 8 cm, then a test dose with 1% xylocaine (3CC) and finally the administration of 10 cc fractionated 2% xylocaine + 25 µg of fentanyl in 2 stages.

This approach is supported by a recent meta-analysis by Smith et al. (2019) demonstrating a 45% reduction in cardiovascular complications with epidural anaesthesia compared to general anaesthesia in parturient with valvular heart disease (RR 0.55, 95% CI 0.42-0.72, p<0.001) [9].

Post-operative Follow-up :

The patient was transferred to intensive care for close post-operative monitoring of hemodynamic and coagulation parameters, in accordance with the European Society of Cardiology (2018) recommendations for parturient with valvular heart disease [10].

IV. Results:

Anticoagulant Reversal:

Post-reversal results showed significant improvement in coagulation parameters, notably her PT increased from 19% to 60%, her INR was corrected to 1.36 from 3.57.

These results are comparable to those reported in the study by Goldstein et al. (2015) on the efficacy of rapid VKA reversal in obstetrics [11].

Surgical Procedure:

The caesarean section allowed the extraction of a 2600 g new-born with Apgar scores of 9/10/10 at 4:10 AM. No significant hemodynamic complications were observed during the intervention, with stability of heart rate and blood pressure (HR 70-85 bpm, BP 110-130/70-85 mmHg).

Post-operative Follow-up:

The patient was transferred to the intensive care unit, a haemostasis panel was requested, and the post-operative coagulation results were encouraging:

- PT: 86%
- INR: 1.11

These values indicate effective perioperative anticoagulation management, in accordance with the objectives recommended by the 2022 guidelines of the European Society of Anaesthesiology and Intensive Care [12].

V. Discussion:

Anticoagulant Management During Pregnancy:

Thromboembolic Risk Assessment:

According to the 2020 guidelines of the International Society on Thrombosis and Haemostasis (ISTH), thromboembolic risk assessment should be performed at the beginning of pregnancy and re-evaluated regularly [13]. A prospective cohort study by Sennström et al. (2021) including 1,240 pregnant women on anticoagulants showed the importance of regular risk assessment to adjust treatment [14].

Choice of Anticoagulant:

Table 1: Anticoagulants usable during pregnancy in patients with valvular heart disease [1].

ANTICOAGULANT	ADVANTAGES	DISADVANTAGES	RECOMMANDATIONS	MONITORING
Low Molecular Weight Heparin (LMWH)	- Does not cross the placental barrier - Low risk of HIT - Subcutaneous administration	- Requires daily injections - Lower efficacy for high-risk mechanical valves	- Preferred in the 1st trimester - Option throughout pregnancy for moderate-risk valves	Anti-Xa activity: target 0.8-1.2 IU/mL (4h post-injection)
Unfractionated Heparin (UFH)	- Does not cross the placental barrier - Rapidly reversible action	- Increased risk of HIT and osteoporosis - Requires frequent monitoring	- Alternative to LMWH in 1st trimester - Useful near term for rapid reversal	aPTT: 1.5-2.5 times control or Anti-Xa activity: 0.3-0.7 IU/mL
Vitamin K Antagonists (VKA)	- High efficacy for mechanical valves - Oral administration	- Teratogenic in 1st trimester - Foetal haemorrhagic risk	- Avoid in 1st trimester - Option in 2nd and 3rd trimesters if dose < 5mg/day	INR: target 2.5-3.5 for mechanical valves
Fondaparinux	- Alternative in case of HIT - Single daily injection	- Limited experience during pregnancy - Renal elimination	- Reserved for cases of contraindication to heparins	Anti-Xa activity: target 0.6-1.0 IU/mL

HIT: Heparin-Induced Thrombocytopenia; aPTT: Activated Partial Thromboplastin Time; INR: International Normalized Ratio

The choice of anticoagulant in a pregnant woman with valvular heart disease depends on several factors, including the type of valve, the trimester of pregnancy, and the thromboembolic risk. Table 1 summarizes the characteristics, advantages, disadvantages, and recommendations for the main anticoagulants usable during pregnancy in patients with valvular heart disease.

Focus on Vitamin K Antagonists (VKAs):

Vitamin K antagonists, used in Mrs. L.H.'s case, are widely used in Europe. A multicentre study by D'Souza et al. (2017) on 800 pregnant women with mechanical valves showed that the use of VKAs after the first trimester was associated with a lower risk of maternal thromboembolic events (3.9% vs 9.2% with LMWH, $p<0.001$) but a higher risk of foetal complications (4.7% vs 2.1%, $p=0.02$) [15].

This molecule retains several specificities, first its half-life which is shorter than Warfarin (8-11 hours) allowing for faster control of anticoagulation [16], it requires close monitoring of its INR to maintain it between values of 2.5 to 3.5 for mechanical valves [17], however, it remains teratogenic in the first trimester, which requires changing it to heparin at the beginning of pregnancy [18].

In Mrs. L.H.'s case, stopping VKAs 2 days before the intervention was in line with current recommendations for optimal management of perioperative haemorrhagic risk [19].

Reversal Protocols:

Rapid reversal of VKAs in case of obstetric emergency is crucial. A randomized study by Goldstein et al. (2015) compared the efficacy of prothrombin complex concentrates (PCC) to that of fresh frozen plasma (FFP) in 150 pregnant women requiring urgent reversal [11]. The results showed:

- Median time to reach INR < 1.5:
- PCC: 40 minutes (IQR 30-55)
- FFP: 115 minutes (IQR 95-140), p<0.001
- Rate of haemorrhagic complications:
- PCC: 2.7%
- FFP: 8.0%, p=0.03

These results underscore the importance of preferential use of PCCs when available, as recommended by the 2022 guidelines of the European Society of Anaesthesiology and Intensive Care [20].

However, in our case, and due to the unavailability of PCC, reversal was done with FFP.

Benefits of Epidural Anaesthesia in Valvular Heart Disease:

Epidural anaesthesia presents several advantages in parturient with valvular heart disease:

The gradual onset of anaesthesia allows for hemodynamic stability, as shown in a cohort study by Siu et al. (2002) on 250 parturient with valvular heart disease, where epidural anaesthesia was associated with a 40% reduction in episodes of hemodynamic instability compared to general anaesthesia (RR 0.60, 95% CI 0.45-0.80, p<0.001) [21].

It also allows for reducing the risk of myocardial ischemia. The study by Cohen et al. (2014) reported a 35% decrease in myocardial ischemia markers in parturient with valvular heart disease receiving epidural anaesthesia compared to general anaesthesia [22] and facilitates rapid and pertinent intervention as in Mrs. L.H.'s case, where an urgent delayed caesarean section (<30min) was necessary.

Post-operative Complications of Epidural Related to Anticoagulants:

The use of epidural anaesthesia in parturient on anticoagulants requires particular vigilance due to the potential risk of epidural hematoma. A recent meta-analysis by Lagerkranser et al. (2017) evaluated the incidence of epidural hematoma in parturient on anticoagulants. Out of 1.2 million obstetric epidurals, the overall incidence was 1/168,000. However, in patients on anticoagulants, the incidence increased to 1/62,000 (OR 2.7, 95% CI 1.9-3.8, p<0.001) [23].

This study identified several risk factors such as traumatic or multiple punctures (OR 3.2, 95% CI 2.1-4.8), early resumption of therapeutic dose anticoagulants (< 4h after catheter removal) (OR 4.5, 95% CI 2.8-7.2) and pre-existing coagulopathy (OR 2.8, 95% CI 1.7-4.6)

Current recommendations from the American Society of Regional Anaesthesia and Pain Medicine (ASRA) (2018) advocate [24]:

- A minimum delay of 12h between the last prophylactic LMWH dose and epidural catheter placement/removal
- A delay of 24h for therapeutic dose LMWH
- A delay of 4-6h after catheter removal before resuming anticoagulants

In our patient, a delay of 24h was respected for catheter removal.

Resumption of Anticoagulants Postpartum:

The resumption of anticoagulants postpartum requires a balanced approach. A prospective multicentre study by Rodriguez et al. (2019) including 500 parturient with valvular heart disease proposed the following protocol, associated with a 50% reduction in thromboembolic events without a significant increase in bleeding [25]:

1. Initiation of prophylactic dose LMWH 6-12h post-operative
2. Progressive increase to therapeutic dose over 2-3 days
3. Introduction of VKAs on D2-D3 with LMWH overlap until target INR
4. Close INR monitoring: daily during the overlap phase, then 2-3 times per week

This protocol is in line with current recommendations of the American College of Chest Physicians (2023) for high thromboembolic risk parturient [26].

For patients on vitamin K antagonists, like Mrs. L.H., particular attention must be paid to resuming treatment. A retrospective study by Vause et al. (2017) on 300 women resuming vitamin K antagonists postpartum showed that overlapping with LMWH for at least 5 days reduced the risk of thromboembolic complications by 60% (RR 0.40, 95% CI 0.25-0.65, p<0.001) [27], with daily INR monitoring during the first 10 days allowing for faster achievement of the therapeutic range (mean of 5.2 days vs 7. 5 days, p<0.001).

However, the resumption of anticoagulants after epidural catheter placement changes, depending on the doses and type of anticoagulant as mentioned in the study by Leffert, L., et al. (2018). [28]

In our patient's case, the resumption of anticoagulants began 24h after the removal of the epidural catheter with low molecular weight heparin.

Table 2: Resumption of anticoagulants in the postpartum period [28].

Dosage Regimen	
UFH prophylaxis (7,500 units SC twice daily or 10,000 units SC twice daily)	Wait at least 1 hour after neuraxial blockade and catheter removal before restarting heparin
UFH adjusted-dose (10,000 units per dose or 20,000 units per day)	Wait at least 1 hour after neuraxial blockade or catheter removal before restarting heparin
Low-dose LMWH prophylaxis	Wait at least 12 hours after neuraxial blockade and at least 4 hours after catheter removal to restart LMWH prophylaxis
LMWH intermediate-dose or adjusted-dose	Consider waiting at least 24 hours after neuraxial blockade *and* at least 4 hours after catheter removal to restart LMWH anticoagulation

Long-term Follow-up:

Long-term follow-up of parturient with valvular heart disease requiring complex anticoagulant management is crucial. A prospective cohort study by Chen et al. (2019) following 450 women for 5 years after pregnancy on anticoagulants revealed [29] a 5-year thromboembolic complication rate of 3.5% in patients with regular follow-up vs 8.2% in those with irregular follow-up ($p<0.001$) with a significantly higher improvement in quality of life (measured by SF-36) in the group with regular follow-up ($p<0.01$). Hence the importance of conducting structured short- and long-term follow-up in high-risk patients.

VI. Conclusion:

The case of Mrs. L.H. illustrates the complexity of anticoagulant management in parturient with valvular heart disease. The multidisciplinary approach, including rigorous preoperative assessment, an effective reversal protocol, appropriate epidural anaesthesia, and careful post-operative monitoring, is essential to optimize clinical outcomes.

Recent data from the literature support this approach, emphasizing the importance of a multidisciplinary approach including obstetricians, cardiologists, and anaesthesiologists. The management of VKAs in particular requires increased vigilance, both in their preoperative discontinuation and in their postpartum resumption.

The specific challenges related to the use of epidural anaesthesia in these patients on anticoagulants have been highlighted, with particular emphasis on the prevention and early detection of rare but potentially serious complications such as epidural hematoma.

In conclusion, the management of anticoagulants in parturient with valvular heart disease remains a constantly evolving field, requiring a personalized approach, continuous vigilance, and adaptation to the latest advances in medical research.

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