BRITISH JOURNAL OF HOSPITAL MEDICINE

Managing anticoagulation in pregnancy for the anaesthetist on the labour ward

Penny Sceales[1]

Sohail Bampoe[2]

Author details can be found at the end of this article

Correspondence to:
Penny Sceales;
p.sceales@nhs.net

Abstract

Pregnancy is a hypercoaguable state. As part of the multidisciplinary team on labour ward, the anaesthetist plays a role particularly in advising the women and the obstetric team regarding the timing and even choice of regional analgesia given the potential risk of complications, as this may be affected by the anticoagulation treatment pregnant women may be on. It is important to understand the type of anticoagulation regimens parturients might be on and what sort of risk assessment they must undergo, as this has obstetric and anaesthetic implications. Although a rare presentation, management of women with mechanical prosthetic heart valves who are pregnant requires detailed and highly specialised care in tertiary care centres with a well-developed multidisciplinary team and pathway. Despite their rare presentation, it is important to understand the intricate and complex management that these women require as they have a high morbidity and mortality rate.

Key words: Anticoagulation in pregnancy; Maternal mortality; Mechanical heart valves; Venous thromboembolism

Submitted: 5 October 2020; accepted following double-blind peer review: 2 December 2020

Introduction

Venous thromboembolism remains the leading cause of direct maternal mortality in the UK (Knight et al, 2018). It is a requirement that all women undergo a documented venous thromboembolism risk assessment at the start of their pregnancy (or pre-pregnancy) and that this is repeated intrapartum or immediately postpartum (Royal College of Obstetricians and Gynaecologists, 2015a). There are differences among institutions and hospitals in the UK with regards to the venous thromboembolism risk assessment (Knight et al, 2018). There are inconsistencies between the person completing the venous thromboembolism risk assessment (each of whom may interpret it very differently); for example, at the point of elective caesarean section is it the midwife, obstetrician or anaesthetist who completes it? Additionally, which risk factors are included varies a great deal from the national guidance (with no clear evidence as to why only a selection of risk factors have been chosen and included) (Knight et al, 2018). This article discusses the prothrombotic risk factors and options for thromboprophylaxis during pregnancy, which includes an oral vitamin K antagonist or a low molecular weight heparin with some evidence for the use of direct oral anticoagulants. This article also briefly outlines the anticoagulation management of parturients with mechanical prosthetic heart valves, who may be a rare presentation, but who carry a high risk of complications and therefore require detailed planning of their anticoagulation needs pre-, intra- and postpartum. These parturients require input from haematology, cardiology and anaesthetic teams, particularly peripartum, with regards to monitoring their anti-factor Xa levels (if on low molecular weight heparin) and timely restarting of their anticoagulation postpartum. The detailed management of these high-risk patients is beyond the scope of this article.

How to cite this article:
Sceales P, Bampoe S. Managing anticoagulation in pregnancy for the anaesthetist on the labour ward. Br J Hosp Med. 2021 https://doi.org/10.12968/hmed.2020.0589

Risk factors for venous thromboembolism in pregnancy

Risk factors that contribute to a woman having an increased risk of developing a venous thromboembolism during her pregnancy can be classified as pre-existing (eg thrombophilia), obstetric, or new or transient, as outlined in Table 1 (Royal College of Obstetricians and Gynaecologists, 2015a).

Table 1. Risk factors for developing venous thromboembolism during pregnancy

Pre-existing	Previous venous thromboembolism	
	Thrombophilia	Heritable or acquired
	Medical comorbidities	Cancer, heart failure, T1 diabetes mellitus, active systemic lupus erythematosus, active sickle cell
	Age >35 years	
	Obesity (body mass index >30 kg/m^2)	
	Parity >3	
	Smoking	
	Varicose veins	Symptomatic or above the knee
	Paraplegia	
Obstetric	Multiple pregnancy	
	Current pre-eclampsia	
	Caesarean section	
	Prolonged labour >24 hours	
	Mid cavity or rotational operative delivery	
	Stillbirth	
	Preterm	
	Postpartum haemorrhage >1 litre or requiring transfusion	
Transient or reversible	Any surgery during pregnancy or puerperium	Excludes repair of perineum
	Hyperemesis or dehydration	
	Ovarian hyperstimulation syndrome	In the first trimester
	Admission or immobility >72 hours	'Bed rest'
	Current systemic infection	Requiring intravenous antibiotics or hospital admission
	Long distance travel	>4 hours

From Royal College of Obstetricians and Gynaecologists (2015a)

In summary, if:

- Four or more risk factors are currently present, low molecular weight heparin should be considered in the antenatal period. This anticoagulation therapy will usually continue for 6 weeks into the postnatal period, although the Royal College of Obstetricians and Gynaecologists' (2015a) guidelines do suggest that, irrespective of risk factors present during the antenatal period, a postnatal venous thromboembolism risk assessment should be repeated
- Three risk factors are currently present (excluding previous venous thromboembolism and thrombophilia), low molecular weight heparin should be considered from 28 weeks' gestation onwards and continue for 6 weeks postnatally, again following an additional postnatal risk assessment (Royal College of Obstetricians and Gynaecologists, 2015a)
- Two risk factors are currently present (excluding previous venous thromboembolism and thrombophilia), prophylactic low molecular weight heparin should be considered for 10 days postpartum (Royal College of Obstetricians and Gynaecologists, 2015a).

Pregnancy with previous venous thromboembolism

Women who have had a venous thromboembolism previously should receive pre-pregnancy counselling (or counselling as early into the pregnancy as possible), with a plan made for

anticoagulation during and after their pregnancy. They should continue with low molecular weight heparin during the antenatal period, unless the venous thromboembolism was a single occurrence in relation to previous surgery (Royal College of Obstetricians and Gynaecologists, 2015b). Women who are on oral anticoagulation because of recurring venous thromboemboli should be counselled (ideally pre-pregnancy) regarding the risks to the fetus of continuing on oral anticoagulation; they should be changed to low molecular weight heparin as early as possible in their pregnancy (Royal College of Obstetricians and Gynaecologists, 2015b).

Women with antithrombin deficiency or antiphospholipid syndrome require higher doses of low molecular weight heparin (an increase of up to 70%), continued for 6 weeks into the postnatal period or until they have been re-established on their regular oral anticoagulation (Royal College of Obstetricians and Gynaecologists, 2015b).

If the venous thromboembolism was unprovoked or the result of a transient cause (other than major surgery), thromboprophylaxis with low molecular weight heparin should be offered (Royal College of Obstetricians and Gynaecologists, 2015a,b). These women should be tested for antiphospholipid antibodies (Royal College of Obstetricians and Gynaecologists, 2015a,b). In the event that the venous thromboembolism was provoked (including by major abdominal surgery), low molecular weight heparin can be withheld until 28 weeks' gestation so long as no additional risk factors are present.

Thromboprophylaxis during labour and delivery

Women who are scheduled for an elective caesarean section, who have been on low molecular weight heparin during the antenatal period, should receive their final thromboprophylactic dose the night before their caesarean section (Royal College of Obstetricians and Gynaecologists, 2015a). No dose should be given on the morning of their caesarean section and ideally the surgery should take place in the morning (Royal College of Obstetricians and Gynaecologists, 2015a).

Anticoagulation for mechanical prosthetic heart valves

This particular subgroup of women have a morbidity rate of 41% and mortality of 9% (Vause et al, 2017). These women carry both increased thrombotic and haemorrhagic risks, given the necessity for ongoing anticoagulation throughout the peripartum period, and therefore are considered particularly high risk. Some women with mechanical prosthetic heart valves choose to avoid pregnancy altogether because of the high rates of maternal and fetal mortality and morbidity rates (Elkayam et al, 2016). The lowest rates of maternal complications have been observed when using warfarin, but dose-dependent fetal complications do occur (Vitale et al, 1999; McLintock, 2011). Low molecular weight heparin has reasonable fetal safety but not without maternal risk (Popelová et al, 2012).

The risk of complications occurring depends on a variety of factors such as the underlying cardiac diagnosis, prosthetic valve position and ventricular function. In terms of valve position, a mechanical prosthetic valve in the mitral position is associated with the highest risk of thrombosis as are right-sided prosthetic valves (Roudaut et al, 2007; Dangas et al, 2016). The risk is also affected by the presence of additional non-cardiovascular comorbidities and so the possibility of an adverse event occurring (eg valve thrombosis) will vary between individuals. When it comes to their anticoagulation needs, there needs to be a degree of individualisation. In terms of risk stratification for these high-risk women, other scoring tools can also be used, such as the modified WHO classification, those described in large studies or the ZAHARA weighted risk scoring system (Siu et al, 2001; Drenthen et al, 2010; Van Hagen et al, 2015; Silversides et al, 2018). However, the woman needs to ultimately comply with both her anticoagulation regimen and follow up, making this perhaps the most important aspect of the management.

Choice of anticoagulant in a patient with a mechanical prosthetic heart valve

Oral vitamin K antagonists may be more effective at preventing valve thrombosis, but they cross the placenta and are associated with multiple fetal developmental abnormalities such

as warfarin-specific embryopathy, fetal ocular and neurological abnormalities (McLintock, 2013). Additionally, late fetal loss and stillbirth have been reported (McLintock, 2013). Evidence supports a dose-dependent effect on the developing fetus with use of oral vitamin K antagonist, suggesting that warfarin <5 mg may be continued throughout pregnancy (McLintock, 2013). This is particularly important when counselling women regarding the risk of warfarin embryopathy and fetopathy. Unfractionated heparin and low molecular weight heparin do not cross the placenta and have also been associated with better fetal outcomes (McLintock, 2013).

The European Society of Cardiology guidelines (Regitz-Zagrosek et al, 2018) recommend oral anticoagulants in the second and third trimester, unless the patient is on warfarin >5 mg/day (Table 2). The American College of Chest Physicians (Bates et al, 2012) suggest that decisions regarding anticoagulation should be individualised, but they do not offer recommendations regarding doses (Table 3).

With regards to therapeutic monitoring when on low molecular weight heparin, peak anti-factor Xa levels 4–6 hours post dosing is recommended, allowing for regular dose adjustment (McLintock, 2013; Regitz-Zagrosek et al, 2018). Further evidence recommends measurement of anti-factor Xa trough levels, suggesting that this ensures women maintain a baseline level of anticoagulation (Goland and Elkayam, 2012; McLintock, 2013). They advise target trough anti-factor Xa levels of 0.6–0.7 IU/ml and peak anti-factor Xa levels of 1.0–1.2 IU/ml or less than 1.5 IU/ml (Elkayam and Goland, 2012; McLintock, 2013). The European Society of Cardiology (Regitz-Zagrosek et al, 2018) recommends monitoring peak levels, aiming for a lower target range of 0.8–1.0 IU/ml.

Table 2. Doses of anticoagulation for women with mechanical prosthetic heart valves as suggested by the European Society of Cardiology

All patients	Oral anticoagulants are recommended during the second and third trimester until the 36th week of gestation
Women taking warfarin <5 mg/day	Continue oral anticoagulants during the first trimester
	Discontinuation of oral anticoagulants between weeks 6 and 12 and replacement by unfractionated heparin or low molecular weight heparin may be considered on an individual basis
Women taking warfarin >5 mg/day	Discontinuation of oral anticoagulants between weeks 6 and 12 and replacement by adjusted-dose unfractionated heparin or low molecular weight heparin twice daily should be considered
	Continuation of oral anticoagulants between weeks 6 and 12 may be considered

From Regitz-Zagrosek et al (2018). Target anti-factor Xa levels for low molecular weight heparin 4–6 hours post dose are 1–1. 2 IU/ml (for right sided and mitral valves) and 0.8–1.2 IU/ml for aortic valves. At 36 hours before delivery, all women should be converted to intravenous unfractionated heparin aiming for activated partial thromboplastin time ≥2 x control. Infusion should be stopped 4–6 hours pre delivery and then restarted 4–6 hours post delivery if bleeding is not evident

Table 3. Anticoagulation for pregnant women with mechanical prosthetic heart valves as suggested by the American College of Chest Physicians

Low molecular weight heparin	Adjusted-dose, given twice daily throughout pregnancy. The dosing is adjusted to achieve manufacturer's peak anti-factor Xa level 4 hours post dose
Unfractionated heparin	Adjusted-dose, given subcutaneously, twice daily throughout pregnancy. Doses are adjusted to aim for mid-interval activated partial thromboplastin time of at least twice the control value or to achieve a plasma heparin concentration level between 0.35 and 0.70 units/ml (by factor Xa inhibition)
Unfractionated heparin or low molecular weight heparin	Continue until the 13th week of gestation and then substitute with vitamin K antagonists until closer to time of delivery. Unfractionated heparin or low molecular weight heparin is then resumed
Women at high risk of venous thromboembolism	Vitamin K antagonists with replacement of unfractionated heparin or low molecular weight heparin (as above) close to time of delivery. This is for women in whom efficacy and/or safety of unfractionated heparin or low molecular weight heparin is deemed to be a concern (eg women with older generation mechanical heart valve in the mitral position)

From Bates et al (2012)

Management of women with mechanical prosthetic heart valves can be complex, especially as they may have multiple underlying health conditions. It might also be difficult to achieve their target anticoagulation range and their compliance may not be 100%. Ideally, their care should include a multidisciplinary team consisting of a cardiology, anaesthetic and haematology consultant, and should take place in a specialised tertiary centre (European Society of Cardiology, 2018).

Use of regional anaesthesia

The main concern surrounding the use of regional anaesthesia and anticoagulation is the development of serious complications such as a spinal haematoma. In individuals without any coagulation abnormalities, these complications are very rare (Cook et al, 2009). The third National Audit Project from the Royal College of Anaesthetists (Cook et al, 2009), reported the incidence of vertebral canal haematoma after neuraxial blockade as 0.85 per 100 000 (95% confidence interval 0–1.8 per 100 000). The extent to which the risk of haemorrhagic complications is increased in patients with abnormalities of coagulation is also likely to be small (Harrop-Griffiths et al, 2013).

Thromboprophylaxis and regional anaesthesia

Regional anaesthesia (spinal, epidural or a combined spinal epidural) should be avoided for 12 hours after a prophylactic dose of low molecular weight heparin and an epidural catheter should not be removed within 12 hours of the most recent injection of therapeutic low molecular weight heparin (Harrop-Griffiths et al, 2013). It is also recommended that prophylactic dose of low molecular weight heparin should not be administered for 4 hours after a spinal injection or removal of an epidural catheter (Harrop-Griffiths et al, 2013).

If on a treatment dose of low molecular weight heparin, then unlike the European Society of Cardiology guidelines, which do not refer to obstetric patients, the Association of Anaesthetists of Great Britain and Ireland suggests categorising patients into three groups (normal, increased and high risk) for epidural bleeding at catheter removal (Table 4) (Harrop-Griffiths et al, 2013). The timing of catheter removal should be assessed on an individual basis. The Association of Anaesthetists of Great Britain and Ireland suggests waiting for 24 hours after administration of a therapeutic dose of low molecular weight heparin before considering regional anaesthesia and that it is safe to administer the next dose of therapeutic low molecular weight heparin 4 hours after removal of an epidural catheter or spinal (Harrop-Griffiths et al, 2013).

Direct oral anticoagulants in pregnancy

Owing to their shorter half life, direct oral anticoagulants have an advantage over oral vitamin K antagonist (Beyer-Westendorf et al, 2016; Steinberg and Krieger, 2017) as they may be stopped rapidly in the event of an emergency delivery. Some evidence suggests that they may not have the same extent of fetal toxicity effects as the oral vitamin K antagonist (Beyer-Westendorf et al, 2016). However, there is not enough evidence to support this currently (Regitz-Zagrosek et al, 2018). They do have a teratogenic effect, particularly rivaroxaban (Drenthen et al, 2010).

Table 4. Risk stratification for epidural bleeding after therapeutic low molecular weight heparin

Risk of epidural bleeding	Time since last dose of therapeutic low molecular weight heparin
Normal risk	More than 24 hours: safe for regional anaesthesia to be performed
Increased risk	12 and 24 hours: increased risk of epidural bleeding. Regional anaesthesia not advised, but risk of bleeding in the presence of abnormal coagulation must be weighed against risk of general anaesthesia when in labour with a full stomach (hypoxaemia and difficulty intubating)
High risk	6 and 12 hours: high risk of epidural bleeding. Regional anaesthesia not advised

From Harrop-Griffiths et al (2013)

Key points

- Careful risk assessment needs to be carried out at the start of a pregnancy to identify any prothrombotic risk factors, as pregnancy is a hypercoaguable state.
- There is guidance in the UK regarding type and dosing of thromboprophylaxis depending on underlying risk factors.
- Parturients with mechanical prosthetic heart valves have complex anticoagulation needs requiring care delivered from a multidisciplinary team in a specialist tertiary centre.
- European guidelines recommend oral vitamin K antagonists at doses of <5 mg in parturients with mechanical prosthetic heart valve throughout pregnancy (with individualised assessment between the 6th and 12th week of gestation regarding replacing to unfractionated heparin/low molecular weight heparin).

Conclusions

Anticoagulation in the obstetric population should remain at the forefront during their management – be it before, during or after a woman's labour – as venous thromboembolism remains the leading cause of maternal mortality. Thorough risk assessment should occur during the woman's pregnancy and an individualised approach with regards to appropriateness for regional anaesthesia and multidisciplinary-led care in a tertiary hospital should occur for women who are pregnant with mechanical prosthetic heart valves.

Conflicts of interest

The authors declare that there are no conflicts of interest.

Author details

[1]Department of Anaesthesia, Queen Charlotte's and Chelsea Hospital, London, UK

[2]Department of Anaesthesia and Perioperative Medicine, University College Hospital NHS Foundation Trust, London, UK

References

Bates SM, Greer IA, Middeldorp S et al. VTE, thrombophilia, antithrombotic therapy, and pregnancy: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2):e691S–e736S. https://doi.org/10.1378/chest.11-2300

Beyer-Westendorf JB, Michalski F, Tittle L et al. Pregnancy outcome in patients exposed to direct oral anticoagulants-and the challenge of event reporting. Thromb Haemost. 2016;116(4):651–658. https://doi.org/10.1160/TH16-04-0305

Cook TM, Counsell D, Wildsmith JAW, Royal College of Anaesthetists Third National Audit Project. Major complications of central neuraxial block: report on the Third National Audit Project of the Royal College of Anaesthetists. BJA. 2009;102(2):179–190. https://doi.org/10.1093/bja/aen360

Dangas GD, Weitz JI, Giustino J, Makkar R, Mehran R. Prosthetic heart valve thrombosis. J Am Coll Cardiol. 2016;68(24):2670–2689. https://doi.org/10.1016/j.jacc.2016.09.958

Drenthen W, Boersma E, Balci A et al; ZAHARA Investigators. Predictors of pregnancy complications in women with congenital heart disease. Eur Heart J. 2010;31(17):2124–2132. https://doi.org/10.1093/eurheartj/ehq200

Elkayam U, Goland S. The search for a safe and effective anticoagulation regimen in pregnant women with mechanical prosthetic heart valves. J Am Coll Cardiol. 2012;59(12):1116–1118. https://doi.org/10.1016/j.jacc.2011.12.018

Elkayam U, Goland S, Pieper PG, Silversides CK. High risk cardiac disease in pregnancy: Part I. J Am Coll Cardiol. 2016;68(4):396–419. https://doi.org/10.1016/j.jacc.2016.05.048

Goland S, Elkayam U. Anticoagulation in pregnancy. Cardiol Clin. 2012;30(3):395–405. https://doi.org/10.1016/j.ccl.2012.05.003

Harrop-Griffiths W, Cook T, Gill H et al. Regional anaesthesia and patients with abnormalities of coagulation: The Association of Anaesthetists of Great Britain and Ireland. The Obstetric

Curriculum checklist

This article addresses the following requirements from the general internal medicine training curriculum:

- Is focused on patient safety and delivers effective quality improvement in patient care
- Managing an acute specialty-related take
- Managing medical problems in patients in other specialties and special cases.

Anaesthetists Association. Regional Anaesthesia UK. Membership of the Working Party. Anaesthesia. 2013;68(9):966–972. https://doi.org/10.1111/anae.12359

Knight M, Bunch K, Tuffnell D et al (eds.). Saving lives, improving mothers' care - lessons learned to inform maternity care from the UK and Ireland confidential enquiries into maternal deaths and morbidity 2014-16. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2018

McLintock C. Anticoagulation therapy in pregnant women with mechanical prosthetic heart valves: no easy option. Thromb Res. 2011;127(Suppl 3):S56–S60. https://doi.org/10.1016/S0049-3848(11)70016-0

McLintock C. Anticoagulant choices in pregnant women with mechanical heart valves: balancing maternal and fetal risks-the difference the dose makes. Throm Res. 2013;131(1):S8–10. https://doi.org/10.1016/S0049-3848(13)70010-0

Popelová J, Zatočil T, Vavera Z et al. Mechanical heart valve prosthesis in pregnancy – multicenter retrospective observational study. Cor Vasa. 2012;54(7–8):e217–e222. https://doi.org/10.1016/j.crvasa.2012.06.003

Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J et al. ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J. 2018;39(34):3165–3241. https://doi.org/10.1093/eurheartj/ehy340

Roudaut R, Serri K, Lafitte S. Thrombosis of prosthetic heart valves: diagnosis and therapeutic considerations. Heart. 2007;93(1):137–142. https://doi.org/10.1136/hrt.2005.071183

Royal College of Obstetricians and Gynaecologists. Reducing the risk of venous thromboembolism during pregnancy and the puerperium period. Green top guideline No 37a. 2015a. https://www.rcog.org.uk/globalassets/documents/guidelines/gtg-37a.pdf (accessed 15 March 2021)

Royal College of Obstetricians and Gynaecologists. Thromboembolic disease in pregnancy and the puerperium: acute management. Green top guideline No. 37b. 2015b. https://www.rcog.org.uk/globalassets/documents/guidelines/gtg-37b.pdf (accessed 15 March 2021)

Silversides CK, Grewal J, Mason J et al. Pregnancy outcomes in women with heart disease. The CARPREG II Study. J Am Coll Cardiol. 2018;71(21):2419–2430. https://doi.org/10.1016/j.jacc.2018.02.076

Siu SC, Sermer M, Colman JM et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. Circulation. 2001;104(5):515–521. https://doi.org/10.1161/hc3001.093437

Steinberg ZL, Krieger EV. Reply: the anticoagulation conundrum of mechanical heart valves in pregnancy: Should DOACs be considered? J Am Coll Cardiol. 2017;70(24):3074–3075. https://doi.org/10.1016/j.jacc.2017.09.1139

Van Hagen IM, Roos-Hesselink JW, Ruys TPE et al. Pregnancy in women with a mechanical heart valve data of the European Society of Cardiology Registry of Pregnancy and Cardiac Disease (ROPAC). Circulation. 2015;132(2):132–142. https://doi.org/10.1161/CIRCULATIONAHA.115.015242

Vause S, Clarke B, Tower CL et al. Pregnancy outcomes in women with mechanical prosthetic heart valves: a prospective descriptive population based study using the United Kingdom Obstetric Surveillance System (UKOSS) data collection system. BJOG. 2017;124(9):1411–1419. https://doi.org/10.1111/1471-0528.14478

Vitale N, De Feo M, De Santo LS et al. Dose dependent fetal complications of warfarin in pregnant women with mechanical heart valves. J Am Coll Cardiol. 1999;33(6):1637–1641. https://doi.org/10.1016/S0735-1097(99)00044-3