

Thromboprophylaxis in IVF

Accepted by the Swedish Society of Obstetrics and Gynecology at January 31st 2014

Revised in 2015

Background

There are approximately 17000 IVF treatments performed annually in Sweden. The risk of both arterial and venous thrombosis increases with ovarian hyperstimulation syndrome (OHSS). The risk of thrombosis in pregnancy decreases by 85-90 % when recommended thromboprophylaxis is used (HEM-ARG, Lindqvist-11).

National guidelines regarding thromboprophylaxis in IVF have previously not been available in Sweden. SFOG (Swedish Association of Obstetrics and Gynecology) requested in 2010 that Hem-ARG (A working and reference group for haemostatic disorders in Obstetrics and Gynecology) would provide evidence based guidelines on this subject. The GRADE system (Grading of Recommendations Assessment Development and Evaluation) should be used and the method accounted for.

Guidelines.

1. Thromboprophylaxis is not indicated in patients without known risk factors undergoing IVF treatment.

GRADE ⊕⊕○○. Strong recommendation.

2. Patients diagnosed with OHSS and who need hospitalization or intervention should be started on thromboprophylaxis immediately. Thromboprophylaxis should be continued until resolution of OHSS or at least until week 12+6 in pregnancy.

In the presence of other risk factors thromboprophylaxis should be continued according to the scoring system in HEM-ARG guidelines (see below).

GRADE ⊕⊕⊕○. Strong recommendation.

3. Thromboprophylaxis can be discontinued 4 weeks after resolution of OHSS in patients that are not pregnant.

GRADE ⊕⊕⊕○. Strong recommendation.

4. A decision regarding thromboprophylaxis (risk score ≥ 2) during IVF stimulation and pregnancy should be made by the referring clinician before referral to an IVF clinic.

GRADE $\oplus\circ\circ\circ$. Strong recommendation.

5. In patients where thromboprophylaxis is indicated during pregnancy this should be initiated at the start of FSH/HMG stimulation.

GRADE $\oplus\oplus\circ\circ$. Strong recommendation.

6. Frozen embryo replacement in women with known risk factors for thrombosis should preferably be done in a natural cycle. If stimulation is considered necessary, thromboprophylaxis should be commenced at the start of stimulation.

GRADE $\oplus\circ\circ\circ$. Strong recommendation.

7. An individual plan is recommended in patients with “very high risk” of thrombosis (see below).

GRADE $\oplus\circ\circ\circ$. Strong recommendation.

8. Discontinuation of normal dose prophylaxis is not needed before a laparocentesis (“normal” thromboprophylactic dose).

To decrease the risk of hemorrhage at follicular aspiration, thromboprophylaxis should be withheld in the morning before a follicular aspiration and restarted in the evening.

GRADE $\oplus\circ\circ\circ$. Strong recommendation.

For references please contact Hem-ARG at www.sfog.se

Table 1. Summation of added risk points decides management according to Table 2

1 point	2 points	3 points	4 points	"Very high risk"
Het FV Leiden	Protein S deficiency	Hom FV Leiden	Prior VTE ⁵	Mechanical aortic valve
Het prothrombin mutation	Protein C deficiency	Hom prothrombin	APS without VTE ^{5,6}	Condition warranting chronic warfarine treatment
Obesity ¹	Immobilisation ⁴	More than one thrombophilic defect		VTE with APS ⁶
Cesarean section				Recurrent VTE
Hereditary factors ²				Antithrombin deficiency
Age >40 years				
Preeclampsia				
Hyperhomocysteinemia ³				
Placental abruption				
Inflammatory bowel disease				
Other major risk factors				

Het: heterozygote, FV: factor V, VTE: venous thromboembolism, Hom: homozygote, APS: antiphospholipid syndrome with lupus anticoagulant or cardiolipin antibodies

1. Obesity (BMI >28 in early pregnancy) at booking to antenatal clinic
2. VTE in a 1st degree relative < 60 years
3. Homocysteine >8 umol/L in pregnancy
4. Thromboprophylaxis should be provided during the period of strict immobilization or if the patient has a cast
5. Patients with previous VTE, or APS without VTE, automatically receive 4 points disregarding other risks.
6. Patients with phospholipid antibodies (APLA) should also be treated with ASA 75 mg x 1, see Table 2

Table 2

Management based on risk score assessment (summation of risk points in Table 1)

1 point	thromboprophylaxis not needed
2 points	thromboprophylaxis postpartum once daily at least 7 days, this includes thromboprophylaxis for a transient risk factor
3 points	thromboprophylaxis once daily 6 weeks postpartum
4 points	thromboprophylaxis once daily throughout pregnancy* and at least 6 weeks postpartum
“Very high risk”	thromboprophylaxis twice daily (=double dose) throughout pregnancy* and at least 12 weeks postpartum

Patients requiring special treatment

Hereditary antithrombin deficiency: High dose thromboprophylaxis twice daily (=double dose) starting at positive pregnancy test and supplement with antithrombin concentrate during delivery and in case of complications

Individual assessment if start of thromboprophylaxis should be before pregnancy or in early pregnancy

APS and previous VTE: thromboprophylaxis twice daily (=double dose) and ASA 75 mg x1

*Antepartum thromboprophylaxis should be started in early pregnancy