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**Date:** 27 June 2019

**Sources Searched:** Medline, Embase.

## Fondaparinux in Pregnancy

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[See full search strategy](#)

### 1. Fondaparinux - data on efficacy and safety in special situations.

**Author(s):** Nagler, Michael; Haslauer, Michael; Wuillemin, Walter A

**Source:** Thrombosis research; Apr 2012; vol. 129 (no. 4); p. 407-417

**Publication Date:** Apr 2012

**Publication Type(s):** Journal Article Review

**PubMedID:** 22133273

**Abstract:** New anticoagulants promise to have better efficacy, more safety and/or a better manageability than traditional anticoagulants. However, knowledge is limited regarding special situations such as renal insufficiency, obesity, pregnancy, long-term therapy, heparin-induced thrombocytopenia, treatment in patients with mechanical heart valves, use for children, and in patients with a high risk of thromboembolic complications. These situations have rarely or even never been the objective of randomised controlled trials. The purpose of the present article is to summarize and discuss available data on efficacy and safety in these special situations for one of the first new anticoagulants, the indirect factor-Xa inhibitor fondaparinux. Furthermore, we discuss safety in licensed indications and management of bleeding complications and comment on measuring of drug concentration in plasma.

**Database:** Medline

### 2. Fondaparinux in pregnancy: Could it be a safe option? A review of the literature.

**Author(s):** De Carolis, S; di Pasquo, E; Rossi, E; Del Sordo, G; Buonomo, A; Schiavino, D; Lanzone, A; De Stefano, V

**Source:** Thrombosis research; Jun 2015; vol. 135 (no. 6); p. 1049-1051

**Publication Date:** Jun 2015

**Publication Type(s):** Journal Article Review

**PubMedID:** 25912931

**Abstract:** During pregnancy thrombo-prophylaxis could be required in high risk women. If a severe allergic reaction to low-molecular-weight-heparin (LMWH) or a heparin-induced-thrombocytopenia (HIT) occurs, it's mandatory to stop the drug. Fondaparinux could be an effective option. In the present review, the maternal and pregnancy outcomes of 65 pregnancies in women using Fondaparinux were reported. It was well-tolerated and rate of pregnancy complications was similar

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to that observed in general population. Regarding congenital malformations, further studies are necessary to investigate the safety of the drug.

**Database:** Medline

### **3. Fondaparinux use in pregnancy-'the Mid-Yorkshire Experience'**

**Author(s):** Herbert L.; Vacchiyat K.; Hussein H.Y.W.

**Source:** BJOG: An International Journal of Obstetrics and Gynaecology; Mar 2019; vol. 126 ; p. 21

**Publication Date:** Mar 2019

**Publication Type(s):** Conference Abstract

Available at [BJOG: An International Journal of Obstetrics and Gynaecology](#) - from Wiley Online Library Science , Technology and Medicine Collection 2017

Available at [BJOG: An International Journal of Obstetrics and Gynaecology](#) - from Unpaywall

**Abstract:**Background Venous thromboembolism (VTE) remains one of the leading causes of maternal death in the UK. RCOG guidelines favour low-molecular-weight heparins (LMWH) for the safe and effective option for prevention and treatment of VTE in pregnancy. Fondaparinux, a synthetic pentasaccharide which works similarly to porcine-based LMWH, is currently only licensed for use outside of pregnancy. Fondaparinux is advised for those intolerant of heparin compounds alongside haematology input. It is being increasingly used in pregnancy despite the RCOG guidelines. Fondaparinux is around three times more expensive than traditional LMWH. Method Retrospective case note review of patients dispensed fondaparinux through the Mid-Yorkshire Hospital Trust (MYHT) pharmacies between September 2017 and September 2018. Results 14 patients identified, and 13 notes reviewed and analysed. One had fondaparinux antenatally, and all 13 had it postnatally. Six had no clear documentation for why fondaparinux was prescribed. Two stated patient refusal of dalteparin, but no reason given. Four patients stated vegetarian reasons, and two stated religious reasons. None had haematology input. The majority of patients were of an Asian background or had Islamic beliefs. Discussion Maternal choice due to LMWH's porcine nature is the most common reason for the use of Fondaparinux. Guidelines suggest haematology advice should be sought; however, this is often not followed. At MYHT, it must be considered if Fondaparinux should be added to guidelines given the high cost and whether maternal request is an appropriate indication. Addition to guidelines would, however, ensure safe prescribing with the inclusion of haematology input.

**Database:** EMBASE

#### **4. Efficacy and safety of venous thromboembolism prophylaxis with fondaparinux in women at risk after cesarean section.**

**Author(s):** Kawaguchi, Ryuji; Haruta, Shoji; Kobayashi, Hiroshi

**Source:** Obstetrics & gynecology science; Nov 2017; vol. 60 (no. 6); p. 535-541

**Publication Date:** Nov 2017

**Publication Type(s):** Journal Article

**PubMedID:** 29184861

Available at [Obstetrics & gynecology science](#) - from Europe PubMed Central - Open Access

Available at [Obstetrics & gynecology science](#) - from Unpaywall

**Abstract:** Objectives Cesarean section is associated with an increased risk for venous thromboembolism (VTE). The safety and efficacy of primary prophylaxis of fondaparinux, a synthetic sulfated pentasaccharide heparin analog, in women at risk after cesarean section is uncertain. Methods This was a retrospective study of 295 cases of pregnant women presenting to a tertiary referral center of Nara, Japan, to evaluate the usefulness of thromboprophylaxis with fondaparinux after cesarean delivery between 2011 and 2012. Patients were initially received unfractionated heparin (once 5,000 IU subcutaneously, twice a day), starting 6 hours after cesarean section for 24 hours, and then treated with fondaparinux (once 2.5 mg daily, subcutaneously) for 5 days. The primary efficacy end-point was an improvement in the incidence of symptomatic VTE or fatal post-cesarean pulmonary thromboembolism. The primary safety end-point was major bleeding during treatment. Results There were neither any episodes of symptomatic VTE cases nor maternal deaths. A total of 10 patients had a bleeding event. Major bleeding complication was observed in 2 (0.68%) of 295 patients receiving fondaparinux. Non-major bleeding into critical sites was observed in 8 patients, often at surgical sites, and recovery was not delayed. Conclusion This study demonstrates the safety and efficacy of fondaparinux in women at high risk of VTE after cesarean section. Large phase trials comparing clinical outcomes with fondaparinux across a wide spectrum of patients are needed to confirm these observations.

**Database:** Medline

**5. Retrospective study of patients who were treated with fondaparinux pre-, peri-and/or postpartum for prophylaxis or treatment of venous thromboembolism (FONDAPPP)**

**Author(s):** Dempfle C.-E.; Koscielny J.; Lindhoff-Last E.; Oldenburg J.; Pollmann H.; Kappert G.; Scholz U.; Kropff S.; Eberle S.; Heinken A.

**Source:** Journal of Thrombosis and Haemostasis; Jun 2015; vol. 13 ; p. 680-681

**Publication Date:** Jun 2015

**Publication Type(s):** Conference Abstract

Available at [Journal of Thrombosis and Haemostasis](#) - from Wiley Online Library Science , Technology and Medicine Collection 2017

Available at [Journal of Thrombosis and Haemostasis](#) - from Unpaywall

**Abstract:**Background: Low-molecular weight heparins (LMWH) are the preferred agents for anticoagulation in pregnancy. Still, in a considerable proportion of pregnancies heparin intolerance (allergic reactions, HIT, increases in liver enzymes or other events) make it necessary to change to another anticoagulant. Fondaparinux is a synthetic selective indirect inhibitor of factor Xa with a favourable efficacy/safety profile compared to LMWH. Aims: In this retrospective multi-center study we descriptively analyzed data of women who had been treated for  $\geq 7$  days with fondaparinux during pregnancy. Methods: In total, 120 women (mean  $\pm$  SD] age 31.5  $\pm$  5.4 years) from 7 specialist centres were included. Of 85 women with former pregnancy 60.0% had suffered  $\geq 1$  abortion. The indication of anticoagulation was prophylactic in 92.5% of all women, in 99 women (82.5%) specifically due to an elevated VTE risk. Of these, 82.8% had known thrombophilia (mostly without previous VTE) and 33.3% a history of VTE. All women received LMWH first-line (median treatment duration: 54 days) (3 additionally received UFH). Mainly due to heparin allergy or heparin-induced thrombocytopenia (HIT-2) treatment was changed to fondaparinux (predominant dose 2.5 mg day<sup>-1</sup>; median treatment duration: 131 days). Results: Fondaparinux was well tolerated, with no complications reported in 111 of 120 patients. Adverse events included one case of abdominal wall hematoma, four cases of vaginal hemorrhage, one hemorrhage of other location, one drop in platelet count without thrombotic complications, one abortion, one premature birth, one stillbirth, and one child born with trisomy 18. Thromboembolic events, allergic reactions, or increased liver enzymes, did not occur during fondaparinux treatment. Conclusion: In this retrospective study, a notable number of pregnant women at risk of VTE and with intolerance to LMWH received successful and safe long-term treatment with fondaparinux.

**Database:** EMBASE



## **6. A retrospective analysis of fondaparinux versus enoxaparin treatment in women with infertility or pregnancy loss.**

**Author(s):** Winger, Edward E; Reed, Jane L

**Source:** American journal of reproductive immunology (New York, N.Y. : 1989); Oct 2009; vol. 62 (no. 4); p. 253-260

**Publication Date:** Oct 2009

**Publication Type(s):** Comparative Study Journal Article

**PubMedID:** 19703143

Available at [American journal of reproductive immunology \(New York, N.Y. : 1989\)](#) - from Wiley Online Library Science , Technology and Medicine Collection 2017

**Abstract:**PROBLEMWe compared the pregnancy success rates and safety parameters of fondaparinux versus enoxaparin, combined with immunotherapy, in patients with a history of miscarriage and/or infertility and coagulant defects.METHOD OF STUDYA total of 127 pregnancies in 110 patients with a history of miscarriage and/or infertility were retrospectively evaluated. Of these, 29 pregnancies used fondaparinux 2.5 mg daily and 98 pregnancies used enoxaparin 30 mg twice daily.RESULTSThe pregnancy success rate was 59% (17/29; 95% CI, 41-75%) for patients receiving fondaparinux and 58% (57/98; 95% CI, 48-68%) for patients receiving enoxaparin. No difference was detected in birth weight (2.7 +/- 0.8 and 2.9 +/- 0.6 kg, respectively) or gestational age at delivery (37.3 +/- 2.2 and 37.7 +/- 2.1 weeks, respectively). No birth defects, severe bleeding-related complications, or serious allergic reactions were observed.CONCLUSIONIn patients with a history of miscarriage, infertility, and coagulant defects receiving immunotherapy, fondaparinux resulted in successful pregnancy outcomes comparable with enoxaparin therapy. Although no difference in outcome was observed in our analysis, a much larger study is required to achieve statistical power.

**Database:** Medline

## **7. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy**

**Author(s):** Regitz-Zagrosek V.; Bauersachs J.; Kintscher U.; Kranke P.; Seeland U.; Hindricks G.; Katus H.A.; Roos-Hesselink J.W.; Pieper P.G.; Delgado V.; Blomstrom-Lundqvist C.; Cifkova R.; De Bonis M.; Presbitero P.; Simoncini T.; Barbato E.; Piepoli M.F.; Iung B.; Aboyans V.; Collet J.-P.; Dean V.;



Leclercq C.; Johnson M.R.; Price S.; Rosano G.M.C.; Swan L.; Fitzsimons D.; McDonagh T.A.; Simpson I.A.; Lang I.M.; Morais J.; Sousa-Uva M.; Warnes C.A.; Windecker S.; Gaemperli O.; Roffi M.; Agewall S.; Bueno H.; Coca A.; Zamorano J.L.; Coman I.M.; Juni P.; Knuuti J.; Lancellotti P.; Ponikowski P.; Richter D.J.; Shlyakhto E.; Hammoudi N.; Piruzyan A.; Mascherbauer J.; Samadov F.; Prystrom A.; Pasquet A.; Caluk J.; Gotcheva N.; Skoric B.; Heracleous H.; Vejlsturp N.; Maser M.; Kaaja R.J.; Srbínovska-Kostovska E.; Mounier-Vehier C.; Vakhtangadze T.; Rybak K.; Giannakoulas G.; Kiss R.G.; Thrainsdóttir I.S.; Erwin R.J.; Porter A.; Geraci G.; Ibrahimi P.; Lunegova O.; Mintale I.; Kadri Z.; Benlamin H.; Barysiene J.; Banu C.A.; Caruana M.; Grati C.; Haddour L.; Bouma B.J.; Estensen M.-E.; Hoffman P.; Petris A.O.; Moiseeva O.; Bertelli L.; Tesic B.V.; Dubrava J.; Kozelj M.; Prieto-Arevalo R.; Furenas E.; Schwerzmann M.; Mourali M.S.; Ozer N.; Mitchenko O.; Nelson-Piercy C.

**Source:** European Heart Journal; Sep 2018; vol. 39 (no. 34); p. 3165-3241

**Publication Date:** Sep 2018

**Publication Type(s):** Review

Available at [European Heart Journal](#) - from Oxford Journals - Medicine

Available at [European Heart Journal](#) - from Unpaywall

**Database:** EMBASE

## **8. Management of Venous Thromboembolism in Pregnancy**

**Author(s):** Fogerty A.E.

**Source:** Current Treatment Options in Cardiovascular Medicine; Aug 2018; vol. 20 (no. 8)

**Publication Date:** Aug 2018

**Publication Type(s):** Review

Available at [Current Treatment Options in Cardiovascular Medicine](#) - from SpringerLink - Medicine

**Abstract:** Purpose of review: This manuscript addresses the risks for venous thromboembolism (VTE) during pregnancy and the associated challenges of both diagnosis and treatment. Recent findings: The obstacles to diagnosis given lack of specificity of typical biomarkers to predict VTE in pregnancy, as well as the unique fetal and bleeding risks introduced by managing massive pulmonary embolism (PE) with thrombolytics or thrombectomy are highlighted. Summary: VTE during pregnancy and the postpartum window occurs at a 6-10-fold higher rate compared with age-matched peers and is a major cause of morbidity and mortality. Hypercoagulability persists for 6-8 weeks after delivery with the highest risk of PE being postpartum. The lack of randomized trials in pregnant women leads to variability in practice, which are largely based on expert consensus or extrapolation from non-pregnant cohorts. The standard treatment of VTE in pregnancy is anticoagulation with low molecular weight heparin (LMWH), which like unfractionated heparin does not cross the placenta and is not teratogenic. LMWH is preferred given the negligible risk for heparin-induced thrombocytopenia and osteoporosis, better bioavailability, and a predictive dose response. Depending on the severity of the VTE, additional treatments including thrombolysis, thrombectomy, inferior vena cava filter placement, or venous stenting may be used. Management requires balancing the competing bleeding and thrombotic risks during labor and delivery and factoring the impact of treatment on the fetus. A multidisciplinary team involving hematology, obstetrics, anesthesia, vascular medicine, and cardiology is critical for safe and timely management. The design and execution of prospective, randomized trials to specifically address optimal diagnosis and management are a top priority in obstetric hematology. Copyright © 2018, Springer Science+Business Media, LLC, part of Springer Nature.

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**Database:** EMBASE

## **9. The Safety of Low-Molecular-Weight Heparin during and after Pregnancy**

**Author(s):** Lu E.; Shatzel J.J.; Salati J.; Deloughery T.G.

**Source:** Obstetrical and Gynecological Survey; Dec 2017; vol. 72 (no. 12); p. 721-729

**Publication Date:** Dec 2017

**Publication Type(s):** Article

**PubMedID:** 29280473

Available at [Obstetrical and Gynecological Survey](#) - from Ovid (LWW Total Access Collection 2019 - with Neurology)

**Abstract:** Importance In industrialized countries, venous thromboembolism remains a leading cause of mortality in pregnant women. Low-molecular-weight heparin (LMWH) is the most commonly recommended anticoagulant in pregnancy, having been proven effective and safe in multiple prospective clinical trials. Objective The aim of this article is to outline existing recommendations for proper use of LMWH in pregnancy and data on risks of LMWH. Evidence Acquisition We reviewed guidelines from a number of professional societies. We also examined the current literature behind the various risks associated with LMWH use. Results and Conclusions Our review outlines the current data that guide the use of LMWH in pregnancy. With prophylactic dosing, LMWH comes with a 0.5% risk of antepartum bleeding and a 1% risk of postpartum hemorrhage that is not different from clinical trial controls. With treatment dosing, there is a 1.5% risk of antepartum bleeding and a 2% risk of postpartum hemorrhage. Overall, current evidence behind these risks is limited, and this review suggests areas of further study moving forward. Target Audience Obstetricians and gynecologists, family physicians. Learning Objectives After completing this activity, the learner should be better able to define the specific risk factors and preexisting conditions that would warrant LMWH use in pregnancy and postpartum; describe the different available doses of LMWH,

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when to use each dose, and when monitoring is appropriate; and discuss the risks of anticoagulation with LMWH during various stages of pregnancy and birth. Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.

**Database:** EMBASE

## 10. Challenges of Anticoagulation Therapy in Pregnancy

**Author(s):** Fogerty A.E.

**Source:** Current Treatment Options in Cardiovascular Medicine; Oct 2017; vol. 19 (no. 10)

**Publication Date:** Oct 2017

**Publication Type(s):** Review

Available at [Current Treatment Options in Cardiovascular Medicine](#) - from SpringerLink - Medicine

**Abstract:**Thrombotic complications in pregnancy represent a major cause of morbidity and mortality. Pregnancy is a primary hypercoagulable state due to enhanced production of clotting factors, a decrease in protein S activity, and inhibition of fibrinolysis. These physiologic changes will yield a collective rate of venous thromboembolism (VTE) of about 1-2 in 1000 pregnancies for the general obstetric population, which represents a five- to tenfold increased risk in pregnancy compared to age-matched non-pregnant peers. A select group of women, however, will carry a significantly higher rate of thrombosis due to primary thrombophilia, either inherited or acquired. This introduces a population of women who may benefit from prophylactic anticoagulation, either antepartum or postpartum. The coagulation changes that occur in preparation for the hemostatic challenges of delivery endure for several weeks postpartum. In fact, daily risk for pulmonary embolism (PE) is the highest postpartum. Use of anticoagulation in pregnancy introduces particular risk at the time of delivery, where bleeding and clotting risk collide. Altered metabolism rates of anticoagulants in pregnant women often necessitate closer monitoring than is required outside of



pregnancy in order to ensure efficacy and safety. Heparin products are the mainstay of treating VTE in pregnancy, chiefly because they do not cross the placenta. In women with mechanical heart valves, the ideal anticoagulation regimen remains controversial as heparin use has shown inferior outcomes for preventing thromboembolic complications compared to warfarin, but warfarin carries risk for fetal embryopathy. Other populations where a heparin alternative is necessary include women with a history of heparin-associated thrombocytopenia (HIT) or other heparin intolerance. Further challenging the management of anticoagulation in pregnancy is the dearth of randomized clinical trials. The evidence governing treatment recommendations is largely based on expert guidelines, observational studies, or extrapolation from non-pregnant cohorts. A careful critique of a woman's history, as well as the available data, is essential for optimal management of anticoagulation in pregnancy. Such decisions should involve a multidisciplinary team involving obstetrics, hematology, cardiology, and anesthesia. Copyright © 2017, Springer Science+Business Media, LLC.

**Database:** EMBASE

**11. Use of fondaparinux for thromboprophylaxis in an unfractionated heparin-intolerant pregnant woman with thrombotic predisposition.**

**Author(s):** Haruta, Shoji; Maruta, Kana; Nakajima, Yoshiyuki; Masaoka, Naoki

**Source:** The journal of obstetrics and gynaecology research; May 2017; vol. 43 (no. 5); p. 943-945

**Publication Date:** May 2017

**Publication Type(s):** Case Reports

**PubMedID:** 28437037

Available at [The journal of obstetrics and gynaecology research](#) - from Wiley Online Library Science , Technology and Medicine Collection 2017

**Abstract:** A 34-year-old primigravida who had undergone thrombectomy for deep venous thrombosis (DVT) in her leg and exhibited low protein S activity, indicating predisposition to thrombosis, developed DVT of the leg. No pulmonary embolism was detected. After anticoagulant therapy with unfractionated heparin was discontinued because of liver dysfunction, danaparoid treatment was administered in hospital. The patient had a normal delivery after 39 weeks' gestation with no recurrence of thrombosis. During her second pregnancy four years later, she gave herself

fondaparinux injections. She delivered normally after 38 weeks' gestation without experiencing DVT. Fondaparinux may be a useful anticoagulant for heparin-intolerant pregnant women.

**Database:** Medline

## **12. Treatment of risk pregnancies and Fondaparinux and acetylsalicylic acid**

**Author(s):** Kiesewetter H.; Schmidt F.-P.; Becker R.

**Source:** Hamostaseologie; 2016; vol. 36

**Publication Date:** 2016

**Publication Type(s):** Conference Abstract

**Abstract:** Introduction: The effectiveness of Fondaparinux (F) in combination of acetylsalicylic acid by patients with risk pregnancies was examined prospectively. Patients and methods: The data of 155 pregnant women between the age of 24-50 (height 154-182cm and weight 48-127kg) have been analyzed. 83 had abortions before the 15th week of pregnancy, between 15th and the 24th week of pregnancy or stillbirth. 76 of them were treated with F 2,5mg. 7 out of them had obesity or heavier inflammation and therefore they were treated with 5mg. 5 out them had a APA- syndrome and were treated in combination of acetylsalicylic acid. 2 patients with missed injections of sperms into cytoplasm were infused subcutaneously with Foundaparinux (2 F 1,5mg, 8 F 2,5mg, 2 F 5 mg) 2 days before the transfer daily. 25 patients had notches recently, 12 had a preeclampsia and 6 had a HELLPsyndrome in the last pregnancy. 28 had a former and 10 had a recent venous thromboembolism (3 out of them had a APA- Syndrome), 4 former sinus venous thrombosis, 10 had a thrombophlebitis (with high thrombophilic risk). 18 out of them infused F2,5mg, 33 F 5mg, 6 F 7,5mg and 3 F 10mg, 43 were treated with acetylsalicylic acid as well (multiple diagnosis are possible). The primer variable was the alive birth rate. Results: 2 of the patients with abortions before the 15th week of pregnancy, between 15th and the 24th week of pregnancy or stillbirth in former pregnancy had abortions in the 8th week of pregnancy (start of the treatment in the 7th week of pregnancy). All 12 patients with missed injections of sperms into cytoplasm got pregnant, at least after the second transfer. All patients born healthy children. All 60 patients with notches preeclampsia or HELLP-syndrome born healthy children. 2 out of them had a caesarean section , because they had a acute preeclampsia. Another 2 had a local allergic reaction and another 2 declared a general indisposition, infused Fondaparinux nevertheless till 3 weeks after birth. Conclusion: Fondaparinux according to the high effectiveness and safety. Fondaparinux can be used safely during pregnancy.

**Database:** EMBASE

## **13. Hypersensitivity reactions to low molecular weight heparin in a pregnant woman**

**Author(s):** Canti V.; Yacoub M.-R.; Della-Torre E.; Colombo G.

**Source:** Current Allergy and Clinical Immunology; 2015; vol. 28 (no. 1); p. 34-35

**Publication Date:** 2015

**Publication Type(s):** Article

**Database:** EMBASE



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#### 14. The use of fondaparinux in pregnancy

**Author(s):** Elsaigh E.; Thachil J.; Nash M.J.; Hay C.R.M.; Tower C.; Bullough S.; Byrd L.

**Source:** British Journal of Haematology; Mar 2015; vol. 168 (no. 5); p. 762-764

**Publication Date:** Mar 2015

**Publication Type(s):** Article

**PubMedID:** 25270038

Available at [British Journal of Haematology](#) - from Wiley Online Library Science , Technology and Medicine Collection 2017

Available at [British Journal of Haematology](#) - from Unpaywall

**Database:** EMBASE

#### 15. A case of heparin allergy with good tolerability of fondaparinux during pregnancy

**Author(s):** Pascolini L.; Buonomo A.; Colagiovanni A.; Pecora V.; Rizzi A.; Aruanno A.; Ricci A.G.; Di Rienzo A.; Centrone M.; Sikora A.; Nucera E.; Schiavino D.

**Source:** Allergy: European Journal of Allergy and Clinical Immunology; Sep 2014; vol. 69 ; p. 356

**Publication Date:** Sep 2014

**Publication Type(s):** Conference Abstract

Available at [Allergy: European Journal of Allergy and Clinical Immunology](#) - from Wiley Online Library Science , Technology and Medicine Collection 2017

**Abstract:**Background: Fondaparinux sodium is a synthetic pentasaccharide which strongly binds to antithrombin and enhances the inactivation of factor Xa without interaction with factor II or platelets. Several studies have shown the lack of cross-reactivity of fondaparinux with unfractionated heparins and low molecularweight heparins. For this reason fondaparinux is the drug of choice in patients with heparin allergy. We report the case of a 40 yearold woman suffering from essential thrombocytemia who had a clinical history of intrauterine fetal death and recurrent pulmonary embolism and developed urticaria and dysphagia during treatment with calcium nadroparin. Method: The patient underwent skin prick test and intradermal test with sodium heparin, calcium heparin, sodium enoxaparin, calcium nadroparin, sodium reviparin, sodium dalteparin and sodium fondaparinux. Since the patient needed anticoagulant treatment because she planned a pregnancy, we decided to perform a challenge test with an alternative compound on the basis of allergy testing results. Results: Skin test with both unfractionated and low molecular weight heparins showed a positive response while skin tests with fondaparinux were negative. These results were consistent an IgE-mediated allergy to heparins and confirmed the lack of cross-reactivity of fondaparinux with other heparins. Then the patient well tolerated a therapeutic dose of 2.5 mg of fondaparinux. When the patient became pregnant treatment with sodium fondaparinux was promptly started. No adverse reactions were observed. At the 36th week, the patient underwent caesarean delivery and a healthy female baby was born. Conclusion: Fondaparinux has shown to be safe and effective in pregnant patients but larger studies are needed to assess tolerability. We recommend to perform allergy testing in case of type I or type IV hypersensitivity reactions to exclude crossreactivity before any treatment with fondaparinux to avoid unexpected reactions.

**Database:** EMBASE



**16. A systematic review on the use of new anticoagulants in pregnancy.**

**Author(s):** Tang, Ai-Wei; Greer, Ian

**Source:** Obstetric medicine; Jun 2013; vol. 6 (no. 2); p. 64-71

**Publication Date:** Jun 2013

**Publication Type(s):** Journal Article

**PubMedID:** 27757159

Available at [Obstetric medicine](#) - from Europe PubMed Central - Open Access

Available at [Obstetric medicine](#) - from Unpaywall

**Abstract:** New anticoagulants such as direct factor Xa inhibitors and direct thrombin inhibitors have been recently developed, but their experience in pregnancy is limited. This review therefore aims to systematically search for studies on the use of these newer anticoagulants in pregnancy and the puerperal period. Searches were performed on electronic databases MEDLINE (from 1966), EMBASE (from 1974) and the Cochrane Library, until October 2011 using terms of 'pregnancy', 'puerperium', 'breastfeeding' and names of specific anticoagulants. The search yielded 561 citations and 11 studies (10 on fondaparinux, 1 on ximelagatran) were included. Newer anticoagulants (fondaparinux, hirudin and argatroban) on the limited evidence appear not to have adverse pregnancy outcomes, but there is currently no experience of new oral anticoagulants (rivaroxaban, apixaban, betrixaban or dabigatran) use in pregnancy. There is a need for reporting on new oral anticoagulation use in pregnancy to provide more information about the safety and risks to the fetus in utero.

**Database:** Medline

**17. Safety of fondaparinux in pregnancy- experience of a north west tertiary referral clinic**

**Author(s):** Musial N.; Byrd L.

**Source:** Archives of Disease in Childhood: Fetal and Neonatal Edition; Apr 2013; vol. 98

**Publication Date:** Apr 2013

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**Publication Type(s):** Conference Abstract

Available at [Archives of Disease in Childhood: Fetal and Neonatal Edition](#) - from BMJ Journals - NHS

**Abstract:** Venous thromboembolism (VTE) is amongst the leading causes of maternal death in developed countries. Several series have confirmed the safety and efficacy of LMWHs in pregnancy and it has become the favoured anticoagulant. Adverse skin reactions to LMWHs are rare but recognised events, whereupon a particular LMWH may be successfully replaced with another one. However if the skin symptoms do not improve an alternative must be sought. Fondaparinux is a synthetic pentasaccharide. Whilst it has been extensively studied for use both in surgical prophylaxis and treatment of thromboembolic diseases; its use in pregnancy is less well documented. We report 4 pregnancies in 3 women using Fondaparinux which adds to the available literature. All required thromboprophylaxis because of previous pregnancy associated VTE when they demonstrated broad cross-reactivity between several heparins and/or heparinoids. In 3 pregnancies Fondaparinux was commenced in the first trimester and continued until 6 weeks postpartum. All continued without event resulting in vaginal delivery of well grown babies at term. There was no minor or major maternal bleeding (mean blood loss 250 mls) or thromboembolic event reported during the pregnancy or post-partum period. All babies were breastfed without effect. There was no congenital abnormality or neonatal bleeding. In a 4th pregnancy LMWH was initially deferred until 20 weeks gestation where upon recurrent allergic skin reaction led to the change to Fondaparinux. Review at 37 weeks gestation was pre-empted by a complaint of reduced fetal movements with pathological CTG necessitating emergency caesarean section at her base hospital.

**Database:** EMBASE

**18. Vaginal delivery in a parturient excessively anticoagulated with fondaparinux.**

**Author(s):** Hime, N; Auchet, T; Guerci, P; Vial, F; McNelis, U; Bouaziz, H

**Source:** International journal of obstetric anesthesia; Oct 2012; vol. 21 (no. 4); p. 385-387

**Publication Date:** Oct 2012

**Publication Type(s):** Letter Case Reports

**PubMedID:** 22918028

**Database:** Medline

**19. VTE, thrombophilia, antithrombotic therapy, and pregnancy - Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines**

**Author(s):** Bates S.M.; Greer A.; Middeldorp S.; Veenstra D.L.; Prabulos A.-M.; Vandvik P.O.

**Source:** Chest; Feb 2012; vol. 141 (no. 2)

**Publication Date:** Feb 2012

**Publication Type(s):** Review

**PubMedID:** 22315276

Available at [Chest](#) - from Free Medical Journals . com

Available at [Chest](#) - from Unpaywall

**Abstract:** Background: The use of anticoagulant therapy during pregnancy is challenging because of the potential for both fetal and maternal complications. This guideline focuses on the management

of VTE and thrombophilia as well as the use of antithrombotic agents during pregnancy. Methods: The methods of this guideline follow the Methodology for the Development of Antithrombotic Therapy and Prevention of Thrombosis Guidelines: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines in this supplement. Results: We recommend low-molecular-weight heparin for the prevention and treatment of VTE in pregnant women instead of unfractionated heparin (Grade 1B). For pregnant women with acute VTE, we suggest that anticoagulants be continued for at least 6 weeks postpartum (for a minimum duration of therapy of 3 months) compared with shorter durations of treatment (Grade 2C). For women who fulfill the laboratory criteria for antiphospholipid antibody (APLA) syndrome and meet the clinical APLA criteria based on a history of three or more pregnancy losses, we recommend antepartum administration of prophylactic or intermediate-dose unfractionated heparin or prophylactic low-molecular-weight heparin combined with low-dose aspirin (75-100 mg/d) over no treatment (Grade 1B). For women with inherited thrombophilia and a history of pregnancy complications, we suggest not to use antithrombotic prophylaxis (Grade 2C). For women with two or more miscarriages but without APLA or thrombophilia, we recommend against antithrombotic prophylaxis (Grade 1B). Conclusions: Most recommendations in this guideline are based on observational studies and extrapolation from other populations. There is an urgent need for appropriately designed studies in this population. © 2012 American College of Chest Physicians.

**Database:** EMBASE

## **20. Spinal anesthesia for cesarean delivery in a patient receiving fondaparinux.**

**Author(s):** Rentz, Jack B; Hart, Stuart R; Russo, Melissa

**Source:** The Ochsner journal; 2011; vol. 11 (no. 1); p. 81-83

**Publication Date:** 2011

**Publication Type(s):** Journal Article

**PubMedID:** 21603340

Available at [The Ochsner journal](#) - from ProQuest (Health Research Premium) - NHS Version

Available at [The Ochsner journal](#) - from PubMed Central

**Abstract:** Fondaparinux sodium, a selective inhibitor of factor Xa, is a new anticoagulant being used for thromboprophylaxis in all patient populations. We outline a case of neuraxial anesthesia for cesarean delivery in a patient with recent fondaparinux use and discuss most recent literature recommendations.

**Database:** Medline

## **21. Anticoagulation with Fondaparinux in a pregnant woman with aortic and mitral valve replacement**

**Author(s):** Mondorf W.; Mahnel R.; Mondorf C.

**Source:** Hamostaseologie; 2011; vol. 31 (no. 1)

**Publication Date:** 2011

**Publication Type(s):** Conference Abstract



**Abstract:** Aim: The following case raises the question whether Fondaparinux can be used in pregnant women with heart valve replacement. Result: A today 40-year old pregnant woman received anticoagulation with Nadroparin 7600 IU BID due to prior aortic and mitral valve replacement. In the 29th week of gestation vaginal bleeding occurred leading to caesarean section in the 32nd week. Anticoagulation was changed to UFH two weeks before and to Coumadin after delivery. Beginning of 2010 the patient again presented in early pregnancy. As in prior pregnancy, anticoagulation was changed from Coumadin to Nadroparin 7600 IU BID. In the 20th week of gestation the patient presented with swelling and rashes at the sight of injection. Because of subsequent spreading of the rashes the anticoagulation was changed to Fondaparinux 7.5 mg OD. The rashes disappeared immediately and the ongoing pregnancy was normal and without bleeding episodes. Due to the long half life of Fondaparinux the anticoagulation was changed to Enoxaparin 8000 IU BID in the 38th week of gestation. Again severe rashes occurred and the anticoagulation was switched to Fondaparinux. Anticoagulation was changed to UFH immediately prior to caesarean section. Fondaparinux was given in the postpartal period and changed to Coumadin later on. Conclusion: Fondaparinux is neither approved in pregnancy nor for anticoagulation after heart valve replacement. Due to limited options it was however used in the demonstrated case. In spite of severe skin reactions with Nadroparin and Enoxaparin no such side effects were seen using Fondaparinux. Pregnancy and child development as well as repeated ultrasounds from the heart valves were normal. Haemoglobin decreased to 10.7 g/dl and D-Dimer increased to 0.68 mg/l which was within the range of normal pregnancies. The case shows that Fondaparinux should further be investigated for pregnancies requiring therapeutic anticoagulation.

**Database:** EMBASE

## **22. Use of fondaparinux in a pregnant woman with pulmonary embolism and heparin-induced thrombocytopenia.**

**Author(s):** Ciużyński, Michał; Jankowski, Krzysztof; Pietrzak, Bronisława; Mazanowska, Natalia; Rzewuska, Ewa; Kowalik, Robert; Pruszczyk, Piotr

**Source:** Medical science monitor : international medical journal of experimental and clinical research; May 2011; vol. 17 (no. 5); p. CS56

**Publication Date:** May 2011

**Publication Type(s):** Case Reports Journal Article

**PubMedID:** 21525816

Available at [Medical science monitor : international medical journal of experimental and clinical research](#) - from Europe PubMed Central - Open Access

Available at [Medical science monitor : international medical journal of experimental and clinical research](#) - from Unpaywall

**Abstract:** BACKGROUND A serious complication of heparin treatment, heparin-induced thrombocytopenia (HIT) is rarely observed in pregnant women. Drug therapy during pregnancy should always be chosen to minimize fetal risk. The management of HIT in pregnancy represents a medical challenge. Unlike heparins, the anticoagulants used in patients with HIT do cross the placenta, with unknown fetal effects. CASE REPORT We present a case of a 24-year-old female presenting for care at 34 weeks of gestation with acute pulmonary embolism treated initially with





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unfractionated heparin (UFH) and low molecular weight heparin (LMWH), who developed HIT. She was then successfully treated with fondaparinux. CONCLUSION To the best of our knowledge, this is one of the first case reports describing a successful use of fondaparinux in the treatment of HIT in a third-trimester pregnant woman, providing a novel approach for this subset of patients.

**Database:** Medline

### **23. Anticoagulant and antithrombotic drugs in pregnancy: What are the anesthetic implications for labor and cesarean delivery**

**Author(s):** Butwick A.J.; Carvalho B.

**Source:** Journal of Perinatology; Feb 2011; vol. 31 (no. 2); p. 73-84

**Publication Date:** Feb 2011

**Publication Type(s):** Article

**PubMedID:** 20559281

Available at [Journal of Perinatology](#) - from ProQuest (Health Research Premium) - NHS Version

Available at [Journal of Perinatology](#) - from Unpaywall

**Abstract:** Neuraxial anesthetic techniques are commonly used during the peripartum period to provide effective pain relief for labor and anesthesia during cesarean delivery. Major neurologic complications are rare after neuraxial anesthesia; however, spinal hematoma is associated with catastrophic neurologic outcomes (including lower-limb paralysis). Anticoagulant and antithrombotic drugs can increase the risk of spinal hematoma after neuraxial anesthesia, and better understanding of the pharmacokinetics and pharmacodynamics of anticoagulants has led to greater appreciation



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for withholding anticoagulation before and after neuraxial anesthesia. A number of national anesthetic societies have produced guidelines for performing neuraxial anesthesia in patients receiving anticoagulation. However, there is limited information about anesthetic implications of anticoagulation during the peripartum period. This article will review the risks of spinal hematoma after neuraxial anesthesia in pregnant patients; current guidelines for neuraxial anesthesia for anticoagulated patients; and relevant pharmacological data of specific anticoagulant and antithrombotic drugs in pregnancy. © 2011 Nature America, Inc. All rights reserved.

**Database:** EMBASE

#### **24. Fondaparinux as an alternative anticoagulant therapy during pregnancy**

**Author(s):** Knol H.M.; Schultinge L.; Meijer K.; Erwich J.J.H.M.

**Source:** Journal of Thrombosis and Haemostasis; Aug 2010; vol. 8 (no. 8); p. 1876-1879

**Publication Date:** Aug 2010

**Publication Type(s):** Letter

**PubMedID:** 20492464

Available at [Journal of Thrombosis and Haemostasis](#) - from Wiley Online Library Science , Technology and Medicine Collection 2017

Available at [Journal of Thrombosis and Haemostasis](#) - from IngentaConnect - Open Access

Available at [Journal of Thrombosis and Haemostasis](#) - from Unpaywall

**Database:** EMBASE

#### **25. Successful prevention or treatment of venous thromboembolism with fondaparinux in pregnant women with allergic skin reactions to lowmolecular- weight Heparins and danaparoid**

**Author(s):** Scharf R.; Bomke B.; Hoffmann T.

**Source:** Vox Sanguinis; Jul 2010; vol. 99 ; p. 447-448

**Publication Date:** Jul 2010

**Publication Type(s):** Conference Abstract

Available at [Vox Sanguinis](#) - from Wiley Online Library Science , Technology and Medicine Collection 2017

**Abstract:**Background: Low-molecular-weight Heparins (LMWHs) are currently the anticoagulants of choice for the prevention or therapy of pregnancy-associated venous thromboembolism. The incidence of venous thromboembolism (VTE) is around 1 in 1000-1500 pregnancies; the risk is



highest during the first 3-6 weeks after delivery. LMWHs can safely be used during pregnancy and the puerperium since heparins, including LMWHs, do not cross the placental barrier and are thus non-teratogenic. However, in case of allergic skin reactions to LMWHs or danaparoid, alternative treatment options are limited. Despite the recent availability of new anticoagulants, data related to their use during pregnancy are lacking. Aim: Here we studied the efficacy and safety of fondaparinux in pregnant women, using prophylactic or therapeutic dosages. Fondaparinux is not officially approved for this indication and therefore currently represents an "off-label use" in this setting. Patients: We report on four women (29-35 years, 2 GII PI, 2 GI PO) with a history of VTE (n = 3) or an acute VTE in the 10th week of gestation. They received enoxaparin, either for prophylaxis (n = 3, beginning at the end of the 1st trimester) or at a therapeutic dosage (n = 1). Because of dermal reactions to enoxaparin at the site of s.c. injections, LMWH had to be switched. Intracutaneous testing of nadroparin, dalteparin, tinzaparin, and danaparoid revealed intolerance in all four women, except for fondaparinux. Thus, this drug was administered, although currently not licensed for that use. Three patients received 2.5 mg, one 7.5 mg, each once daily. Methods: Fondaparinux plasma levels were monitored every 4 weeks during pregnancy and 6 weeks postpartum and expressed in mug/ml of a fondaparinux calibrator three h after s.c. injection. Diagnostic work-up included testing for antithrombin, protein C/S, lupus anticoagulant, PAI- 1 levels, resistance to APC, prothrombin (G20210A) and factor V (G1691A) mutations or a deletion/insertion (4G/5G) polymorphism of PAI-1. Results: Screening for thrombophilia was negative in all four women. Platelet count remained within the normal range; no antibodies to PF4- heparin complexes were detected. Fondaparinux was tolerated without any cutaneous reactions in all patients. Its plasma levels were within the target range for prophylactic treatment (0.2-0.5 mug/ml) or effective anticoagulation (0.6-0.9 mug/ml) in the patient with recent VTE. Anticoagulation was discontinued 24 h prior to delivery. No adverse effects of fondaparinux were noted in the newborns. Conclusions: Our data document that fondaparinux may be a valuable, effective and safe alternative for prevention or therapy of VTE in pregnant women with intolerance to LMWHs or danaparoid. However, controlled trials are required, particularly on fetal safety of fondaparinux when using prophylactic and therapeutic dosages.

**Database:** EMBASE

## **26. Fondaparinux versus enoxaparin treatment in women with infertility or pregnancy loss**

**Author(s):** Winger E.; Reed J.

**Source:** Haematologica; Jun 2010; vol. 95 ; p. 185

**Publication Date:** Jun 2010

**Publication Type(s):** Conference Abstract

**Abstract:**Background: Unexplained miscarriage and infertility affect approximately 6% of couples trying to start a family. Immunologic and clotting disorders have been reported in many of these patients. Enoxaparin has been a preferred anticoagulant therapy due to its relative safety and effectiveness in pregnancy. However, it requires more frequent dosing compared with newer anticoagulants such as fondaparinux. Aims. We compared the pregnancy success rates and safety parameters of fondaparinux versus enoxaparin, combined with immunotherapy, in patients with a history of miscarriage and / or infertility and coagulation defects. Methods: A total of 126 pregnancies in patients with a history of miscarriage and / or infertility were retrospectively evaluated. Of these, 63 pregnancies used fondaparinux 2.5 mg daily and 63 pregnancies used enoxaparin 30 mg twice daily. The treatment groups were similar in terms of maternal age (37.1+/- 4.3 versus 36.8+/- 4.5 years), the number of previous miscarriages (2.2+/- 1.8 versus 2.4+/- 1.8

losses), and maternal immunologic and thrombophilic status. Elevated antiphospholipid antibodies were present in 41% (26/63) of patients administered fondaparinux and 43% (27/63) of patients administered enoxaparin. Elevated NK cytotoxicity (K562 killing at an effector: target ratio of 50:1) was present in 44% (28/63) of patients administered fondaparinux and 52% (33/63) of patients administered enoxaparin. Inherited thrombophilia (polymorphism of one or more of the following genes: heterozygous or homozygous factor V Leiden R506Q, prothrombin G20210A, or plasminogen activator inhibitor 4G / 5G; homozygous methylene tetrahydrofolate reductase (MTHFR) C677T; or compound heterozygous MTHFR C677T/A1298C) was present in 63% (40/63) of patients administered fondaparinux and 73% (46/63) of patients administered enoxaparin. The most common immunotherapy protocol used in the two groups was IVIG [(87% (55/63) versus 81%(51/63)] and corticosteroid [57%(36/63) versus 75%(47/63)]. Informed consent was obtained by all patients for off label use of relevant drugs. The study was approved by the Institutional Review Board (WIRB Study Number 1094182). Patient confidentiality was strictly maintained. Results: The pregnancy success rate was 67% (42/63) for patients receiving fondaparinux and 67% (42/63) for patients receiving enoxaparin. No difference was detected in birth weight (2.8+/- 0.7 and 3.0+/- 0.8 kg, respectively) or gestational age at delivery (37.7+/- 2.3 and 38.1+/- 2.8 weeks, respectively). Vaginal bleeding occurred in 14% (9/63) of fondaparinux-treated patients and 17% (11/63) of enoxaparin-treated patients (P=0.81), typically between 7 and 9 weeks of gestation. No birth defects, severe bleeding-related complications, or serious allergic reactions were observed. Summary/Conclusions: In women with miscarriage and /or infertility treated with a combination of immunotherapies and anticoagulants, fondaparinux is well-tolerated and enables successful pregnancy outcomes at a rate comparable with that of enoxaparin therapy. Because fondaparinux also offers more convenient once-daily dosing and, in previous studies, fewer side effects than enoxaparin, we propose that fondaparinux may offer an attractive therapeutic alternative to enoxaparin in immune-treated pregnancy. Although equivalent outcomes were observed in our analysis, a larger study is required to achieve statistical power.

**Database:** EMBASE

## **27. Successful management of term pregnancy complicated with deep vein thrombosis and heparin-induced thrombocytopenia**

**Author(s):** Sioulas V.; Mourtzakis S.; Salamalekis G.; Karanikolopoulos P.; Chrelas C.; Grouzi E.; Brountzos E.; Kassanos D.

**Source:** Journal of Maternal-Fetal and Neonatal Medicine; May 2010; vol. 23 ; p. 211

**Publication Date:** May 2010

**Publication Type(s):** Conference Abstract

**Abstract:** Brief Introduction: The aim of this study is to present a case of deep vein thrombosis (DVT) and heparin-induced thrombocytopenia type II (HIT II) during term pregnancy, treated with inferior vena cava (IVC) filter insertion and fondaparinux administration. Clinical Cases or Summary Results: A 31-year-old nulliparous woman at 37 weeks of gestation was referred to our Department for further management of left popliteal vein thrombosis. Her medical history was significant for systemic lupus erythematosus and a prior episode of DVT. During the course of pregnancy, she was



treated with azathioprine, dexamethasone and tinzaparin (4500 U/24 h). On admission, the woman was switched to IV infusion of unfractionated heparin, but, 24 h later, a marked decrease in platelet count was recorded. Functional and ELISA assays confirmed the diagnosis of HIT. An IVC filter was inserted and the patient underwent cesarean section. A baby boy weighing 2510 gr, with umbilical artery pH of 7.32 and Apgar score of 7/1'9/5', was delivered. Postpartum anticoagulation consisted of fondaparinux (7.5 mg/24 h), gradually replaced by oral anticoagulants, for a period of 6 months. IVC filter was removed 5 weeks after deployment. Conclusions: Fondaparinux, an alternative option for the treatment of HIT, may be safely used in pregnant or lactating women. However, when therapeutic anticoagulation is contraindicated or fails, the placement of IVC filter during pregnancy complicated with DVT is not, probably, associated with adverse maternal or fetal outcomes.

**Database:** EMBASE

## **28. Neuraxial anesthesia in obstetric patients receiving anticoagulant and antithrombotic drugs.**

**Author(s):** Butwick, A J; Carvalho, B

**Source:** International journal of obstetric anesthesia; Apr 2010; vol. 19 (no. 2); p. 193-201

**Publication Date:** Apr 2010

**Publication Type(s):** Journal Article Review

**PubMedID:** 20202816

**Database:** Medline

## **29. Regional anaesthesia in patients taking anticoagulant drugs**

**Author(s):** Checketts M.R.

**Source:** Anaesthesia and Intensive Care Medicine; Nov 2009; vol. 10 (no. 11); p. 541-544

**Publication Date:** Nov 2009

**Publication Type(s):** Review

**Abstract:**Increasing numbers of patients are taking drugs that impair normal coagulation, and this causes concern about the risk of perioperative bleeding events. The anaesthetist is particularly concerned about compressive vertebral canal haematomas, which may occur after spinal or epidural anaesthetic techniques. Fortunately, the risk of this complication is very low. The major risk factors are coagulopathy or technical difficulties with the block. There is also concern about perineural

haematomas, which may be associated with peripheral nerve blocks. This article attempts to put the risks of these complications into context, with reference to different classes of anticoagulant drugs.  
© 2009.

**Database:** EMBASE

### **30. Alternative anticoagulation with fondaparinux in pregnant patients with heparin-intolerance**

**Author(s):** Schindewolf M.; Linnemann B.; Luxembourg B.; Lindhoff-Last E.

**Source:** Journal of Thrombosis and Haemostasis; Jul 2009; vol. 7 ; p. 752

**Publication Date:** Jul 2009

**Publication Type(s):** Conference Abstract

Available at [Journal of Thrombosis and Haemostasis](#) - from Wiley Online Library Science , Technology and Medicine Collection 2017

Available at [Journal of Thrombosis and Haemostasis](#) - from IngentaConnect - Open Access

**Abstract:** Objectives: The use of heparins in pregnancy in association with thromboembolic diseases, thrombophilia or recurrent abortions has been increasing over the past decade. Thus, the rising number of heparin-associated adverse effects necessitates alternative anticoagulatory strategies. So far, only limited data exist on the use of the pentasaccharide fondaparinux in pregnancy. Methods: Literature search was performed in Medline, Medscape and Cochrane Library from 1983 to 2008 using the terms: pregnancy, fondaparinux, arixtra, pentasaccharide, SR90107/Org31540. Results: We found eight patients treated with fondaparinux due to heparin-intolerance (7/8: cutaneous allergic reactions; 1/8: acute immune heparin-induced thrombocytopenia (HIT) with pulmonary embolism. The average duration of therapy was 76.5 days [range 1-224 days]. The patient with HIT received 2.5 mg fondaparinux s.c. bid, all others were treated with 2.5 mg qd. Neither recurrent skin reactions, nor thromboembolic events nor bleeding complications pre-and intra partum occurred. All pregnancies were carried to term and a healthy infant was delivered. Chromogenic anti-FXa-monitoring was performed in five pregnancies. Conclusion: In spite of these promising results, the use of fondaparinux-unless more data are available-should be limited to pregnant women with no further treatment options in refractory heparin-intolerance, which is mostly due to cutaneous allergic reactions or HIT, but here, yielded excellent therapy outcome due to the very low or, respectively, non-existing cross-reactivity with conventional heparins or heparinoids. Although an in-vitro model with perfused human cotyledons suggests no placental transfer, in-vivo fondaparinux has been detected in umbilical cord blood in minor concentrations. Thus, adverse fetal impacts are not excluded, although this is not suggested after analysis of the manufacturer's preclinical data derived from animal models.

**Database:** EMBASE

### **31. Fondaparinux for a pregnant woman with deep vein thrombosis and heparin allergy**

**Author(s):** Almomen A.M.; Abdel Gader A.M.

**Source:** Journal of Thrombosis and Haemostasis; Jul 2009; vol. 7 ; p. 748

**Publication Date:** Jul 2009

**Publication Type(s):** Conference Abstract

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Available at [Journal of Thrombosis and Haemostasis](#) - from Wiley Online Library Science ,  
Technology and Medicine Collection 2017

Available at [Journal of Thrombosis and Haemostasis](#) - from IngentaConnect - Open Access

**Abstract:** A 34 years old lady (gravida 4 para-two plus one, body weight was 68 kg) who was pregnant in her 26th gestational week was admitted with extensive right ilio-femoral Deep Vein Thrombosis (DVT) that was documented by duplex. She was started on unfractionated heparin sodium at 10 000 units intravenously as a bolus dose, followed by heparin infusion at 1000 unit/h. Within a few hours she developed generalised, diffuse erythematous rash and itching all over her body. She was given methylprednisolone and shifted to Enoxaparin sodium (Clexane, Sanofi-Aventis, France), 60 mg subcutaneously twice/day. After an initial improvement, her diffuse erythematous rash and itching started to worsen. Enoxaparin was discontinued and methyl prednisolone was given. Twenty four hour later she was started on Tinzaparin sodium (Innohip, Leo Denmark) at 10 500 unit/day subcutaneously, but the itching, erythematous rash continued to worsen. At this point she was given a test dose of Fondaparinux (Arixtra, Glaxo-Smith-Kline, USA) 2.5 mg subcutaneously, followed by 5 mg daily. The erythematous rash and itching disappeared over the next few days and Fondaparinux was continued until the spontaneous delivery of a full term normal baby on the 39 gestational week and continued for six weeks thereafter. No complications were reported neither in the mother nor in the baby. Conclusion: Fondaparinux could be used safely in patients with heparin allergy even in pregnant women. Safety and efficacy of Fondaparinux need to be confirmed by proper clinical trials.

**Database:** EMBASE

### **32. Treatment of a woman with lupus and thromboembolism and cutaneous intolerance to heparins using fondaparinux during pregnancy.**

**Author(s):** Harenberg, Job

**Source:** Thrombosis research; 2007; vol. 119 (no. 3); p. 385-388

**Publication Date:** 2007

**Publication Type(s):** Letter Case Reports

**PubMedID:** 16647746

**Database:** Medline

### **33. Fondaparinux is an effective alternative anticoagulant in pregnant women with high risk of venous thromboembolism and intolerance to low-molecular-weight heparins and heparinoids.**

**Author(s):** Gerhardt, Andrea; Zotz, Rainer Bernd; Stockschlaeder, Marcus; Scharf, Rüdiger Eberhard

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**Source:** Thrombosis and haemostasis; Mar 2007; vol. 97 (no. 3); p. 496-497

**Publication Date:** Mar 2007

**Publication Type(s):** Letter Case Reports

**PubMedID:** 17334521

**Database:** Medline

### **34. Fondaparinux is a safe alternative in case of heparin intolerance during pregnancy.**

**Author(s):** Mazzolai, Lucia; Hohlfeld, Patrick; Spertini, Francois; Hayoz, Daniel; Schapira, Marc; Duchosal, Michel A

**Source:** Blood; Sep 2006; vol. 108 (no. 5); p. 1569-1570

**Publication Date:** Sep 2006

**Publication Type(s):** Case Reports Journal Article

**PubMedID:** 16645165

Available at [Blood](#) - from HighWire - Free Full Text

Available at [Blood](#) - from Unpaywall

**Abstract:** Heparin is the drug of choice for the treatment or the prevention of thromboembolic disease during pregnancy. However, treatment options are limited when heparin cannot be used because of hypersensitivity skin reactions. Despite the recent availability of new anticoagulant agents, data relating to their use during pregnancy are lacking. This report describes the successful management with fondaparinux, during 150 days, of a pregnant patient with protein S deficiency and prior deep vein thrombosis (DVT) who developed heparin and danaparoid hypersensitivity.

**Database:** Medline

### **35. Fondaparinux as anticoagulant in a pregnant woman with heparin allergy.**

**Author(s):** Wijesiriwardana, Ajith; Lees, David A R; Lush, Christopher

**Source:** Blood coagulation & fibrinolysis : an international journal in haemostasis and thrombosis; Mar 2006; vol. 17 (no. 2); p. 147-149

**Publication Date:** Mar 2006

**Publication Type(s):** Case Reports Journal Article

**PubMedID:** 16479197

Available at [Blood coagulation & fibrinolysis : an international journal in haemostasis and thrombosis](#) - from Ovid (LWW Total Access Collection 2019 - with Neurology)

**Abstract:** We report a patient who had a history of deep vein thrombosis in a previous pregnancy. She was treated with heparins without any reactions in the index pregnancy. Subsequently, when the patient became pregnant again, she developed an acute cutaneous reaction to the low molecular heparin enoxaparin 3 weeks after initiation of therapy. She developed a similar reaction to delteparin as well. She was therefore treated with warfarin until 36 weeks of gestation. Then she was treated with fondaparinux (Arixtra, Sanofi-Synthelabo, Paris, France) 2.5 mg daily for the remainder of the pregnancy. Delivery was at term by induction of labour. Fondaparinux was stopped on the day of the induction of labour. It was re-started 6 h post-delivery and the patient was



anticoagulated with warfarin in the post-partum period. There were no bleeding tendencies or recurrences of thrombosis during fondaparinux therapy. Both mother and baby were well after delivery.

**Database:** Medline

### **36. Minimising the risk of heparin-induced osteoporosis during pregnancy.**

**Author(s):** Hawkins, David; Evans, Jeffrey

**Source:** Expert opinion on drug safety; May 2005; vol. 4 (no. 3); p. 583-590

**Publication Date:** May 2005

**Publication Type(s):** Journal Article Review

**PubMedID:** 15934862

**Abstract:**Unfractionated heparin (UFH) may lead to symptomatic vertebral fractures in up to 3 out of every 100 people on long-term therapy. Ten-times that many people will experience a significant reduction in bone density leading to osteopenia or osteoporosis. Low molecular weight heparins (LMWH) have been shown to be as effective as UFH in the prevention and treatment of venous thromboembolism. Several well-established advantages of LMWH over UFH include increased bioavailability, more predictable dose response, less intensive coagulation monitoring, and a lower probability of causing immune-mediated thrombocytopenia. There is also some evidence that long-term LMWH therapy is less likely to cause osteoporotic fractures and significant reductions in bone mass than UFH. Both UFH and LMWH undergo pharmacokinetic changes during pregnancy, which sometimes necessitates dosage adjustments. Fondaparinux is a synthetic antithrombotic agent, which specifically binds to antithrombin. It has been shown to be comparable to, or even more effective than, LMWH in the management of both arterial and venous thrombosis. Fondaparinux does not appear to have a negative effect on bone metabolism. Therefore, fondaparinux may be a safe and effective alternative to UFH and LMWH in women who require anticoagulation during pregnancy.

**Database:** Medline

### **37. Fondaparinux (ARIXTRA) as an alternative anti-thrombotic prophylaxis when there is hypersensitivity to low molecular weight and unfractionated heparins.**

**Author(s):** Parody, Rocio; Oliver, Arturo; Souto, Juan Carlos; Fontcuberta, Jordi

**Source:** Haematologica; Nov 2003; vol. 88 (no. 11); p. ECR32

**Publication Date:** Nov 2003

**Publication Type(s):** Case Reports Journal Article

**PubMedID:** 14607764

**Abstract:**During the last decade, new anticoagulant drugs with anti-factor-Xa properties have been described (1, 2). Among them is fondaparinux that has been licensed recently. It is a pentasaccharide mimicking the site where heparin binds to antithrombin III (1). This new drug has produced very promising clinical results in the prophylaxis of venous thrombosis after orthopedic surgery (3). Here we report two different clinical situations in which fondaparinux has yielded a successful outcome: first, a patient with repeated cutaneous reaction to several different low molecular weight heparins





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(LMWH), and second, a patient with severe heparin-induced thrombocytopenia (HIT). We decided to use fondaparinux in both cases since it is commercially available in Spain and mostly because the absence of in vitro cross-reaction with heparins, as discussed later.

**Database:** Medline

**38. Fondaparinux sodium does not cross the placental barrier: Study using the in-vitro human dually perfused cotyledon model**

**Author(s):** Lagrange F.; Saux M.C.; Bannwarth B.; Brun J.-L.; Leng J.-J.; Vergnes M.C.; Paolucci F.; Nadal T.

**Source:** Clinical Pharmacokinetics; 2002; vol. 41 ; p. 47-49

**Publication Date:** 2002

**Publication Type(s):** Article

**PubMedID:** 12383045

Available at [Clinical Pharmacokinetics](#) - from SpringerLink - Medicine

**Database:** EMBASE

**39. Absence of placental transfer of pentasaccharide (Fondaparinux, Arixtra) in the dually perfused human cotyledon in vitro.**

**Author(s):** Lagrange, F; Vergnes, C; Brun, J L; Paolucci, F; Nadal, T; Leng, J J; Saux, M C; Banwarth, B

**Source:** Thrombosis and haemostasis; May 2002; vol. 87 (no. 5); p. 831-835

**Publication Date:** May 2002

**Publication Type(s):** Research Support, Non-u.s. Gov't Comparative Study Journal Article

**PubMedID:** 12038785

**Abstract:** The synthetic pentasaccharide, fondaparinux, is the first of a new antithrombotic class: selective factor Xa inhibitors. Comparative clinical trials of fondaparinux versus heparins in prevention and treatment of venous thromboembolism are ongoing. Little is known about fondaparinux during pregnancy, as women of child-bearing potential were excluded from clinical trials. No particular safety issue, for either mother or fetus, has been reported for heparins. The objective of this study was to compare in vitro the steady state placental transfer of fondaparinux and enoxaparin at the plasma concentrations reached during acute treatment of venous thromboembolism (1.75 microg/mL and 1 anti-Xa IU/mL respectively), using antipyrine (20 mg/L) as reference. No biological activity was detectable in the fetal venous effluent during perfusion of enoxaparin-antipyrine, fondaparinux-antipyrine or control media. Furthermore, fetal venous samples did not differ significantly from fetal arterial samples. This apparent absence of placental transfer supports further evaluation of fondaparinux in pregnant women.

**Database:** Medline

## Strategy 677022

#	Database	Search term	Results
1	Medline	(Fondaparinux OR Arixtra OR Quixidar).ti,ab	1647
2	Medline	exp FONDAPARINUX/	1058
3	Medline	(1 OR 2)	1866
4	Medline	(pregnan*).ti,ab	466920
5	Medline	exp PREGNANCY/	865828
6	Medline	(lactation OR breastfeeding OR "breast feeding").ti,ab	62533
7	Medline	exp "BREAST FEEDING"/ OR exp LACTATION/	72385
8	Medline	((obstetric OR intrapartum OR postpartum) ADJ2 (hemorrhag* OR haemorrhag*)).ti,ab	6218
9	Medline	exp "POSTPARTUM HEMORRHAGE"/	6674
10	Medline	exp "ANALGESIA, OBSTETRICAL"/	3831
11	Medline	exp "ANESTHESIA, EPIDURAL"/	13347
12	Medline	(regional ADJ2 analgesi*).ti,ab	1155
13	Medline	(cesarean* OR caesarean*).ti,ab	56015
14	Medline	exp "CESAREAN SECTION"/	43152
15	Medline	exp "DELIVERY, OBSTETRIC"/	76497




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16	Medline	(4 OR 5 OR 6 OR 7 OR 8 OR 9 1038367 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15)	
17	Medline	(3 AND 16)	81
18	EMBASE	(Fondaparinux OR Arixtra OR Quixidar).ti,ab	2794
19	EMBASE	exp FONDAPARINUX/	7103
20	EMBASE	(18 OR 19)	7303
21	EMBASE	(pregnan*).ti,ab	596736
22	EMBASE	exp PREGNANCY/	634397
23	EMBASE	(lactation OR breastfeeding OR "breast feeding").ti,ab	74086
24	EMBASE	exp "BREAST FEEDING"/	48935
25	EMBASE	((obstetric OR intrapartum OR postpartum) ADJ2 (hemorrhag* OR haemorrhag*)).ti,ab	9207
26	EMBASE	exp "OBSTETRIC HEMORRHAGE"/	15659
27	EMBASE	exp "ANALGESIA, OBSTETRICAL"/	4251
28	EMBASE	exp "ANESTHESIA, EPIDURAL"/	32392
29	EMBASE	(regional ADJ2 analgesi*).ti,ab	1454
30	EMBASE	(cesarean* OR caesarean*).ti,ab	79003
31	EMBASE	exp "CESAREAN SECTION"/	89808



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32	EMBASE	exp "OBSTETRIC DELIVERY"/	136597
33	EMBASE	(21 OR 22 OR 23 OR 24 OR 25 993648 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32)	
34	EMBASE	(20 AND 33)	510
35	EMBASE	34 [English language]	466