West Middlesex University Hospital

Date of Search: 07/07/2016
Sources Searched: Medline, Embase, Google Scholar

Search History:
3. Medline; ("intraventricular hemorrhage" OR "intraventricular haemorrhage").ti,ab; 5311 results.
4. Medline; exp FETUS/; 146005 results.
5. Medline; (foetal OR fetal).ti,ab; 216446 results.
6. Medline; 4 OR 5; 301386 results.
7. Medline; 3 AND 6; 559 results.
8. Medline; " low-molecular-weight heparin*".ti,ab; 10368 results.
9. Medline; exp HEPARIN, LOW-MOLECULAR-WEIGHT/; 10680 results.
10. Medline; 8 OR 9; 14774 results.
11. Medline; 7 AND 10; 1 results.
12. Medline; (neonat* OR newborn).ti,ab; 296289 results.
13. Medline; 3 AND 10 AND 12; 5 results.
14. Medline; exp INFANT, NEWBORN/; 533400 results.
15. Medline; 3 AND 10 AND 14; 3 results.
16. EMBASE; ("intraventricular hemorrhage" OR "intraventricular haemorrhage").ti,ab; 6931 results.
17. EMBASE; exp BRAIN HEMORRHAGE/; 103296 results.
18. EMBASE; 16 OR 17; 104712 results.
19. EMBASE; exp FETUS/; 160715 results.
20. EMBASE; (foetal OR fetal).ti,ab; 258901 results.
21. EMBASE; 19 OR 20; 330340 results.
22. EMBASE; 18 AND 21; 2341 results.
23. EMBASE; " low-molecular-weight heparin*".ti,ab; 15236 results.
24. EMBASE; exp HEPARIN, LOW-MOLECULAR-WEIGHT/; 49101 results.
25. EMBASE; 23 OR 24; 50423 results.
26. EMBASE; 22 AND 25; 42 results.
27. EMBASE; 16 AND 21 AND 25; 3 results.
28. EMBASE; exp NEWBORN/; 491720 results.
29. EMBASE; 18 AND 25 AND 28; 57 results.
30. Medline; exp INTRACRANIAL HEMORRHAGES/; 60481 results.
31. Medline; 6 AND 10 AND 30; 4 results.
32. Medline; 10 AND 12 AND 30; 6 results.
33. Medline; infant.af; 1049635 results.
34. Medline; 3 AND 10 AND 33; 3 results.
35. Medline; 10 AND 30 AND 33; 12 results.
36. EMBASE; exp PREMATURITY/; 80445 results.
37. EMBASE; 18 AND 25 AND 36; 23 results.
38. EMBASE; exp PREGNANCY/; 621069 results.

39. EMBASE; 18 AND 25 AND 38; 151 results.
40. EMBASE; *LOW MOLECULAR WEIGHT HEPARIN/; 7959 results.
41. EMBASE; 18 AND 38 AND 40; 8 results.
42. Medline; pregn*.ti,ab; 404878 results.
43. Medline; exp PREGNANCY/; 788424 results.
44. Medline; 42 OR 43; 871004 results.
45. Medline; 3 AND 10 AND 44; 1 results.
46. Medline; 10 AND 30 AND 44; 14 results.
47. EMBASE; 16 AND 24; 24 results.
48. EMBASE; 16 AND 40; 3 results.
49. Medline; exp STROKE/; 100727 results.
50. Medline; 6 AND 10 AND 49; 7 results.
51. Medline; 10 AND 33 AND 49; 16 results.
52. EMBASE; exp CEREBROVASCULAR ACCIDENT/; 126784 results.
53. EMBASE; 21 AND 25 AND 52; 32 results.
54. EMBASE; perinatal.ti,ab; 71472 results.
55. EMBASE; 18 AND 25 AND 54; 29 results.
56. Medline; perinatal.ti,ab; 55950 results.
57. Medline; 10 AND 30 AND 56; 1 results.
58. EMBASE; *BRAIN HEMORRHAGE/; 24583 results.
59. EMBASE; 25 AND 38 AND 58; 6 results.
60. Medline; exp CEREBRAL HEMORRHAGE/; 29551 results.
61. Medline; 10 AND 14 AND 60; 6 results.
62. Medline; 10 AND 33 AND 60; 7 results.
63. Medline; heparin.ti; 27387 results.
64. Medline; 3 AND 63; 14 results.
65. EMBASE; 16 AND 25; 26 results.
1. EMBASE; exp LOW MOLECULAR WEIGHT HEPARIN/; 49101 results.
2. EMBASE; exp BRAIN HEMORRHAGE/; 103296 results.
3. EMBASE; exp FETAL HEMORRHAGE/; 268 results.
4. EMBASE; 1 AND 2 AND 3; 23 results.
5. EMBASE; 1 AND 2; 2782 results.
6. EMBASE; exp NEWBORN/; 491720 results.
7. EMBASE; 5 AND 6; 55 results.
8. EMBASE; exp FETOMATERNAL TRANSFUSION/; 12788 results.
9. EMBASE; 5 AND 8; 2 results.

Title: Intrauterine subdural hemorrhage in a preterm neonate possibly associated with maternal low-molecular weight heparin treatment.

Citation: Journal of perinatology : official journal of the California Perinatal Association, Jul 2009, vol. 29, no. 7, p. 521-523, 1476-5543 (July 2009)

Author(s): Bauder, F, Beinder, E, Arlettaz, R, Albisetti, M, Boltshauser, E, Gessler, P

Abstract: We report intrauterine subdural hemorrhage in a preterm infant delivered by cesarean section at 32 weeks following vaginal bleeding of a mother treated with low-molecular weight heparin (LMWH) for deep vein thrombosis. The subdural hematomas were partially calcified, proving antenatal occurrence. Maternal trauma during pregnancy, intrauterine infection, cerebral vascular malformation and congenital coagulopathy as known etiologies of subdural hemorrhage could be ruled out. Intrauterine subdural hemorrhage may be an exceptional complication of maternal LMWH treatment.

Source: Medline

Title: Use of low-molecular-weight heparin from the first trimester of pregnancy: A retrospective study of 111 consecutive pregnancies

Citation: European Journal of Obstetrics Gynecology and Reproductive Biology, July 2006, vol./is. 127/1(73-78), 0301-2115 (01 Jul 2006)

Author(s): Deruelle P., Denervaud M., Hachulla E., Ducloy-Bouthors A.-S., Valat A.-S., Puech F., Trillot N., Hatron P.-Y., Subtil D.

Language: English

Abstract: Background: During the first trimester of pregnancy, unfractionated heparin is the standard anticoagulant treatment for pregnant women at high risk of thrombosis. Objective: To observe maternal and fetal tolerance for low-molecular-weight heparin begun in the first trimester of pregnancy. Methods: Observational study conducted from 1 January 1997 to 31 May 2001. All patients began treatment before the 15th week of pregnancy. The outcome measures were the incidence and causality of adverse events in mother and fetus. Results: The study included 97 patients (and 111 pregnancies) at very high risk for thrombosis. Seven fetal losses (6.3%) were observed: three early spontaneous abortions, three late spontaneous abortions and one medically indicated abortion. Twenty-five (22.5%) bleeding events occurred during pregnancy, seven (6.3%) of which required medical intervention: five curettages for first trimester spontaneous abortions, one late abortion at 21 weeks and one placental abruption at 25 weeks. Of nine (8.1%) primary postpartum hemorrhages involving a blood loss >500 mL, three involved losses of 1000 mL or more and one required embolization of the uterine arteries. Five patients had thrombocytopenia, but none was

treatment-related. Local cutaneous reactions occurred in 33 (29.7%) patients. Six (5.4%) maternal thromboembolic complications occurred during pregnancy or postpartum. At birth, two children had non-chromosomal congenital malformations (pyelectasia, cleft lip and palate). No fetal or neonatal complication was attributed to the treatment. Conclusion: The use of low-molecular-weight heparin (LMWH) for patients requiring anticoagulant treatment from the first trimester appears safe for mother and fetus. © 2005.

Publication Type: Journal: Article

Source: EMBASE

Title: Maternal medication part of infant mortality

Citation: Journal of Maternal-Fetal and Neonatal Medicine, June 2014, vol./is. 27/(320-321), 1476-7058 (June 2014)

Author(s): Jashi R., Gorgadze N.

Language: English

Abstract: Brief Introduction: In Georgia, the greater part of infant mortality falls to perinatal mortality. Perinatal mortality is a useful integrated indicator of the quality of services provided to pregnant women, delivering mothers and infants. However, to achieve a further improvement in the quality of services, individual components of this indicator should be analyzed. The common causes of perinatal mortality are respiratory disorders specific to the perinatal period, including Respiratory Distress Syndrome (RDS) of newborn - 21.6% and intrauterine hypoxia and birth asphyxia -8.5%. Understanding the etiology of these conditions is a very important step towards developing preventive strategies. Materials & Methods: Objectives: Our aim is to identify medicationrelated risk factors. Methods: Retrospective and pharmacological analysis of diseased newborns and maternal medical records (total number 225). Maternal data: age, diagnosis, medications used during pregnancy and delivery; newborn data: gestational age at delivery, birth weight, diagnosis and medications used. We analyzed the mortality risks associated with pharmacologic treatment for newborns and medications used by mothers during pregnancy and delivery. Clinical Cases or Summary Results: The study revealed that RDS in newborns was often associated with maternal use of certain medications during pregnancy(RDS is mostly associated with gestational age). 1 Magnesium Sulfate: 11% newborns had symptoms of Magnezium Sulfate intoxication, such as CNS disturbances 2 Diazepam: newborn asphyxia was related to maternal Diazepam use during delivery (9%) - apnea, hypothermia and feeding problems identified in these newborns could be caused by this medication. 3 Naphthyzinum: in one case, during pregnancy, the mother routinely used Naphthyzinum, because of the difficulty with breathing. Four hours after the birth signs of neural excitation, periodic breathing, apnea and convulsions developed in the newborn 4 Nadroparin: premature infants are predisposed to coagulopathy, which may increase the incidence of intraventricular haemorrhage (IVH). Coagulation values vary with gestational age. There is only limited clinical data concerning transplacental passage of a blood thinner nadroparin in pregnant women. We observed twins born at 28 weeks of gestational age. Their mother was

treated with nadroparin during pregnancy 10 days before delivery. Our Analysis shows that Activated Partial Thromboplastin Time (APTT) values were the highest at 1 day of life (DOL) (twin I: APTT 90,8 at 1 DOL and APTT 50,1 at 2 DOL;TWIN II:APTT 54,5 at 1 DOL, and APTT 40,8 at 2 DOL.) Ultrasound images show IVH II in both infants. Conclusions: For appropriate treatment of neonates, it is necessary to take into consideration maternal medication use during pregnancy and delivery. This is important because of both the direct side effects of these medications newborns and their potential for altering kinetics of other medications in the fetus as well as in the newborn. We think that the information on the maternal medication use during pregnancy must be included in the patient care system software (PCS, IBM) for immediate detection of possible drug-interactions in newborns. Using computerizing methods of documentation for improving quality of drug therapy is currently limited due to the absence of patients' clinical database in hospital information systems. The inclusion of such a database could be useful for the systematic detection of adverse drug reactions and improvement of drug safety in neonatal patients. Using computerized methods should lead to significant time savings and improvements in cost effectiveness.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: Maternal complications and pregnancy outcome in women with mechanical prosthetic heart valves treated with enoxaparin

Citation: BJOG: An International Journal of Obstetrics and Gynaecology, November 2009, vol./is. 116/12(1585-1592), 1470-0328;1471-0528 (November 2009)

Author(s): McLintock C., McCowan L.M.E., North R.A.

Language: English

Abstract: Objective To determine maternal and fetal outcomes in women with mechanical heart valves managed with therapeutic dose enoxaparin during pregnancy. Design Retrospective audit. Setting Hospital-based high-risk antenatal clinics. Population Pregnant women with mechanical heart valves attending high-risk antenatal clinics, treated with enoxaparin (1 mg/kg twice daily) during pregnancy. Methods Women with mechanical heart valves treated with enoxaparin at any stage during pregnancy (1997-2008) identified using a database of women with mechanical heart valves attending the high-risk clinics and a prospective database of women prescribed enoxaparin for any indication during pregnancy. Main outcome measures Maternal outcomes included thromboembolic and haemorrhagic complications. Pregnancy and fetal outcomes included miscarriage, stillbirth, baby death and live birth, small-for-gestational-age infants, warfarin embryopathy and warfarin-related fetal loss. Results Thirty-one women underwent 47 pregnancies. In 34 pregnancies (72.3%), anticoagulation was with predominantly enoxaparin and 13 (27.7%) pregnancies women received mainly warfarin, with enoxaparin given in the first trimester and/or peri-delivery.

Seven (14.9%) thrombotic complications occurred, of which five (10.6%) were associated with enoxaparin treatment. Non-compliance or sub-therapeutic anti-Xa levels contributed in each case. Antenatal and postpartum haemorrhagic complications occurred in eight (17%) and 15 (32%) pregnancies respectively. Of 35 pregnancies continuing after 20 weeks' gestation, 96% (22/23) of women taking predominantly enoxaparin had a surviving infant compared with 75% (9/12) in women taking primarily warfarin. Four perinatal deaths occurred, three attributable to warfarin. Conclusions Compliance with therapeutic dose enoxaparin and aspirin during pregnancy in women with mechanical heart valves is associated with a low risk of valve thrombosis and good fetal outcomes, but close monitoring is essential. © RCOG 2009 BJOG An International Journal of Obstetrics and Gynaecology.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in BJOG: An International Journal of Obstetrics and Gynaecology
Available from *John Wiley and Sons* in BJOG: An International Journal of Obstetrics and Gynaecology

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Title: Low-molecular-weight heparin during pregnancy and delivery: Preliminary experience with 41 pregnancies

Citation: Obstetrics and Gynecology, March 1996, vol./is. 87/3(380-383), 0029-7844 (March 1996)

Author(s): Dulitzki M., Pauzner R., Langevitz P., Pras M., Many A., Schiff E.

Language: English

Abstract: Objective: To describe experience with 41 pregnancies treated with the low-molecular-weight heparin enoxaparin. Methods: The medical charts of 34 women (a total of 41 pregnancies) treated between January 1992 and March 1995 with the low-molecular-weight heparin enoxaparin were reviewed. Most patients (87.5%) received one daily 40-mg injection. In all cases, treatment was continued throughout tabor, delivery, and the immediate postpartum period. Results: Therapy was administered for 5-280 days (median 91). One case of a thromboembolic event was recorded during treatment. No systemic or local side effects were reported. During pregnancy, only one patient had mild vaginal bleeding, which resolved spontaneously while therapy was continued. There was no excessive intrapartum bleeding in any of these patients, whether delivered vaginally or abdominally. During treatment, 19 of the 34 patients underwent 24 surgical procedures, including 13 cesarean deliveries, without excessive bleeding. Epidural anesthesia was used during labor in nine of the patients, with no specific complications. The corrected perinatal mortality rate, (ie, the rate of fetal death after 24 weeks' gestation plus neonatal death, excluding a neonate with multiple anomalies) for those neonates delivered after 24 weeks'

gestation was 2.7%. There were no cases of intraventricular hemorrhage in any of the neonates. Conclusion: This preliminary series, the largest reported to date, demonstrates the relative safety and efficacy of low-molecular-weight heparin therapy in pregnancy and delivery.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *Obstetrics and Gynecology* in Patricia Bowen Library and Knowledge Service West Middlesex university Hospital
Available from *Ovid* in Obstetrics and Gynecology

Title: Heparin and the risk of intraventricular hemorrhage in premature infants.

Citation: The Journal of pediatrics, Sep 1997, vol. 131, no. 3, p. 362-366, 0022-3476 (September 1997)

Author(s): Chang, G Y, Lueder, F L, DiMichele, D M, Radkowski, M A, McWilliams, L J, Jansen, R D

Abstract: This study was carried out to determine whether the routine use of low-dose heparin in umbilical catheter infusates increases the risk of intraventricular hemorrhage or alters the coagulation profile in premature infants. In a randomized, blinded trial, 113 infants born at less than 31 weeks' gestation were assigned to receive, in their umbilical catheter infusate, either 1 unit of heparin per milliliter (n = 55) or no heparin (n = 58). Prothrombin time, activated partial thromboplastin time, fibrinogen concentration, and antithrombin III activity levels were determined at the start and the completion of the study. Cranial ultrasonography was performed during the first week of life. There was no difference in the incidence of intraventricular hemorrhage between the heparin and no heparin groups, 35.8% and 31.5%, respectively (p = 0.6). Similarly, no difference was detected in the incidence of severe intraventricular hemorrhage (grades III/IV). Prothrombin time, activated partial thromboplastin time, and fibrinogen levels were not significantly different between the two groups. However, the use of heparin was associated with a lower antithrombin III activity level. Antenatal indomethacin use was associated with a 2.9 increased risk of intraventricular hemorrhage (95% confidence interval, 1.15 to 7.17). A low dose of heparin added to umbilical catheter infusates does not increase the incidence or severity of intraventricular hemorrhage or significantly alter the coagulation profile in premature infants.

Source: Medline

Full Text:
Available from *Journal of Pediatrics* in Patricia Bowen Library and Knowledge Service West Middlesex university Hospital

Title: Low molecular weight heparin for the prophylaxis of thromboembolism in women with prosthetic mechanical heart valves during pregnancy

Citation: Thrombosis and Haemostasis, October 2004, vol./is. 92/4(747-751), 0340-6245 (October 2004)

Author(s): Oran B., Lee-Parritz A., Ansell J.

Language: English

Abstract: Increased thromboembolic events occur in women with mechanical prosthetic valves during pregnancy, and selecting an effective and safe anticoagulant is still a challenge. Low molecular weight heparin (LMWH) is a promising alternative, but a recent warning and label change about its use in patients with mechanical prosthetic valves has caused confusion among physicians. The aim of the present study was to review the risks of maternal and fetal complications with mechanical heart valves treated with LMWH during pregnancy. We performed a review of the current medical literature through MEDLINE and EMBASE (1989 to 2004).Additional data sources included abstract proceedings, and reference lists of selected articles. Among 81 pregnancies in 75 women, the proportion of valve thrombosis was 8.64% (7/81; 95% CI, 2.52%-14.76%). The frequency of overall thromboembolic complication (TEC) was 12.35% (10/81; 95% CI, 5.19%-19.51%). Nine of ten patients with TEC received a fixed dose of LMWH and two of these received a fixed low dose of LMWH. Among 51 pregnancies whose anti-factor Xa levels were monitored, only one patient was reported to have a thromboembolic complication.The frequency of live births with LMWH was 87.65% (95%CI, 80.49%-94.81%). In pregnant women with mechanical heart valves, LMWH appears to be a suitable option to a vitamin K antagonist. The use of LMWH warrants monitoring and appropriate dose adjustments to maintain a 4-6 hr post-injection anti-factor Xa level at a minimum of 1.0 U/ml to decrease the incidence of TEC. © 2004 Schattauer GmbH, Stuttgart.

Publication Type: Journal: Review

Source: EMBASE

Title: Subdural hemorrhages associated with antithrombotic therapy in infants with cerebral atrophy

Citation: Pediatrics, September 2014, vol./is. 134/3(e889-893), 1098-4275 (Sep 2014)

Author(s): Dang L.T., Shavit J.A., Singh R.K., Joshi S.M., Leber S.M., Barks J.D., Shellhaas R.A.

Language: English

Abstract: Low-molecular-weight heparins, such as enoxaparin, are often used to treat thrombosis in infants. We present 4 infants with diffuse brain injury who developed cerebral

venous sinus thrombosis or deep vein thrombosis and were treated with enoxaparin. These infants subsequently developed subdural hemorrhages, and enoxaparin was stopped. In 3 cases, the subdural hemorrhages were found on routine surveillance brain MRI, and in 1 case imaging was urgently obtained because of focal seizures. Two patients needed urgent neurosurgical intervention, and all subdural hemorrhages improved or resolved on follow-up imaging. Each infant developed severe neurologic deficits, probably from the coexisting diffuse brain injury rather than from the subdural hemorrhages themselves. The risk of intracranial hemorrhage from enoxaparin may be accentuated in patients with diffuse brain injury, and careful consideration should be given before treatment in this population.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *Pediatrics* in Patricia Bowen Library and Knowledge Service West Middlesex university Hospital
Available from *Highwire Press* in Pediatrics
Available from *Free Access Content* in Pediatrics

Title: Anticoagulant choices in pregnant women with mechanical heart valves: Balancing maternal and fetal risks - The difference the dose makes

Citation: Thrombosis Research, January 2013, vol./is. 131/SUPPL.1(S8-S10), 0049-3848;1879-2472 (January 2013)

Author(s): McLintock C.

Language: English

Abstract: Long-term anticoagulation is required in all patients with mechanical prosthetic heart valves to prevent complications with valve thrombosis and valve failure or systemic thromboembolism. The prothrombotic environment of pregnancy further increases the risks of these complications. Anticoagulant choices for pregnant women include oral vitamin K antagonists such as warfarin, or heparin-either unfractionated heparin (UFH) or low molecular weight heparin (LMWH). None of the options is without risk for the mother or her baby. Warfarin crosses the placenta and is associated with warfarin embryopathy and fetopathy but is very effective at preventing thromboembolic complications. The dose of warfarin may play a role in the risk of some, but not all fetal complications. Heparin does not cross the placenta but is less effective at preventing thrombosis and LMWH may be more effective than UFH. The optimal dose and target anti-Xa levels for LMWH have not been established. Measurement of trough anti-Xa levels in addition to peak anti-Xa levels may be important. © 2013 Elsevier Ltd. All rights reserved.

Publication Type: Journal: Article

Source: EMBASE

Title: Subdural hemorrhage associated with antithrombotic therapy in infants with cerebral atrophy

Citation: Annals of Neurology, December 2013, vol./is. 74/(S150-S151), 0364-5134 (December 2013)

Author(s): Dang L., Shavit J.A., Singh R.K., Joshi S.M., Leber S.M., Barks J.D., Shellhaas R.A.

Language: English

Abstract: Objective: Neonates and infants are treated with antithrombotic therapy such as low molecular-weight heparin (LMWH) for several reasons, including cerebral venous sinus thrombosis (CVST), and deep vein thrombosis (DVT). Anti-thrombotic therapy with LMWH in infants is reported to be safe, because resultant intracranial hemorrhage (ICH) is rare, and in cases with ICH, there is usually no significantly increased morbidity or mortality from the ICH. Anticoagulation in the setting of coexisting diffuse brain injury, such as hypoxic-ischemic injury, has not been well studied. Methods: Case series of infants with CVST or DVT and comorbid diffuse brain injury that were treated with enoxaparin. Results: Four infants (ages 1-11 weeks) were studied. Three had CVST and one catheter-associated DVT, treated with LMWH. Each infant subsequently developed subdural hemorrhage (SDH) in the setting of evolving brain atrophy. Two infants had diffuse brain injury from a hypoxicischemic insult, and one from severe hypernatremia and dehydration. One infant had multiple congenital abnormalities and progressive brain atrophy of unknown etiology. While three had significant SDH discovered on surveillance imaging with a brain MRI/MR venogram, only one was detected by urgent imaging due to new-onset, refractory, focal seizures. Two required urgent neurosurgical intervention. Developmental outcomes at 4-8 months of age have been unfavorable. Conclusions: Infants at risk for cerebral atrophy, whether from a diffuse ischemic insult or another cause, are vulnerable to clinically significant SDH when treated with LMWH. Comorbid diffuse brain injury may be a relative contraindication to anticoagulation for small, nonprogressive CVST or DVT.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: The search for a safe and effective anticoagulation regimen in pregnant women with mechanical prosthetic heart valves

Citation: Journal of the American College of Cardiology, March 2012, vol./is. 59/12(1116-1118), 0735-1097;1558-3597 (20 Mar 2012)

Author(s): Elkayam U., Goland S.

Language: English

Publication Type: Journal: Note

Source: EMBASE

Full Text:
Available from *ProQuest* in Journal of the American College of Cardiology
Available from *Free Access Content* in Journal of the American College of Cardiology

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Title: Fetal warfarin syndrome.

Citation: BMJ case reports, Jan 2012, vol. 2012, 1757-790X (2012)

Author(s): Starling, Luke D, Sinha, Ashutosh, Boyd, Duncan, Furck, Anke

Abstract: A case of a baby born preterm with an antenatal diagnosis of aortic coarctation for which prostin was electively started at birth. The baby was found to be profoundly anaemic with no clear obstetric cause. Features consistent with antenatal intracerebral haemorrhage were noted on cranial ultrasonography in the context of severe coagulopathy, prompting investigations which confirmed fetal-maternal haemorrhage. It transpired that, following aortic and mitral valve replacements, the mother was anticoagulated with warfarin at conception, having misunderstood her cardiologist's advice that: 'you cannot get pregnant whilst on warfarin'. Following conversion to low molecular weight heparin, she suffered a stroke, thus warfarin was restarted, with an international normalised ratio of 3-4.7 during pregnancy. Following transfer to the paediatric intensive care unit, fetal warfarin syndrome was diagnosed. The coagulopathy and anaemia were corrected and aortic coarctation was excluded. The baby returned to the neonatal intensive care unit for ongoing care and was discharged home in good condition around his due date. At the present time, there is no clinically overt neurological deficit.

Source: Medline

Full Text:
Available from *Highwire Press* in BMJ Case Reports
Available from *National Library of Medicine* in BMJ Case Reports

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Title: Foetal cerebral hemispheric atrophy and porencephaly after intrauterine exposure to maternal warfarin for mechanical prosthetic heart valve

Citation: Prenatal Diagnosis, February 2008, vol./is. 28/2(157-159), 0197-3851;1097-0223 (February 2008)

Author(s): Simonazzi G., Pilu G., Palareti G., Bernardi B., Rizzo N.

Language: English

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *John Wiley and Sons* in Prenatal Diagnosis
Available from *John Wiley and Sons* in Prenatal Diagnosis

Title: Perinatal stroke--risk factors and management.

Citation: British journal of haematology, Aug 2005, vol. 130, no. 3, p. 333-343, 0007-1048 (August 2005)

Author(s): Chalmers, Elizabeth A

Abstract: Stroke is an uncommon but increasingly recognised cause of mortality and long-term neurological morbidity in children. A significant number of these events appear to be caused by thromboembolic disease and, as with other childhood thrombotic problems, the incidence of central nervous system events appears highest during the neonatal period. In contrast to peripheral arterial and venous thrombotic problems, it is likely that a proportion of cerebral thromboembolic events occur either in utero or perinatally and reflect different risk factors from those occurring in older infants and children. The pathophysiology of perinatal stroke is complex and in many cases is likely to be multifactorial. It is now recognised that risk factors may relate to both maternal and placental problems as well as fetal and neonatal disorders. Large prospective studies of perinatal stroke are currently lacking and efforts to define the relative contribution from each of these areas are at an early stage. The complex nature of these disorders requires collaboration between a number of different disciplines including obstetrics, fetal medicine, pathology, neonatology and neurology. Of particular interest to haematologists is the possible impact of prothrombotic abnormalities in the pathophysiology of these events and also the potential for the use of antithrombotic agents in both management and prevention.

Source: Medline

Full Text:
Available from *John Wiley and Sons* in British Journal of Haematology
Available from *John Wiley and Sons* in British Journal of Haematology

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Title: Perinatal intraventricular hemorrhage (IVH) related to maternal warfarin

Citation: Journal of Thrombosis and Haemostasis, July 2011, vol./is. 9/(477), 1538-7933 (July 2011)

Author(s): Komvilaisak P., Kiatchoosakun P., Jirapradittha J., Kitkhuandee A., Vannaprasaht S.

Language: English

Abstract: Introduction: Warfarin can cross the placental barrier. It might cause of perinatal IVH irrespective of maternal INR (International normalized ratio) level. Incidence of perinatal IVH related to maternal warfarin is 4.6-5.1% in autopsy studies of stillbirth. Results: A 35-week male neonate was born by emergency cesarean section due to fetal distress. His mother, a 27-year old, had underlying rheumatic heart disease status post mitral valve replacement requiring life-long warfarin with INR level of 2.65. Anticoagulation was switched to enoxaparin between 8 and 12-week gestation then was on warfarin until delivery. She reported of decrease fetal movement, fetal monitoring showed abnormal variability compatible with acute fetal hypoxia. His Apgar scores were 1, 3, 3 at 1, 5, 10 min, respectively. He had markedly pale, widening and tensed anterior fontanelle, fixed pupils with no response to light. Initial hematocrit was 16% requiring blood transfusion. Coagulogram revealed prolonged both prothrombin time and activated partial thromboplastin time requiring fresh frozen plasma replacement. Platelet count and fibrinogen level were normal. CT of brain demonstrated IVH and a 4.3 x 5.7 x 4.9 cm. in size intracerebral hemorrhage at right parietotemporal region with evidence of subfal-cine and descending transtentorial brain herniation. At age of 4 h, he developed seizure requiring anticonvulsant. Multidisciplinary team and parents made decision to treat palliatively. He deceased from respiratory failure at age of three months. Genotype of VKORC1 showed 1173CC>TT and 1639GG>AA in both mother and child. These polymorphism decreased vitamin K epoxide reductase activity lead to reduce active form of vitamin K. Conclusion: Perinatal intracranial hemorrhage related to maternal warfarin is caused of neurocognitive morbidity and mortality in neonate. Monitoring for fetal well-being and pharmacogenomics of warfarin in pregnant women should be warranted.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: Warfarin-associated Fetal Intracranial Hemorrhage: A Case Report

Citation: Journal of Korean Medical Science, October 2003, vol./is. 18/5(764-767), 1011-8934 (October 2003)

Author(s): Lee H.-C., Cho S.Y., Lee H.J., Kim C.J., Park J.S., Chi J.G.

Language: English

Abstract: A 27-yr-old woman who had been taking warfarin for 10 yr after mitral valve replacement became pregnant. After knowing her pregnancy, she received heparinization for nine weeks instead of warfarin, and took oral anticoagulant again. At 24 weeks of gestation, fetal ultrasound and MRI showed a left subdural hematoma, and the pregnancy was terminated. Subdural hematoma was demonstrated on autopsy. Fatal bleeding of the fetus is a rare complication of maternal warfarin medication, occurring mostly in the second or third trimester. There is no alternative regimen available, so that regular monitoring by fetal ultrasound and strict control of warfarin dose with regular measurement of prothrombin time are the best way to prevent intrauterine fetal death due to bleeding.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *National Library of Medicine* in Journal of Korean Medical Science
Available from *National Library of Medicine* in Journal of Korean Medical Science
Available from *Free Access Content* in Journal of Korean Medical Science

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Title: The contribution of prothrombotic disorders to peri- and neonatal ischemic stroke

Citation: Seminars in Thrombosis and Hemostasis, August 2003, vol./is. 29/4(415-424), 0094-6176 (August 2003)

Author(s): Golomb M.R.

Language: English

Abstract: Prothrombotic disorders are believed to be important contributors to the etiology of peri- and neonatal arterial ischemic stroke and sinovenous thrombosis, which may lead to life-long disability. This article reviews hematological issues unique to the perinatal period, including: the significance of the placenta as the interface between maternal and fetal circulations; normal changes in the coagulation system of mothers during and just after gestation; and the significance of prothrombotic disorders in the mother and/or fetus. Other possible maternal and neonatal contributors to peri- and neonatal stroke are discussed, including: infection, pre-eclampsia, diabetes, and drug use in the mother; and infection, dehydration, complex congenital heart disease, extracorporeal membrane oxygenation, and catheter placement in the neonate. Possible approaches to preventing and treating perinatal and neonatal stroke are presented.

Publication Type: Journal: Review

Source: EMBASE

Title: Venous thromboembolism during pregnancy: a retrospective study of enoxaparin safety in 624 pregnancies.

Citation: BJOG : an international journal of obstetrics and gynaecology, Nov 2001, vol. 108, no. 11, p. 1134-1140, 1470-0328 (November 2001)

Author(s): Lepercq, J, Conard, J, Borel-Derlon, A, Darmon, J Y, Boudignat, O, Francoual, C, Priollet, P, Cohen, C, Yvelin, N, Schved, J F, Tournaire, M, Borg, J Y

Abstract: To assess the maternal, fetal and neonatal safety of enoxaparin in pregnant women who require antithrombotic therapy. Retrospective analysis of case notes of women who received enoxaparin during pregnancy, irrespective of dose, duration and reason for treatment. Fifty-five French perinatal centres. Data from 624 pregnancies in 604 women between 1988 and 1997. The incidence of previous thromboembolism was 29.8%, known thrombophilia 15.2%. Indication, regimen of enoxaparin and outcome measures were reported for each pregnancy. Information was obtained from case records, validated by research staff and analysed by an independent scientific committee. Incidence, seriousness and causality of maternal, fetal and neonatal adverse events, pregnancy outcome, and incidence of venous thromboembolism. Enoxaparin was administered for treatment of an acute episode in 49 cases and for thromboprophylaxis in 574 cases. Serious maternal haemorrhage occurred in 11 cases during pregnancy (1.8%), one being reasonably related to enoxaparin, and in nine cases at delivery (1.4%), all unrelated to enoxaparin. Maternal thrombocytopenia was reported in 10 cases (1.6%). two being serious but unrelated to enoxaparin. Eight pregnancies ended in stillbirth (1.1%). Among the 693 live births, 17 major congenital abnormalities (2.5%) and 10 serious neonatal haemorrhages (1.4%) were reported. None of the fetal or neonatal adverse events was related to enoxaparin. Eight venous thromboembolic events (1.3%) were reported. The incidence of adverse events reported could be explained by the high risk profile of the study population. Overall, this retrospective study suggests enoxaparin is well tolerated during pregnancy.

Source: Medline

Title: The role of heparin in the etiology of intraventricular hemorrhage: A controlled trial

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Title: The association of heparin exposure with intraventricular hemorrhage among very low birth weight infants.

Citation: Journal of perinatology : official journal of the California Perinatal Association, May 1995, vol. 15, no. 3, p. 185-191, 0743-8346 (1995 May-Jun)

Author(s): Malloy, M H, Cutter, G R

Abstract: To determine whether there is a relationship between exposure to heparin and an increased risk of intraventricular hemorrhage (IVH), we analyzed data from a cohort of infants who had been subjects in a randomized clinical trial of umbilical artery catheter placement. Data from 862 infants who survived the first 6 days of life were used for analysis. The incidence of IVH (grades 1 through 4) was 28.6%. The mean (SD) birth weight for infants with IVH was 954 gm (247 gm) compared with 1053 gm (253 gm) among infants without IVH ($p < 0.01$). The mean (SD) heparin intake among infants with an IVH was 83.5 units/kg/day (48.7) compared with 59.4 units/kg/day (48.7) among infants without an IVH ($p < 0.01$). With the use of logistic regression modeling to adjust for a number of potentially confounding variables, including fluid intake and birth weight, we observed an odds ratio for an IVH of 1.96 (95% confidence interval = 1.32, 2.91) for infants with second through fourth quartile intakes of heparin compared with that for infants with first quartile heparin intakes. Although we cannot rule out the possibility that the observations from this model may be confounded by factors associated with the severity of illness of the infant, these data support the findings of previous reports of an association between heparin exposure and the risk for an IVH.

Source: Medline

Title: The role of heparin in the etiology of intraventricular hemorrhage: A controlled trial

Citation: Journal of Maternal-Fetal Investigation, 1993, vol./is. 2/6(283-287), 1057-0802 (1993)

Author(s): Stec T., Metcalf M., Anwar M., Hiatt M., Hegyi T.

Language: English

Abstract: The prevalence and severity of intraventricular hemorrhage (IVH) were comparable in two groups of very low birthweight infants managed with different intravenous flush solutions. Nineteen infants, BW 1,097 +/- 390 g (mean +/- SD) and GA 28 +/- 3 wk, were treated with heparin (1 U/ml) containing IV fluids infused into the umbilical artery and 23 control infants, BW 1,001 +/- 416 g and GA 28 +/- 3 wk were managed in an identical manner but without the administration of heparinized fluids during the first week of life. All infants, randomly assigned and managed with a double-blind protocol, were enrolled prior to 24 hr of age. Except for two infants, one in each group, all infants had negative neurosonographic evaluations and normal platelet counts during the first day of life. Neurosonograms were obtained at 1, 3, and 7 days of age. At 7 days of age, there were seven infants with IVH in the heparin group and fourteen among the controls (37% vs. 61%). Severe IVH (grades 3 or 4) occurred in four heparin and four control infants. Two infants in the heparin group and one in the control group expired. Thrombotic umbilical artery-associated complications occurred in five heparin infants and 10 control infants. None of these differences approach statistically significant levels. In this population of very low birthweight infants the administration of heparinized solution in the first week of life did not

increase the incidence or severity of IVH, nor did it affect the number of catheter related complications.

Publication Type: Journal: Article

Source: EMBASE

Title: The comparison of the pharmacokinetics of a low molecular weight heparin in the newborn and adult pig

Citation: Thrombosis Research, 1989, vol./is. 56/4(529-539), 0049-3848 (1989)

Author(s): Andrew M., Ofosu F., Brooker L., Buchanan M.R.

Language: English

Abstract: Standard heparin (SH) is frequently used in the sick neonate to prevent catheter related thrombosis. SH can cause significant bleeding complications in the adult and its use in the neonate is linked to an increased incidence of intraventricular hemorrhage. Recently available low molecular weight heparins (LMWH) offer potential advantages over SH in the adult by exhibiting a longer half life and decreased bleeding side effects compared to SH. Whether LMWHs would offer similar therapeutic advantages to the sick neonate is unknown. Using the porcine model of neonatal hemostasis we measured the pharmacokinetics of a LMWH (Choay 222) in the pig (ATIII level: 100%), in the piglet (ATIII level: 50% of adult) and in the piglet given exogenous ATIII. All pigs were bolused with ¹²⁵I-LMWH (5, 25 or 100 anti-factor Xa units/kg) and blood samples collected for the measurement of ¹²⁵I-radioactivity, and anti-factor Xa activity. The half life of LMWH, measured as either ¹²⁵I-radioactivity or as anti-factor Xa activity, was not dose dependent and was similar in pigs and piglets; however, the volume of distribution was greater in the piglet resulting in an increased total clearance compared to the pig. As well, the supplementation of the piglet with exogenous ATIII did not influence the pharmacokinetics of LMWH. The half life of the LMWH in both pigs and piglets was approximately twice as long as previously reported values for SH in the same animal model. Thus the longer half life of LMWH in the piglet, and the similarity of the half life in piglets and pigs suggest that LMWH may have a therapeutic advantage in the newborn over SH.

Publication Type: Journal: Article

Source: EMBASE

Title: Heparin use as a risk factor for intraventricular hemorrhage in low-birth-weight infants.

Citation: The New England journal of medicine, May 1986, vol. 314, no. 18, p. 1156-1160, 0028-4793 (May 1, 1986)

Author(s): Lesko, S M, Mitchell, A A, Epstein, M F, Louik, C, Giacoia, G P, Shapiro, S

Abstract: In a systematic review of data on drug use and adverse clinical events in infants with birth weights under 2000 g, we observed an association between germinal matrix-intraventricular hemorrhage and the use of heparin to maintain the patency of vascular catheters. Sixty-six infants with germinal-matrix (periventricular) or intraventricular hemorrhage or both (cases) were matched with 254 infants with other conditions (controls), and analysis, taking the matching factors into account, yielded an odds ratio of 14.0 (95 percent confidence interval, 5.4 to 34). When potential confounding factors were taken into account, the odds ratio was 3.9 (1.4 to 11). The association did not appear to vary according to the severity of hemorrhage or to the method of administration or dose of heparin. The data suggest that the routine use of heparin in neonatal intensive care units is associated with a four-fold increase in the risk of germinal matrix-intraventricular hemorrhage. Because of the possibility that confounding may have been incompletely controlled for, the true risk cannot be determined from these data, and a controlled clinical trial of heparin use in low-birth-weight infants is recommended.

Source: Medline