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President's Column


Prof. Dr. Samina Naeem

Assalam o aliakum. The historical city of Lahore is honoured to host the 16 th annual conference of PSH along with 37 th annual PAP conference in December from 20th to 22nd 2013. Zinda Dilan e Lahore will give you a warm welcome in this winter season Insha Allah. This conference is a joint venture of all the sub specialties of pathology. Pre conference workshops will be followed by didactic lecture sessions and paper presentations. Enthusiastic participation from all the members of PSH and pathology community will turn this mega event into a success Insha Allah.

Tremendous efforts for revival of local chapter meetings of PSH have started to bear the fruit. These meetings are regularly conducted in almost all the provincial capitals of Pakistan as well as Rawalpindi / Islamabad. These interactive meetings not only serve as a good source of exchange of knowledge and experience, they also provide a platform for social interaction. Participation of haematologists from distant areas and neighboring cities in these meetings will be highly appreciated .This will help us to develop PSH into a more active and stronger body.

The threat of Dengue fever is not yet over. Mass education, improved hygienic conditions, media campaigns and vigilant monitoring has helped to reduce the burden of disease. Public awareness and education is a most beneficial tool to combat any disease. These efforts should continue to achieve the desired results.

Looking Forward to see you all in Lahore.

With warm regards,
Prof.Dr.Samina Naeem

ACADEMICS

Anticoagulants and Thrombolytics in Pregnancy

Contributed by Dr.Humera Rafiq and Professor Samina Naeem , Chairperson and Dean of Pathology Department KEMU

Normal pregnancy is associated with a hypercoagulable state due to multiple causes. The foremost reason is the increased serum levels of procoagulants, such as factor II, VII, VIII, X, XII ,and fibrinogen. Decreased levels of protein S and increased resistance to activated protein C are also observed in the second and third trimesters of pregnancy. Concomitantly, serum levels of plasminogen activator inhibitor-1 (PAI-1) and placental plasminogen activator inhibitor-2 (PAI-2) increase which lead to a decreased fibrinolytic state. Venous stasis resulting from pressure of the gravid uterus on the inferior vena cava and decreased venous tone are other predisposing factors to venous thrombosis in pregnancy.

Pregnancy is associated with 4 times increased risk of venous thromboembolism (VTE) and the risk increases to 14-fold during puerperium. This risk increases further if an underlying thrombophilia is present. Anticoagulant therapy is indicated in pregnancy for the treatment of acute VTE, valvular heart disease, prevention of pregnancy-related complications in women with antithrombin deficiency or antiphospholipid antibody syndrome (APLAs) and pregnant women with other thrombophilias who have had prior episode of VTE. Most (approximately 85%) of DVT of the lower extremity occur on the left side during pregnancy. This is attributed to the more tortuous course of the venous drainage of the left leg through the pelvis and compression of the left common iliac vein by the overlying right iliac artery.

Indications for the Use of Antithrombotic Agents

Anticoagulant therapy is indicated in pregnancy for

- treatment of acute VTE,
- valvular heart disease,
- prevention of pregnancy-related complications women with antithrombin deficiency
- antiphospholipid antibody syndrome (APLAs)
- Pregnant women with other thrombophilias who have had prior episode of VTE.

Antithrombotic agents (i.e., anticoagulants and thrombolytic agents) are first-line therapy for pathological thromboses. Anticoagulants are available in oral or parenteral forms. They interrupt the coagulation cascade to prevent thrombus formation and extension while endogenous thrombus lysis occurs. Thrombolytic agents promote thrombus lysis and are administered parenterally.

Unfractionated heparin, low molecular weight heparin (LMWH), heparinoids, synthetic pentasaccharide inhibitors (e.g., fondaparinux), and direct thrombin inhibitors (i.e., hirudin and argatroban) are the used parenteral anticoagulants. They inactivate thrombin and/or factor Xa without depleting circulating levels of clotting factors. Warfarin, Rivaroxaban and Dabigatran are examples of oral anticoagulant. Warfarin interferes with liver synthesis of vitamin K-dependent clotting factor , Rivaroxaban is a factor Xa inhibitor whereas Dabigatran is a direct thrombin inhibitor. Unlike warfarin, the pharmacokinetics of rivaroxaban and dabigatran are predictable; thus, routine monitoring of coagulation parameters is not required when one of these agents is used. Warfarin is being used in pregnancy (with some reservations) especially in patients with mechanical valve replacement (replacing with LMWH during first 3 months and discontinuing 4-6 weeks before delivery).The safety and efficacy of the newer oral agents (rivaroxaban or dabigatran) in pregnancy however has not been established.

Traditional thrombolytic agents include streptokinase (SK), anisoylated plasminogen streptokinase activator complex (APSAC), urokinase, and recombinant tissue plasminogen activator (t-PA).These agents mediate the dissolution of fibrin clots by promoting the conversion of plasminogen to plasmin, which causes degradation of fibrin to fibrin degradation products.

Risk Factors in Pregnancy and Recommendations

(Prophylactic, Adjusted and Intermediate Doses of LMWH, UFH are given at the end Of Table)

Risk Factor	Recommendations
Women with a single episode of VTE associated with a transient risk factor that is no longer present.	Clinical surveillance and anticoagulant prophylaxis postpartum*
Women with a single episode of VTE and thrombophilia (confirmed laboratory abnormality) and a strong family history of thrombosis who are not receiving long-term anticoagulants.	Prophylactic or intermediate-dose LMWH or unfractionated heparin (UFH), plus postpartum anticoagulation for at least 6 weeks (for a total minimum duration of therapy of 6 months)
Women with antithrombin deficiency and no previous VTE	Antepartum and postpartum prophylaxis.
Women with thrombophilia (other than antithrombin deficiency) and no previous VTE.	Clinical surveillance or prophylactic LMWH or UFH and anticoagulant prophylaxis postpartum*
Women with multiple (= 2) episodes of VTE who are not receiving long-term anticoagulants.	Prophylactic, intermediate-dose or adjusted-dose UFH or adjusted-dose LMWH followed by long-term anticoagulation postpartum
Women with multiple (= 2) episodes of VTE who are receiving long-term anticoagulants.	Adjusted-dose UFH or LMWH followed by resumption of long-term anticoagulation postpartum.
All women with previous DVT, antenatal and/or postpartum	Use of graduated elastic compression stockings
Women with recurrent pregnancy loss (= 3 miscarriages) and women with severe or recurrent preeclampsia, placental abruption, or otherwise unexplained intrauterine growth retardation.	Screen for thrombophilia and antiphospholipid antibodies
Women with antiphospholipid antibody syndrome and a history of multiple (= 2) early pregnancy losses or = 1 late pregnancy losses, preeclampsia, intrauterine growth retardation (IUGR), or abruption.	Antepartum aspirin plus prophylactic or intermediate-dose UFH or LMWH.
Women with APLAs and a history of VTE who are receiving long-term oral anticoagulation therapy.	Adjusted-dose LMWH or UFH therapy plus low-dose aspirin and resumption of long-term oral anticoagulation therapy postpartum

* If the previous risk factor is pregnancy or estrogen-related or additional risk factors (such as obesity) are present, antenatal anticoagulant prophylaxis is recommended.

Prophylactic Dose

LMWH : 110 to 199 lb. (50-90 kg); 40 mg SC daily: < 110 lb.; 20 mg SC daily: > 199 lb.; 40 mg SC every 12 hours. UFH : 1st trimester; 5,000 IU SC twice daily: 2nd trimester; 7,500 IU SC twice daily: 3rd trimester; 10,000 IU SC twice daily.

Intermediate dose

LMWH :< 50 kg; 60 mg subcutaneously once-daily :50 kg to < 70 kg; 80 mg subcutaneously once-daily: 70 kg to < 100 kg; 100 mg subcutaneously once-daily:100 kg or above; 120 mg subcutaneously once-daily.
UFH : An antifactor Xa assay concentration of 0.1-0.3 unit/ml is used as the target range.

Adjusted-dose

LMWH : antifactor Xa target peak range (3-4 hours after dosing) should be 0.5 - 1 IU/mL
UFH : UFH SC every 8 to 12 hours ,adjusted to prolong the activated partial thromboplastin time (APTT) to 1.5 - 2.5 times the control when tested at mid-interval between subcutaneous injections.

Recommendations in Pregnant Women with Acute VTE

The following 2 alternative approaches are reasonable:

- Subcutaneous LMWH can be used initially and for long-term treatment with dose adjustment based on monitoring of anti-Xa levels.
- Intravenous (IV) UFH bolus is followed by continuous infusion to maintain APTT in the therapeutic range for at least 5 days, followed by subcutaneous LMWH or dose-adjusted subcutaneous UFH for the remainder of pregnancy.

LMWH is preferred over UFH for the prevention and treatment of VTE because of ease of use and better efficacy and safety profile. Anticoagulants should be administered for at least 6 weeks postpartum for a minimum total duration of therapy of 6 months.

In women receiving dose-adjusted LMWH or UFH therapy, discontinuing anticoagulant therapy 24 hours prior to elective induction of labor is recommended. If spontaneous labor occurs, careful monitoring of APTT or anti-Xa levels is required. If APTT is markedly prolonged near delivery, protamine sulfate may be required to reduce the risk of bleeding.

Valvular Heart Disease

Women with valvular heart disease who are pregnant or planning to conceive require careful evaluation and management. Physiologic changes associated with pregnancy are poorly tolerated in some cases of valvular heart disease. These include aortic stenosis, mitral regurgitation, aortic regurgitation with NYHA class 3-4 symptoms, mitral stenosis with NYHA class 2-4 symptoms, valvular heart disease that results in severe pulmonary hypertension, and left ventricular (LV) dysfunction with an ejection fraction (EF) less than 40%. Patients with mechanical prosthetic valve requiring anticoagulation are exposed to special risks during pregnancy.

Whenever possible, symptomatic or severe valvular lesions should be addressed before conception. Anticoagulation is recommended in most pregnant patients with a mechanical prosthetic heart valve, whereas those with a bioprosthetic valve do not require anticoagulation. Warfarin (Coumadin) is more efficacious than UFH for thromboembolic prophylaxis of pregnant women with mechanical valves. Unfortunately, warfarin therapy in the first trimester of pregnancy is associated with a substantial increase in fetal anomalies, and anticoagulation with any agent is associated with an increased incidence of fetal wastage (approximately 30%), prematurity (approximately 45%), and low birth weight (approximately 50%). In a systematic review of fetal and maternal outcome of pregnancy with mechanical heart valves, the regimen associated with the lowest risk of valve thrombosis (3.9%) was warfarin throughout pregnancy. However, its use throughout pregnancy was associated with warfarin embryopathy in 6.4% of live births. The substitution of heparin at or prior to 6 weeks, and continued until 12 weeks, eliminated the risk of warfarin embryopathy. Using heparin only from 6-12 weeks' gestation was associated with an increased risk of valve thrombosis (9.2%).

Recommendations for anticoagulation of pregnant women with prosthetic heart valves

- Adjusted dose (twice daily) subcutaneous LMWH throughout pregnancy to achieve a peak anti-Xa level of 1-1.2 U/mL 4 hours after injection or

- Adjusted dose (twice daily) subcutaneous UFH throughout pregnancy to achieve mid-interval APTT at least twice control or an anti-Xa level of 0.35-0.70 U/mL or
- UFH or LMWH (as above) until 13 weeks' gestation, change to warfarin until the middle of the third trimester, and then restart UFH or LMWH

Long-term anticoagulants should be resumed postpartum with all regimens.High-risk women with prosthetic heart valves, such as women with LV dysfunction and women with prior thromboembolic episodes, should have the addition of low-dose aspirin 75-162 mg/d.

Fetal complications of anticoagulants during pregnancy

Warfarin crosses the placenta and can cause both fetal bleeding and teratogenicity, with the latter occurring mainly during the first trimester.Neither UFH nor LMWH cross the placenta; therefore, these agents do not cause fetal bleeding or teratogenicity, although bleeding at the uteroplacental junction and fetal wastage is possible.

Maternal complications of anticoagulants during pregnancy

The rate of major bleeding in patients treated with UFH therapy is 2%.

Approximately 3% of patients receiving UFH develop immune thrombocytopenia (heparin-induced thrombocytopenia [HIT]), which predisposes to venous and arterial thrombosis.

Heparin-induced osteoporosis causes vertebral fracture in 2-3% of patients and significant reduction in bone density is seen in about 30% of patients receiving long-term UFH. LMWH causes less osteoporosis and HIT than UFH.

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FCPS Haematology Intensive Course

The Children hospital Lahore organized an orientation course in collaboration with PSH, focusing on preparation of FCPS PART II (written) examination on 7th September 2013 at Shaukat Raza Khan Auditorium. It was followed by 7TH FCPS Haematology intensive course on October 9-12,2013. This course comprised of modules on transfusion, coagulation and morphology. Eminent haematologists from all over Pakistan were facilitators of the course.

The Sindh Prevention and Control of Thalasemia Ordinance 2013

An ordinance was passed by honourable Governor Sindh Mr.Ishratulabad on 8th May 2013 comprising of following salient points

1. Government shall arrange and approve the dissemination of information and education of thalassemia and its trait and using instructions, guidelines,etc. Government shall also set up a system of genetic counseling and diagnostic facilities and encourage as well as ensure easy access and use to these facilities.
2. Screening of blood relatives of thalassemia patients will be ensured, blood relatives of thalassemia patients shall be advised and counseled at the time of marriage.
3. Antenatal tests shall be carried out on carrier pregnant women whose husbands are also known to be carriers with approval from the couple. They will be told about the results and results be entered in a data bank for registration.
4. Diagnostic facilities and counseling on risk of consangous marriages of persons having thalassemia trait be provided.
5. All individuals of child bearing age should have their thalassemia status checked by electrophoresis with their consent.
6. All NGO's working for thalassemia will ensure that 10% of their budget will be spent on prenatal diagnosis and developing facilities for thalassemia screening.
7. It will be compulsory for health facilities (which includes government, non-government, semi-government, private organization and medical practitioners providing medical care to thalassemia patient) to provide all above facilities. In case a facility fails to do so, penalty of one hundred thousand Rupees shall be charged.
8. Government will establish a thalassemia and hemoglobinopathy foundation.

2nd Joint Conference of PAP/ 16th PSH conference

Date:18.12.2013 :Bone Marrow Morphology
Date:19.12.2013: Coagulation Workshop ,Transfusion Workshop ,Workshop on Flow Cytometry

DAY 1 20Th December 2013	DAY 2 21st December 2013	DAY 3 22nd December 2013
9:00 AM INAUGRATION	9:00 AM-10:30 AM PLENARY LECTURES Speakers: Prof. Mohammad Khurshid Maj.Gen. Suhaib Ahmed: Non-Transfusion Dependent Thalassaemia Brig.Pervaiz Ahmed: Haemopoietic stem cell transplantation issues and opportunities. Dr.Bushra Moiz : Hemostatic Disorders in females . Brig. Saleem Ahmed Khan: Quality Management in Blood Transfusion.	09:00 AM - 11:00 AM PLENARY LECTURES 3 Speakers: Prof. Khalid Hassan : Myelodysplastic syndrome Prof. Mehfooz ur Rehman: Haemovigilance In Transfusion. Dr. Nisar Ahmad : Congenital dyserthropoetic anemia. Professr Syed Irfan: CML- Molecular genetics and Targeted Therapies Dr Shahida MOHSIN: Role of microparticles in various clinical settings.
09:30 AM - 10:30 AM RAAZI LECTURE	10:30 AM - 11:00 AM Tea	11:00 AM - 11:30: AM Tea
10:30 AM - 11:15 AM EXHIBITION OPENS	11:00 AM - 12:00 PM PLENARY LECTURES 2 Speakers: Prof. Khalid Zafar Hashmi: Hepatitis-C virus related thrombocytopenia" Dr. Tahir Shamsi: Gama Globin Gene Switching in Beta Thalassaemia Abolishes Transfusion Requirement. Dr.Saba Jamal : Centralized Blood Banking System in Pakistan- Challenges & Solutions General Body Meeting PSH	11:30 AM - 1:30 PM Free Paper Session 3
11:15AM-1:15PM Common Scientific Session	12:00 PM - 1:00 Pm General Body Meeting PAP	1:30 PM LUNCH
1:15PM-2:30 PM LUNCH & PRAYERS	1:00 PM - 02:00 PM LUNCH	
2:30PM-4:30 PM Free Paper Session I	2:00 PM - 4:30 PM Free Scientific Paper Session 2	

Activities of Lahore chapter of PSH

Local chapter of PSH Lahore has been active as like previous year and regular monthly meetings are being held in different institutions. PSH meetings were hosted by Ittefaq hospital, Shalamar Hospital, King Edward Medical University, and Children's Hospital & ICH in June, July, August and September. Discussions of rare and interesting cases were held which benefited the trainees and participants .

Lahore local chapter meeting at King Edward Medical University

Dear Colleagues

We request you to join us in newsletter by sending your comments, short communications, case reports, issues of national interest, new developments in your departments, and scientific activities in your institutes. Your contribution is the back bone of this newsletter. It is requested that report/write up should be brief and concise. For information, suggestions, and correspondences please e-mail to: humerarafiqsheikh@hotmail.com In case you are a member and you are not receiving mails from us please update your postal and e address urgently. You can find us at www.psh.org.pk

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