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Abstracts

ORAL COMMUNICATIONS

OC-1a
Rivaroxaban use in women with antiphospholipid syndrome and previous poor anticoagulation control with vitamin K antagonists

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Background: Management of antiphospholipid syndrome (APS) centres on long term anticoagulation with vitamin K antagonists (VKA).In a minority of APS patients treated with VKAs instability of INR control is of major concern and we had switched such patients to rivaroxaban 20 mg od.
Methods: Data on APS women with poor anticoagulation control with VKA who had been a switched to rivaroxaban 20 mg was collected. All such patients were APS patients treated with VKA with INR target 2–3 for secondary prevention of venous thromboembolism (VTE) and whose time in therapeutic range (TTR) was 65% or less.
Results: 24 APS patients were included (mean±SD age 45.2±15.1 yrs, mean disease duration 8.9±7.4 yrs, mean age at onset of disease 37.1±8.7 yrs). All patients had previous deep vein thrombosis and seven had both deep vein thrombosis and pulmonary embolism. Mean TTR was 58% [42–62]. 18 patients had erratic INR control (mean 16 [11–21] INR tests within the last 6 months) and six patients had INRs constantly in sub-therapeutic range. Patients were followed for a mean of 11.8 months [6–24] after starting rivaroxaban. No further VTE or major bleeding events were observed. Two women reported menorrhagia, which was treated with conservative management.
Conclusion: The use of rivaroxaban therapy for secondary thromboprophylaxis for previous VTE in APS patients appeared safe. A larger trial RAPS (Rivaroxaban in AntiPhospholipid Syndrome, IRSCTN 68222801) is ongoing and results will be available next year. In the interim, rivaroxaban may be considered cautiously as an alternative anticoagulant in APS patients with poor anticoagulant control with VKA.

OC-1b
Von Willebrand syndrome and pregnancy

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In patients with von Willebrand disease the bleeding symptomatic depends on the type of the disease. The following study investigates the influence of the specific type of von Willebrand disease on the clinical course of the disease and the therapeutic implications during pregnancy.
Patients and methods: The diagnosis of the bleeding disorder was preconceptional. Clinical data of bleeding events, medication and delivery were documented. The duration of the von Willebrand factor and factor VIII from beginning to 6 weeks after delivery were analysed.
Results: We detected during 2005–2013 67 patients with 79 pregnancies. Type 1 was found in 56 patients, type 2A in 7, type 2B in 2, type 2N in 1 and type 3 in 1 patient. The age of the patients was between 16 and 40 years. Only the patient with von Willebrand type 3 was on a regular prophylaxis with a von Willebrand plasma derived product. Type 1 showed a normalized von Willebrand-Antigen without a severe clinical complication associated with the disease in all patients. A vaginal bleeding complication was seen in one type 2B patient. Minor bleeding symptoms (epistaxis, hematomas) were more often in type 2 than in type 1. Plasma derived von Willebrand products were indicated only in 6 patients, transexamic acid in 9 patients and desmopressin in 7 patients.
Conclusion: The therapy of patients with von Willebrand syndrome and pregnancy depends on the type of the disease. The clinical observation and a patient-related therapy is important for a successful pregnany.

OC-2a
Clinical outcomes of implementing evidence-based practice on venous thromboembolism prevention for cancer patients in Qatar, a retrospective study

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Background: Venous ThromboEmbolism (VTE) disease is a serious condition; approximately 20% of VTE cases occur in cancer patients and it is a significant cause of morbidity and mortality especially during the first year among all types and stages of cancer [1,2]. Most hospitalized patients with cancer require thromboprophylaxis throughout hospitalization [3]. Breast cancer is considered a very high risk for VTE due to different factors (malignancy, surgery, chemotherapy, hormonal therapy, hospitalization, and female gender) [4].
Objectives: This study focuses on the assessment of the clinical outcome in preventing VTE amongst cancer population in Qatar after implementation of evidence based thromboprophylaxis guidelines.
Methods: A retrospective study was conducted to evaluate the incidence of DVT by evaluating doppler ultrasound, database for 364 cases of inpatients and outpatients over 24 month (January 2011–December 2012), findings were analyzed by a hematologist to identify patients who developed DVT due to current or previous admission (within 30 days). The relationship between the incedence of devloping VTE overtime and the complinece to VTE prevention protocol were established.
Results: The study showed that the increase in the overall compliance to VTE prophylaxis protocol introduced to inpatients population (n=2595) increased from 61.5% to 84.6% (P=0.0297), led to decreased DVT incidence by 66.4% (P=0.0145). 50% of cancer cases developed DVT were breast cancer patients (n=24), 92% of them were outpatients.
Conclusion: Appropriate thrombophylaxis could considerably improve the incidence of DVT in cancer patients, breast cancer patients are very high risk for VTE, which raises the importance of implementing thromboprophylaxis in both hospital and ambulatory sittings.
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OC-2b
Reducing venous thromboembolic events associated with ovarian cancer: are we winning the battle?

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We previously reported a venous thromboembolism (VTE) incidence of 9.7% in a large cohort of women with ovarian cancer from 2006 to 2010. Of these, 33% occurred in the first 28 days following surgery. In keeping with current international guidelines we introduced a policy of extended VTE prophylaxis with low molecular weight heparin (LMWH) for four post-operative weeks in January 2012. This is a study of VTE outcomes in the first two years.
Patients treated for ovarian cancer from Jan 2012 to Dec 2013 in St. James' Hospital were identified from the gynaecology oncology database
Fourteen VTE events occurred in 146 (9.5%) women with ovarian cancer. Eight (57%) occurred prior to treatment, 4 (29%) events occurred in the post-operative period with only 1 case (7%) occurring in the first 28 days post op. Two cases (14%) occurred during subsequent chemotherapy. Analysis of the postoperative events revealed the following: One patient had PE on Day 1 prior to starting LMWH (she had massive intraoperative haemorrhage); the other 3 patients all had PEs at 3, 6 and 12 months post operatively. The incidence of immediate post-operative VTE events (first 28 days) was 0.7%, a reduction from 3.2% in the original study (p=0.2).
Conclusion: Extended postoperative VTE prophylaxis has had no impact on the overall incidence of VTE in ovarian cancer patients. However, we did see a reduction in the number of events in the first post-operative month. Commencement of LMWH pre-operatively and mechanical compression boots have been introduced in a further attempt to reduce post-operative VTE.

OC-3a
Role of p45-NF-E2 in regulating syncytiotrophoblast formation in human placenta

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The transcription factor p45-NF-E2, known to regulate megakaryocyte maturation, has been associated with impaired placental vascularization and intrauterine growth restriction (IUGR) in mice, where p45-NF-E2 expression is required for normal syncytiotrophoblast formation. The role of p45-NF-E2 in regulating syncytiotrophoblast formation and placental vascularization in human placenta and its relevance for placental dysfunction in humans remains unknown.
To address this question, we evaluated Gcm-1 and p45-NF-E2 expression (immunoblotting and immunofluorescence) in human placenta from healthy controls and patients with pregnancy complications (IUGR). Furthermore, a human choriocarcinoma cell line, Bewo, was stimulated with 8-Br-cAMP and in-vitro syncytia formation was evaluated using E-cadherin staining and marker gene expression (Gcm-1, Syn-1, hCG-β). Expression of p45-NF-E2 under these experimental conditions and its functional role using p45-NF-E2 knock-down Bewo cells were evaluated. Overall acetylation in human tissues and Gcm-1 acetylation were studied using HAT/HDAC inhibitors and immunoprecipitation experiments.
The diseased placenta samples showed enhanced syncytiotrophoblast formation, altered acetylation and reduced expression of p45-NF-E2 as compared to controls. In-vitro, p45-NF-E2 deficiency was sufficient to increase spontaneous syncytiotrophoblast formation. Increased Gcm-1 expression in the absence of p45-NF-E2 is dependent on enhanced protein acetylation, including acetylation of Gcm-1 itself. Modulating acetylation in Bewo cells regulates syncytiotrophoblast formation via NFE-2 and Gcm-1.
We identify a novel function of p45-NF-E2 during human placental development. Reduced p45-NF-E2 expression alters placental protein acetylation and may be an early cause and a suitable marker of placental dysfunction. Potential mechanisms and biomarkers associated with altered acetylation and p45-NF-E2 expression in human IUGR need to be further evaluated.

OC-3b
The low-molecular weight heparin-associated early variations in circulating angiogenic factors predict clinical outcomes in pregnant women with treated obstetric antiphospholipid syndrome

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In pure obstetric antiphospholipid syndrome (APS) women treated with prophylactic-dose low-molecular weight heparin (LMWH) plus low-dose aspirin (LDA), stillbirths and late placenta-mediated complications (PMCs: pre-eclampsia, placental abruption, birth of a small-for-gestational age neonate) remain higher than in non-APS women sharing the same clinical manifestations (NOH-APS cohort. Blood 2014;123:404–13).
LMWHs are beneficial on the antiphospholipid antibody (aPLAb)-mediated inhibition of endometrial endothelial cell angiogenesis (D'Ippolito S. et al. PLoS One 2012;7: 229660).
We thus used stored frozen plasma samples from the APS women included in our NOH-APS cohort (citrated blood taken for platelet count checks performed before the initiation of LMWH and 4 days after the first injection) and assayed the concentrations of fms-like tyrosine kinase 1 sFlt1 and of free placental growth factor PlGF using commercially available ELISAs (R&D Systems, Abingdon, UK).
LMWH injections were associated with sustained increases of sFlt1 and of free PlGF plasma concentrations. The LMWH-associated increases in sFlt1 (precipitating effect) and of free PlGF (protecting effect) were both independent risk factors for the occurrence of PMCs ($p<0.0001$), or of PMCs plus stillbirths ($p<0.0001$).
The LMWH-induced early mobilisation of releasable sFlt1 and PlGF stores indicate the clinical prognosis in treated obstetrical APS women.