Comprehensive and Multidisciplinary Approach to Evaluation of Young Women with Heavy Menstrual Bleeding: Impact on diagnosis, management and outcomes

Subcommittee: Women’s Health Issues in Thrombosis and Hemostasis

- Person responsible (Chair / Principal Investigator):
  - Rezan Kadir (chair)
  - Ayesha Zia (PI)

- Aims / Mandate of the project:
  - To prospectively determine menstrual bleeding patterns and prevalence of bleeding disorders and prescribed interventions in young women with anovulatory HMB
  - To prospectively determine menstrual bleeding patterns and prevalence of bleeding disorders and prescribed interventions in young women with ovulatory HMB
  - To prospectively examine the utility of a comprehensive diagnostic testing algorithm in the diagnosis of young women with HMB
  - To examine the utility of a bleeding score of > 2 and/or global hemostatic assays in young women with HMB as screening tools for underlying bleeding disorders
  - To measure the change in overall health-related quality of life (HRQOL) before and after multidisciplinary comprehensive care in young women with HMB and to compare their HRQOL with age-matched healthy controls
  - To assess the degree and impact of dysmenorrhea on QOL in relation to whether an underlying bleeding disorder is present

- Methodology (in very brief, not more than 1 paragraph):
  - Young Women (ages 11-21 years) will be evaluated in a multidisciplinary ‘Young Women with Blood Disorders Clinic’ and undergo a standardized diagnostic and testing approach (Figure below). Subjects will be seen at 3 months interval until heavy menstrual bleeding is controlled and subsequently every 6-12 months if an underlying bleeding disorder is established. Subjects in whom heavy menstrual bleeding is controlled and a bleeding disorder is ruled out will continue regular care with their primary adolescent physician or gynecologist. PBAC, fatigue and QOL scores will be collected at each visit until heavy menstrual bleeding is controlled and at 6 and 12 months post diagnosis for all subjects.
Subjects will be asked to maintain menstrual diaries in between visits. Changes in scores of physical and psychosocial fatigue perception, QOL and fatigue severity will be documented at all these visits. To control the effects of depression on fatigue, common in the adolescent population, a HEADSS assessment will be separately performed at the initial visit for all subjects to screen for depression. A database containing their demographic and clinical information, laboratory testing results, final diagnoses, response to therapeutic modalities, serial fatigue and quality of life scores and long-term outcomes will be maintained prospectively to study aims as above.

- Inclusion / recruitment criteria (if applicable): As above
- Year of starting: 2014
- Annual report of project: ISTH meeting 2015 (interim report)
- Year of completion (expected): 2016
**COMPREHENSIVE EVALUATION OF YOUNG WOMEN WITH HMB**

**FIRST TIER**
- Hematologic tests: CBC with reticulocyte count, peripheral blood smear for platelet morphology, iron profile
- Endocrine tests: FT4, TSH
- Gynecologic tests: Pregnancy test, pelvic ultrasound (select cases)
- Blood bank: ABO blood group
- Coagulation tests: PT, APTT, fibrinogen, TT, PFA-100, whole blood platelet aggregation, VWF Ag, FVIII:C, VWF:RCoF, VWF:CB assay, thromboelastography (TEG or ROTEM)
- Fibrinolysis

**SECOND TIER (select cases)**
- Endocrine tests: prolactin, FSH, LH, testosterone (if suspicion of PCOS high)
- Liver Function tests: ALT, bilirubin (with prolonged PT)
- Repeat VWD testing, +VWF multimers: Only if initial VWF <80% and suspicion high (BAT score 4 or more) or for any discrepancy between Ag: Activity ratio, RIPA
- Repeat Platelet aggregation: If initial results are abnormal
- Dysfibrinogenemia panel: TT, reptilase time (if TT or fibrinogen abnormal), fibrinogen antigen Coagulant factor assays: FIX:C, FXI:C, FVII:C (if the R time is prolonged on the TEG); Hyperfibrinolysis: Chromogenic FXIII assay (if lysis-30 time is prolonged on the TEG)
- Platelet glycoprotein expression/flow cytometry: based on platelet aggregation testing
- Electron microscopy: Platelet granules (based on platelet aggregation testing)

**THIRD TIER (select cases)**
- Repeat VWD testing
- Genetic testing as needed

**BLEEDING ASSESSMENT TOOLS**
- Patient administered:
  - PBAC
  - Fatigue scores
  - QOL questionnaire

**LABORATORY ASSESSMENT**
- Physician administered:
  - History
  - Physical exam
  - ISTH BAT
  - Beighton Score

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