Navigating Hormones and Gynecologic Concerns among Female Adolescents in the Settings of Thrombophilia and Anticoagulation

Jennifer E. Dietrich MD, MSc [1,*], Laskhmi Srivaths MD [2]

[1] Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston, Texas
[2] Division of Hematology, Department of Pediatrics, Baylor College of Medicine, Houston, Texas

A B S T R A C T

In the setting of an inherited or acquired thrombophilia, managing a gynecologic concern can be challenging. Nonetheless, careful consideration of the history along with a team approach to management, in which hematologists and gynecologists work together is critical. Thombophilias are important to understand, because certain types pose more risk than others. In addition, it is important to balance baseline factors, which might affect decisions regarding the best way to manage a concurrent gynecologic condition. Relative risks for thrombosis have been well studied for a variety of inherited and acquired conditions. Because of these risks, organizations such as the Centers for Disease Control and Prevention, World Health Organization, and American College of Obstetricians and Gynecologists have compiled clinical guidance recommendations to aid providers when hormonal management might be necessary (ie, to treat conditions such as delayed puberty, ovarian cysts, heavy menstrual bleeding, contraception). It is important to use these resources because there are limited prospective studies on this specific population who present with concurrent gynecologic conditions.
Key Words: Thrombophilia, Hemorrhagic ovarian cyst, Menstrual disorders, Hormone use

Introduction

Understanding thrombophilia is critical from a hematologic and a gynecologic perspective. Relative risks have been established with regard to the baseline population risk for thrombosis (4 per 100,000).[1] Fortunately, among the general population, the risk for thrombosis is low. However, among patients with known thrombophilias, patients who present with reproductive concerns or concurrent gynecologic conditions can pose a challenge to the provider. Within a woman's lifetime, she might be faced with concerns regarding puberty, menses, the child-bearing years, a surgical need or other reproductive tract problems, including conditions expected to occur normally, such as functional ovarian cysts.[2] Not all patients will be at the same stage in life, and therefore, an understanding of the time at which various conditions might be of concern is important to review. Even more important is that of targeting the specific conditions for which hormones might be needed for treatment and wherein increased thrombotic risk exists for hormonal therapy in the presence of a concurrent thrombophilia. Specific situations include sexual activity, the need for gynecologic surgery, pubertal delay, heavy menstrual bleeding, management of menstrual symptoms, and ovarian cysts. In this review we highlight each of these areas and aim to provide guidance for the practitioner faced with these concurrent situations.[2]

Gynecologic Concerns in Children and Adolescents

A number of gynecologic concerns might present within a woman's lifetime. Some of these are expected, such as puberty. Some conditions might be unexpected, such as a hematometrocolpos due to an imperforate hymen.[2] A few of these important common conditions will be highlighted because these might be times when hormonal intervention is necessary.

Scenario 1: Delayed Puberty Dilemma

Puberty is an important time of life for adolescents because this is when teens will face changes in their bodies internally and externally.[1] Over time, puberty appears to be beginning earlier. For a small percentage of girls, however, puberty will be delayed in onset. The exact incidence of delayed puberty in girls is not known, however, approximately 0.1% of girls might experience primary amenorrhea (lack of menses by age 16 years), indicating the absence of any menses.[3] A variety of conditions can cause this delay: genetic, anatomic, constitutional, nutritional, and other chronic health conditions. The most common etiology is constitutional (53% of cases), and in this setting, usually allowance of additional time without intervention, is the goal. However, for adolescents who present with delayed puberty due to genetics (10%) or anatomic reasons (7%), intervention is necessary. For instance, Turner syndrome presents in 1 of 2500 girls. As a result, many of these girls will face a need for hormonal therapy initiation, when height interventions are complete, to allow for secondary sexual characteristic development, reproductive organs to

The authors indicate no conflicts of interest.

* *Address correspondence to*: Jennifer E. Dietrich, MD, MSc, Department of Obstetrics and Gynecology, Baylor College of Medicine, 6651 Main St, Suite F1020, Houston, TX 77030; Phone (832) 826-7464
E-mail address: jedietri@bcm.edu (J.E. Dietrich).

1083-3188/$ - see front matter
http://dx.doi.org/10.1016/j.jpag.2015.05.005

reach adult size, and for these girls to be similar to their peers.[3]

Scenario 2: Risk of Unplanned Pregnancy in Adolescents with Thrombophilia Dilemma

In the United States, the Centers for Disease Control and Prevention conducts high school surveys every few years known as the Youth Risk Behavior Surveillance. These surveys aim to assess a number of risk factors that teens face today (ie, exposure to alcohol or drugs) in addition to evaluation of health habits, such as exercise and nutrition. In addition, a portion of this survey is devoted to assessmet of sexual health.[4] In the recent survey from 2013, from more than 6000 participants, more than 60% of girls and boys were reportedly sexually active by grade 12. In addition, the survey assessed how many teens became sexually active before the age of 13 years (approximately 3%). Additional findings included limited condom use among this group (46.9%) and limited contraceptive use before the last sexual encounter (10.2%). A number of more recent initiatives have been established in the United States to attempt to improve access and knowledge for teens who face reproductive health decisions. Nonetheless, a need for contraception clearly exists in this population to prevent unplanned pregnancy.[4]

Scenario 3: Hemorrhagic Cysts in Adolescents and Surgical Dilemma

Functional ovarian cysts are common in adolescents and might be discovered during routine imaging studies for other reasons up to 50% of the time.[2] Functional cysts occur because of the inherent follicular and luteal activity of the ovary. In cases in which a cyst fails to involute or there is a failure of ovulation, a persistent cyst might be found. In many cases these cysts will resolve spontaneously. In other cases, a cyst requires medical or surgical management. The recurrence of functional cysts (follicular or nonexpanding hemorrhagic) can be aided by the use of hormones for central gonoadotropin supression. In cases in which the size of the cyst has resulted in acute abdominal pain, the concern for adnexal torsion arises, which is a surgical emergency. In other cases, surgical need might also arise in the setting of an expanding hemorrhagic cyst.[2]

Scenario 4: Heavy Menstrual Bleeding and Thrombophilia—Medical Management Dilemma

Heavy and irregular menstrual bleeding is a common complaint in adolescents, with prevalence rates as high as 30%, because of a variety of reasons ranging from physiologic immaturity, infection, pelvic abnormalities, underlying bleeding disorders, and endocrine disorders.[5] Because heavy menstrual bleeding can have a signifcant negative effect on the quality of life of the teenagers, and could lead to missed school days, sports limitations, and impedance in social activities, it becomes crucial to regulate the menstrual cycle and reduce the bleeding for effective functioning of the adolescent. Hormonal therapy is a key element of acute therapy and maintenance regimens in this scenario. In patients with underlying thrombophilia, the thrombotic risks vs the benefit of bleeding control with hormonal therapy should be carefully weighed and medication choices discussed in detail with the patient. Hematology consultation will aid in assessment of the severity of thrombotic risk for the range of hormonal options in various thrombophilic states and help to guide appropriate therapeutic choices.

Scenario 5: The Anticoagulated Patient with Gynecologic Bleeding Dilemma

Heavy menstrual bleeding has been documented in up to 60% of women who receive anticoagulant therapy.[6] In addition, intermenstrual bleeding, postcoital bleeding, and hemorrhagic ovarian cysts[7] are other reported complications of anticoagulation therapy in women of reproductive age. Whereas anticoagulation might be required for management of their underlying illness, optimal hormonal therapy for gynecologic bleeding complications without escalation of thrombotic risk in these patients requires a collaborative approach between hematology and gynecology.

Screening for Thrombophilia; a Gynecologic Perspective

From a gynecologic point of view, any of the aforementioned gynecologic concerns do not require strict screening before the initiation of hormonal therapy. Nonetheless, there is some guidance regarding patients who might require screening before hormonal therapy initiation and patients who might not require screening. Current evidence suggests that it is not cost-effective to screen every individual before hormone therapy initiation.[8,9] Screening is costly, therefore, screening is recommended in certain situations: in the setting of personal history of thrombosis, strong family history of thrombosis, or when the screening could affect the management.[8] One principle to consider in the absence of an indicated need to screen, is the age of the patient (thrombosis risk increases after age 20 years and exponentially increases after age 40 years).[8] In addition, there are a few things to keep in mind for comparison: the baseline risks of thrombosis for certain populations and the risk in the setting of hormone use (Table 1).[8] If thrombophilia screening is undertaken, the following should be evaluated: coagulation studies including factor VIII level and fibrinogen activity, Protein C, S, and antithrombin III levels, factor V Leiden and prothrombin gene mutation 20210A, homocysteine level, lupus anticoagulant, anticardiolipin antibody, and anti-beta 2 glycoprotein 1 antibody panel. Consider consulting a hematology expert before undertaking screening if any uncertainty remains.[8] Nonetheless, if a thrombophilic condition is detected, in general there is relative or absolute contraindication to estrogen therapy depending on the severity of thrombotic risk. However, in some situations, if a need for estrogen therapy exists (ie, delayed puberty that occurs with Turner syndrome),[10] this therapy might need to be intiated only after careful family counseling about