Systemic lupus erythematosus (SLE) is an autoimmune disease that primarily affects women of reproductive age. Cyclophosphamide (CYC) is typically used in severe cases of SLE where there is renal or central nervous system involvement. The use of CYC can have several reproductive implications such as reduced fertility and teratogenic effects.

CYC can be toxic to the ovaries resulting in premature ovarian insufficiency (POI). POI is defined as amenorrhea for at least four months with two follicle-stimulating hormone levels in the menopausal range that are done at least one month apart. This risk is dependent on the dose of CYC exposure and cumulative dose of CYC. The risk for POI is less in women who received CYC at age 25 or younger and have a cumulative dose of less than 10 g. One retrospective study found that the risk for POI was 12% in women younger than 26, while 37% in the 26-30 age group. The risk increased to 60% if exposure occurred in the first trimester.

CYC is the recommended 10 g dose of CYC was often not discussed. Most females were not counseled on the effects of CYC in relation to ovarian function, the other reproductive aspects of CYC were often not discussed. Finally, most females were not followed up by a gynecologist after completing CYC treatment despite their known risk of menstrual abnormalities. This study highlights the reproductive needs of females receiving CYC for SLE.

Background

Premenarcheal girls who received CYC from the dates 2000 to 2015 were identified by ICD 9 codes. Demographics include Age, ethnicity, menarchal status, and use of contraceptive medications. The time to return of menstruation was calculated from the date of CYC treatment. Data were entered into Access 2016 and analyzed using Microsoft Excel. All females who received CYC were counseled prior to treatment about the risk of POI and the teratogenic effect of CYC, and 37% on the need for birth control.

Purpose/Objectives

1) Evaluate if patients received counseling for treatment risks with CYC including its teratogenic effect, need for contraception, and risk of premature ovarian failure.

2) Evaluate if and when GnRH-a was given for ovarian protection

3) Evaluate for effects CYC treatment had on menstrual function following treatment

Methods

• IRB approval was obtained from Baylor College of Medicine

• Texas Children’s Hospital has a large cohort of pediatric and adolescent SLE patients who received CYC. A retrospective chart review was performed of females younger than 21 with diagnosis of SLE who received CYC from the dates 2000-2015.

• Patients were identified ICD 9 codes.

• Descriptive statistics were calculated with Microsoft Excel 2013.

Results

A total of 70 females received CYC due to SLE from 2000 to 2015. Please refer to the table for demographics of the 70 females. Of the 29 premenarchal females who were treated with CYC, 27 have achieved spontaneous puberty following treatment. One female had been diagnosed with delayed puberty, and it was still too young to diagnose delayed puberty. Of the 41 females who were post- menarchal, 100% received leuprolide acetate (GnRH-a) during CYC treatment. Only 5% of females had the GnRH-a administered during the recommended 10-14 days prior to onset of CYC treatment. The rest had the GnRH-a administered within 10 days of starting CYC treatment due to urgency of symptoms. Following treatment, all 41 post-menarchal female resumed menses. Please refer to the graph for time to return of menses in study participants. All females who received CYC were counseled prior to treatment about the risk of premature ovarian failure; however, only 12% were counseled on the teratogenic effect of CYC, and 37% on the need for birth control during treatment. On 39% of females have been seen by gynecology during the study period. In addition, only 19% had laboratory evaluation of ovarian function performed after treatment.

Discussion/Future Work

We felt this study is important as SLE is an autoimmune disease that primarily affects women of reproductive age. CYC can have long-term effects on menstruation. Our study has been few studies looking at the reproductive health of women younger than 21 who received CYC. Texas Children’s Hospital has one of the largest cohorts of SLE patients under who received CYC. We also felt this study is warranted as we are initiating a quality improvement project at our institution to improve care of reproductive health in our SLE patients.

Based on the results, most females who received CYC maintained their ovarian function and had resumption of their menstrual function within 6 months of completing CYC treatment. Although providers did counsel patients on the effects of CYC in relation to ovarian function, the other reproductive aspects of CYC were often not discussed. Finally, most females were not followed up by a gynecologist after completing CYC treatment despite their known risk of menstrual abnormalities. This study highlights the reproductive needs of females receiving CYC for SLE.