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Ovarian protection in patients receiving cyclophosphamide for lupus nephritis

Dr Sarah Gleeson[1], Dr Srivathsan Thiruvengadam[1], Dr Christopher Uy[1], Ms Rachna Bedi[1], Dr Hannah Wilson[2], Dr Tom Cairns[1], Prof Liz Lightstone[2]
[1]Imperial Healthcare Trust, London, United Kingdom, [2]Imperial College London, London, United Kingdom

Background:
Systemic Lupus Erythematous (SLE) affects mainly women of child bearing age. Up to two thirds of women with SLE develop lupus nephritis (LN). Cyclophosphamide (CyP) treatment can impair fertility, causing azoospermia in males and amenorrhoea in a dose and age dependent manner in females.
GNRH analogues are thought to temporarily suppress ovarian function and reduce the incidence of premature ovarian failure. Both the KDIGO and EULAR guidelines recommend their use. Our LN protocol recommends use of leuprorelin and ganirelix in females and andrology referral in males undergoing intravenous cyclophosphamide therapy.
Aim:
To audit adherence with our protocol for ovarian protection in an unselected cohort of patients.
Methods:
All patients having undergone a kidney biopsy showing LN between January 2017 and September 2018 were identified from pathology records. Demographic and clinical information was extracted from their electronic medical records. Descriptive statistics were performed using Microsoft Excel.
Results:77 patients (70 female) were identified. Mean age was 42.8 ± 16.1 years. Clinical information was unavailable in 6 females- these were excluded from our analysis.
Of those remaining (n=71) 28 biopsies were performed to investigate possible de novo LN, 43 in those with known LN.
55 patients required (re)induction therapy. 26 patients (24 female) received a regimen that included cyclophosphamide. (Eurolupus regimen). Mean CyP dose was 4.7 ± 1.7g.
The average age of females receiving CyP was 39.5± 13.6 years.
Females receiving ovarian protection (n=14, 58%) were significantly younger than those who did not (mean ages 30.5 ± 4.9 years and 50.6 ± 14.0 years, respectively; $p<0.0001$). 6 of the 14 women receiving ovarian protection had their treatment instigated as an inpatient(IP), 8 were outpatients(OP). Further information on those who didn't receive ovarian protection in table 1.

Two males received CyP. One (47 years, IP) was critically unwell and was not referred to andrology. One (24 years, OP) was referred to andrology.
Overall 42% of females treated with CypP did not receive ovarian protection. This was likely appropriate (age 40+ years) in 80%. 20% should have received ovarian protection.
An unexpected finding, highlighting the importance of ovarian protection, is that 5 females (9.8%)aged <45 years became pregnant during our short follow up period (mean 16.3 ± 6.9. months, max 2 years)-one had received CyP with ovarian protection.
Conclusion:
Fertility preservation is an important issue in LN management. As a tertiary LN centre with many complex patients, we regularly use Eurolupus CyP as induction therapy. Despite our strong obstetric-nephrology links and protocolised approach to ovarian protection in patients receiving CyP, a small but significant proportion of women did not receive this. The importance of both proactive fertility management and contraception, in this patient group is underscored by their high pregnancy rates.