

P1085 EVALUATION OF GONADAL FUNCTION IN YOUNG WOMEN DIAGNOSED WITH HODGKIN AND NON-HODGKIN LYMPHOMA

Topic: 17. Hodgkin lymphoma - Clinical

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Background:

ABVD chemotherapy (CT) is the standard treatment approach for Hodgkin lymphoma (HL), with a negative interim PET. R-DA-EPOCH and R-CHOP are the most frequently used regimens used in primary mediastinal/high grade B-NHL and DLBCL, respectively. Young women are often affected by these types of lymphoma and may be cured in >80% of the cases. Thus, treatment-related complications are being increasingly recognized, among which, gonadal insufficiency with its major psychological consequences. This is more prevalent in female patients, in whom collection and cryopreservation of oocytes/ovarian tissue are not applied in everyday clinical practice. Published data are scarce on this subject. Moreover, little is known about the kinetics of gonadal function and sex hormones during chemotherapy to safely guide contraceptive measures.

Aims:

The aim of this study is the prospective evaluation of gonadal function in young women with malignant lymphoma who are receiving CT. We here present our preliminary results on 50 patients with HL and B-NHL.

Methods:

This is a prospective study of gonadal function in female patients ≤ 40 years. Hormonal measurements were performed at pre-specified time points: before treatment (t0), during CT (t1), at the end of CT (t2) and every six months (t6, t12) thereafter. The following hormones were measured: follicle-stimulating hormone (FSH), luteinizing hormone (LH), progesterone (PG), estradiol (E₂), anti-Mullerian hormone (AMH). The study included: 32 HL [median age: 29 years, 32 ABVD] and 18 B-NHL patients [median age: 27 years, 9 RDAEPOCH, 7 RCHOP, 2 other]. FSH reflects gonadal function in women (increased levels indicate gonadal dysfunction). AMH is considered to be the most sensitive biomarker for gonadal reserve (decreasing values correlate with ovarian insufficiency). E2 and progesterone are the major sex hormones.

Results: HL-ABVD: FSH constantly increased from the beginning, peaking in the middle (fsh0-1 $p < 0.0001$), remaining high until the end (fsh0-2 $p < 0.0001$), without reaching normal levels at 6 months (fsh0-6 $p = 0.002$), finally normalizing at 12 months after the end of treatment. Consistently with FSH, AMH sharply decreased during treatment: [median values: 2,85IU/mL (t0), 0,45IU/mL (t1), 0,62IU/mL (t2), $p < 0.0001$ for both]. A rebound increase was observed at 6 months and slowly decreased again to normal values at 12 months after the end of CT. Estradiol and progesterone were not affected throughout the treatment.

B-NHL: Gonadal damage, reflected by the increase in FSH, was evident, though with slightly different kinetics compared to HL: [median values: 4,1IU/mL (t0), 8,3IU/mL (t2), fsh0-2 $p = 0,035$]. FSH gradually increased during treatment, reaching a peak towards the end. FSH slowly reached normal values after six months from the end of

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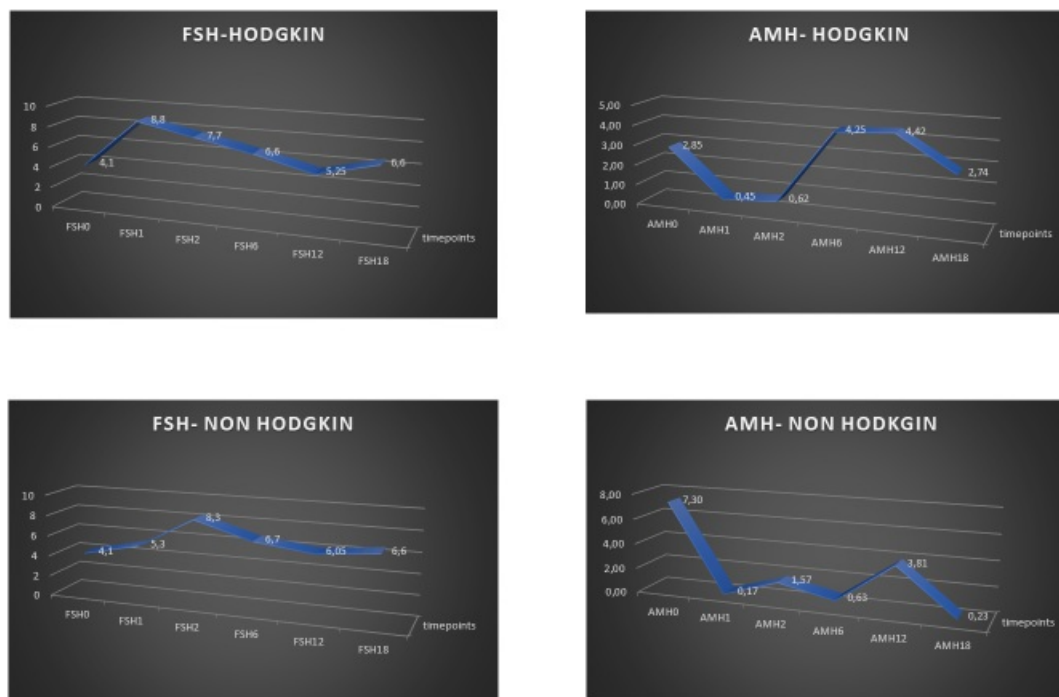
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treatment. In parallel to HL, AMH values sharply decreased during CT: [median values: 7,3IU/mL(t0), 0,17IU/mL(t1), 1,57IU/mL(t2), amh0-1 p=0.002, amh0-2 p=0,043). However, in contrast to HL, no clear rebound was seen and AMH values remained extremely low, even at 18 months after the end of treatment (median values: 0,23IU/mL), highlighting the gonadotoxic effect of CT. Estradiol and progesterone did not change significantly.

Image:



Summary/Conclusion: Gonadal function in female patients with malignant lymphomas is affected during CT in both HL and B-NHL, though with different kinetics. In HL patients treated with ABVD, gonadal function normalized at 6 months, whereas, in B-NHL gonadal dysfunction remained even at 18 months after the end of CT, possibly indicating a chemotherapy-dependent genotoxic effect.

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