Serum HE4 predicts progestin treatment response in endometrial cancer and atypical hyperplasia: a prospective observational study

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Abstract

Abstract Objective: To investigate serum human epididymis-4 (HE4) as a predictive biomarker of intrauterine progestin response in endometrial cancer and atypical endometrial hyperplasia (AEH). Design: Prospective observational study. Setting: Consecutive sample of women attending a tertiary gynaecological oncology centre in the North West of England. Population: Women with AEH or early stage, low grade endometrial cancer who were unfit or declined primary surgical management; 48 in the discovery cohort and 28 in the validation cohort. Methods: Women were treated with a levonorgestrel intrauterine system (LNG-IUS) for 12 months. Endometrial biopsies and imaging were performed to assess treatment response. Pre-treatment serum HE4 was analysed by chemiluminescence immunoassay and diagnostic accuracy and logistic regression analyses performed. Main outcome measure: Progestin response at 12 months defined by histology and imaging. Results: Baseline serum HE4 was significantly higher in non-responders than responders in both discovery [134.6pmol/L (IQR:94.0-292.4) vs 76.5pmol/L (IQR:59.7-87.3), p<0.001] and validation cohorts [108.2pmol/L (IQR:80.3-119.2) vs 64.4pmol/L (IQR:53.0-73.0), p=0.004]. An HE4[?]77pmol/L had a sensitivity and specificity for progestin treatment response of 83.3% and 53.3% in the discovery cohort, and 85.7% and 76.2% and in the validation cohort, respectively. When expressed as a continuous variable, the AUC was 0.81 (95%CI:0.67-0.95) and 0.87 (95%CI:0.73-1.00) for the discovery and validation cohorts, with every 1pmol/L of HE4 increasing the likelihood of progestin treatment failure by 2% and 5%, after adjustment for age and histology, respectively (p=0.02 and p=0.18). Conclusion: Serum HE4 shows promise as a predictive biomarker of progestin treatment response in endometrial cancer and AEH.

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