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Original Research

Hormone replacement therapy after risk-reducing salpingo-oophorectomy minimises endocrine and sexual problems: A prospective study

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Abstract ***Background:*** There has been some doubts raised in earlier studies about the efficacy of hormone replacement therapy (HRT) in reducing endocrine and sexual problems in women who have undergone a risk-reducing salpingo-oophorectomy (RRSO).
Methods: In this prospective, observational study, we recruited 178 premenopausal women with a high risk for ovarian cancer. Fifty-seven women opted for RRSO and 121 for gynaecological screening (GS). Women completed questionnaires before surgery (T1) and 3 (T2) and 9 (T3) months post surgery, or at equivalent time points for the GS-group. Menopausal symptoms were assessed with the Functional Assessment of Cancer Therapy–Endocrine Subscale (FACT-ES) and sexual functioning with the Sexual Activity Questionnaire (SAQ). Groups were compared using repeated measures mixed effect models for continuous variables, and generalised estimating equations for longitudinal ordered categorical data.

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Results: Twenty-seven women who underwent RRSO used HRT after surgery (HRT-users) and 30 did not (HRT-non-users). There were no significant group differences at baseline on the outcome variables. Compared to the HRT-users, the HRT-non-users exhibited a significant increase in overall endocrine symptoms ($p = 0.001$, effect size (ES) $= -0.40$ and $p < 0.001$, ES $= -0.59$ at T1 and T2, respectively), and in sexual discomfort ($p < 0.001$, ES $= 0.74$ and $p < 0.001$, ES $= 1.17$). The effect size provides an indication of the magnitude of the observed group differences. An effect size of 0.50 or greater is generally considered to be clinically relevant. No significant differences over time were observed between the HRT-users and the GS-group on any of the outcomes.

Conclusion: Our results suggest that HRT use in the first year after RRSO has beneficial effects in terms of minimising endocrine symptoms and sexual symptoms in premenopausal women who have undergone RRSO.

1. Introduction

Approximately 10% of all epithelial ovarian cancers (OCs) can be attributed to an inherited predisposition. Gynaecological screening (GS) in women at high-risk for OCs has not been demonstrated to be effective either in detecting cancer at an earlier stage or in improving prognosis. Most interval carcinomas are detected in staging classification of International Federation of Gynaecology and Obstetrics (FIGO) stage III [1]. In Stage III ovarian cancer, cancer cells have spread to tissues outside the pelvis or to regional lymph nodes in the back of the abdomen (retroperitoneal lymph nodes). Cancer cells may be found on the outside of the liver. About 60% of all cases of ovarian cancer are diagnosed when they are Stage III. Therefore, many high-risk women choose risk-reducing salpingo-oophorectomy (RRSO), which lowers the risk of OC by 80%–96% [2], with low surgical morbidity [3]. However, RRSO in premenopausal women causes immediate onset of menopause with accompanying symptoms and sexual dysfunction [4].

In naturally evolved postmenopausal women, HRT is highly effective in decreasing endocrine symptoms and urogenital atrophy [5]. Studies on the safety of short-term use of HRT have not reported adverse effects on oncological outcomes in high-risk women who have undergone RRSO [6–11]. The Dutch, United States of America (USA), United Kingdom (UK) and Australian guidelines state that HRT can be offered after RRSO for a short period of time in premenopausal women without a history of breast cancer until the age of natural menopause [12–15].

Only a limited number of studies have focussed on HRT use, endocrine symptoms and sexual functioning after RRSO [16–22] (See the Online Appendix for a summary of these studies). One prospective study ($n = 75$) showed a decline in endocrine symptoms and sexual dysfunction while using HRT, but symptoms did not return to pre-surgical levels [16]. In a previous cross-sectional, observational study, Madalinska *et al.* [17] reported significantly fewer endocrine symptoms after RRSO among HRT-users ($n = 77$) compared to non-users ($n = 87$). However, symptom levels remained well above those of premenopausal women undergoing screening, and sexual discomfort was not alleviated by HRT [17].

We conducted a prospective, observational study to (dis)confirm the cross-sectional results of Madalinska *et al.* [17] on the effects of HRT on endocrine symptoms and sexual dysfunction in high-risk, premenopausal women who opted for RRSO.

2. Patients and methods

2.1. Sample and procedures

Patients were recruited in seven hospitals in the Netherlands between 2002 and 2004. The inclusion criteria for this prospective observational study were: (1) age between 30 and 70 years; (2) member of a hereditary breast and ovarian cancer (HBOC) family with a risk estimated to exceed 10% or proven BReast CAncer susceptibility gene1 or gene2 (BRCA1/2) mutation carrier; and (3) referred to a gynaecologist to discuss the prevention of ovarian cancer. Exclusion criteria were: (1) prior oophorectomy and (2) metastatic cancer or any other severe comorbidity.

For the purpose of the current analysis, we selected the women who were premenopausal at the time of study entry and opted either for RRSO or for GS. If HRT was prescribed after surgery, this was a standard dosage of hormones (tibolone or oestrogen and progestin) administered either orally, transdermally or topically. This cohort of premenopausal women was divided into three groups: RRSO HRT-users, RRSO HRT-non-users, and women undergoing GS.

Patients received an informed consent form, a baseline-questionnaire by mail. Patients were included in the