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Original Research

Outcome of 3-day bleomycin, etoposide and cisplatin chemotherapeutic regimen for patients with malignant ovarian germ cell tumours: A Taiwanese Gynecologic Oncology Group study

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Abstract ***Background:*** The combination of bleomycin, etoposide and cisplatin (BEP) is currently the most widely used treatment for malignant ovarian germ cell tumours (MOGCTs). The aim of this study was to evaluate the efficacy and adverse effects of the 3-day BEP regimen in Taiwan. The prognostic factors of the MOGCT patients were also analysed.
Patients and methods: Two hundred and thirty-nine cases of MOGCTs were identified from the Taiwanese Gynecologic Oncology Group database, and 204 of those who received postoperative BEP chemotherapy were then analysed.

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Results: The estimated rate of no evidence of disease was 94.0% for 204 patients with adjuvant BEP regimen. Seven grade 3/4 haematological adverse effects including four subjects with neutropenia, one with pancytopenia and two with neutropenic fever were recorded in the 853 total courses of chemotherapeutic cycles. The rates of haematological and non-haematological adverse effects were 0.82% and 2.3%, respectively. No treatment-related mortality was noted. In the analysis of prognostic factors, only tumour stage had a significant impact on disease recurrence (95% confidence interval (CI), 4.2–94.4, $p < 0.001$) and disease-related mortality (95% CI, 2.2–163.9, $p = 0.007$).

Conclusions: The current 3-day adjuvant BEP regimen was effective and safe for patients with MOGCTs.

1. Introduction

Malignant ovarian germ cell tumours (MOGCTs) that affect young females are uncommon but highly chemo-sensitive malignancies. Therapy has evolved along similar lines to that of testicular germ cell tumours. The first effective combination chemotherapy regimen for patients with advanced MOGCTs was vincristine, actinomycin D and cyclophosphamide (VAC). However, more than 50% of the patients with advanced MOGCTs still died of the disease [1,2]. After applying a cisplatin-based chemotherapeutic regimen (cisplatin, vinblastine and bleomycin, PVB), the survival of patients with testicular tumours obviously improved [3]. In addition, this PVB regimen was also found to be more effective than the VAC regimen for women with MOGCTs [4].

The substitution of etoposide for vinblastine has been shown to be equally active but less toxic in the treatment of patients with testicular cancer. Therefore, the combination of bleomycin, etoposide and cisplatin (BEP) is now the most common treatment for patients with MOGCTs [5,6]. In the standard BEP regimen, bleomycin (30 units, days 1, 8 and 15), etoposide (100 mg/m^2, days 1–5) and cisplatin (20 mg/m^2, days 1–5) are suggested every 3 weeks for a planned total of three to four cycles [7]. With this regimen, 25% of the patients have been reported to develop grade 3 or 4 neutropenia, and 10% of patients had febrile neutropenic episodes [6,8]. Furthermore, bleomycin-induced pulmonary toxicity may occur in 10% of patients and can occasionally be fatal [8].

Since the 1990s, we have used fertility-preserving surgery, comprehensive staging surgery or maximal cytoreduction followed by a 3-day BEP regimen including lower total doses of bleomycin and etoposide to decrease chemotherapy-related complications. Therefore, the aim of this retrospective study was to evaluate the efficacy and adverse effects of this chemotherapeutic regimen for patients with MOGCTs using the Taiwanese Gynecologic Oncology Group (TGOG) database. In addition, we further aimed to identify the prognostic factors of these patients treated with this 3-day regimen.

2. Patients and methods

2.1. Study population

Patients with histologically proven malignant ovarian germ cell tumours (MOGCTs) were eligible for the study. The histological types were defined according to the World Health Organisation classification [9], and disease was staged based on the International Federation of Gynecology and Obstetrics (FIGO) staging system for ovarian cancer [10]. In this study, FIGO stage I/II and FIGO stage III/IV MOGCTs were considered to be early and advanced disease, respectively. The TGOG tumour registry databases were searched, and 239 patients diagnosed with MOGCTs were identified between January 1991 and December 2012. In all hospitals, the institutional review boards approved this multi-centre cooperation study. Detailed clinicopathological characteristics of this study population were retrospectively abstracted from the medical records until December 2013.

2.2. Surgery, chemotherapy and follow-up of the patients with MOGCTs

All of the patients with MOGCTs underwent surgical treatment for pathologic diagnosis. The surgeries including debulking or staging surgery, total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO), TAH and unilateral salpingo-oophorectomy (USO), BSO, USO or oopho-cystectomy, with or without intra-abdominal tumour excision depended on the patients' age, disease severity and desire of fertility. The frozen sections for diagnosis were obtained by pathologists during surgery. The maximum diameter of the residual tumour after surgery was also recorded. Optimal debulking surgery was defined as the maximum diameter of the residual tumour $\leqslant$1 cm. Otherwise, the debulking surgery was considered to be sub-optimal. In this study, USO, and oopho-cystectomy were defined as fertility sparing operational methods. TAH + BSO, TAH + USO, BSO, debulking and staging surgery