INTRODUCTION

Breast cancer is one of the leading fatal cancers in the world. Patients with early, localized disease may be cured by resection of the tumor followed by adjuvant chemotherapy.[1] However, there are still significant numbers of patients who ultimately die of metastatic breast cancer during follow-up.[2] Metastatic breast cancer is possibly not very responsive to additional hormonal therapy or chemotherapy.[3] The median survival duration in relapsed metastatic breast cancer patients ranges from 16 to 24 months, and 5-year survival is less than 5%.[4]

Current chemotherapy may produce a response rate of 40%-70% with a response duration of about 12 months. Anthracycline-containing regimens, such as CAF (cyclophosphamide, adriamycin or epirubicin and 5-fluorouracil), are most commonly used for first-line chemotherapy. When treatment of patients with metastatic breast cancer fails with anthracycline-containing regimens, the response to second-line chemotherapy is about 10%-40% and median survival is 4 to 6 months.[1] Due to the poor prognosis of these patients, a well-designed effective and less-toxic chemotherapeutic regimen is obviously necessary for improving the preliminary outcome.

These days, treatment advances have achieved higher response rates than ever, although many of these advances provide more palliative than curative effects.[2] Paclitaxel is one of the most-exciting new anticancer drugs among recent advances in this field, and it has shown significant clinical activity in breast, ovarian, lung, and head and neck cancers.[6] Utilizing paclitaxel as salvage chemotherapy in patients with metastatic breast cancer has been documented to have satisfactory tolerability and definite activity.[7]

Paclitaxel is a diterpene plant product derived from the crude bark extract of the western yew *Taxus brevifolia*.[8] It represents the first of a group of compounds developed that have a unique mechanism of action.[2] The cellular target appears to be the microtubular apparatus, but unlike vinca alkaloids or podophyllotoxins, paclitaxel actually promotes microtubular assembly in vitro via direct high-affinity binding to polymerized tubulin, while in the meantime, it decreases the critical tubulin concentration required for polymerization.[8] In vitro studies of drug-treated cells, it was found that they can be depolymerized by their microtubular cytoskeleton, and this phenomenon is the putative mechanism of the anti-tumor activity. Treated cells experience blocked replication in the G2 and M phases of the cell cycle.[9]

A 24-h intravenous infusion of paclitaxel in a dosage of 250 mg/m^2 showed an objective regression rate of 56% to 62% in patients without heavy treatment.[2] Several studies have reported that paclitaxel might possibly still retain its therapeutic activity on patients with anthracycline-refractory breast cancer by using the 3-h, 24-h, and 96-h infusions of paclitaxel.[10] Several toxicities, including hematologic, neuromuscular, cardiac, gastrointestinal, and hypersensitivity reactions have been reported for paclitaxel while leukopenia, anemia, and neuromuscular side effects, such as paresthesias and arthralgia are among the most frequently encountered ones.[11] By giving standard premedications, including steroids and antihistamines before giving paclitaxel, we can now easily prevent the occurrence of unwanted hypersensitivity reactions.[12] Neutropenia is a dose-limiting toxicity in most studies and is dose and schedule dependent, but there is less neutropenia seen with the 3-h infusion. Thrombocytopenia and anemia are also not common in the 3-hour infusion regimen.[13] Prolonged infusion of paclitaxel increases the possibility of cytotoxicity; hypersensitivity reactions and the response rate may also increase.[14] We adopted an infusion regimen of 175 mg/m^2 in 3-h because we assumed that this regimen might lead to fewer adverse effects and allow patients to better tolerate it compared to other higher-dosage regimens. This study evaluates the efficacy and toxicities of this paclitaxel regimen.

METHODS

Patients

Between November 1995 and November 1996, a total of 25 women was enrolled in this study (Table 1). The average age of these 25 patients was 46.9 (range