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ORIGINAL ARTICLE

Cisplatin-Dependent Nephrotoxicity in Patients with Lung Cancer

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OBJECTIVE
The aim of the present study was to investigate nephrotoxicity development ratios and clinical results of nephrotoxicity in patients diagnosed with lung cancer who received cisplatin in chemotherapy protocol.

METHODS
A total of 170 lung cancer patients were enrolled in the present prospective study. Renal functions were recorded for each patient before and after chemotherapy. Nephrotoxicity was defined as doubling in plasma creatinine concentration. Modification in treatment due to nephrotoxicity (reduction in cisplatin dosage, cisplatin interruption, or discontinuation of chemotherapy) was recorded during chemotherapy courses.

RESULTS
Decreasement of creatinine clearance levels was observed following each course of chemotherapy, but was especially noteworthy following the 1st and 5th courses (p=0.002; p=0.007, respectively). Nephrotoxicity was observed in 19 of the 170 patients (11%), in 10 of whom (53%) cisplatin dosage was reduced, and in 8 of whom (42%), cisplatin treatment was interrupted. Chemotherapy was discontinued in 1 patient (5%).

CONCLUSION
Particularly following the fourth course, chemotherapy must be carefully administered due to risk of nephrotoxicity.

Keywords: Lung cancer; cisplatin; nephrotoxicity.

Introduction

Nephrotoxicity is the most common side effect of chemotherapy drugs. Renal damage in cancer patients can occur due to malignancy or iatrogenic causes.[1] Cisplatin is a broad-spectrum antineoplastic agent used for treatment of solid tumors such as those of the lung.[2] However, occurrence of nephrotoxic effect, dependent on dose, limits the area of usage.[3] While the cellular mechanism of cisplatin nephrotoxicity has yet to be made clear, it has been shown that oxidative stress plays an important role in its pathophysiology.[4]

The aim of the present study was to investigate creatinine clearance rate, growth rate of nephrotoxicity, and

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clinical results of nephrotoxicity in patients who underwent a chemotherapy regime that included cisplatin for the treatment of lung cancer.

Material and Methods

A total of 170 patients with lung carcinoma who underwent chemotherapy regimes that included cisplatin, administered by members of the Department of Chest Diseases of Trakya University Faculty of Medicine between March 2004 and September 2006, were included in the present prospective study. Diagnosis was cytological and histological in all patients. Chemotherapy protocol that included cisplatin-etoposide was performed in 137 patients, and taxotere-cisplatin protocol was performed in 33 patients. Hydration was provided with physiological saline solution in all patients before and after chemotherapy. Drugs administered were etoposide (100 mg/m^2/day), cisplatin (80 mg/m^2/day), and taxotere (75 mg/m^2/day). Renal functions were recorded before and after chemotherapy. Creatinine clearance rates were determined using the Calvert scale, according to surface area, age, and serum creatinine values. Two-fold increase in serum creatinine level from base was accepted as nephrotoxicity. Changes in treatment as response to nephrotoxicity (cisplatin dose reduction, cessation of cisplatin, or termination of chemotherapy) were recorded during chemotherapy cycles.

The present study was conducted following approval from the ethics committee of the Trakya University Faculty of Medicine. Properties of patients were recorded using SPSS software (version 15.0; SPSS Inc., Chicago, IL, USA). Statistical significance was accepted as $p<0.05$. Creatinine clearance determined before and after chemotherapy was compared using paired sample t-test.

Results

Average age of patients was 59.9±10.6. Study population comprised 154 males (90.6%) and 16 females (9.4%). General patient features are shown in Table 1. Creatinine clearance was 77±21 prior to and 73±21 following the first cycle of chemotherapy. It was 72±18 after the 2nd cycle, 70±20 after 3rd, 71±19 after 4th, 68±19 after 5th, and 63±18 after the 6th cycle. Although decrease in creatinine clearance was observed following each cycle, decreases following the 5th and 6th cycles were remarkable ($p=0.002$; Figure 1).

Cisplatin-dependent nephrotoxicity developed in 19 patients (11%), in 10 of whom (53%) dose of cisplatin was reduced, and in 8 of whom (42%) cisplatin treatment was terminated. While chemotherapy was continued with different platinum-based agents in the majority of these patients, it was terminated in 1 (5%).

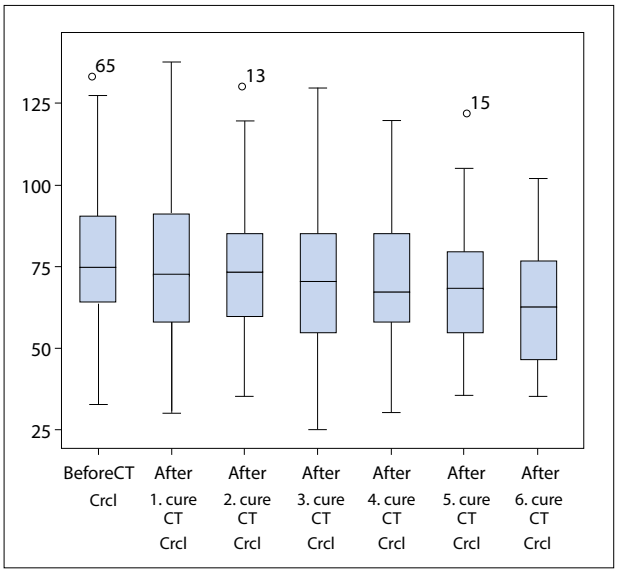

Fig. 1. Creatinine clearance of each chemotherapy course

Discussion

Cisplatin is one of the most commonly used antineoplastic drugs, and its nephrotoxic effect is relatively well known; nephrotoxicity is the most significant side effect that delimits clinical use. Cisplatin-dependent nephrotoxicity can appear in many forms, including acute renal failure, electrolyte disturbance (hypomagnesemia, hypocalcemia, hypokalemia), distal renal tubular acidosis, renal concentration defects, temporary proteinuria, and chronic kidney failure.[5]

Table 1 General characteristics of patients treated with cisplatin-based chemotherapy

Age	59.9±10.6
Men	154 (90.6%)
Women	16 (9.4%)
Cell type	
NSCLC	117 (68.8%)
SCLC	41 (24.1%)
Type unclear	12 (7.1%)
Chemotherapy	137 (80.6%)
Cisplatin+etoposide	
Taxotere+cisplatin	33 (19.4%)

NSCLC: Non-small-cell lung carcinoma
SCLC: Small-cell lung carcinoma

No studies were found that related to growth rates of nephrotoxicity in lung cancer patients treated with chemotherapy that included cisplatin. However, acute renal failure was observed in some cases following single-dose cisplatin.[6] In a study conducted by Kurt et al., creatinine clearance rates prominently decreased after first cycle of a chemotherapy regime that included cisplatin (60 mg/m^2) in 28 lung cancer patients.[7] Likewise, in the present study, significant decrease in creatinine clearance rate was determined, particularly following the 1st and 5th cycles.

Hydration with physiological saline solution (150-200 ml/h) was administered 8-12 hours before and 6 hours after treatment. Diuresis with hypertonic saline infusion, mannitol, and furosemide can also be performed to reduce nephrotoxic effect of cisplatin. When improvement of nephrotoxicity is observed in patients treated with cisplatin, methods such as dose reduction, continuation with different agent, or termination of chemotherapy are options.[3,8] In spite of hydration, cisplatin-dependent nephrotoxicity was observed in 11% of patients in the present study (n=19). Dose reduction was performed in 53% of those patients, (n=10), continuation of chemotherapy with a different agent was performed in 42% (n=8), and chemotherapy was terminated in 5% (n=1).

Cisplatin-related nephrotoxicity is the most common side effect, leading to important changes in chemotherapy regimes. Renal functions should be closely followed before, during, and after chemotherapy. Gain:loss ratios should be taken into consideration, particularly after the fourth cycle, in terms of nephrotoxicity risk.

Disclosure Statement

The authors declare no conflicts of interest.

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