Efficacy and Tolerability of Amifostine in Elderly Cancer Patients

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ABSTRACT

Background: Amifostine is a cytoprotective agent used to prevent cisplatin nephrotoxicity. It is associated with dose-limiting acute toxicities of emetic symptoms (nausea and vomiting) and transient hypotension.

Objective: The aim of this study was to analyze the efficacy and tolerability of amifostine in elderly cancer patients.

Methods: This 18-month, prospective, comparative study was conducted at the Department of Internal Medicine, Adnan Menderes University Hospital (Aydin, Turkey). Adult (aged 40–<85 years) hospitalized patients with advanced-stage cancer without comorbid diseases were enrolled. Patients were divided into 2 groups: age <70 years (group 1) and ≥70 years (group 2). All patients were treated with amifostine + cisplatin-based chemotherapy (CT). Amifostine 910 mg/m² (maximum, 1500 mg) was administered as a 15-minute IV infusion. Clinical systolic and diastolic blood pressures (SBP and DBP, respectively) were measured at 0 minute (baseline), at 8 and 15 minutes of amifostine infusion, and at 30 minutes after the start of amifostine infusion. In addition to physical examination, chest radiography, electrocardiography, blood chemistry (including serum electrolytes and renal function tests), complete blood count, and complete urinalyses were performed before each CT administration and at the post-CT day of toxicity assessment.

Results: Thirty-five consecutive patients were enrolled (22 men, 13 women; mean [SD] age, 61 [12] years; group 1, n = 22; group 2, n = 13). Patients received a total of 153 CT cycles (median, 4 cycles/patient; group 1, 96 cycles; group 2, 57 cycles). Amifostine caused significant SBP and DBP reductions at 8 minutes of infusion compared with baseline in groups 1 (both $P < 0.001$) and 2 ($P = 0.002$ and $P = 0.006$, respectively). Overall, 20 patients (57.1%) experienced ≥1 symptomatic hypotensive episode; these rates were not significantly different between groups 1 (11 cases, 50.0%) and 2 (9 cases, 69.2%). Amifostine infusion

was interrupted a similar number of times (6 times in group 1 and 4 times in group 2 [6.3% and 7.0% of administrations, respectively]) due to hypotension, but could be restarted in all. At 15 minutes, mean SBP and DBP values were not significantly different from baseline in either group. The mean baseline SBP values were similar between groups at baseline, and, overall, the differences in mean SBP and DBP values were not significant between groups at any time point. All other toxicities were comparable, and serum creatinine concentrations did not change significantly from baseline with CT in either group.

Conclusions: In this study of the efficacy and tolerability of amifostine in elderly patients with advanced-stage cancer without comorbid diseases, amifostine was effective in reducing cisplatin-induced nephrotoxicity, with transient systolic and diastolic hypotension being the most prominent adverse effect. All other toxicities were either low grade or preventable. No significant differences in amifostine tolerability or toxicities were observed between the study groups. (*Curr Ther Res Clin Exp.* 2004;65:113–124) Copyright © 2004 Excerpta Medica, Inc.

Key words: amifostine, adverse effects, elderly cancer patients, tolerability, cisplatin, nephrotoxicity.

INTRODUCTION

A cytoprotective agent, amifostine is used against the adverse effects (AEs) of certain radiation and antineoplastic drugs,^{1–9} such as cisplatin, which causes dose-related nephrotoxicity in addition to various other AEs.¹⁰ Amifostine has been approved by the US Food and Drug Administration and in Turkey for use to reduce the cumulative nephrotoxicity of cisplatin-based chemotherapy (CT) regimens.^{1–3,9–11} It is a prodrug with little or no intrinsic effect. After dephosphorylation by alkaline phosphatase, it forms an activated free thiol that appears selective in its entry into nonmalignant cells, and exerts a protective effect on healthy tissues through free-radical scavenging, hydrogen donation, and direct binding to the active species of alkylating and platinum agents. Other protective mechanisms include reversal of cisplatin-DNA adduct formation and chemical repair of the DNA.^{1,12} Although it is used to improve the quality of life of cancer patients, amifostine is associated with various AEs.¹² Its dose-limiting toxicities include emetic symptoms (nausea and vomiting) and transient hypotension.^{3,9,12,13}

Traditionally, until the past 3 or 4 years, elderly (aged ≥ 65 –70 years) patients have been excluded from oncology studies. Although 60% of all cancers arise after age 65 years, only 20% to 40% of Phase II and III study patients were in this age range, a large proportion (60%–80%) of them aged <70 years.¹⁴ According to a MEDLINE search (key terms: *amifostine*, *elderly cancer patients*, and *tolerability*; years: 1950–2003), only 1 study exists in the medical literature concerning amifostine tolerability, but not efficacy, in elderly cancer patients.²

The aim of this study was to analyze the efficacy and tolerability of amifostine in elderly cancer patients undergoing cisplatin-based CT regimens.

PATIENTS AND METHODS

Study Design

This 18-month, prospective, comparative study was conducted at the Department of Internal Medicine, Adnan Menderes University Hospital (Aydin, Turkey). The study protocol was approved by the institutional review board.

Patients

Eligible patients were hospitalized and had histopathologically diagnosed advanced-stage cancer; indication of cisplatin-based CT; age 40 to <85 years; and Eastern Cooperative Oncology Group (ECOG) performance status^{15*} ≤ 3 . Patients who were frail; who had abnormal cardiac, hepatic, bone marrow, or renal functions (serum creatinine concentration [SCC], ≥ 1.6 mg/dL); or hypertension (systolic/diastolic blood pressure [SBP/DBP], $>140/90$ mm Hg) were excluded. All patients provided written informed consent to participate.

Methods

Treatment

Patients were divided into 2 groups according to their ages: <70 years (group 1) and ≥ 70 years (group 2). All patients received CT regimens in a supine position, administered by an oncology nurse. Premedication included 1000 mL IV of 0.9% isotonic saline infused over 2 hours, followed by a 20-mg IV bolus of dexamethasone (with a 40-mg IV bolus of omeprazole for gastric mucosa protection) and 3 mg granisetron in 150 mL of 5% dextrose water as a 30-minute IV infusion. Amifostine[†] 910 mg/m² (maximum, 1500 mg) was administered in 150 mL of 0.9% isotonic saline as a 15-minute IV infusion. Cisplatin was administered in 1000 mL of 0.9% isotonic saline as a 2-hour IV infusion, starting 30 minutes after the end of amifostine administration. Cisplatin dose was 80 to 100 mg/m² every 3 to 4 weeks depending on the CT regimen. All CT regimens included an additional accompanying agent (etoposide, vinorelbine tartrate, gemcitabine hydrochloride, paclitaxel, or 5-fluorouracil) to amifostine + cisplatin, depending on the underlying neoplasm of the patient. All patients received ≥ 3 L/d oral hydration on study days 2 to 5, with granisetron 1 mg/d orally.

*ECOG performance status scale: 0 = fully active, able to carry on all predisease performance without restriction; 1 = restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (eg, light housework, office work); 2 = ambulatory and capable of all self-care but unable to carry out any work activities, up and about $>50\%$ of waking hours; 3 = capable of only limited self-care, confined to bed or chair $>50\%$ of waking hours; 4 = completely disabled, cannot carry on any self-care, totally confined to bed or chair; 5 = dead.

[†]Trademark: Ethyol® (Er-Kim Medical, Istanbul, Turkey).

Efficacy and Tolerability Assessments

An experienced nurse and a physician monitored patients' clinical signs and symptoms, including body temperature, BP, arterial pulse, cardiac rhythms, symptoms related to hypotension, acute/early chemotherapy toxicities such as allergic reactions, and extravasation. SBP and DBP were obtained at 0 minute (baseline), at 8 and 15 minutes of amifostine infusion, and at 30 minutes after the start of amifostine infusion. BP was measured using a sphygmomanometer with the patient in the supine position. The first and fifth phases of Korotkoff sounds were noted as SBPs and DBPs, respectively.

Patients also were assessed using physical examination, chest radiography, and electrocardiography (all performed by a physician), blood chemistry (including sodium, potassium chloride, calcium, phosphorus, creatinine, blood urea nitrogen [BUN], aminotransferases, alkaline phosphatase, gamma-glutamyl transferase, total protein, albumin, uric acid, and lactate dehydrogenase) (performed by a biochemist), complete blood count (performed by a hematologist), and complete urinalyses (performed by a nephrologist) before each CT administration and at the post-CT toxicity assessment (between days 10 and 15, depending on the regimen). For blood analysis, samples were centrifuged at 3000 rpm for 10 minutes at room temperature. CT toxicities were assessed according to ECOG criteria.¹⁵ The primary outcome measures were emetic symptoms, hypotension, and serum creatinine concentration. BUN, hematuria and proteinuria, hematologic toxicities, and neurotoxicity were the secondary outcome measures.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for Social Sciences software version 10.0 (SPSS Inc., Chicago, Illinois). A *t* test was used for comparison of the body surface area and the SCCs of the study groups. The Fisher exact test and Mann-Whitney *U* test were used for the between-group sex and performance status differences, respectively. The Tamhane test¹⁶ was used to compare the significance of the changes in SBP and DBP values related to the time of infusion. To compare the SBP and DBP values between the 2 groups, the Kruskal-Wallis test was used. The cisplatin doses of the 2 groups were compared using the chi-square test. The *t* test and Wilcoxon ranked sum test were used to analyze the change in SCC in each group. Statistical significance was set at $P \leq 0.05$.

RESULTS

Thirty-five consecutive patients were enrolled (22 men, 13 women; mean [SD] age, 61 [12] years; group 1, *n* = 22; group 2, *n* = 13). Patients received a total of 153 CT cycles (median, 4 cycles/patient; group 1, 96 cycles; group 2, 57 cycles). The demographic and clinical characteristics were similar between groups and are presented in **Table I**. The types of treated neoplasms are shown in **Table II**.

Table I. Demographic and clinical characteristics of the study patients.*

Characteristic	Group 1 (n = 22)	Group 2 (n = 13)	All Patients (N = 35)
Age, y			
Mean (SD)	54 (8)	74 (3)	61 (12)
Median (range)	56 (40–67)	73 (70–77)	62 (40–77)
Sex, no. (%)			
Men	12 (54.5)	10 (76.9)	22 (62.9)
Women	10 (45.5)	3 (23.1)	13 (37.1)
Race, no. (%)			
White	22 (100.0)	13 (100.0)	35 (100.0)
Body surface area, mean (SD), m ²	1.69 (0.11)	1.59 (0.17)	1.65 (0.14)
Performance status (ECOG), ¹⁵			
median (range) [†]	2 (1–3)	2 (2–3)	2 (1–3)
Chemotherapy cycles			
Total cycles, no.	96	57	153
Cycles/patient, median (range)	4 (1–11)	4 (1–10)	4 (1–11)

ECOG = Eastern Cooperative Oncology Group.

*No significant between-group differences were found.

[†]ECOG performance status scale: 0 = fully active, able to carry on all predisease performance without restriction; 1 = restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (eg, light housework, office work); 2 = ambulatory and capable of all self-care but unable to carry out any work activities, up and about >50% of waking hours; 3 = capable of only limited self-care, confined to bed or chair >50% of waking hours; 4 = completely disabled, cannot carry on any self-care, totally confined to bed or chair; 5 = dead.

The effects of amifostine infusion on the clinical BP values of the study groups are shown in **Table III** and **Table IV**. The mean (SD) of median per patient reductions in SBP and DBP values at 8 minutes of infusion were significant compared with baseline in group 1 (16 [12] and 8 [7] mm Hg, respectively; both $P < 0.001$), group 2 (18 [12] and 13 [8] mm Hg; $P = 0.002$ and $P = 0.006$, respectively), and in all patients (17 [11] and 10 [7] mm Hg; both $P < 0.001$). The mean reductions at 8 minutes in groups 1 and 2 for SBP were similar.

A total of 30 symptomatic hypotensive episodes (19.6% of the infusions) occurred in 20 (57.1%) patients; 18 were experienced by 11 patients (50.0%) in group 1 (5 patients [22.7%] had 2 episodes, and 1 patient [4.5%] had 3 episodes), and 12 episodes were experienced by 9 patients (69.2%) in group 2 (3 patients [23.1%] had 2 episodes). No significant differences were found between groups 1 and 2 in the number of hypotensive episodes. In patients who experienced these episodes, no significant difference was observed between groups 1 and 2 in mean (SD) reductions in SBP (34 [10] vs 34 [11] mm Hg, respectively) or DBP (24 [10] vs 24 [8] mm Hg, respectively). Overall, in patients who experienced these episodes, the mean (SD) reductions in SBP and DBP were 34 (10) and 23 (9) mm Hg, respectively. Hypotensive symptoms included

Table II. Number (%) of study patients with neoplasms.**†

Neoplasm	Group 1 (n = 22)	Group 2 (n = 13)	All Patients (N = 35)
Lung cancer	5 (22.7)	4 (30.8)	9 (25.7)
Ovarian cancer	4 (18.2)	3 (23.1)	7 (20.0)
Head/neck cancer	4 (18.2)	2 (15.4)	6 (17.1)
Stomach cancer	4 (18.2)	1 (7.7)	5 (14.3)
Cervical cancer	2 (9.1) [‡]	0 (0.0)	2 (5.7)
Cancer of unknown primary origin	1 (4.5)	2 (15.4)	3 (8.6)
Breast cancer	1 (4.5)	0 (0.0)	1 (2.9)
Hepatocellular carcinoma	1 (4.5)	0 (0.0)	1 (2.9)
Esophageal cancer	0 (0.0)	1 (7.7)	1 (2.9)

*No significant between-group differences were found.

†Percentages do not add to 100 because of rounding.

‡One of these patients had concomitant gallbladder cancer.

mild lightheadedness, dizziness, and tachycardia. Amifostine infusion was interrupted a similar number of times in each group (6 times in group 1, and 4 times in group 2 [6.3% and 7.0% of administrations, respectively]) when these symptoms were moderate or severe and accompanying diaphoresis and visual blurring due to hypotension were noted. Amifostine administration could be restarted in all patients after an interruption of ~5 minutes and lower extremity elevation. No chest pain, dyspnea, or syncope was reported, and amifostine + cisplatin-based treatment was continued in all of these symptomatic patients.

Mean SBP and DBP values increased significantly at 15 minutes (end of infusion) compared with 8 minutes in both groups and overall (group 1: SBP, $P = 0.004$; DBP, $P = 0.003$; group 2: SBP, $P = 0.004$; DBP, $P = 0.007$; all patients: SBP, $P = 0.007$; DBP, $P = 0.003$), but the values at 15 minutes were not significantly different from baseline. Mean SBP and DBP values continued to increase

Table III. Blood pressure (mm Hg) during amifostine infusion.* (Values are expressed as mean [SD].)

Group	0 Min (Baseline)		8 Min		15 Min		30 Min	
	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
Group 1	112 (14)	78 (10)	98 (12)	60 (7)	108 (12)	70 (8)	116 (14)	76 (10)
Group 2	120 (11)	80 (8)	100 (12)	60 (9)	110 (12)	70 (8)	122 (12)	78 (9)
All patients	120 (14)	80 (9)	100 (12)	60 (8)	110 (12)	70 (8)	122 (12)	78 (8)

SBP = systolic blood pressure (normal value, ≤ 140 mm Hg); DBP = diastolic blood pressure (normal value, ≤ 90 mm Hg).

*No significant between-group differences were found. Differences between time points are shown in Table IV.

Table IV. *P* values found for differences in blood pressure during amifostine infusion.

Group	8 Min Versus 0 Min (Baseline)		15 Min Versus 8 Min*		30 Min Versus 8 Min*		30 Min Versus 15 Min*	
	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
Group 1	<0.001	<0.001	0.004	0.003	<0.001	<0.001	0.009	0.034
Group 2	0.002	0.006	0.004	0.007	0.002	0.005	0.028	0.042
All Patients	<0.001	<0.001	0.007	0.003	<0.001	<0.001	0.016	0.022

*No significant differences versus baseline were found.

significantly at 30 minutes. The differences in BP at 30 minutes versus 8 minutes were as follows: group 1: SBP, $P < 0.001$; DBP, $P < 0.001$; group 2: SBP, $P = 0.002$; DBP, $P = 0.005$; and all patients: SBP, $P < 0.001$; DBP, $P < 0.001$. The differences in BP at 30 minutes versus 15 minutes were as follows: group 1: SBP, $P = 0.009$; DBP, $P = 0.034$; group 2: SBP, $P = 0.028$; DBP, $P = 0.042$; and all patients: SBP, $P = 0.016$; DBP, $P = 0.022$. The values at 30 minutes were not significantly different from baseline. No significant between-group differences in SBP or DBP were found at any time point throughout the study.

Toxicity assessment is summarized in **Table V**. Overall, the toxicities were comparable in both groups. Hematologic toxicities were mostly due to the agent accompanying the amifostine + cisplatin CT regimen. Neutropenia and thrombocytopenia were similar between groups. Mean cisplatin doses were similar in the 2 study groups. Vomiting was not observed before cisplatin infusion in any patient. All other toxicities were either low grade or preventable. Allergic reactions and symptomatic hypocalcemia as well as other electrolyte abnormalities did not develop. No changes in BUN levels were noted. At the end of the last CT cycle in both groups (**Table VI**), the changes in mean SCC with amifostine and cisplatin-based CT regimens were not significantly different from baseline. In the complete urinalyses, neither proteinuria nor hematuria was observed in any patient.

DISCUSSION

Amifostine is a widely used agent because protection of healthy cells from the toxicity of CT is an evolving strategy in current oncology practice.¹⁷ The only existing study in the literature was conducted by Genvresse et al,² in which the investigators examined whether age and/or comorbidity influenced amifostine tolerability by comparing its AEs in 268 consecutive administrations at a dose of 740 mg/m² in patients aged <70 years or ≥70 years. Our study differs in that we used the highest acceptable tolerated dose in clinical practice (910 mg/m² of amifostine) so that the differences between the 2 study groups would be

Table V. Number (%) of patients with toxicities in study patients.*†

Toxicity/ECOG Grade ¹⁵	Group 1 (n = 22)	Group 2 (n = 13)	All Patients (N = 35)
Anemia			
1	14 (63.6)	7 (53.8)	21 (60.0)
2	3 (13.6)	3 (23.1)	6 (17.1)
3	0 (0.0)	0 (0.0)	0 (0.0)
4	0 (0.0)	0 (0.0)	0 (0.0)
Emesis			
1	11 (50.0)	6 (46.2)	17 (48.6)
2	6 (27.3)	5 (38.5)	11 (31.4)
3	3 (13.6)	1 (7.7)	4 (11.4)
4	0 (0.0)	0 (0.0)	0 (0.0)
Nephrotoxicity			
1	2 (9.1)	1 (7.7)	3 (8.6)
2	2 (9.1)	3 (23.1)	5 (14.3)
3	0 (0.0)	0 (0.0)	0 (0.0)
4	0 (0.0)	0 (0.0)	0 (0.0)
Thrombocytopenia			
1	2 (9.1)	2 (15.4)	4 (11.4)
2	0 (0.0)	0 (0.0)	0 (0.0)
3	0 (0.0)	0 (0.0)	0 (0.0)
4	0 (0.0)	0 (0.0)	0 (0.0)
Peripheral neurotoxicity			
1	2 (9.1)	1 (7.7)	3 (8.6)
2	0 (0.0)	0 (0.0)	0 (0.0)
3	0 (0.0)	0 (0.0)	0 (0.0)
4	0 (0.0)	0 (0.0)	0 (0.0)
Neutropenia			
1	1 (4.5)	2 (15.4)	3 (8.6)
2	1 (4.5)	2 (15.4)	3 (8.6)
3	3 (13.6)	3 (23.1)	6 (17.1)
4	3 (13.6)	3 (23.1)	6 (17.1)
Oral mucositis			
1	1 (4.5)	0 (0.0)	1 (2.9)
2	0 (0.0)	0 (0.0)	0 (0.0)
3	0 (0.0)	0 (0.0)	0 (0.0)
4	0 (0.0)	0 (0.0)	0 (0.0)

*Patients are accounted for in the highest grade of toxicity they had experienced.

†No significant between-group differences were found.

more easily determined.¹⁸ Also, we did not include patients with comorbid diseases and studied only cisplatin-based CT regimens for better identification of toxicities and the renoprotective efficacy of amifostine, contrary to the study by Genvresse et al,² in which patients received platinum-, taxol-, or cyclophosphamide-based treatments.

Table VI. Serum creatinine concentrations* (mg/dL) with amifostine and cisplatin-based chemotherapy regimens.† (Values are expressed as mean [SD].)

Measurement	Group 1 (n = 22)	Group 2 (n = 13)	All Patients (N = 35)
Baseline	1.0 (0.2)	1.1 (0.3)	1.0 (0.2)
Last	1.0 (0.3)	1.2 (0.3)	1.1 (0.3)

*Normal value, 0.6 to 1.2 mg/dL.

†No significant between-group differences were found.

Cisplatin is a widely used antineoplastic agent that causes dose-related renal dysfunction. In addition to increased SCCs, electrolyte abnormalities such as transient hypomagnesemia and hypokalemia are among the commonly reported AEs. Previous studies have confirmed the efficacy of amifostine in protecting against cisplatin-induced nephrotoxicity.^{1-3,9,19} Cytoprotection by amifostine also was reported in hematopoietic stem cells, myocardial cells, neural cells, and mucosa, without detectable protection of malignant cells.^{3,8,9,12} Because amifostine is activated after dephosphorylation by alkaline phosphatase, the absence of this enzyme in the tumoral endothelium and stromal components, and the acidity of the tumor environment, may explain this cytoprotective selectivity.²⁰ Although various other drugs, such as sodium thiosulfate and diethyldithiocarbamate,²¹ work against cisplatin-induced nephrotoxicity, we selected amifostine because it was the only agent registered for this use in Turkey.

We assessed general and age-related tolerability of amifostine in this study. Amifostine was reported as a generally well-tolerated agent with acceptable toxicity^{17,22}; the 2 most common AEs associated with this treatment are emetic symptoms and hypotension.^{1,9,10,13,17,19} These AEs generally are considered reversible following treatment discontinuation, most likely because >90% of the drug is cleared from plasma within 6 minutes and peak tissue concentration occurs 10 to 30 minutes after IV administration.^{1,13,19}

In contrast to the study by Genvresse et al,² in which 20.8% of the elderly and 10.0% of the younger patients experienced nausea and vomiting, amifostine-related emetic symptoms were effectively prevented by premedication in our study, and the prevalence of emetic symptoms was not significantly different between the 2 groups. Also, we did not find any cases of hypocalcemia, a less common AE associated with this treatment.^{2,19}

Amifostine has been shown to induce hypotension episodes after ~20% of administrations, according to 1 report.¹³ In our study, the frequency of symptomatic hypotensive episodes (19.6%) was comparable with that rate. Several studies^{3,22} have shown that the dose-limiting toxicities of amifostine (emetic symptoms and hypotension) might be better controlled by reducing the duration of infusion. Rapid infusion of amifostine over as short as 10 to 15 seconds

has been associated with much less toxicity, particularly less nausea, than longer infusions. The subcutaneous route also has been shown to result in less severe nausea, vomiting, and hypotension, but more frequent cutaneous toxicity.^{23,24} We used a longer infusion time because the registration of the drug in Turkey states a “15-minute infusion.”

Transient systolic and diastolic hypotension was prominent in both groups in the present study. The mechanism of amifostine-induced hypotension appears to be direct relaxation of vascular smooth muscle. Smooth muscle relaxation is not related to the production of nitric oxide, prostaglandins, or cyclic nucleotides; α -adrenergic receptor antagonism; or interference with receptor-dependent increases in intracellular calcium. Administration of the adrenergic receptor agonist ephedrine was reported to attenuate the hypotension induced by amifostine in anesthetized rats.^{12,25}

Genvresse et al² reported transient hypotension as the most common AE, and decreases in SBP were of similar frequency in their study groups. They interrupted amifostine infusion 8 times in the younger patients and 16 times in the older patients (5% and 13% of administrations, respectively), mainly because of hypotension. In our study, hypotension was also the most common AE, and amifostine infusion was interrupted in groups 1 and 2 equally (6.3% and 7.0% of administrations, respectively) but could be restarted.

Both SBP and DBP values were not significantly different between groups 1 and 2 in relation to time of amifostine administration in this study. Although both SBP and DBP values seemed to reach their baseline values later in group 2 compared with group 1, both SBP and DBP values at 15 minutes (end of infusion) were not significantly different from baseline in either group. Age did not appear to have a remarkable influence on amifostine-induced hypotension in view of the data obtained in our study.

Genvresse et al² concluded that AEs associated with amifostine were not observed more frequently in the older patients than in the younger ones. In our study also, despite the higher dose of amifostine (910 mg/m²), AEs did not occur more frequently in group 2.

Gridelli et al²⁶ studied the toxicity of the combination of cisplatin + vinorelbine + amifostine in 40 patients with advanced non-small cell lung cancer. The investigators reported nephrotoxicity as one of the most prominent AEs. We compared the efficacy of amifostine in the prevention of cisplatin-induced nephrotoxicity. Although grade 2 nephrotoxicity was more prominent in group 2, the mean changes in SCC due to cisplatin-based CT were not significantly different between the 2 groups in our study. Also, no significant changes were found in other parameters such as hematuria, proteinuria, and blood urea nitrogen levels to suggest nephrotoxicity.

Because elderly patients may have more comorbid diseases than their younger counterparts, amifostine administration should be closely monitored in this age group. Also, further studies would be appropriate to prevent and/or to control amifostine-related AEs more effectively.

CONCLUSIONS

In this study of the efficacy and tolerability of amifostine in elderly patients with advanced-stage cancer without comorbid diseases, amifostine was effective in reducing cisplatin-induced nephrotoxicity, with transient systolic and diastolic hypotension being the most prominent AE. All other toxicities were either low grade or preventable. No significant differences in amifostine tolerability or toxicities were observed between the study groups.

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