INTRODUCTION

Hypercalcemia is a common metabolic complication of malignancy which occurs in 5% to 10% of patients with advanced cancers.[1,2] If appropriate medical treatment is not given promptly, patients suffering from hypercalcemia are likely to go rapidly downhill and be exposed to dangerous clinical events. Accurate diagnosis and timely interventions are not the only life saving procedures; appropriate calcium-lowering agents are also necessary for long term survival and are beneficial in improving the life quality.[2]

It has already been demonstrated that giving a combination of fluid-repletion and bisphosphonates is one of the most effective therapies for cancer-associated hypercalcemia.[3,4] Pamidronate (3-amino--1-hydroxypropylidene-1,1-bisphosphonic acid, APD) is a second generation bisphosphonates and in randomized, comparative trials, it was demonstrated that the calcium levels of patients in the pamidronate group regained normocalcemia faster and were able to sustained longer.[3,5,6] To test the efficacy and toxicity of intravenous pamidronate, we performed a prospective, open phase-II clinical trial on patients with cancer-associated hypercalcemia.

PATIENTS AND METHODS

Patients

In total, 18 patients with cancer-associated hypercalcemia of various types were enrolled in this study. Their characteristics are shown in Table 1. Eligibility for this study was based on the following criteria: proven malignant diseases with an elevated serum calcium level (adjusted for serum albumin) of > 10.4 mg/dL persisting after 48 h of hydration with 3 L of normal saline per day. Patients had to be older than 18 years, and signed informed consent before entering to this study. Exclusion criteria included patients undergoing concurrent administration of other medications containing bisphosphonate or any other treatments for hypercalcemia with steroids; patients with severe renal impairment with serum creatinine > 3 mg/dL; patients known to have an allergy to pamidronate or other bisphosphonate; and patients with familial benign hypercalcemia, vitamin D intoxication or hyperparathyroidism. Lactating mothers and pregnant women were also excluded in this study.

Because pamidronate produces a dose-dependent decrease in plasma calcium,[7] patients were allocated into 3 groups with different doses of pamidronate based on the severity of the hypercalcemia at presentation (Table 2).

Methods

Blood samples were collected daily for analysis during the period of 2 days before and 7 days after medication; then the samples were collected once a week in the following 8 weeks. Tests included white blood cell count, differential cell count, hemoglobin, platelets, serum albumin, serum calcium, phosphate, urea, creatinine, and magnesium. Serum calcium level was adjusted according to the serum albumin level by

Table 1. Details of Tumor Type and Bony Metastasis

Tumor type	Bony met (+)	Bony met (-)	Total
breast carcinoma	5	0	5
multiple myeloma	0	3	3
lymphoma	0	2	2
squamous cell lung cancer	2	0	2
hepatocellular carcinoma	0	2	2
renal cell carcinoma	1	0	1
ovarian carcinoma	1	0	1
laryngeal carcinoma	0	1	1
TCC of urinary bladder	1	0	1

met = metastases; TCC = transitional cell carcinoma.