

Analgesia and curative effect of pamidronate disodium combined with chemotherapy on elderly patients with advanced metastatic bone cancer

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Abstract. The curative effect and adverse reactions of pamidronate disodium in elderly patients with advanced metastatic bone cancer were evaluated. A total of 160 elderly patients with advanced metastatic bone cancer admitted to Affiliated Hospital of Nantong University from February 2012 to January 2015, were divided into the chemotherapy group (n=60) that received routine therapy and the pamidronate disodium group (n=100) that received pamidronate disodium therapy based on the chemotherapy. Pain relief, analgesic time, analgesic duration and side effects were compared between the two groups after treatment. The effect of pain relief in the pamidronate disodium group was significantly higher than that in the chemotherapy group ($P<0.001$). The total effective rate of the pamidronate disodium group was significantly higher than that of the chemotherapy group ($P<0.001$). The analgesic onset time in the pamidronate disodium group was earlier than in the chemotherapy group ($P<0.001$). The analgesic duration in the pamidronate disodium group was longer than that in the chemotherapy group ($P<0.001$). The incidence of adverse reactions and complications after treatment in the

pamidronate disodium group was significantly less than that in the chemotherapy group ($P<0.001$). The results indicated that pamidronate disodium is effective in the treatment of elderly patients with advanced metastatic bone cancer and patients are less prone to adverse reactions, complications and pain, which is worthy of clinical application.

Introduction

Bone metastasis, a common complication of solid tumors such as advanced breast cancer, prostate cancer and lung cancer, has high incidence (1-3). Patients with advanced tumors suffer from bone pain and fracture due to the deterioration of tumors and bone metastases, causing bone cell absorption and osteolysis, or even bone destruction (4,5). Patients with bone metastases endure severe pain resulting in low quality of life and poor mental health, as well as loss of confidence in life (6). Morphine is a routine analgesic in the late stage of clinical treatment but with poor effect for patients with bone metastasis because of short onset time and side effects (7). Therefore, the effective analgesic treatment for patients with bone metastases is currently a hot topic in clinical research (8).

Chemoradiotherapy, radionuclide, analgesic and bisphosphonate therapies are currently important methods for bone metastases from malignant tumors (9-11). In the treatment and prevention of complications of bone metastasis from malignant tumors, some studies have indicated that bisphosphonates are effective in alleviating pathological bone pain of patients (12). Bisphosphonates play an important role in reversing bone destruction such as bone cell absorption and osteolysis, especially pamidronate disodium, one of the bisphosphonates, which was effective in inhibiting bone resorption and osteolytic bone metastasis (13). Zoledronic acid and pamidronate disodium are widely-used bisphosphonates clinically (14,15). Therefore, this study aimed to analyze the curative effect and side effects of pamidronate disodium in the treatment of elderly patients with advanced metastatic bone cancer.

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Table I. General data of the two groups [n (%)].

Variables	Pamidronate disodium group (n=100)	Chemotherapy group (n=60)	t/ χ^2	P-value
Age (years)	53.67±4.81	53.15±4.93	0.656	0.513
Sex			0.220	0.639
Men	63 (63.00)	40 (66.67)		
Women	37 (37.00)	20 (33.33)		
BMI (kg/m ²)	18.93±4.12	18.42±3.84	0.778	0.438
Types of cancer				
Esophageal carcinoma	15 (15.00)	7 (11.67)	0.351	0.553
Lung cancer	24 (24.00)	16 (26.67)	0.142	0.706
Cervical cancer	20 (20.00)	12 (20.00)	0.000	1.000
Prostate cancer	13 (13.00)	5 (8.33)	0.818	0.366
Nasopharyngeal cancer	28 (28.00)	20 (33.33)	0.508	0.476
Number of bone metastases			0.886	0.347
1	68 (68.00)	45 (75.00)		
>1	32 (32.00)	15 (25.00)		

BMI, body mass index.

Patients and methods

Patients data. A total of 160 elderly patients with advanced metastatic bone cancer admitted to Affiliated Hospital of Nantong University (Nantong, China) from February 2012 to January 2015 were divided into the chemotherapy group (n=60) that received routine therapy and the pamidronate disodium group (n=100) that received pamidronate disodium therapy based on the chemotherapy. Patients in the chemotherapy group ranged in age from 46 to 72 years, with an average age of 53.15±4.93 years. Patients in the pamidronate disodium group ranged in age from 47 to 69 years, with an average age of 53.67±4.81 years. Inclusion criteria were as follows: i) patients who met the international diagnostic criteria for malignant tumors and were diagnosed as bone metastases through pathological examination and medical imaging technology (16); and ii) patients who did not have surgical treatment. Exclusion criteria were as follows: i) presence of neurological diseases, liver and renal dysfunction and organic diseases, severe complications, failure of chemotherapy and follow-up.

The study was approved by the Ethics Committee of Affiliated Hospital of Nantong University. Signed informed consents were obtained from the patients or guardians.

Methods. Treatment methods: Both groups received chemotherapy according to the clinical medication guidelines for primary tumors. Based on the chemotherapy group, patients in the pamidronate disodium group were treated with 45 mg pamidronate disodium (SFDA approval no. H19980200; Shenzhen Neptunus Pharmaceutical Co., Ltd.) and 500 ml sodium chloride solution with 0.9% concentration twice a week, once a day, four weeks a course and three courses for the treatment. Liver and kidney functions were measured each week.

Evaluation of curative effect. Criteria of pain relief effect and bone lesions were as follows: according to Verbal Rating Scale (VRS) (17), pain is divided into grade 0 to III: the higher the grade, the more severe the pain. The pain grading standard is as follows: downregulation by one level indicating effectiveness, by two levels indicating marked effectiveness, upregulation or unchanged indicating ineffectiveness. The total effective rate of pain relief = (marked effectiveness)/effectiveness + effectiveness/total number of cases x100%. Evaluation of curative effect of bone lesions: CR indicates the disappearance of bone lesions for 4 weeks or less. PR indicates that the area of diseased tissue reduced and the density of calcification of bone lesions was 4 weeks or less. NC indicates no change in the area of bone lesions. PD indicates that new bone lesions or the area of original bone lesions increased. The total effective rate of bone lesions = (CR+PR)/total number of cases x100%.

Statistical analysis. SPSS19.0 (Bizinsight Information Technology Co., Ltd.) software was used for statistical analysis. The enumeration data were expressed as the number of cases/percentage [n (%)] and tested by χ^2 test. The measurement data were expressed as mean ± standard deviation and tested by independent sample t-test at the same time-point. P<0.05 was considered to indicate a statistically significant difference.

Results

General data of patients. There was no significant difference in general data between the two groups (P>0.05; Table I).

Comparison of pain relief between the two groups after treatment. The pain relief effect in the pamidronate disodium group was as follows: patients with marked effectiveness: 39 cases,

Table II. Comparison of pain relief between the two groups after treatment [n (%)].

Groups	n	No. of marked effectiveness	No. of effectiveness	No. of ineffectiveness or deterioration	Total effective rate
Pamidronate disodium	100	39 (39.00)	46 (46.00)	15 (15.00)	85 (85.00)
Chemotherapy	60	21 (35.00)	12 (20.00)	27 (45.00)	33 (55.00)
χ^2		-	-	-	17.430
P-value		-	-	-	<0.001

Table III. Comparison of the curative effect of bone metastases between the two groups after treatment [n (%)].

Groups	n	CR	PR	SD	PD	Total effective rate
Pamidronate disodium	100	35 (35.00)	19 (19.00)	24 (24.00)	22 (22.00)	54 (54.00)
Chemotherapy	60	11 (18.33)	1 (1.67)	28 (46.67)	20 (33.33)	12 (20.00)
χ^2		-	-	-	-	18.360
P-value		-	-	-	-	<0.001

Table IV. Comparison of analgesic time and duration (h) between the two groups.

Groups	Pamidronate disodium group	Chemotherapy group	t	P-value
Analgesic onset time	4.59±0.74	8.12±0.62	30.990	<0.001
Analgesic duration	21.01±2.45	12.45±3.15	19.180	<0.001

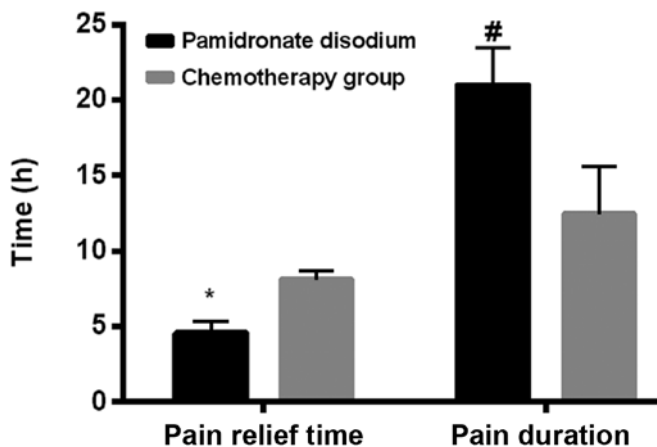


Figure 1. Comparison of analgesic time and duration between the two groups. The analgesic onset time of the pamidronate disodium group was earlier than that of the chemotherapy group ($P<0.001$); The duration of analgesic time in the pamidronate disodium group was longer than that in the chemotherapy group ($\#P<0.001$).

effectiveness: 46 cases, ineffectiveness: 15 cases. While in the chemotherapy group, patients with marked effectiveness: 21 cases, effectiveness: 12 cases, ineffectiveness: 27 cases. The total effective rate of pain relief in the pamidronate disodium group was 85%, higher than that in the chemotherapy group ($P<0.001$; Table II).

Comparison of curative effect of bone metastases between the two groups after treatment. The curative effect of bone metastases in the pamidronate disodium group was: CR cases: 35, PR cases: 19, SD cases: 24, PD cases: 22; while in the chemotherapy group was: CR cases: 11, PR cases: 1, SD cases: 28, PD cases: 20. The total effective rate of pain relief in the pamidronate disodium group was 54%, higher than that in the chemotherapy group ($P<0.001$; Table III).

Analysis of analgesic time and duration between the two groups. The analgesic onset time in the pamidronate disodium group was 4.59 ± 0.74 h, while the chemotherapy group was 8.12 ± 0.62 h. Compared between the two groups, the onset time in the pamidronate disodium group was earlier than that in the chemotherapy group ($P<0.001$). The duration of analgesic time in the pamidronate disodium group was 21.01 ± 2.45 h, while the chemotherapy group was 12.45 ± 3.15 h. The duration of analgesic time in the pamidronate disodium group was longer than that in the chemotherapy group ($P<0.001$; Table IV and Fig. 1).

Analysis of side effects between the two groups. The total incidence of adverse reactions and complications, such as hypercalcemia, oesophagus damage, renal dysfunction, nausea and vomiting, body aches and chills in the pamidronate disodium group was 28.00% after treatment, which was significantly lower than that in the chemotherapy group (63.33%) ($P<0.001$; Table V).

Table V. Comparison of adverse reactions and complications between the two groups [n (%)].

Groups	Hypercalcemia	Oesophagus damage	Renal dysfunction	Nausea and vomiting	Body aches	Body chills	Total
Pamidronate disodium	2 (2.00)	4 (4.00)	12 (12.00)	4 (4.00)	3 (3.00)	3 (3.00)	28 (28.00)
Chemotherapy	2 (3.33)	5 (8.33)	13 (21.67)	6 (10.00)	6 (10.00)	6 (10.00)	38 (63.33)
χ^2	-	-	-	-	-	-	19.320
P-value	-	-	-	-	-	-	<0.001

Discussion

In this study, the general data of elderly patients with advanced metastatic bone cancer in the two groups were comparable according to different treatment methods. Differences in pain relief effect in bone metastasis lesions, analgesic onset time and duration, adverse reactions were compared between the two groups after treatment. The total effective rate of pain relief in the pamidronate disodium group was 85%, higher than that in the chemotherapy group. The total effective rate of bone lesion metastases in the pamidronate disodium group was 54%, higher than that of the chemotherapy group. Pathological fracture or complications caused by advanced metastatic bone cancer have a serious impact on physiology and psychology of patients (18). At present, great importance has been attached to studies on patients with bone metastases. A large number of studies have indicated that different treatment methods had different effects on pain in patients with metastatic bone cancer (19).

Chemotherapy is a common treatment for patients with metastatic bone cancer, but it cannot alleviate the pathological pain caused by bone metastasis (20). Pamidronate disodium, a second-generation bisphosphonate drug, is a bone resorption inhibitor (21). Relevant studies have demonstrated that pamidronate disodium was effective in cancer-related hypercalcemia and bone pain caused by malignant tumors (22). Therefore, it is likely that pamidronate disodium therapy based on chemotherapy is more effective than conventional chemotherapy in relieving bone pain. Goblirsch *et al* suggested that bisphosphonates showed a good effect in the treatment of patients with bone metastases of malignant tumors (23), which is similar to the results of the study. The analgesic onset time and duration of the pamidronate disodium and the chemotherapy groups were analyzed. It was found that the analgesic onset time of the pamidronate disodium group was earlier than that of the chemotherapy group while the duration of analgesic time in the pamidronate disodium group was longer than that in the chemotherapy group, indicating statistical differences.

A large number of studies have shown that pamidronate disodium and other bisphosphonates could shorten analgesic onset time and increase duration of analgesic effect, which is of great significance for improving the curative effect and quality of life (24). According to adverse reactions of the two groups, the total incidence of adverse reactions, such as hypercalcemia, oesophagus damage, renal dysfunction, nausea and vomiting, body aches and chills, in the pamidronate disodium group was significantly lower than that in the chemotherapy group

after treatment. Some studies indicated that complications such as bone pain, pathological fracture and hypercalcemia caused by bone metastasis of malignant tumors not only had a serious impact on quality of life of patients, but also caused death of patients with malignant tumors (25). Nausea and vomiting, body aches and chills are common adverse reactions in chemotherapy (26). Wong and Wiffen suggested that bisphosphonates in the treatment of bone metastasis of malignant tumors enhanced the prevention of complications and adverse reactions, and reduced the incidence of adverse reactions (27). Therefore, pamidronate disodium therapy based on chemotherapy is more effective than the conventional chemotherapy in preventing the complications and adverse reactions.

In conclusion, pamidronate disodium therapy based on chemotherapy can improve the analgesic effect and curative effect and prevent complications and adverse side effects of elderly patients with advanced metastatic bone cancer, which is worthy of clinical promotion.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

JL, CZ and BL led the conception and design of the study. JL and CZ were responsible for evaluation of curative effect. BL and LW were responsible for the general data collection and analysis. HL and LW were in charge of interpreting the data and drafting the manuscript. CZ and BL made revision from critical perspective for important intellectual content. The final version was read and approved by all the authors.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Affiliated Hospital of Nantong University (Nantong, China).

Signed informed consents were obtained from the patients or guardians.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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