Original Article

Pre-Emptive Value of Methylprednisolone Intravenous Infusion in Patients With Vertebral Metastases. A Double-Blind Randomized Study

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Abstract

Context. The vertebral column is the most common site of bone metastases irrespective of the primary tumor. Vertebral metastases are a major cause of motor deficit of the lower extremities. The use of radiotherapy is the treatment of choice in these patients. A temporary worsening of pain shortly during the course of palliative radiotherapy is clinically a common problem. Steroid infusion has well-documented neuroprotective effects.

Objectives. Our study objective is to evaluate the effect of pre-emptive infusion of methylprednisolone on pain flare and motor function in patients with vertebral metastases.

Methods. One hundred twenty patients with vertebral metastases received short-course external beam radiotherapy as high-voltage irradiation with a 6 MeV, via linear accelerator. In addition to the short-course radiotherapy, 60 patients received pre-emptive methylprednisolone infusion (5 mg/kg) the day just before initiation of radiotherapy (Group 1 [G1]). The other 60 patients received short-course radiotherapy without pretreatment methylprednisolone infusion, and only normal saline was infused (Group 2 [G2]). The Brief Pain Inventory, incidence of pain flare during radiotherapy, and motor functions were evaluated using the Tomita scale at the time of initial assessment, at the end of external beam radiotherapy, and after two weeks.

Results. Four patients (6.6%) in G1 experienced pain flare compared with 12 patients (20%) in G2 during the two-week short-course radiotherapy. The mean values of pain scores were significantly reduced in both groups at the end of radiotherapy; the mean value of worst, average, and current pain scores in G1 remained statistically significant in comparison to pretreatment and G2 mean values two weeks later. Significant increase was noticed in patients with normal motor and ambulatory status in G1 at two and four weeks of initial assessment.

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Conclusion. Pre-emptive methylprednisolone infusion is an effective prophylactic agent in the prevention of radiation-induced pain flare and improves functional motor status after short-term radiotherapy in patients with vertebral metastases. J Pain Symptom Manage 2014;48:762–769.

Key Words
Methylprednisolone, vertebral metastasis, pain flare

Introduction

Vertebral metastases commonly cause both cancer pain and neurological deficit.[1] Palliative radiotherapy is a well-established treatment option for symptomatic bone metastases. External beam radiotherapy has been considered the standard treatment for spine metastasis.[2] It is the initial treatment for most patients with metastases to a vertebral body.[3]

External beam radiotherapy is associated with treatment-related side effects, most of which are dependent on the site of radiation. Pain flare or temporary worsening of pain in the irradiated site is a well-known side effect.[4]

The incidence of pain flare has been reported in about 40% of patients undergoing palliative radiotherapy.[5] Pain flare is defined as a two-point increase in the worst pain score compared with baseline worst pain with no decrease in analgesic intake or a 25% increase in daily analgesic intake with no decrease in worst pain score.[6]

Controversial reports of variable effects regarding neurological status after external beam radiotherapy have been reported with different degrees of improvement or deterioration.[7] Previous studies reported that infusion of steroids had a neurological protective function, especially methylprednisolone, as it reduces pretumoral edema, improving the sensory or motor manifestation or both in patients with vertebral metastases.[8]

The objective of this study is to determine the effect of pre-emptive methylprednisolone infusion on the changes in the Numerical Rating Scale (NRS), incidence and duration of pain flare, functional interference items of the Brief Pain Inventory (BPI), and motor function of the lower extremities in patients who received a palliative course of radiotherapy for vertebral metastases.

Methods

After study approval by the Investigational Review Board of the Faculty of Medicine, Tanta University, informed consent was obtained from patients participating in the study. This study was registered in the Pan African Clinical Trials Registry with unique identification number PACTR201211000432357.

A total of 155 patients with Class I–III Harrington classification of vertebral metastases were admitted to the Department of Clinical Oncology, Faculty of Medicine, Tanta University, and were enrolled into the study from November 2012 to May 2013. Thirty-five patients were excluded; 15 patients did not meet the inclusion criteria, whereas 20 patients refused to participate in the study (Table 1).

One hundred twenty patients were included in the study; 60 patients received short-course radiation therapy in addition to methylprednisolone infusion (5 mg/kg; Solu-Medrol®; Pfizer Manufacturing Belgium NV, Puurs, Belgium) the day just before initiation of radiotherapy (Group 1 [G1]) and another 60 patients received short-course radiotherapy without pretreatment infusion (Group 2 [G2]) (Fig. 1).

High-voltage short-course external beam radiotherapy in the form of 6 MeV, via linear accelerator (DMX System, Varian Medical Systems, Inc., Palo Alto, CA) was applied to all patients participating in the study. The target volume included the entire affected vertebrae, transverse process, and soft tissue component of the lesion as imaged by computed tomography or magnetic resonance imaging. The adjoining vertebrae were included in the treatment volume as 30 Gy of radiation delivered in 10 Gy fractions over a two-week period.

Diagnosis of bone metastases was based on the history taking, the presence of symptoms,